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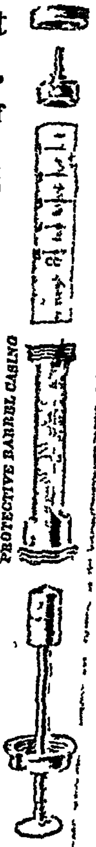

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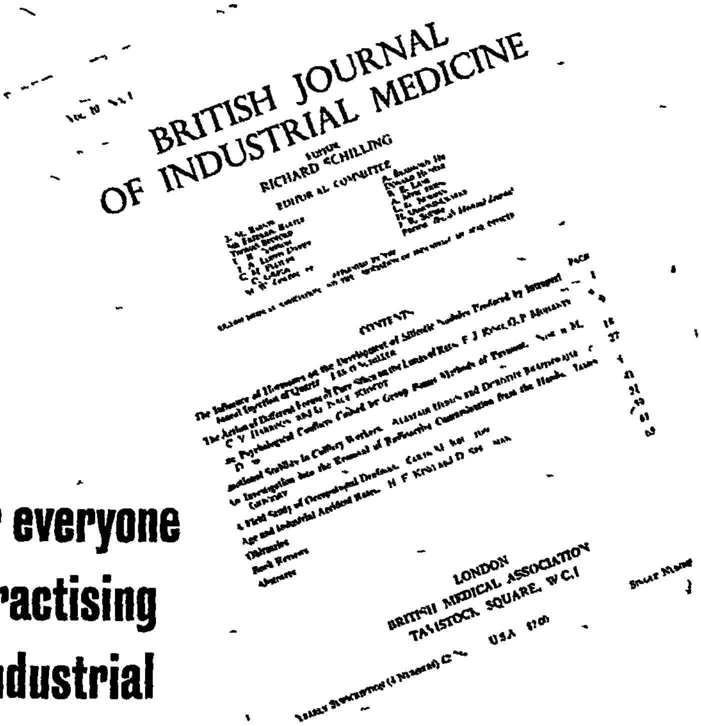

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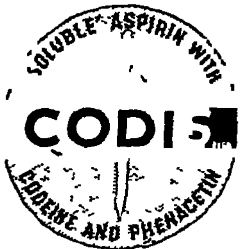

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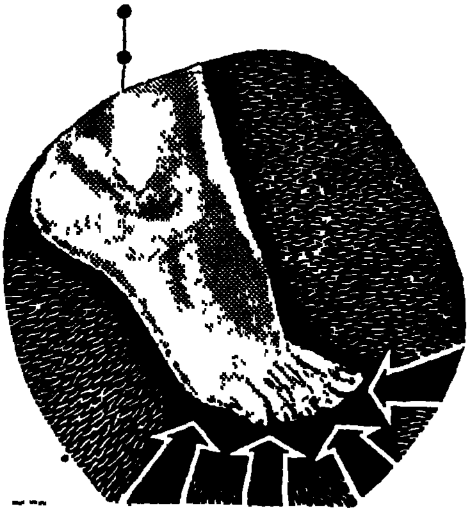

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INTRACRANIAL HYPOTENSION

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Magendie (1825) described vertigo and unsteadiness following removal of cerebrospinal fluid (C.S.F.), and attributed them to cerebral anæmia due to pressure on basal blood-vessels by the brain no longer supported by its cushion of C.S.F. Until the early part of the present century the possible clinical importance of a low C.S.F. pressure passed unnoticed. It was then noted that many unconnected medical conditions might be associated with a low C.S.F. pressure, but no specific clinical picture was recognised.

Leriche (1915) described the value of lumbar puncture in head injuries sustained in the war which broke out in 1914. Later (Leriche 1920) he described in detail the clinical picture of intracranial hypotension, discussed its possible causation, and showed the value of subcutaneous serum and intravenous distilled water in treatment. Still later (Leriche 1931) he described his further experience of this condition and stated that little interest had been aroused by his previous reports, although a few cases had been reported by his pupils. Since then many reports, mostly by French workers, have been published on the Continent, but little attention has been paid to intracranial hypotension in this country. This subject was discussed at a combined meeting of the neurological section of the Royal Society of Medicine and the Neurological Society of Paris in 1948 (*Proceedings of the Royal Society of Medicine* 1948). Thorsén (1947) extensively reviewed the published reports of intracranial hypotension following spinal anæsthesia, and Chorobski (1950) discussed intracranial hypotension following cranial operations and suggested its pathogenesis.

In the earlier reports of cases in which a low C.S.F. pressure was found the lack of accurate methods of measuring the pressure detracts from the value of the observations, and it is only since the more general use of manometry that the clinical significance of intracranial hypotension has been realised. Leriche's early suspicions that headaches, vertigo, nausea, convulsions, and stupor sometimes progressing to coma and death could be associated equally with hypotension as with hypertension of the C.S.F. seemed to be supported by the case which he described with Emery (Leriche and Emery 1922):

> "A young man sustained a basal fracture of the skull with escape of cerebrospinal fluid from the ear. When seen the patient was comatose and the loss of cerebrospinal fluid had ceased. Following an intravenous injection of 40 ml. of distilled water the patient rapidly became conscious and talked normally although still complaining of headache and giddiness. At the same time cerebrospinal fluid again spurted from his ear and after a short interval he relapsed into semicoma, the flow of cerebrospinal fluid ceasing. The intravenous injection was twice repeated with similar results and following the third injection the flow of cerebrospinal fluid ceased completely and the patient made an uninterrupted recovery."

Leriche and Wertheimer (1921) described hypotension complicating other closed and compound head injuries, a case of jacksonian epilepsy, and one of generalised epilepsy, in which the intravenous injection of distilled water led either to recovery of consciousness or to cessation of fits. They summarised the causes of cerebral hypotension as:

(1) Diagnostic or therapeutic lumbar puncture and, especially, spinal anæsthesia.

(2) Closed or compound head injuries with or without loss of C.S.F. from the ear.

(3) Cranial operations.

(4) Unrelated medical or neurological disorders.

ÆTIOLOGY

There can be little doubt that most cases of cerebral hypotension fall into Leriche's first three groups, but his fourth group is composed of several apparently unrelated conditions.

Fontan et al. (1946) describe the case of an infant with "*serous*" *meningitis*, with raised cells and protein in the C.S.F., who lapsed into deep coma. Repeated lumbar puncture gave only a few drops of C.S.F. under no measurable pressure. Ventricular puncture showed a similar low C.S.F. pressure. Considerable improvement followed the intraventricular injection of 15 ml. of saline solution and the intravenous injection of saline solution and distilled water. A further lapse into coma associated with ventricular collapse was rapidly and completely cured by injecting 35 ml. of saline solution into the ventricles, with vigorous intravenous fluid therapy.

A case of acute *meningococcal meningitis* and one of *acute encephalitis* with coma were described by Thieffry et al. (1943). Both these cases showed evidence of cerebral hypotension and improved remarkably under appropriate treatment.

Puech et al. (1942b) reported a case showing mental depression, wasting, insomnia, and confusion followed by sudden coma. Cerebral hypotension was diagnosed, and trephine holes were made. The brain was found to have shrunk away from the dura, and ventricular pressure was low. Injection of serum and air into the ventricles produced a rapid recovery. The patient later relapsed into coma, with identical physical findings and a similar response to treatment. This was repeated three more times, the last coma being fatal eighteen months after the onset of his illness. At necropsy no macroscopic pathological process was seen, but histologically the choroid plexus showed gross sclerosis of the capillaries with hyaline degeneration. The epithelium showed no evidence of secretory activity. A possible pathological basis for the causation of spontaneous intracranial hypotension is suggested by this case.

The association of low C.S.F. pressure in cases of chronic *subdural hæmatoma* is well known. The ventricles are sometimes reinflated with air or with saline solution after evacuation of the blood-clot in this condition (Krebs et al. 1937).

Two cases of *intraventricular hæmorrhage* with hypotension cured by evacuation of the blood-clot and reinflation of the ventricles with air were described by Puech et al. (1935).

Two cases of *intracerebral hæmorrhage* with hypotension have been seen and successfully treated by evacuation of blood-clot and rehydration by Miss D. J. K. Beck (personal communication).

The apparently anomalous association of *cerebral œdema* and cerebral hypotension has been described by Puech et al. (1948), who also reported the case of a child developing diabetes insipidus, headaches, drowsiness, narcolepsy, and coma after an operation for a persistent urachus. The brain was sunken, gelatinous, and dehydrated, and the ventricular pressure was very low. Rapid cure followed reinflation of the ventricles.

A case of *sunstroke* in a child, with coma of several days' duration in which clinical and manometric evidence of intracranial hypotension was present, was described by Sorel et al. (1951). Rapid relief followed the intraventricular injection of 20 ml. of physiological saline solution. After a few hours intracranial hypertension supervened; this was rapidly relieved by the withdrawal of a few millilitres of C.S.F. through the trephine holes. This lability of the C.S.F. pressure has often been noted, and lends a note of caution about the introduction of fluid into the subarachnoid space.

Various *psychological syndromes* associated with intracranial hypotension have been reported: depression (Puech et al. 1942a); and maniacal and narcoleptic forms (Puech et al. 1942c). Acute hypotension as a cause of irreversible coma during insulin shock therapy has also been noted (Delay et al. 1948). Low C.S.F. pressures occur not infrequently in schizophrenia (S. Sherwood, personal communication).

CLINICAL PICTURE

The symptoms of cerebral hypotension are not specific and may equally be present in intracranial hypertension and other conditions They do not seem to be directly related to the degree of hypotension

Headache is the chief symptom Its occurrence after lumbar puncture is usually attributed to hypotension of the C S F

Jacobæus and Frumerie (1923) reported two cases, with severe headache following lumbar puncture, in which repeated puncture revealed a pressure of zero both cases responded immediately to raising of the C S F. pressure with intrathecal saline solution 35 ml and 90 ml.

Alpers (1925) found headache after lumbar puncture in sixteen out of ninety-one patients in whom 15–25 ml of C S F had been removed In all these cases the C S F pressure fell notably after removal of C S F Alpers suggested treatment with pituitary posterior-lobe extract for mild cases and intravenous hypotonic fluids in more severe cases, and recommended a small needle for the puncture and a period of recumbency after the puncture.

Pickering (1948), discussing 11 cases of reaction to lumbar puncture, described headache and pain in the occiput, neck, shoulders, and back, with or without neck stiffness The headache was worsened by sitting upright, by jugular pressure, and by shaking the head, and was lessened by lying down In all the cases repeat lumbar puncture showed a low pressure

Kunkle et al (1943) constantly induced headache by drainage of about 20 ml of C S F with the patient in the erect position The headache was reduced by tilting the patient towards the horizontal or by flexion or extension of the head, and was exacerbated by the erect position These postural changes were independent of estimated intravenous pressure Drainage headache was reduced in intensity by intrathecal injections of physiological saline solution and restoration of the volume of C S F These workers agreed with MacRobert (1918) that headache after lumbar puncture was due to a fall in C S F pressure as a result of prolonged leakage through the hole in the dura

The character of the headache in other conditions associated with a low C S F pressure is similar to that seen after lumbar puncture It may be mild or severe, frontal or, more often, occipital, spreading down the neck and back to the shoulders, is accentuated by the erect position and movement of the head, is relieved by lying down, and may be associated with various degrees of neck stiffness and a positive Kernig's sign

Vertigo often occurs with headache and is also worsened by changes of posture and movement of the head. With it may be seen various degrees of ataxia and disorders of equilibrium

Vomiting may occur, especially at the height of headache, and is often preceded by nausea, which may be present alone in milder cases Evidence of general dehydration can be seen after prolonged vomiting

Symptoms of diabetes insipidus and narcolepsy are sometimes present

Generalised epileptiform *convulsions* and jacksonian epilepsy have been described and are relieved by raising the C S F pressure Focal neurological signs—e g, hemiplegia and aphasia—may occur

Disorders of consciousness, ranging from apathy to deep coma, are common and, if untreated, may proceed to death

Disturbance of autonomic centres, with fever and alteration in pulse-rate and blood-pressure, may also be noted

Psychological changes have been mentioned above

ILLUSTRATIVE CASE-RECORDS

After Lumbar Puncture

Case 1.—A married woman, aged 27, was admitted to the neurological wards of this hospital, where early disseminated sclerosis and hysterical retention of urine were diagnosed For the previous month, after an emotional shock, the patient had not passed urine normally and had been catheterised once daily in the casualty department of another hospital During this time her fluid intake had been reduced to about a pint daily Shortly after admission a history from her

Lumbar puncture was done the day after admission, in the left lateral position A pressure of 50 mm H_2O was recorded After 7 ml *of C S F had been removed, the pressure* fell to zero The foot of the bed was raised on blocks Both before and after lumbar puncture the patient refused to take *adequate fluids* Shortly after the puncture she complained *to the nurses of* giddiness and a 'sense of oppression' in her head, *these diminished* during the evening Next morning *she had no* symptoms until her bed was taken down from blocks, when she again noticed giddiness and headache At 11 A M she asked for a bedpan, on to which she was helped by *a nurse* A few moments later she was found lying *unconscious in the bed*

On examination her respiration was slow and stertorous, *pulse rate 80*, and blood pressure 84/60 mm Hg She was deeply comatose and unresponsive to painful stimuli She had *pin point* unreacting pupils, normal optic fundi, and absent corneal reflexes Her limbs were hypotonic, deep reflexes absent, and plantar responses extensor

Diagnosis and treatment—Acute cerebral hypotension was diagnosed, but in view of the gravity of her condition no attempt was made to confirm this diagnosis by further lumbar puncture Her bed was placed on high blocks, and she was given three pints of intravenous physiological saline solution in an hour She responded to this treatment by suddenly becoming more conscious and moving her limbs spontaneously Her, pupils became widely dilated, her corneal and deep reflexes returned, and her plantar responses became feebly flexor

Progress—In the next few hours, during which the intravenous saline solution was injected slowly, her condition showed remarkable variation from deep coma with pin point pupils, absent corneal and deep reflexes, and bilateral extensor plantar responses, to violent semi-coma during which she flung herself about the bed and needed restraint and sedation her pupils were widely dilated, her corneal and deep reflexes were present, and her plantar responses were flexor These changes occurred with great rapidity, and it was noticeable that each period of violence was followed by sudden collapse into deep coma By 11 P M she was screaming and moaning hysterically, and she resisted actively any interference or attempted examination No abnormality apart from an apparent inability of lateral conjugate deviation of the eyes was detected Her blood pressure was 130/80 mm Hg, having slowly risen from its previous low level in the preceding twelve hours Next morning she was fully conscious, complaining of no symptoms, but was difficult, noisy, uncoöperative, and resistant to examination Her eventual recovery was complete, and her further stay in the neurological ward was characterised only by a hysterical anæsthesia of her left leg and a very hysterical gait She was discharged to the mental wards of the hospital for further treatment

Comments—This dramatic, and fortunately rare, reaction to lumbar puncture was due, in all probability, to a sudden fall in C S F pressure in a patient with a latent dehydration occasioned by a very deficient fluid intake in the month preceding lumbar puncture This diagnosis is supported by the low initial C S F pressure and its fall to zero after removal of a small amount of C S F for diagnostic purposes Although C S F pressure readings were not repeated, owing to the gravity of her condition, it is a reasonable presumption (in view of her history and her recovery with rehydration) that her symptoms were due to sudden intracranial hypotension The immediate cause of her collapse was undoubtedly the adoption of the erect position with its attendant lowering of intracranial pressure Such an event must indeed be most unusual, but it is perhaps expedient that the possibility of collapse and even death may be known to occur in certain special circumstances following lumbar puncture

In Association with Subdural Hæmatoma

Case 2—A married woman, aged 55, sustained a very mild blow on the head while getting into a car on Aug 22, 1948 A week later she complained of sudden onset of vertical and occipital headache She gradually became drowsy, and for eighteen hours was stuporose She vomited twice during this time Recovery from the incident was rapid, but com adache persisted for a week. She then again became uporose, and on admission was in semi-coma.

On examination her temperature was 99·8°F, pulse-rate 70, espirations 26 a minute. She was incontinent of urine and esponded slowly to painful stimuli. Her right pupil was arger than her left and moderately dilated. Evidence of a eft hemiplegia was present, but both plantar responses were xtensor. She had mild neck stiffness.

Lumbar puncture showed clear C.S.F. under a pressure of 0 mm. H_2O and containing protein 40 mg. per 100 ml., ed cells 17 per c.mm., and lymphocytes 15 per c.mm. A subdural hæmatoma was diagnosed.

Treatment and progress.—On Aug. 5, 1948, bilateral exploratory posterior parietal burr-holes were made. When the dura on the left side was opened, dark altered blood gushed out, and the brain was found to be depressed 7 mm. below the surface of the dura. The blood was sucked out and saline solution run through until clear. About 30 ml. of blood was removed. On the evening of the operation the patient became conscious, spoke rationally to relations, and complained of headache. She was again drowsy next morning and later stuporose. Her pupils were small but equal, and the signs of hemiplegia remained unchanged. Radiography of the skull showed considerable recession of the brain from the front of the skull in the face-up position. In view of the possible reaccumulation of fluid or of blood the patient was re-explored. No evidence of fresh subdural hæmorrhage was found, but the brain had shrunk from the dura on both sides of the skull. The intraventricular pressures were not measured. Intracranial hypotension was diagnosed, the patient was nursed in the head-down position, she was given plenty of fluids, and an intravenous drip of physiological saline solution was set up. The patient gradually improved and within three days had returned to normal consciousness, her hemiplegic signs disappearing by the seventh day. She was discharged entirely normal at the end of a month.

Comments.—The initial C.S.F. pressure in case 2 was low (30 mm. H_2O), a finding which is well known to accompany chronic subdural hæmatoma. The patient's partial recovery after operation is consistent with the removal of 30 ml. of subdural blood, and her relapse into semi-coma with evidence of cerebral dehydration strongly suggests intracranial hypotension. Her recovery with rehydration confirms this impression.

Spontaneous

Case 3.—A female clerk, aged 38, had had a duodenal ulcer diagnosed in 1945. She had been treated medically until 1947, when a vagotomy was done, since when she had had no further dyspepsia. After vagotomy she had remained in hospital for three weeks and then been sent to a convalescent home. On the third day, while looking in a shop window, she had felt a sudden shooting pain through the front of her head. This was followed by unconsciousness lasting $1^1/_2$ hours. The attack was described as "unlike an ordinary faint," because she bit her tongue and went stiff. She felt dazed and muzzy in the head for three days. Some weeks later she began to experience muzzy heavy headaches, later increasing in severity and frequency until she was admitted to hospital in June, 1949, for investigation. In July, 1948, during a twenty-mile bus ride she noticed a thumping muddled headache with dizziness. On leaving the bus she fainted; she awoke in hospital, feeling weak and dazed, and with a frontal headache. She was discharged the same day. In May, 1949, after a worrying day she had had a similar headache and again lost consciousness while leaving a bus. She bit her tongue, foamed at the mouth, passed her urine, and went stiff. She was unconscious for two hours. Headache remained severe after this attack, and she lost consciousness twice two days later. Hypoglycæmic attacks had been tentatively diagnosed before her first admission in June, 1949.

Physical examination showed no abnormality. A glucose-tolerance test, an insulin-glucose-tolerance test, electrocardiography, electro-encephalography, lumbar puncture, radiography of the skull, a blood-count, a Wassermann reaction of the blood, and liver-function tests were normal, but the C.S.F. was under a low normal pressure of 60 mm. H_2O. Hypoglycæmic attacks, induced with intravenous insulin, bore no resemblance to her usual attacks. No certain diagnosis was made, and the patient was discharged.

Readmission.—Her symptoms gradually increased in severity, necessitating readmission in March, 1950. A more detailed history of her headaches revealed certain important characteristics. The headache was mainly frontal in distribution but travelled to the occiput and back of the neck when severe. The severity varied from a mild muzzy heavy feeling to severe incapacitating pain with stiffness of her neck, photophobia, vertigo and nausea, but no vomiting. The pain was sometimes much exacerbated by coughing, sneezing, straining, jolting, turning the head quickly, and noise. The headache never occurred at night and usually started shortly after the patient got up in the morning. When the pain was severe, the patient felt the need to lie down, which act consistently relieved the pain within a few minutes. She noticed that aspirin hastened the relief of pain if she lay down, but alone, or combined with rest in the upright position in a chair, it had no effect. A recumbent position therefore appeared necessary for relief. After a headache the patient felt weak, dazed, and shaky. In association with headache she was often giddy, with objects rotating in an anti-clockwise direction. This symptom was also rapidly relieved by lying down. Apart from a mild but definite loss of concentration she had no other symptoms. She admitted to being slightly highly strung but did not relate her symptoms to periods of stress and anxiety, and she showed no apparent evidence of emotional instability.

Physical examination was entirely negative, and in view of the characteristics of her headache a diagnosis of intracranial hypotension was considered.

Lumbar puncture was done without difficulty. The C.S.F. pressure was 30 mm. H_2O, rising rapidly on jugular pressure to 120 mm. H_2O and falling equally rapidly to its former pressure; 7 ml. of C.S.F. was removed for examination, and after its removal the spontaneous flow of C.S.F. ceased. The C.S.F. was normal in constitution.

Treatment and progress.—The foot of the patient's bed was placed on blocks, but the same evening she developed headache, which was greatly increased next morning, when the blocks were removed. The headache was similar to her usual headache, was frontal and occipital in distribution, extending down the back of the neck, which felt stiff, to her shoulders. The bones of her neck were tender, and she had photophobia, vertigo, and increased headache on raising her shoulders from the bed. The headache was much increased by shaking her head, coughing, and, to a less extent, by jugular compression. Her neck showed slight stiffness and was painful on movement. The foot of the bed was again raised, the patient was given as much fluids as she would take, and after four days her symptoms had entirely disappeared. This reaction was that of a typical moderately severe post-lumbar-puncture syndrome, but the resemblance between these symptoms and those for which she was admitted was striking. Two attempts were made to induce symptoms by lowering intracranial pressure with 50% intravenous sucrose (50 ml. and 75 ml.) but without success. The patient next induced an attack by spending the day among the noise and bustle of London traffic. She returned with moderately severe headache. Two hours later lumbar puncture produced C.S.F. under a pressure of 35 mm. H_2O. Entirely without the patient's knowledge 20 ml. of physiological saline solution was introduced into the spinal theca, raising the C.S.F. pressure to 100 mm. H_2O. After 12 ml. had been injected she said that the headache had completely disappeared. Eight hours later headache returned with considerable severity combined with nausea and giddiness. After the ingestion of 750 ml. of water and an intramuscular injection of 10 units of 'Pitressin' considerable improvement took place for three hours. After diuresis the headache returned. In view of the effect of oxygen in raising intracranial tension under certain conditions the patient was treated in an oxygen tent with a flow of 6 litres a minute for two hours, with almost complete relief of symptoms. She was discharged symptom-free a week later. When she resumed work her symptoms recurred, and fluids and salt in large amounts, pitressin snuff, ephedrine, *d*-amphetamine sulphate, and sedatives have been used without effect.

Comments.—The unusual characteristics of this patient's headaches first drew attention to the possibility of intracranial hypotension as a cause. The low C.S.F. pressure and the rapid relief obtained by raising this pressure are strong evidence that this presumption was correct.

After Torkildsen's Operation for Hydrocephalus

Case 4.—A schoolgirl, aged 15, had hydrocephalus. Preoperative ventriculography revealed gross hydrocephalus, probably due to stenosis of the aqueduct, since the fourth ventricle and the aqueduct of Sylvius were not filled. Ventricular pressures of 20 mm. H_2O were recorded. Ventriculography was followed by Torkildsen's operation, a ventriculo cisternostomy.

Postoperatively the patient's condition remained excellent for the next two days. At lumbar puncture the C.S.F. pressures on these days were 210 mm. and 240 mm. H_2O, and 20 ml. and 30 ml. of C.S.F. were withdrawn. On the third postoperative day the child's condition began to deteriorate, and she complained of severe headache; the C.S.F. pressure had fallen to 60 mm. H_2O. Next day she was worse, being drowsy and responding with difficulty to questions. Her headache remained severe; she was incontinent of urine, and her pulse-rate had slowed to 60. Her pupils were large, eccentric, and sluggish in reaction; a divergent squint was present. A combined ventricular and lumbar puncture was done. The lumbar pressure remained at 60 mm. H_2O, but no ventricular pressure was recordable. The child was now nearly comatose. An intravenous drip of physiological saline solution was started, two pints being given rapidly, and then continued more slowly. For the first four hours after the drip began the patient remained comatose, with dilated unresponsive pupils, a divergent squint, flaccid extremities, a low blood pressure, a rising irregular pulse rate, slow irregular respiration, and slight cyanosis. After six hours voluntary movement to command began to return. Hypotonic saline solution and, later, distilled water were substituted for physiological saline solution. By twelve hours she was complaining of an "awful headache" and could answer simple questions and move her limbs voluntarily. After twenty-four hours she was fully conscious and had no headache or abnormal neurological signs apart from those that existed before operation. By this time she had been given eight and a half pints of intravenous fluid. Her further convalescence was uneventful.

Comments.—This girl's condition on the fourth postoperative day was so serious that it was thought she would die. Within twenty-four hours she had returned almost to normal through vigorous rehydration, showing the remarkable and gratifying response to early treatment in intracranial hypotension. Since this complication may occasionally follow the Torkildsen procedure it should be suspected whenever alterations of consciousness, pulse-rate, respirations, temperature, or blood-pressure appear, with or without evidence of meningeal irritation or focal neurological abnormality.

PATHOGENESIS

Various mechanisms may play a part in the production of intracranial hypotension; these mechanisms resolve themselves largely into the following three main groups.

(1) *Excessive loss of C.S.F.* may follow compound fractures of the skull, intracranial operations with leakage of C.S.F., and, occasionally, prolonged dural leakage after lumbar puncture or spinal anæsthesia.

(2) *Insufficient production of C.S.F.*—Under normal conditions C.S.F. is produced by the choroid plexuses, circulates throughout the subarachnoid space, and is absorbed into the arachnoid villi. Its formation within the choroid plexus depends on active secretion by these cells and not on simple filtration (Flexner 1934). This process may therefore be affected by alterations in the nervous control of, or blood flow through, the plexus or by degenerative changes within the plexus. After head injuries spasm of cerebral blood-vessels may occur in man and be seen experimentally in animals. A sudden fall of blood pressure, or peripheral vascular failure with consequent diminution of blood flow through the choroid plexus, may lead to diminished formation of C.S.F. Dehydration may have a similar effect. Severe toxæmia may affect either the cerebral blood flow or the secretory cells of the choroid plexus. Degenerative changes in the plexus may occasionally lead to a chronic and progressive diminution of production of C.S.F., as in the case described by Puech et al. (1942b).

(3) *Increase in size of subarachnoid space*.—A relative insufficiency of C.S.F. can be the result of an increase in the capacity of the subarachnoid space due to cortical atrophy such as follows head injuries and cerebrovascular accidents, or of the removal of the space-occupying lesions within the skull. The first mechanism may be present in chronic cases but is otherwise unlikely to be of importance.

Cause and effect are clear in groups 1 and 3, but much remains to be learnt about the factors operating in group 2. It is tempting to incriminate disturbances of the hypothalamus as the cause of diminished production of C.S.F. and of certain symptoms of intracranial hypotension. Changes in consciousness seen in intracranial hypotension may resemble the "arrested consciousness" sometimes observed in hypothalamic lesions, and alterations in temperature control, blood-pressure, and pulse rate may indicate dysfunction of vegetative centres. Chorobski (1950) believes that a centre may exist in the diencephalon for the production of C.S.F., which can be affected, through alterations in cerebral blood flow, by (1) simple exposure of the brain to the atmosphere, (2) the effect of afferent nerve impulses from the operation site, and (3) tissue metabolites released from the area of trauma. It seems equally possible, however, that any disturbance of the hypothalamus which occurs may be the result, and not the cause, of the hypotension, both, perhaps, being produced by diminished cerebral blood-flow. Russell (1948) also considered the possibility of a hypothalamic disorder, but through its action on general body-water control. Ryder et al. (1952) have produced evidence, by estimation of cerebral blood-flow and C.S.F. pressure in man, that variations in cerebral blood-flow induce changes in C.S.F. pressure in the same direction. They have also shown that changes in cerebral blood-flow and in the arterial and jugular venous pressures may be completely dissociated, and that, when C.S.F. pressure varies concomitantly with changes in systemic arterial pressure, it is because the cerebral blood-flow varies concomitantly with the changes in systemic arterial pressure. These findings strongly support the view that diminished cerebral blood-flow may be of the greatest importance in the causation of intracranial hypotension.

TREATMENT

Pressure within the subarachnoid space may be increased either by the introduction of fluid or of air directly into the space, by increasing the production of C.S.F., or by retaining fluid within the body.

Lumbar-puncture reactions usually respond satisfactorily to nursing with the foot of the bed raised and forced fluids. As suggested by Alpers (1925) pituitary posterior-lobe extracts may be used to inhibit diuresis. Possibly a large intake of fluids and sodium before lumbar puncture may lessen the likelihood of reactions.

In acute cases of intracranial hypotension more drastic measures are indicated. Intravenous injection of 20–40 ml. of distilled water was successfully used by Leriche and should be tried first. Hypotonic solutions increase the production of C.S.F. (Weed and Hughson 1921), and the danger of hæmolysis is minimal with this dosage. Intravenous infusion of hypotonic or of physiological saline solution, or of plasma is also effective, but its action is slower. Pressure within the theca may be rapidly raised by the introduction of either physiological fluid or air into the subarachnoid space or into the ventricle. We have been able largely to abolish lumbar-puncture reactions after the removal of 30 ml. of C.S.F. in a few cases of disseminated sclerosis, in which reactions are common, by the immediate introduction of physiological saline solution. Only 20–25 ml. of physiological saline solution is needed to restore the original pressure, which fact suggests that a reactive increase in the production of C.S.F. has taken place. This method of treating intracranial hypotension is easy and satisfactory, but the strictest aseptic precautions must be taken. There is also the disadvantage that further C.S.F. may leak through the hole in the dura and cause the gradual return of symptoms. The use of air in reinflation of the ventricles (" regonflage du cerveau " or " pneumothérapie cérébrale ") is widely recommended by Delay and Sizaret (1947), partly because of its action of re-establishing intraventricular pressure and partly because of its "irritant" effect on the choroid plexus. Since some French workers insist that direct measurement of the intraventricular pressure is essential in the diagnosis of intracranial hypotension they recommend the introduction of air into the ventricles through a needle passed through the trephine holes. The lumbar route may also be used. The value of reinflation of the ventricles with air has a diagnostic, in addition to a therapeutic, value because radiography of the skull after this procedure may reveal some unsuspected focal abnormality.

For less acute cases other measures may be taken. Many drugs—e.g., adrenaline, ephedrine, d-amphetamine sulphate, and pilocarpine—are thought to increase C.S.F. pressure. None of these exerts much therapeutic effect. The inhalation of oxygen causes a large increase in C.S.F. pressure in patients with emphysema and cor pulmonale, due to carbon dioxide retention, and oxygen has also been used to relieve symptoms following air encephalography. Although there is no evidence that oxygen can cause an increased C.S.F. pressure in normal people, it was tried with success in case 3 and might prove a valuable therapeutic measure in other cases.

In chronic idiopathic intracranial hypotension such measures are either impracticable or valueless, and for these cases certain radical surgical measures have been suggested—e.g., ligature of the inferior longitudinal sinus or of the internal jugular vein, and pericarotid sympathectomy. Until we know more about intracranial hydrodynamics, these procedures can only be considered as experimental. Early diagnosis is essential, when appropriate therapy may be effective, because some cases progress to irreversible intracranial hypotension and death.

SUMMARY

The history, clinical picture, ætiology, pathogenesis, and treatment of intracranial hypotension are discussed.

Clinicians should be aware of the occurrence of intracranial hypotension as a complication in certain cases of head injury, infective or vascular intracranial conditions, and following lumbar puncture, spinal anæsthesia, and cranial operations.

Intracranial hypotension is diagnosed from a combination of certain non-specific symptoms and signs in association with a low C.S.F. pressure, and its significance must remain uncertain until we know more about intracranial hydrodynamics.

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RECOGNITION OF PRIMARY TUBERCULOUS INFECTION OF SKIN AND MUCOSÆ

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With illustrations on plate

WHEN Ghon (1912) described the anatomical and pathological characteristics of the primary tuberculous infection in childhood he recognised that the primary focus with enlargement of regional lymph-nodes could be in the skin or on any mucosa as well as in the lungs or abdomen. From that time onwards a constant trickle of cases has been published of primary complexes situated in almost every part of the human body. Nearly always, however, these reports are of one or two cases, and the inference is drawn that primary infection in sites other than lung and abdomen is curious and interesting but uncommon. Indeed I have found only one published report of more than 6 cases: Stokes (1925) reported 10 from the Mayo Clinic. He made the point which is the object of the present paper:

> "A better acquaintance with the clinical characteristics of this lesion would result in the identification of more cases, especially by those who as surgeons, internists, pediatricians, and roentgenologists are required to deal with the superficial tuberculous adenopathies."

Because I believe that this statement is true, and that primary tuberculous infection of the skin and mucosæ is often unrecognised, I describe and illustrate here the characteristics of primary infection of the skin and of the mucosæ of the mouth and the conjunctiva in 28 patients.

PRIMARY LESION OF TUBERCULOSIS

The recognition of a primary infection of tuberculosis in a child, adolescent, or adult is possible because the body reacts to an initial infection with tubercle bacilli in a unique recognisable way. Wherever the site of infection may be, the reaction is the same; some bacilli remain to form a small local lesion, while others pass rapidly along lymphatics to the nearest node, which enlarges and, from about two to four weeks later, caseates. As caseation occurs, the body becomes sensitive to tuberculo-protein. This altered sensitivity has a profound influence on the body's reaction to any subsequent infection; for, if that takes place, there is a local reaction of variable severity, but the regional lymph-nodes do not caseate. This type of lesion was previously seen on the skin as the " butchers' wart " or on mucosa as the shallow painful tuberculous ulcer of lip or mouth in persons with phthisis. But wherever the combination of a tuberculous lesion with caseous tuberculosis of the regional lymphatic glands can be demonstrated, we have strong presumptive evidence that the patient is undergoing his primary infection. If we have also observed tuberculin conversion, the presumption becomes certainty. It is apparent, however, that this will be uncommon under ordinary conditions of clinical study, and all but 2 of my patients were tuberculin-positive when first seen Simultaneous infection at different sites (e g, lung and skin) or further infection before sensitivity has developed will produce the same reaction of the primary complex—a focus and regional adenitis at each site of infection

GENERAL FEATURES OF CASES

My study of this condition began early in 1947, when I saw 2 children

(1) An infant, aged six months, was brought for routine examination to the Contact Clinic in Newcastle Her mother was dying of phthisis, and the child had a primary complex in the lung, but since the age of six weeks she had also had an indolent ulcer on her chin and a submental swelling which at first had been hard but had softened and was discharging The ulcer, set in the skin without surrounding inflammation, was small and circular, with two nodules of "apple jelly" material in its rather elevated edge We could not obtain permission for biopsy, but both the skin lesion and the regional gland, after a further abscess in the neck, healed slowly, with subsequent calcification at the sites of the gland abscesses

(2) I saw the second child shortly afterwards, when she was four months old Her father had phthisis, but she was well and was tuberculin negative Two months later she was seen by a colleague in a child-welfare centre She was still well but had developed a small hard papule on the face and a firm swollen gland at the angle of the jaw, and her tuberculin reaction was positive In this child we watched the slow evolution of the lesion without biopsy which would have destroyed its appearance Fig 1 shows the second child six months after the lesion was first seen, fig 2 the development of satellite nodules (see below), and fig 3 shows the lesion after natural healing was complete twelve months later

With interest stimulated I undertook a wider search and more systematic investigation, and in the five years to February, 1952, with the help of friends in the children's, surgical, ophthalmological, and dental departments of the Royal Victoria Infirmary, I have been able to record, photograph, and study 28 examples of primary infection of the skin, mouth, or eye This number excludes 9 other cases of which I possess notes and in some instances photographs, but which I have not been able to see often enough to make a sufficiently detailed and prolonged study

With 1 exception, a farm labourer aged nineteen, the patients were all children aged less than twelve years In 20 cases the primary infection was situated on the skin, in 5 on the conjunctiva, and in the remaining 3 the mouth All the children with infections of skin or mouth lived in the industrial areas along Tyneside in North-eastern England, whereas 3 of the 5 children with infection in the eye lived in the country areas, of them on farms The ages and salient facts of the cases are given in the accompanying table, which shows that in 22 of the 28 cases we were able to prove the tuberculous nature of the primary focus The 6 exceptions include the child who had been examined when tuberculin-negative and we did not wish to disturb the evolution of the lesion, a child with the primary lesion on the sole of the foot, where biopsy was considered inadvisable because a painful scar might remain, though tubercle bacilli were recovered from the inguinal glands, and 4 others where we could not obtain a biopsy for other reasons In 2 of these 6 patients additional information supporting the diagnosis of tuberculosis has been the observation of a change in the tuberculin reaction, in 2 others the appearance of erythema nodosum at the expected time, and the calcification in the regional glands which has appeared in every case These factors, together with the clinical course of the illness, leave no reasonable doubt that all the cases included in this series are examples of primary tuberculous infection

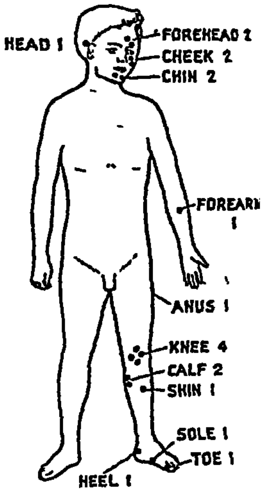

Fig 4—Anatomical distribution of 19 primary tuberculous lesions of skin

PRIMARY LESIONS IN SKIN

There were *20 such cases* In 3 the children were aged less than one year when the lesion first appeared 2 were in the second year, 8 were between two and five years old, and the eldest of the remaining 7 was nearly eleven years old All but 1 of the lesions were

SYNOPSIS OF DATA OF 28 CASES OF PRIMARY TUBERCULOUS INFECTION

Case no	Age at onset (yr)	Site	Contact	Trauma	Primary focus histology	Regional gland		First symptom
						Calcification	Histology or bacteriology	
1	$3^{2}/_{12}$	Shin	Mother	No	+	+	+	Swelling in groin
2	$2^{4}/_{12}$	Cheek	None	Yes	+	+	+	Spot on face, and swelling in front of ear
3	4	Knee	Mother	No	+	+	+	Acute inguinal adenitis
4	7	Heel	None	Yes	+	+	+	Inguinal adenitis and lack of healing
5	$5^{10}/_{12}$	Knee	None	No	+	+	+	Inguinal swelling
6	8	Foot	None	Severe injury	−	+	+	Lack of healing after accident
7	$1^{10}/_{12}$	Arm	Father	No	+	+	+	Axillary adenitis
8	8	Toe	None	Yes	+	+	+	Swelling in groin
9	$^{4}/_{12}$	Knee	Mother	No	+	+	+	Red area on knee
10	$2^{9}/_{12}$	Calf	Uncle	No	+	+	+	Acute inguinal adenitis
11	$3^{6}/_{12}$	Knee	Father	Yes	+	+	+	Scab did not heal
12	$10^{9}/_{12}$	Chin	None	Yes	+	−	+	Swelling under chin
13	$1^{8}/_{12}$	Anus	Father	Yes	+	+	+	Swelling in groin
14	$^{6}/_{12}$	Chin	Mother	No	−	+	−	Lesion on chin, submental abscess
15	$^{8}/_{12}$	Cheek	Father	No	−	+	−	Spot on face, tonsillar gland swelling
16	$2^{7}/_{12}$	Forehead	Aunt	Yes	−	+	−	Wound did not heal
17	$4^{6}/_{12}$	Forehead	Aunt	No	−	+	+	Scab on forehead, and abscess in front of ear
18	$6^{9}/_{12}$	Head	None	Severe injury	−	+	+	Postauricular abscess
19	4	Calf	None	No	Tubercle bacilli isolated	−	+	Ill on admission after measles
20	$3^{6}/_{12}$	Foot	None	Yes	−	+	+	Septic foot and acute adenitis
21	9	Eye	None	?	+	−	+	Sore eye
22	$11^{9}/_{12}$	Eye	None	No	+	+	+	Swelling of tonsillar gland
23	$10^{9}/_{12}$	Eye	None	?	Tubercle bacilli isolated	+	+	Chronic conjunctivitis
24	10	Eye	None	?	−	+	+	Irritability of eye
25	$^{9}/_{12}$	Eye	Aunt	No	Tubercle bacilli isolated	+	+	Small swelling in front of ear
26	$7^{10}/_{12}$	Mouth	None	No	+	+	+	Ulcer in mouth
27	$8^{9}/_{12}$	Mouth	None	Yes	+	−	+	Submaxillary swelling
28	2	Mouth	None	Yes	+	+	+	Submaxillary swelling

found on skin surfaces exposed to injury and to contamination from outside dust and dirt. This distribution about the face and the legs below the knee can be seen in fig. 4: 7 lesions were on the face and head; 11 on the knee, lower leg, and foot; 1 on the forearm, and 1 at the anus. In one child (case 6, not illustrated in fig. 4), the whole of the foot was involved in the primary infection. In 11 of the 20 children there was known contact with an infective adult, either a member of the family or a frequent visitor. In 10 cases there was a history of trauma, including 2 major injuries from road accidents. Yet only in 3 cases were both injury and contact combined and only 2 were without either; nor was there evidence of trauma in one area and contact in another, an equal division of each between face and leg being seen.

Thus the presence of either contact or trauma is important, but it is unusual to get a history of both, and I do not know if slight injury is always necessary before a primary infection can be established. Yet it might be reasonable to think that, where there is a frequent contact with an infective adult, the chance of infection of a minute skin lesion is fairly high, whereas with larger cuts or injuries the possibility of dust infection, presumably with small numbers of tubercle bacilli, increases.

PRESENTING SYMPTOMS

Only 1 child presented with a systemic illness, pyrexia following measles, later becoming miliary tuberculosis. In all the 19 others the mother found a local lesion when her child was otherwise well: in 6 it was a spot or a scab in the skin or a small wound or abrasion which did not heal; in 13 a swelling of a lymph-node in the groin, in front of the ear, or in the neck first gave rise to complaint and raised suspicion of tuberculosis. This lymph-node swelling in 10 cases was slow and painless, but in 3 the reaction was much more acute, 1 presenting with high pyrexia, great pain, and tenderness, and the other 2 with moderate tenderness, sufficient nevertheless to simulate a "septic" infection.

I do not yet know whether the acute type of reaction with rapid softening indicates the presence of a simultaneous infection with tubercle bacilli and pyococcal organisms, but the circumstances of infection are such that this is at least possible; it might also, however, indicate a severe reaction to tuberculous infection only. This point remains to be studied later.

Attention may therefore be directed to the primary infection in three ways:

(1) Reference may be made to a papule, a scab, or a small wound which does not heal.

(2) A painless glandular swelling may be found in the groin, axilla, neck, or in front of the ear.

(3) Occasionally the presenting symptom is a more acute type of glandular reaction, simulating an acute pyococcal infection.

CHARACTERISTICS OF PRIMARY FOCUS IN SKIN

The 20 cases comprised lesions in all stages of development: the earliest had been present only three weeks when first seen (and was not photographed for some time later), and others at least eighteen months when first seen. The natural course of healing was often interrupted, sometimes by surgical intervention for biopsy; others were healed by streptomycin therapy. I have not, therefore, found it possible to describe the evolution and healing of a "typical" lesion, and indeed, if it had been easily possible to do so, the appearance would have been well known long ago. The first characteristic is therefore variability; and, since the most significant factors in determining the shape and size of the primary focus are undoubtedly the presence and the type of visible injury into which the bacilli have been introduced, the natural division, for purposes of description, is into those cases with or without a history of trauma.

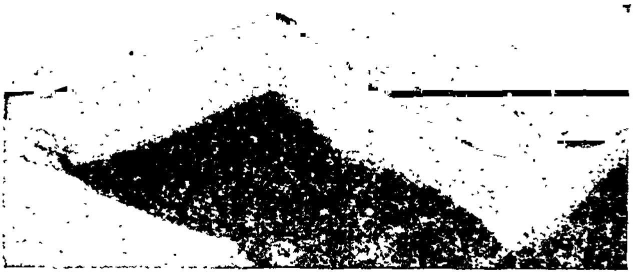

Fig. 5—Primary tuberculous lesion of skin of left foot, with painless enlarged lymph-node in left groin, in a boy, aged 7 years, eight weeks after he had cut his foot.

Primary Infection of Skin Following Injury

Of the 20 skin cases 10 had a history of injury, varying from a scratch by a puppy to a serious road accident. The wound at first seemed to heal but unexpectedly broke down about the end of the first week. The two road accidents were both major injuries: in the first, a compound dislocation of the ankle did not heal, the whole foot became a large tuberculous lesion, and a tuberculous abscess appeared in the groin; in the second, the boy was admitted to hospital with multiple injuries, including a large scalp wound. His tuberculin skin reaction was negative on admission, and he made a good recovery except for a ragged granulating area behind the right ear and a postauricular gland abscess from which tubercle bacilli were recovered. These two infections may have been from one of several sources: from tubercle bacilli in the road dust, by contact infection on the way to hospital, or within the hospital wards. All but 1 of the remaining lesions were in smaller cuts or abrasions and presented as small ulcers or scabs which had refused to heal for several weeks yet had remained without pain or surrounding inflammation and with slight, if any, discharge. The one exception was a boy who cut his foot on a piece of glass and within a few days had a painful lesion on the sole of the foot, with rapid swelling and extreme tenderness of the regional glands. Probably there were coincident tuberculous and pyococcal infections.

I shall give the history of 1 other child in rather more detail:

In July, 1949, a healthy lively boy, aged seven years, was paddling in a pool in a public park, when he cut the inner side of his left heel on a piece of glass, making a wound about 1 in. long. When he came home, his mother dressed it, and for the first week healing seemed satisfactory; by the end of the second week, however, it had broken down, forming an indolent painless ulcer. A month later, while bathing him, his mother found a painless swelling in his left groin. Within another fortnight this had become red, and he was then referred to hospital, where an abscess was incised. Like the wound on the foot, the incision did not heal, and another small incision was necessary. On this occasion tubercle bacilli were found in the pus, and I was asked to see the child. Biopsy of the lesion on the foot showed *tuberculous granulation* tissue, and the appearance of the primary complex at the time of the diagnosis, eight weeks after the onset, is shown in figs. 5 and 6.

When a wound is infected with tubercle bacilli, the appearance of the primary lesion is determined by the size and shape of the original injury. The clue to diagnosis is to suspect any wound which has broken down after initial healing and is accompanied by a painless enlargement of regional lymph-nodes.

Primary Lesions without History of Injury

Turning for comparison to the 10 other primary skin infections, without a history of trauma but mostly with a history of contact, we find the lesions are much less conspicuous and have not the same ulcerous appearance. Rather do they give the impression that, after the bacilli have gained entry, most of the activity takes place below the surface of the epidermis The distribution is still on exposed areas, the face and the leg below the knee Most of the lesions are $^1/_2$–1 in in diameter roughly circular or ovoid, with a depressed centre and a raised edge, and are set in the skin just below the epidermis Over the surface, especially in the centre of the focus, there are usually adherent silvery epidermal scales, while on close inspection of the edge or on pressure with a glass slide small "apple-jelly" nodules, similar to those seen in lupus vulgaris, can be observed The whole lesion looks innocent and indolent, it often passes unseen or is described as a "healed or healing septic spot" (figs 7 and 8) Only closer inspection and histological examination reveal its true nature In 1 case the primary focus did merit its first description of impetigo and indeed one wondered if an impetiginous area had not become infected with tubercle bacilli

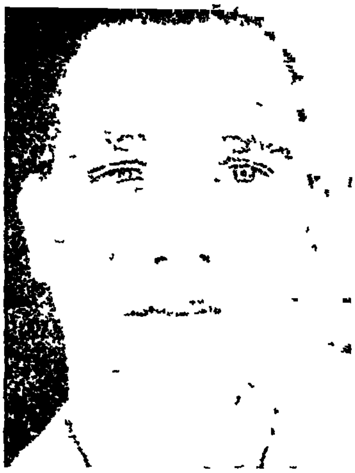

Fig 10—Œdema of right eyelid and swollen preauricular gland in youth aged 19

A boy, aged seven years, was seen in a children's sanatorium with a large fluctuating swelling in the right iliac fossa and the scar of a recently healed tuberculous sinus below the right inguinal ligament Further search revealed a circular lesion with a depressed centre and a raised edge in the skin over the patella (fig 9) So far as I could discover, this had never ulcerated, and no complaint had ever been made about it Histologically it was tuberculous, and eventually the large abscess in the right iliac fossa was opened, and caseous material obtained

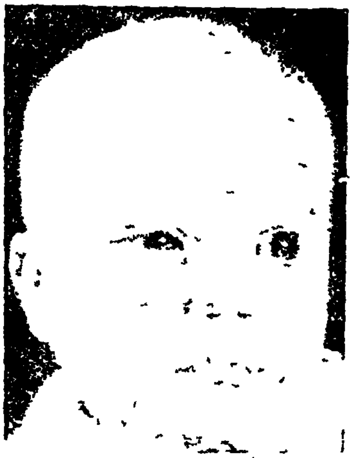

Fig 12—Œdema of eyelid on same side as swollen preauricular gland in boy aged 9 months

Several cases presented a phenomenon which may be peculiar to primary tuberculous lesions This was the development of scattered small nodules in the skin in a zone about the main lesion In 1 such case there was a history of trauma and the nodules disappeared as the lesion healed under streptomycin therapy In another case the primary focus healed naturally, leaving a serpiginous scar and small clear cut craters (fig 3) where the nodules (fig 2) had been In neither of these cases was a nodule removed for biopsy but in a 3rd case where the toe had previously been amputated, careful search at the base of the operation scar revealed a similar small lesion, which was removed and found to consist of tuberculous tissue The presumption is, therefore, that these nodules are tiny tuberculous foci, but we do not know how they arise, they might be examples of direct implantation from an explosive cough with bacilli laden sputum, or they might result from lymphatic spread from the primary focus, but, if so, I would have expected them

The examples described and illustrated here are enough to demonstrate the wide variety of forms of the primary infection Tuberculosis should certainly be suspected whenever a wound does not heal but does not show much inflammation The primary lesion without history of injury is more deeply set in the skin and often inconspicuous In 19 of 20 cases the primary lesion was painless, in the other secondary infection with pyococcal organisms was likely Indeed, whenever a tuberculous lymphadenitis is seen in groin, axilla or neck careful search should be made in the area drained by the gland, and any small nodules or ulcers should be closely examined

PRIMARY LESIONS IN EYE

Lesions on the conjunctiva were seen in 5 cases in the same period in 3 children aged between nine and twelve years, in 1 aged eight months, and in a youth aged nineteen Only the baby had a definite story of contact, 3 had a history of irritation of the eye, said to be due to a fly, exposure to artificial fertilisers, and dust and chaff at threshing-time, but there was no definite story of trauma Whereas all the 20 children with skin lesions lived in towns, 3 of these 5 lived in the country, 2 on farms Unfortunately I do not know if the organisms were human or bovine types of tubercle bacilli

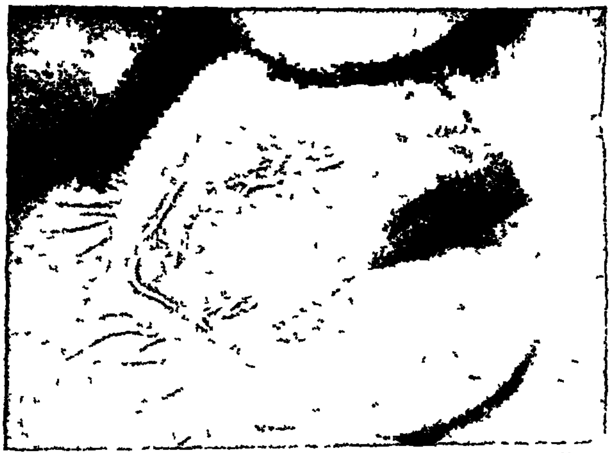

Fig 13—Shallow ulcer under eyelid in same case as in fig 12.

Three complained first of irritation in the eyes, and all 3 had enlargement of the preauricular gland, in the small infant the mother discovered a preauricular gland accidentally while washing the child, the remaining child attended outpatients with erythema nodosum and

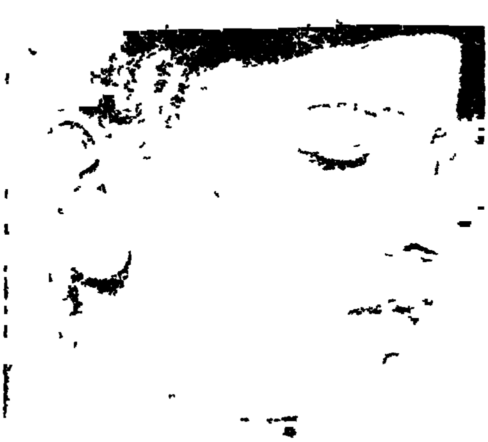

Fig 14—Swollen right submandibular gland in boy with ulcer on gum

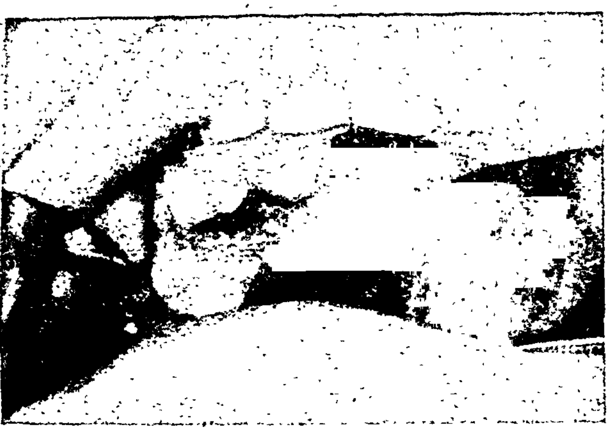

Fig. 15—Circular tuberculous ulcer of gum of right upper jaw in same case as in fig. 14.

a swollen tonsillar gland. Only in 1 case was the primary lesion easily visible as a mass of granulation tissue on the scleral conjunctiva towards the medial canthus; the 4 other lesions were all under the upper lid, but each could have been suspected by the presence of œdema of the eyelid on the same side as the glandular swelling (figs. 10 and 12). When the lids were turned up, the change revealed was uniformly greater than expected, either a fungating mass of granulations (fig. 11) or, as in the infant, a shallow ulcer with a yellow base and much surrounding œdema (fig. 13).

Painless preauricular lymphadenitis should always raise the suspicion of tuberculosis. If there is any complaint about the eyes, or if there is swelling of an eyelid, eversion, if necessary under anæsthesia, should disclose the primary focus. Even in the routine examination of children with cervical adenitis a quick look at the eyelids may be profitable.

A child, aged nine months, was born healthy, the only infant of artisan parents. At the end of April, 1950, while his mother was washing his face she found a small lump in front of his right ear. She consulted various doctors and was seen in the children's department. The swelling was larger, and œdema of the right upper eyelid was apparent (fig. 12). Eversion of the lid under anæsthesia revealed a shallow ulcer (fig. 13), which histological examination showed to be tuberculous. The tuberculin skin reaction was positive, and later, when the preauricular adenitis became an abscess, tubercle bacilli were recovered. The child had been in regular contact with a phthisical aunt, who died a few months afterwards.

PRIMARY TUBERCULOSIS OF MOUTH

Up to now, excluding lesions in or on the tonsils, I have seen only 3 cases with proved tuberculous lesions in the mouth and regional tuberculous lymphadenitis:

(1) A girl, aged two years, developed a painless ulcer in her mouth and a submental adenitis after her mother had found her sucking several small sharp stones from the roadway. There was no known source of infection.

(2) A child, aged eight years, had a ragged painless ulcer over her upper incisors and a small, similarly painless, enlargement of her facial and submental lymphatic glands.

(3) A boy, previously healthy, came to hospital in April, 1949, with three weeks' history of a firm painless swelling of his right submandibular gland (fig. 14). Examination of his mouth revealed a circular ulcer on the gum of his right upper jaw (fig. 15). This ulcer was about $^{1}/_{2}$ in. in diameter, with raised and rather irregular edges and a red granulating base. The boy knew the ulcer was present but had not complained of it. He had had it for three weeks, and it had appeared fourteen days after two teeth had been extracted. Biopsy revealed tuberculous granulation tissue, and tubercle bacilli were later recovered from the gland. There was no known contact.

These 3 lesions were all conspicuous, and the regional glands were in no way distinguishable from many other cases in which no lesion was found in the mouth. The chances of infection in the mouth must be great, and it seems strange that we do not see tuberculous lesions in the mouth more often. Perhaps it is because we have not yet learnt to recognise them. In these 3 cases there was no history of contact; 2 had trauma to the mucosa; and all 3 had the combination of a painless mouth lesion with a regional tuberculous lymphadenitis.

CONCLUSION

This paper is concerned only with the recognition and simple description of the primary lesion of tuberculosis developing in visible sites on skin and mucosæ. In five years I have seen more than 30 cases, and here I have given details of 28. This form of infection must be more common than we have hitherto appreciated, and it must often go unrecognised. Yet it is important because collection and study of such cases should help our understanding of the pathogenesis and natural history of tuberculous lymphadenitis and might make a firm foundation for a study of the treatment of that condition. To the clinical scientist it is material for study which comes near to the conditions which are necessary for experimental work.

SUMMARY

28 cases of primary tuberculous infection are described: 20 of skin, 5 of eye, and 3 of mouth.

A history of trauma was present in 10 cases of skin infection and 2 in the mouth.

In 11 cases of skin infection there was a history of contact; in only 3 cases was there a history of both trauma and contact.

The appearances of the primary focus on the skin are determined largely by the presence or absence of trauma.

The lesion in the eye is usually under an œdematous upper lid.

The regional glands in all the cases have softened to form abscesses.

Although I have seen all these cases in the course of everyday clinical work, a consistent study has only been made possible by the help I have received from many friends in the pædiatric, surgical, ophthalmological, dental, and pathological departments of the Royal Victoria Infirmary, and from the Director and staff of the department of medical photography in King's College, Newcastle upon Tyne.

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AUGMENTED RESPIRATION

STUDIES IN ATELECTASIS NEONATORUM

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With illustrations on plate

Atelectasis, or failure in expansion of the lung, is often found in premature babies and commonly accompanies cerebral damage, aspiration of foreign matter, hyaline membrane, and congenital defects such as diaphragmatic hernia, œsophago-tracheal fistula, and pulmonary hypoplasia. In some of these conditions —and especially in prematurity—removal of the handicap of atelectasis would improve the chances of survival.

Every year in England and Wales about 14,000 children die in the first month of life, and of these about 2300 are certified as dying of asphyxia and atelectasis.

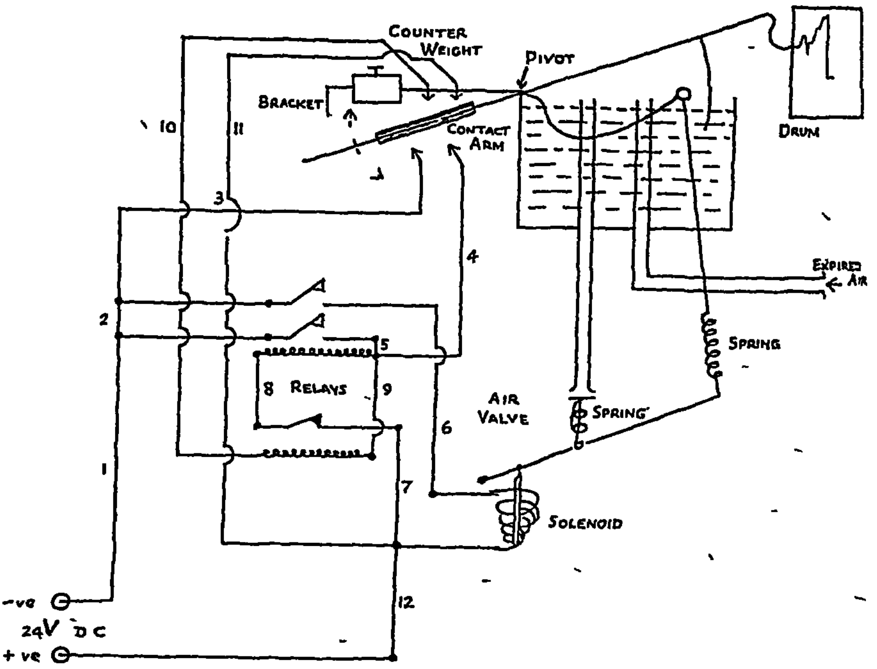

Fig 1—Trip spirometer

Cruickshank (1930) analysed the necropsy findings in 800 deaths in the first month and found that 540 of the deaths were due to asphyxia resulting from atelectasis, cerebral hæmorrhage, or prematurity Among the babies dying during the first day of life, premature birth was four times as common as full-term delivery Claireaux (1952), in a similar analysis of 100 cases in a consecutive series at Queen Charlotte's Hospital, found that 70 of the babies were premature, and 34 (48%) of these died from atelectasis and 18 (26%) from intracranial hæmorrhage

The standard treatment of atelectasis is largely a matter of laisser faire and relies on good nursing, airway clearance, and a supply of oxygen Particularly if premature, a baby with gross atelectasis may be too weak to avail itself of the oxygen, and fruitless inspiratory efforts exhaust it, so that within a few hours the struggle ends in peripheral circulatory failure

The servo respirator here described was evolved as a means of actively assisting lung expansion and rapid oxygenation, and, although the success of any such treatment may be reflected in the survival-rate of asphyxiated babies, its efficacy can only be assessed by an objective study of the rate and degree of pulmonary expansion so obtained A simple method of clinical spirometry has therefore been devised to assess respiratory efficiency of babies with atelectasis before and after treatment and to compare it with that of healthy infants

Trip Spirometer

The apparatus at present in use (fig 1) consists of a Krogh spirometer of known capacity in which expired air is collected via a simple non-return flap valve, so that the individual breaths are represented on a kymograph by a series of steps of different sizes arranged like a staircase The steepness of the staircase slope varies with the child's respiratory activity As soon as the spirometer float is filled, an electrical trip mechanism comes into play, and, by means of a simple system of relays, a solenoid lifts the balancing weight off the counter arm of the spirometer and simultaneously releases the accumulated expired air by opening a spring-loaded valve The float chamber immediately drops to the empty position, whereupon another relay circuit is closed This not only interrupts the solenoid circuit, thereby allowing the spring-loaded valve to close and the balancing weight to resume contact with the counter arm, but also interrupts itself, so that no current is used except in the process of emptying The spirometer then fills again with the next series of breaths, and the process is repeated A time-marker is used and a number (N) of complexes are thus traced over a known number of seconds (S), each complex representing the same known spirometer capacity (C) The minute volume is easily calculated by the following formula

$$\text{Minute volume} = \frac{N \times C}{S} \times 60$$

The size of each step gives an indication of the amount of tidal air (fig 2)

A more rough and-ready method is to measure the angle of slope of each complex with a protractor and then

The expired air is collected by using a rubber oxygen mask of U S Army pattern upside down so that the base fits over the forehead, including the eyes, and the chin fits into the apex, which would normally rest over the bridge of the nose in an adult This mask fits well and can be used on any size of baby

When the child is in the servo respirator, the trip spirometer is simply connected to the head or face chamber Until six months ago recording was by a variable-leak method (Paton 1949), but this was found to be inadequate in dealing with the intermittent and periodic breathing of premature infants, and calibrating errors were too great

Plethysmographic methods, such as that of Cro (1949), probably give more accurate results but involve disturbing an ill baby The above described method is sufficiently accurate for diagnostic purposes

Certain defects in the apparatus are admitted

(1) *Inaccuracies occur at both ends of the scale* very minute breaths are under registered owing to inertia, and very *large* breaths are exaggerated owing to overswing

(2) The concentration of carbon dioxide in the dead space of the mask tends to rise and may artificially stimulate respiration This is not a serious objection, because the periods of recording are necessarily short in the case of sick children and we are more concerned with maximum than minimum respiratory capacity

(3) *The figures for quiet respiration have to be tabulated* separately from those of crying respiration because the two are not comparable

(4) Any leak in the fit of the mask over the face causes under registration

The advantages of this method, however, easily outweigh the drawbacks in clinical practice

(1) The degree of atelectasis can be assessed without removing the child from its incubator or disturbing it any extent

(2) A record is obtainable within a few minutes, and the apparatus is very simple to use We have tested six babies in about three quarters of an hour, and this included proper cleaning of the mask between cases

(3) The apparatus can be constructed cheaply for only a few pounds if home made One of us (I D) built one in less than eighteen hours

We have taken recordings from healthy infants of all sizes and at different ages to find out what normal figures to expect. Our figures are higher than those of Cross and Oppé (1952), but this is because, in clinical work, it has not been practicable (even if desirable) to achieve absolute rest on the part of the baby for five minutes before recording. Babies with atelectasis or cerebral irritation are incapable of resting.

Expansion of the Lung

Lung expansion in the normal infant has been studied both by spirometry and by radiography.

Edith Potter (1952) believes that, normally, all alveolar ducts and alveoli are expanded within the first few minutes of extra-uterine existence, and Morrison (1952) states that lung aeration is more or less complete shortly after birth, although areas of non-aeration may persist for many days, particularly in premature babies.

Clement Smith (1951), on the other hand, claims that some degree of primary atelectasis may persist for more than a week after birth in quite normal babies.

Most radiographs of the chest during the neonatal period are taken during expiration. The newborn infant has a small volume of residual air; so differing opinions have been published about the rate of expansion of normal lungs. Our own radiographs taken within thirty minutes of birth in normal cases show full aeration (fig. 3), but spirometry gives readings which are directly proportional to the birth weight and increase considerably during the first twenty-four hours of life. This increase in the case of the healthy infant usually levels off within forty-eight hours.

Lung Expansion in Abnormal Infants.—The above-mentioned standards have to be modified in the light of prematurity, anoxic depression, atelectasis, and cerebral irritation, or the subsequent development of pulmonary disease; in fact, readings may run parallel with the progress of the case and may fall progressively.

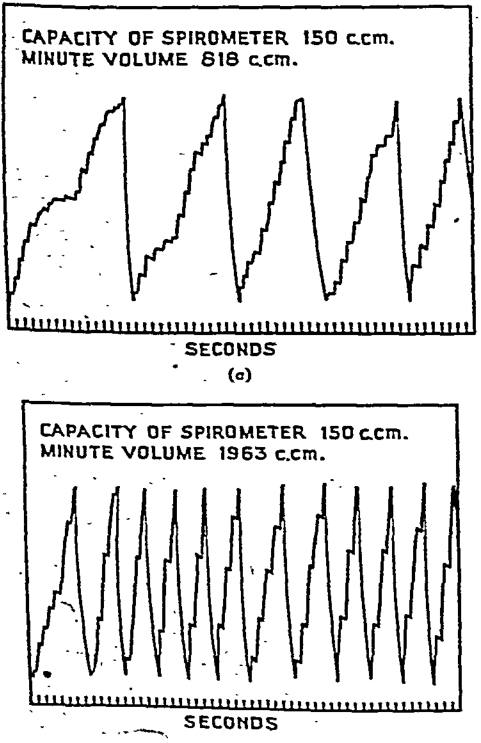

Fig. 2—Specimen tracings from normal baby (birth weight 6 lb. 12 oz.) at ages of (a) 12 minutes and (b) 25 hours.

Pathology and Rationale of Treatment of Neonatal Asphyxia

The small premature baby has a relatively inadequate surface area in the lung available for respiratory exchange, and the blood-supply to the air sacs is small. The infant has weak respiratory muscles with which to overcome the cohesion of the moist walls of the air-passages. If those parts of the lung which are sufficiently mature are not expanded promptly, the baby is liable to suffer irreversible damage from asphyxia.

Asphyxia, in mature as well as premature babies, is most commonly due to intra-uterine anoxia. Firstly, the stimulus of anoxia may cause premature respiratory efforts, with the inhalation of liquor amnii and debris. This is absorbed or eliminated by the healthy infant, but it may be lethal to the baby already damaged by intra-uterine anoxia.

The most important effect of this anoxia is congestion of the fœtal veins and capillaries, accompanied by hæmorrhages and œdema. In the brain the resulting circulatory embarrassment makes the respiratory centre unresponsive. In the lung the congestion and hæmorrhagic œdema of the parenchymal tissue impair expansion. In fact full expansion may be long delayed or may never take place. The pulmonary air sacs, too, contain excess fluid, which so limits aeration that their capillaries continue to be filled with venous blood. This alters the permeability of the capillary walls and causes increasing pulmonary œdema of local origin. This fluid cannot be absorbed by a failing circulation. In addition, some asphyxiated babies have generalised œdema at birth. If there is a widespread but compensated excess of extravascular fluid, the absorption of fluids from the lungs will be delayed. Also, elimination of these fluids via the air-passages is slow when the baby suffers from shock and poor muscle tone. In such a baby partial absorption or elimination of fluid may be followed by further atelectasis (resorption non-aeration).

An initial atelectasis may thus cause death within the first few hours, or the baby may remain in a damaged and precarious state for several days.

Atelectasis is both the effect and the cause of anoxic damage to the fœtus. Expansion of the lung will promote oxygenation, aid the elimination of pulmonary fluid, and improve the circulation. Most of the severely asphyxiated full-term babies soon achieve an adequate lung expansion after pharyngeal aspiration and the prompt administration of endotracheal oxygen. Some small premature infants, nursed in a warm oxygen tent and given postural drainage and gastric oxygen, likewise do well. In others regular respiratory efforts are achieved, but the signs of atelectasis persist. These babies are considered to be in urgent need of oxygenation, and an attempt is being made to break the vicious circle of anoxia, œdema, and atelectasis by gentle and gradually assisted lung expansion with the servo respirator.

SECONDARY ATELECTASIS

Though primary atelectasis is common, true secondary atelectasis, in which collapse of the lung follows adequate expansion, seems to be rare. It may be secondary to traumatic cerebral damage or to certain congenital defects, but usually these conditions are associated with an initial non-aeration. In certain conditions inspired debris or infected material, which at first moves freely in the air-passages, may become plastered round the bronchioles and proximal air sacs, causing pulmonary collapse, possibly with the formation of a hyaline membrane, or even causing pneumonia.

The necropsy finding of "atelectasis" in a child who showed previous evidence of adequate pulmonary expansion is of doubtful significance. Potter (1952) claims that secondary atelectasis is found at necropsy in almost all infants who die in the first few weeks of life; but in the

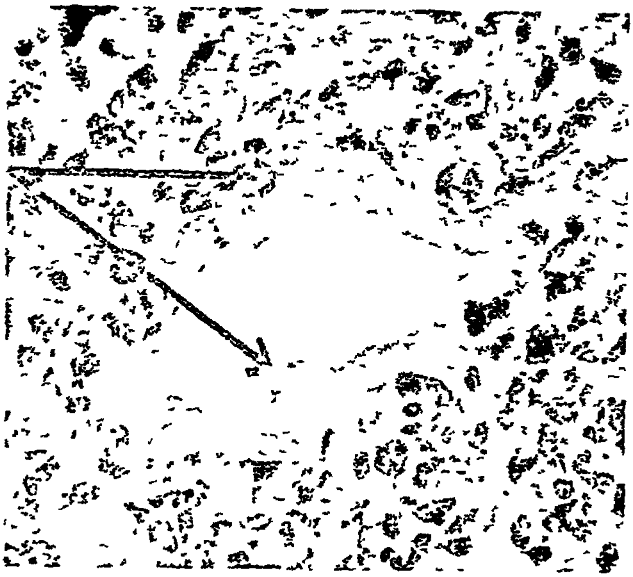

Fig 7—Twin D1 Hyaline membrane in alveolar duct

absence of hyaline membrane it is not the primary cause of death The newborn lung is highly elastic and contains little residual air A large share of this is absorbed during the agonal period

We are studying, by radiography and spirometry, the evolution of "secondary" atelectasis It is possible that, if the child can be kept oxygenated by aided respiration, the condition may be self-limited or reversible

It is interesting to note the development of atelectasis in five of our cases which came to necropsy Initial respiratory difficulty had originally been present at birth in all of them

Triplet L3 achieved a minute volume of 1100 ml after treatment with the servo respirator but died some hours later The lungs were solid, and hyaline membrane was present

Baby Su breathed promptly if inadequately at birth but died after 8 hours, with total non aeration of the lungs and again hyaline membrane

Baby Je showed at necropsy no evidence of ever having breathed though it was grunting on admission, lived for 5 hours, and was observed breathing, and though radiography at the age of 4 hours showed some aeration of the right base (fig 4) This is a point of some forensic importance Air (4 ml) was present in the stomach and probably supplied the greater part of what little oxygen the baby received

Baby D1 had minute volumes (after respirator treatment) of 1150 ml and 1050 ml 2 hours and 1$^1/_2$ hours respectively before death, *yet at necropsy only the anterior aspect* of the right upper lobe was aerated (figs 5 and 6) All the remainder of the lung tissue was solid Hyaline membrane was present (fig 7)

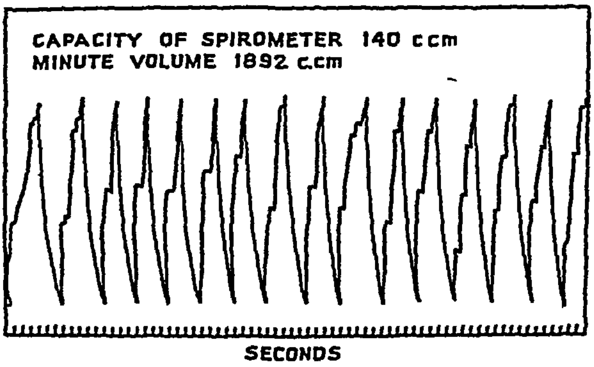

Fig 8—Baby Aa aged 22 hours Spirometer tracing

Baby R1 showed, radiologically, full expansion at 9 h and just before and immediately after the moment of de yet at necropsy the picture was that of partial atelec chiefly affecting the lower lobe of each lung, many of t *alveoli and alveolar ducts being filled with cornified* c and acidophil fluid owing to excessive aspiration of liq amnii There was no hyaline membrane Death was d to subdural and subarachnoid hæmorrhage as the result asphyxia The child weighed 2 lb 12 oz, and was admit at the age of 1 hour Clinically there was no evidence air entry, rib recession was pronounced Minute volume *348 ml and 360 ml were recorded at 5 hours and 12 hour* which were considered reasonably adequate in relation birth weight, and because of this, as well as the satisfacto radiographs, the respirator was not switched on Death which took place at 29 hours, was *correctly* attributed to intracranial hæmorrhage

Spirometry as a Diagnostic Aid

Spirometry helps to clarify the clinical diagno at least in the direction of excluding atelectasis

Baby Aa weighing 7 lb 13 oz, was delivered after a rapid second stage with fœtal distress Its condition for the next 2 days was unsatisfactory, and atelectasis was diagnosed Spirometry at 22 hours, however *(crying), recorded 1802 ml* minute volume (fig 8), and the diagnosis was disputed, treatment with the servo respirator was therefore withheld Next day chest radiography showed pneumonic consolidation of the right middle lobe with lung fields otherwise clear (fig 9) The child recovered

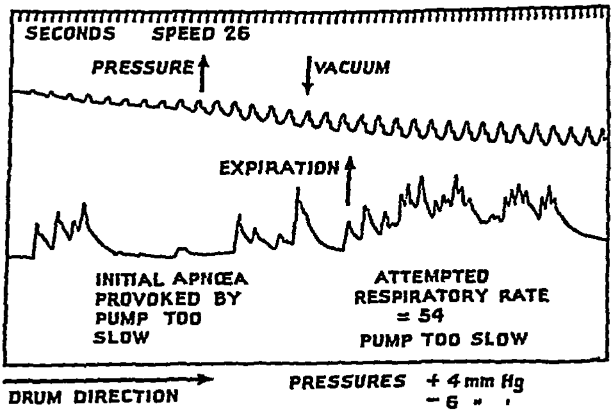

Fig 11—Baby, aged 23 minutes birth weight 1 lb 15 oz Spirometer reading with artificial respiration not adjusted to natural respiratory rhythm (variable leak method)

The spirometer is even more useful in assessing the degree and progress of established atelectasis We have had two sets of twins and one set of triplets in which, by spirometry, we were able to select the most severely affected with atelectasis for treatment in the respirator

Triplets L were delivered in the 33rd week The first born, L1, weighed 3 lb $^1/_2$ oz, and at 1$^1/_2$ hours the minute volume was 450 ml, which was regarded as satisfactory, and the respirator was not used L1 progressed well on its own and, during a phase of crying, *at 8 hours achieved a recording of* 1021 ml, a figure which was not again reached during the *next 4 days* This suggests that the baby achieved full expansion in the first 8 hours The other two triplets are described in more detail below

Baby RcR was interesting It was delivered naturally at 32 weeks gestation and weighed 3 lb 7 oz Its condition initially was good At 45 minutes, when it was breathing quietly, its minute volume was 235 ml, and it was decided to *observe progress before putting it in the respirator* At 11 hours the minute volume had increased to 304 ml, and at 35 hours it was 701 ml On the 3rd day, however, the baby s condition deteriorated, and the minute volume was found at 56 hours to have fallen to 397 ml Apnœic attacks developed and cerebral irritation was diagnosed *Radiography* a few hours earlier revealed a spontaneous pneumothorax on the *right side (fig 10) The respirator had not been used*

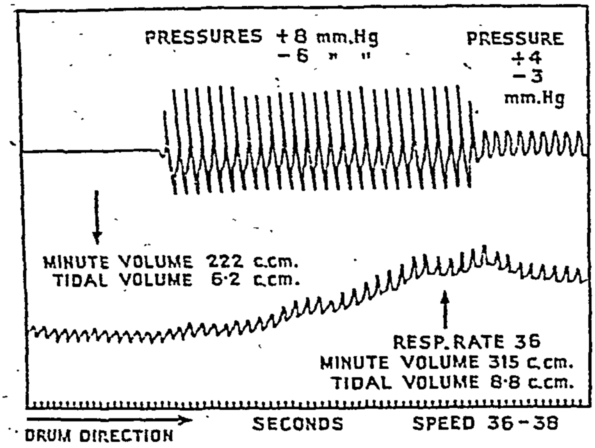

Fig. 12—Baby, aged 2 hours, born at 29½ weeks. Spirometer reading with artificial respiration adjusted to natural respiratory rhythm (variable leak method).

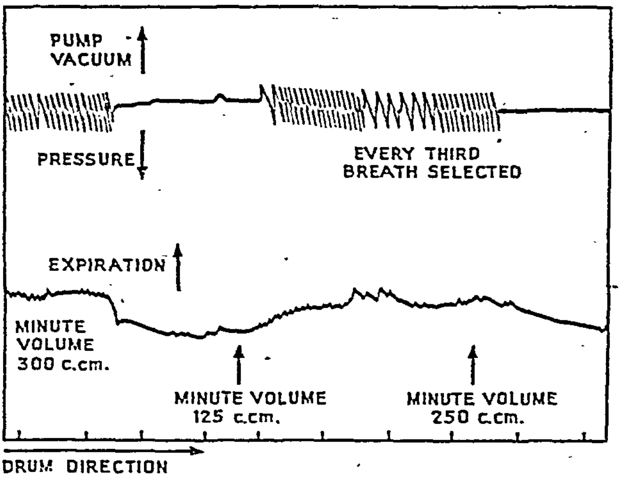

Fig. 13—Baby, aged 9 hours; birth weight 1 lb. 10¼ oz. Spirometer reading with amplified respiration (variable leak method).

Servo Patient-cycled Respirator

This apparatus has no place in the treatment of asphyxia at birth due to fœtal shock. It has been designed to deal with cases in which the signs of atelectasis persist or develop subsequently. The large majority of infants in this category are premature.

Considerable experience was gained originally with a Drinker type of apparatus in which speeds of operation and pressure could be varied within wide limits by means of a crank of variable throw driving a large-capacity bellows. Results obtained, however, were never convincing, even when the child survived. One of three things usually happened:

(1) The baby fought the rhythm of the machine with its own variable rhythm if strong enough to do so, with the result that, at best, no good was done.

(2) The baby promptly went into apnœa—we call this "protest apnœa"—after which some large breaths might or might not be forced on it.

(3) Alkalotic tetany was liable to develop as a result of hyperventilation; it was therefore considered unsafe to leave the apparatus switched on for more than three consecutive minutes at a time.

It was not until the taking of recordings was instituted that the limitations of the Drinker principle became apparent in treating the newborn. At that time, the trip spirometry method had not been developed, and the variable-leak method was in use. This served at least to reveal what was wrong.

Figs. 11 and 12 show the striking difference in efficiency achieved when it was possible to adjust the respirator so that it was exactly in step with the baby's natural rhythm.

It became obvious that what was needed was a machine which would amplify spontaneous respiratory efforts however irregular. This has been achieved with a photo-electric pick-up mechanism whereby, by means of a light mirror attached to the flap of the inspiratory valve, the very start of each inspiration (the first 0·1 or 0·2 ml.) causes a light beam to be deflected from a photo-electric cell. The resulting electrical impulse is then amplified to trigger the machine into action. The baby therefore controls the machine with its own feeble respiratory efforts, the danger of alkalosis is removed, and the machine can safely be run for hours on end. This principle of respiratory amplification seems to be physiologically sound.

Cranks, bellows, and pistons have too much inertia to be of any use in such a machine. The operating pressures are therefore tapped from vacuum and pressure reservoirs by solenoid-operated valves. The apparatus and its circuit have been described elsewhere (Donald and Young 1952). The effect on respiration is shown in fig. 13, while fig. 14 illustrates one form of the present apparatus.

SEALING THE FACE

For the proper operation of the sensitive photoelectric pick-up, and also for accurate recordings, it is essential to have an efficient method of sealing the neck or face from the main body chamber.

Inflatable cuffs and sponge-rubber seals were discarded because, even with considerable contact pressure, which is undesirable, they remain inefficient and permit "pistoning" of the whole child. A search for a suitable plastic material which could be poured or squirted into place and would then set, without pressure, to the consistence of firm wet rubber led to the present use of an alginate ('Duplit') which contains sodium triple phosphate as a retarder and sets in about three minutes. This material is non-toxic and harmless. We mix it with water in roughly equal volumes in ordinary kitchen

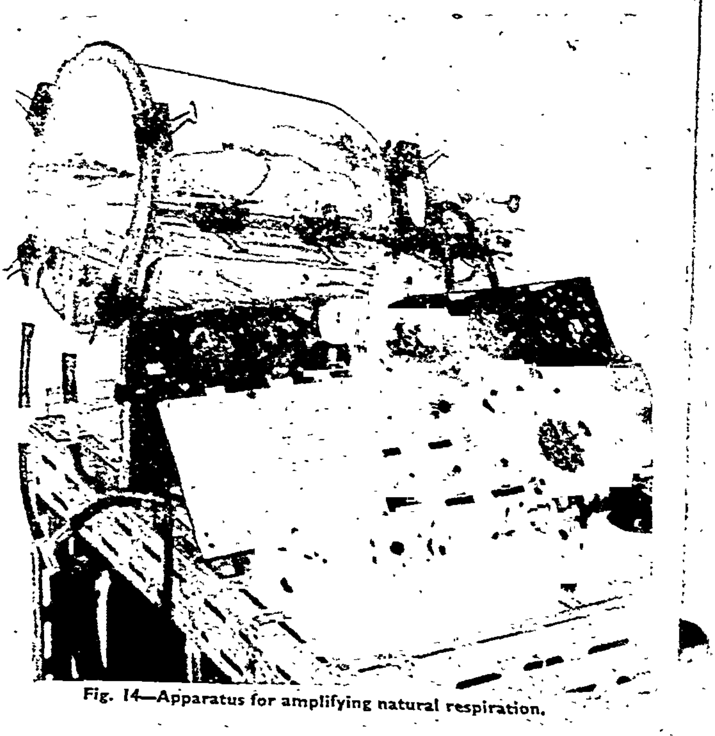

Fig. 14—Apparatus for amplifying natural respiration.

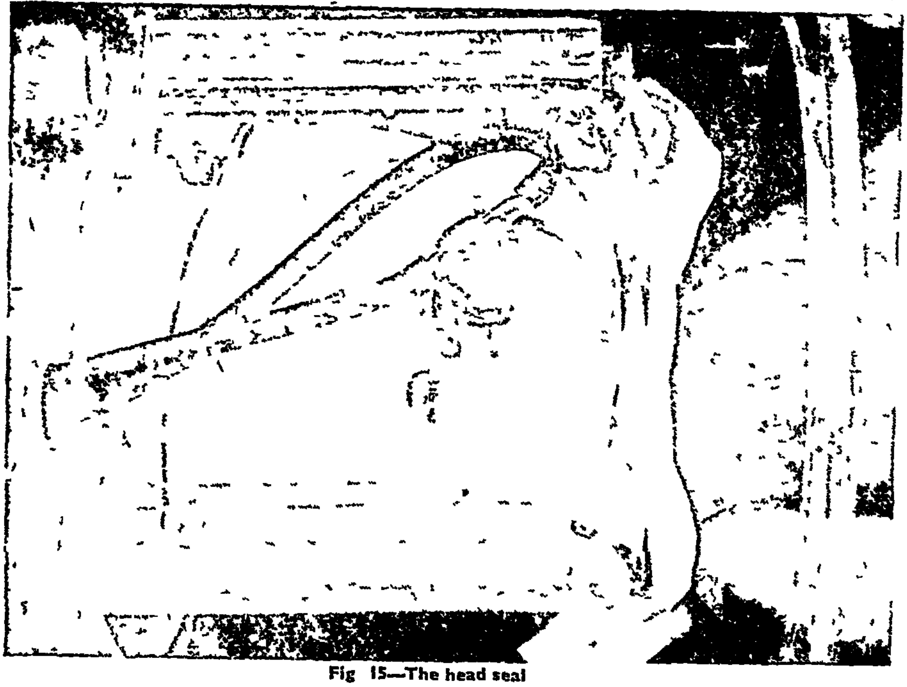

Fig 15—The head seal

egg-mixers The addition of glycerin seems to increase the durability of the seal but prolongs the setting-time, and experiments to improve the mixture continue

This material flows readily into position and conforms with all the natural shapes and crevices of the child's neck

Two alternative methods of sealing are used according to the requirements of the case Firstly, the neck may be sealed by injecting the solution by means of a metal ear syringe between two light latex diaphragms round the child's neck Although a firm fat cushion is thus formed between shoulders and occiput, slight pistoning due to elasticity is still liable to take place Though it does not interfere with treatment, this prevents accurate recording, and light metal baffle plates are necessary Even then a displacement compensator, connected with the outside atmosphere, has to be adjusted to eliminate recording errors completely

The second and newer method is therefore preferred A latex bib, edged with a wire half loop, is applied round the neck, and the child is laid in a sliding 'Perspex' trough with a deep well for the head The alginate is then poured into the well until the entire head and neck, except the eyes, nose, and mouth, are submerged Into this setting helmet the face mask is embedded, and the perspex trough is slid into the respirator case on runners (fig 15) After setting, the whole case can be rotated half-way to one or other side if desired Normally 50% oxygen and 50% nitrogen mixtures are carburetted and supplied at atmospheric pressure, but the proportions can be altered at will

The alginate breaks away very easily in the fingers and removal of the seal is therefore easy

After birth the routine resuscitative measures are applied as usual or appropriate, particularly the extraction of mucus Only when atelectasis persists is the respirator considered, and this may not be for an hour or two after birth In such cases oxygen supplied through a fine 'Polythene' tube passed into the stomach (Ylppo 1935) as a temporary measure often gives a period of grace for the transfer of the baby to the respirator a manœuvre which must not be hurried

CONTROL OF PRESSURE CYCLES

The operating pressures are determined by aircraft

seconds Allowances have to b made for changes in baromet pressure, but the corrections be applied are read directly fro an altimeter

The pressure waves can al be altered in form by bla gates on the reservoir manifol system

Either negative pressur (only) can be used, or th full cycle can be operated a desired With an electron "weld-timer" filter it is possible to select only a proportion of the child's breaths for ampli fication, and this is useful where respiration is very rapid

OPERATING PRESSURES

Minimum effective pressures are sought because the range of safety is not yet fully known The negative pressures applied to the body are potentially dangerous, but we have found pressures up to −40 cm of water harmless. The alginate seal, however, will not remain competent at these levels, and the usual ranges of *−15 to −30 cm* of water suffice

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LEGENDS TO ILLUSTRATIONS ON PLATE

DR MILLER

Fig 1—Scab on face and soft gland at angle of the jaw 6 months after infection in child aged 12 months

Fig 2—Nodules round tuberculous skin lesion, for scars left on healing see fig 3

Fig 3—Same tuberculous lesions as in fig 1 after natural healing twelve months later Note serpiginous scar with clear-cut craters where nodules had been

Fig 6—Same lesion of skin as in fig 5

Fig 7—Typical tuberculous lesion of skin without history of trauma Note silvery epidermal scales

Fig 8—As fig 7 Another lesion similar to that shown in fig 7

Fig 9—Circular tuberculous lesion with depressed centre and raised edge in skin over patella of a boy, aged 7 years, without trauma

Fig 11—Tuberculous granulations in same case as in fig 10

DR DONALD AND DR LORD

Fig 3—Aged 30 minutes Normal aeration of lungs

Fig 4—Baby Je aged 4 hours Slight aeration at right base At subsequent necropsy there was no sign of the child having breathed

Fig 5—Twin Dl, aged 9¹/₂ hours General stippling throughout lungs Slight depression of horizontal fissure ? alveolar collapse.

Fig 6—Twin Dl post mortem Total bilateral pulmonary collapse

Fig 9—Baby Aa, aged 2 days No evidence of pulmonary deflation, but small area of consolidation in right middle zone

Fig 10—Baby RcR aged 2 days Spontaneous right pneumothorax

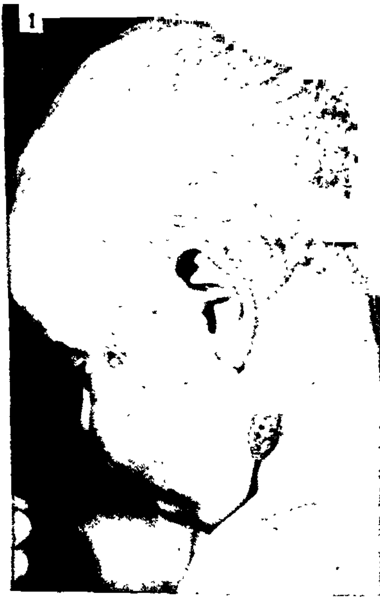
Fig 17—Baby B aged 8 hours After 3 hours in respirator Collapse of left lower lobe Fine mottling throughout lung suggesting alveolar atelectasis

Fig 21—Triplet L2, aged 6 hours Lungs fully expanded after treatment in respirator

Fig 22—Triplet L3 aged 6 hours Pulmonary collapse at bases and in left middle and upper zones with bronchi clearly visible on both sides extending to periphery As yet untreated in respirator

DR TREVETHICK

DR. MILLER: PRIMARY TUBERCULOUS INFECTION OF SKIN AND MUCOSÆ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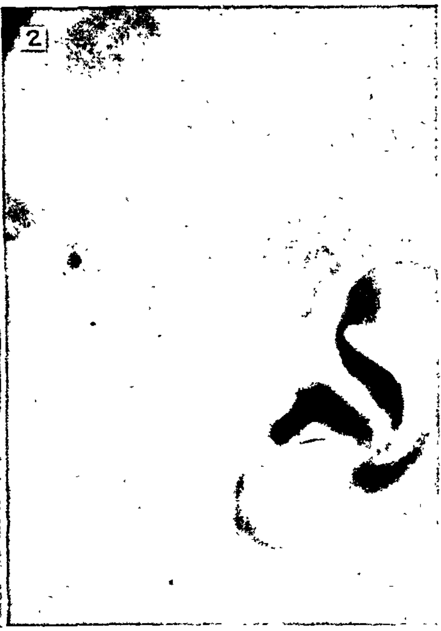
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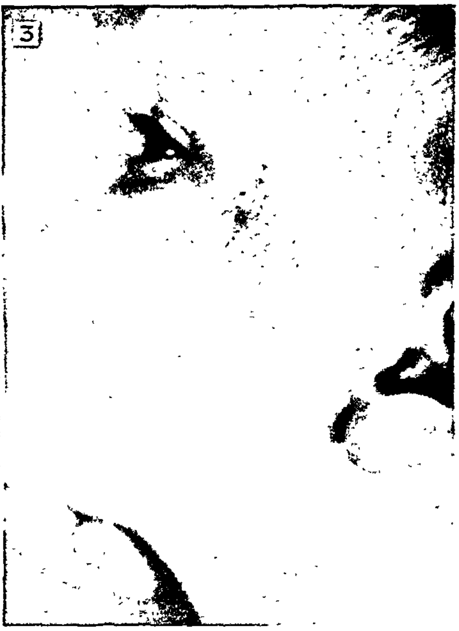
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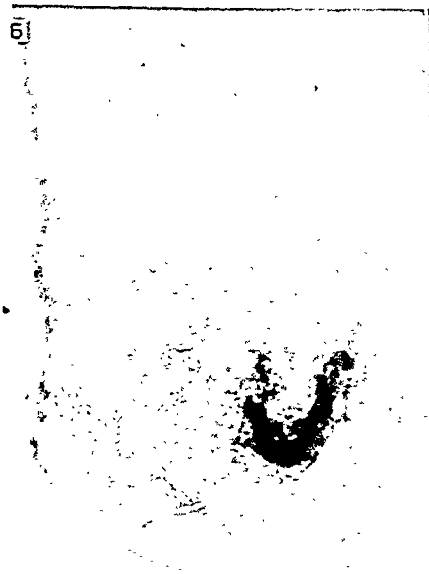
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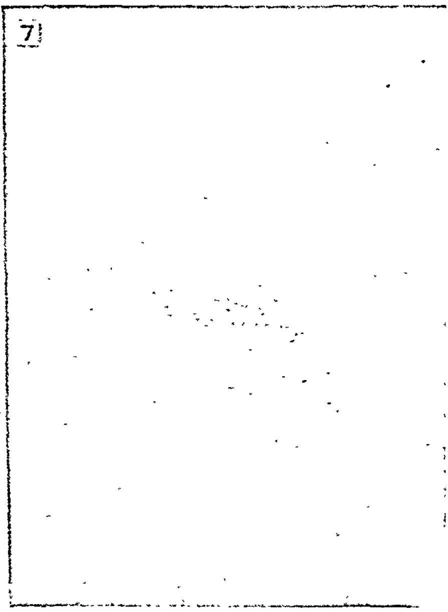
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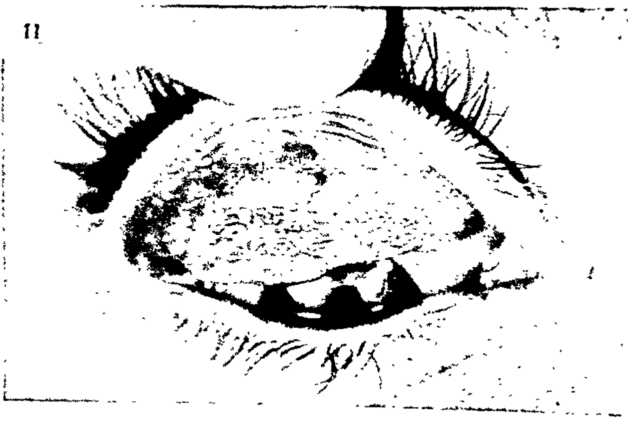
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R DONALD AND DR LORD ATELECTASIS NEONATORUM

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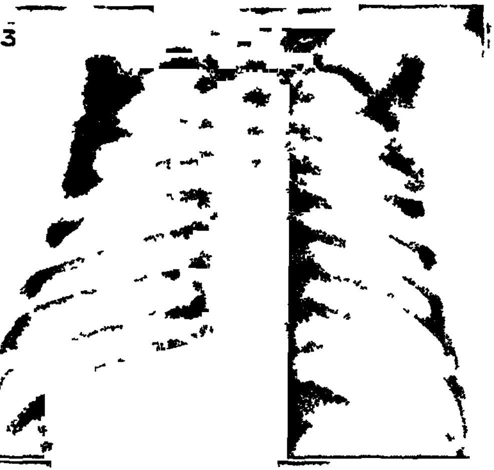

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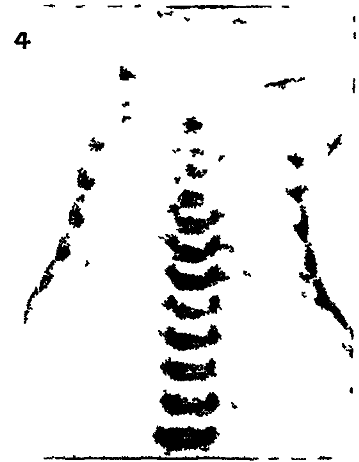

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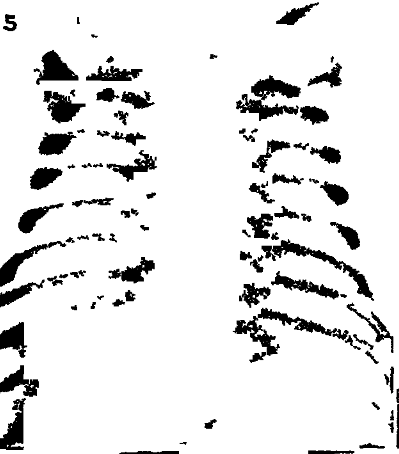

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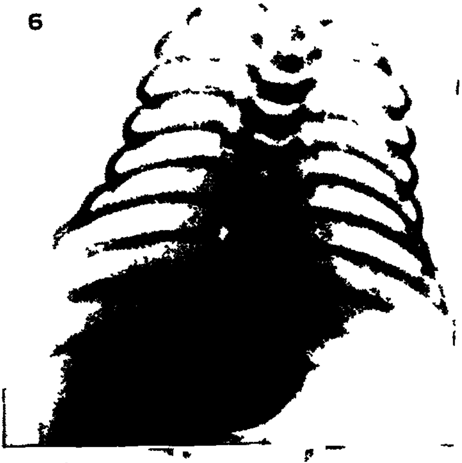

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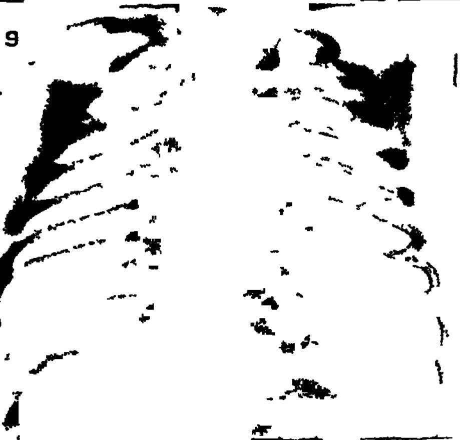

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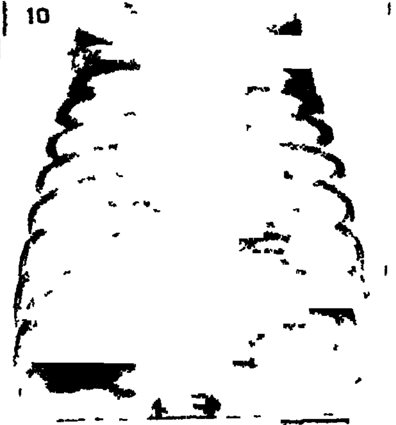

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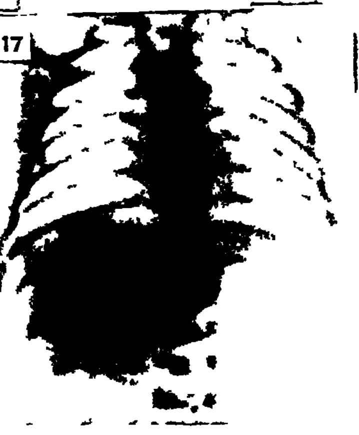

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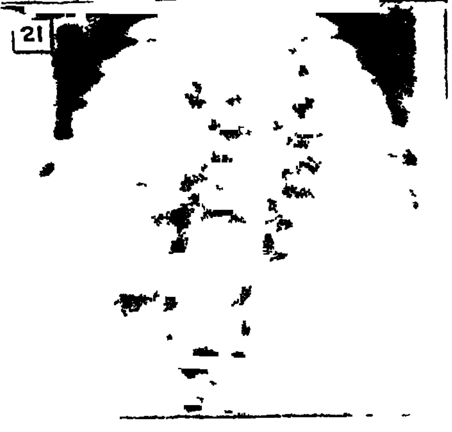

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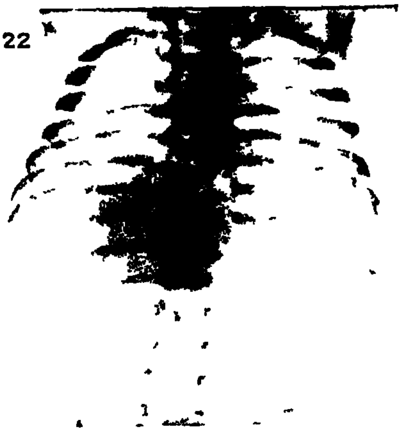
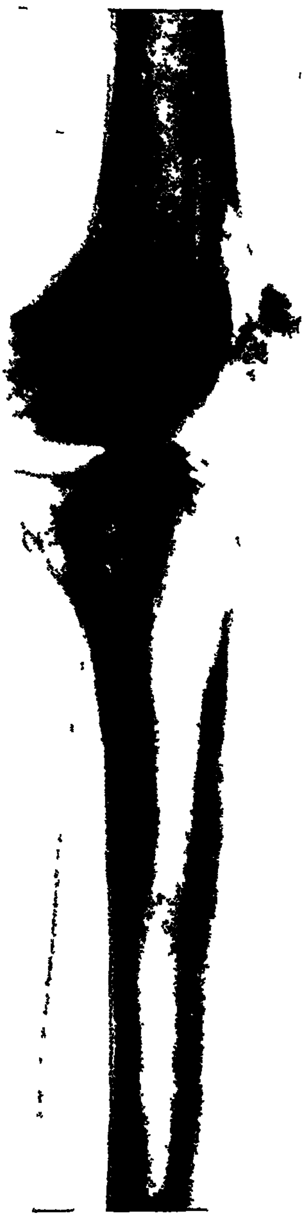
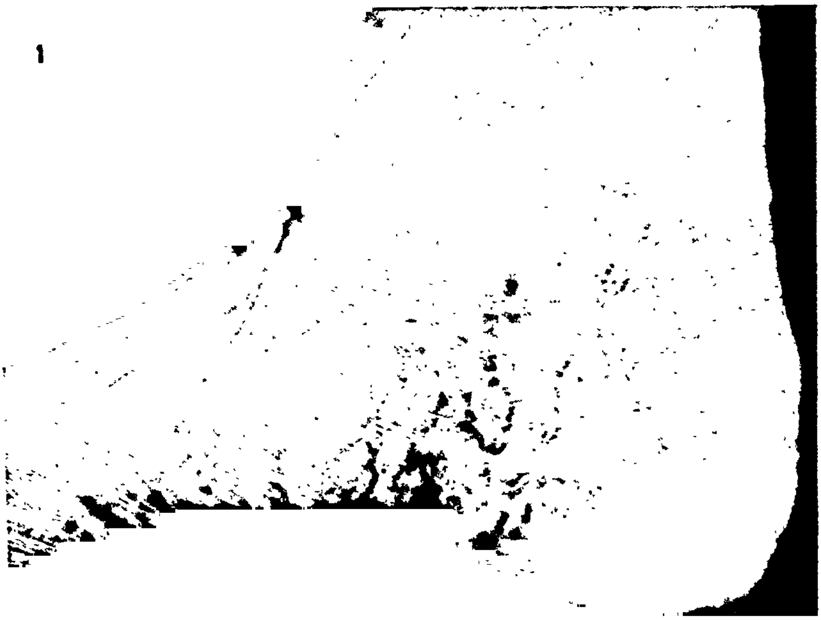


COCKET

DR TREVETHICK

MELORHEOSTOSIS

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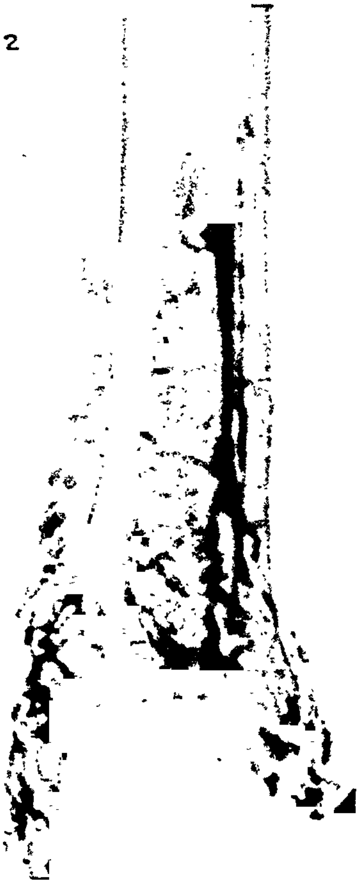
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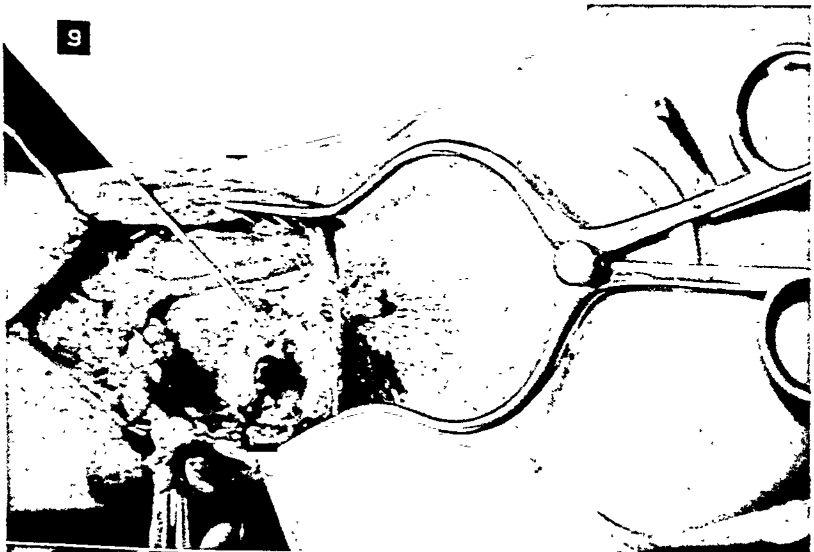
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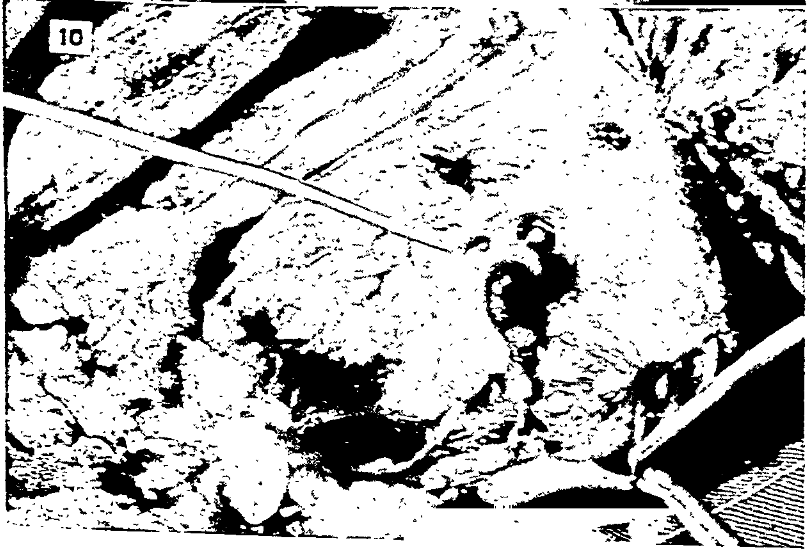
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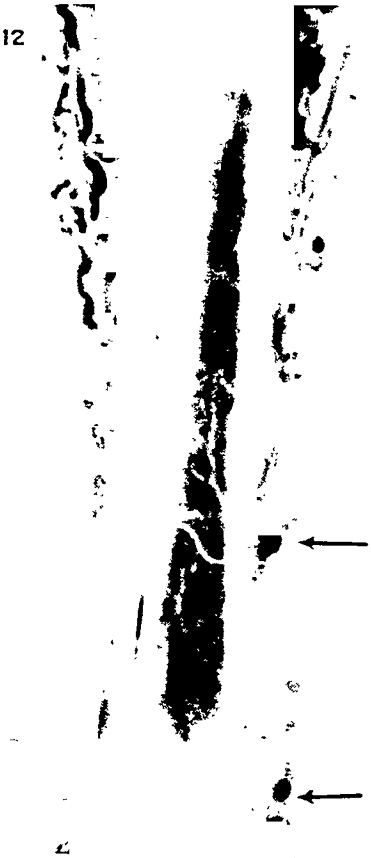
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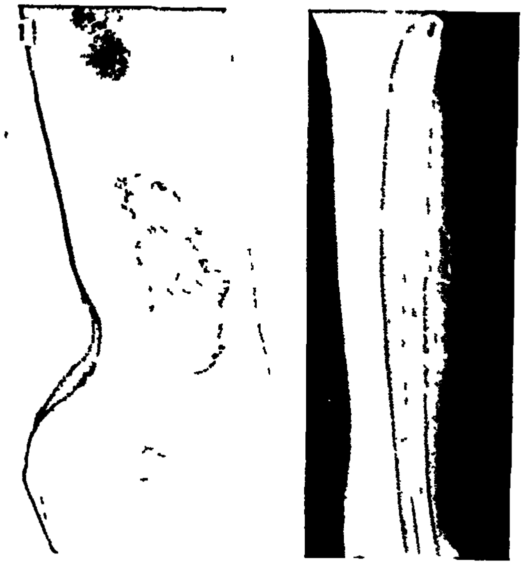
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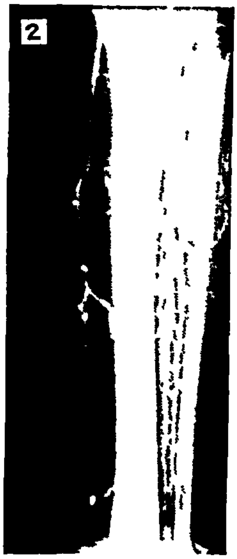
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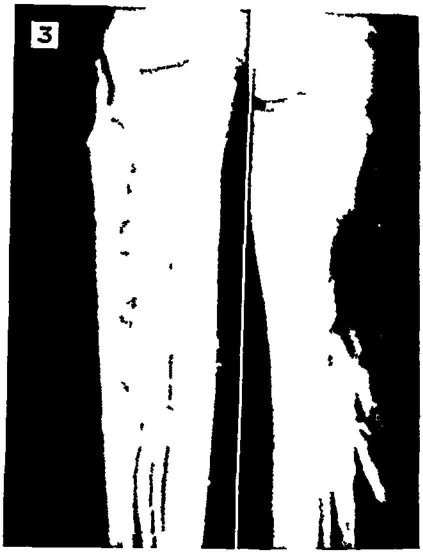
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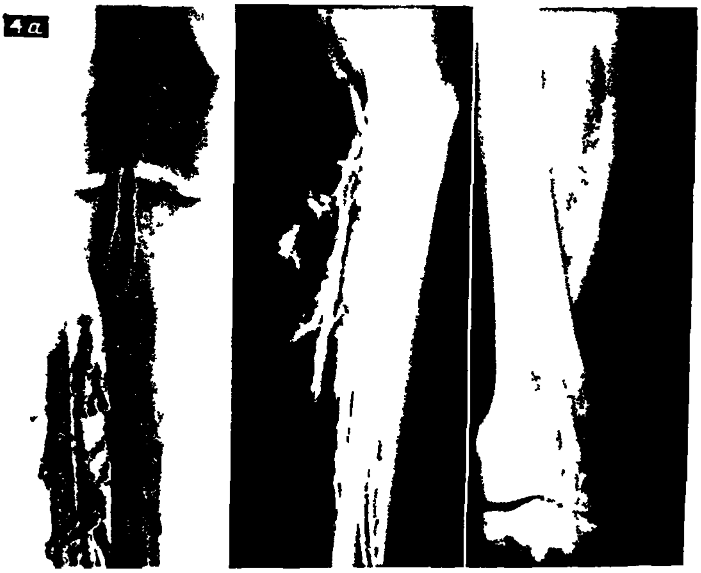
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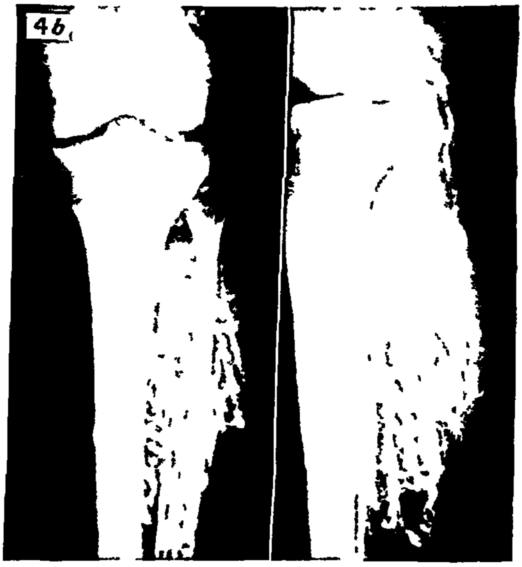
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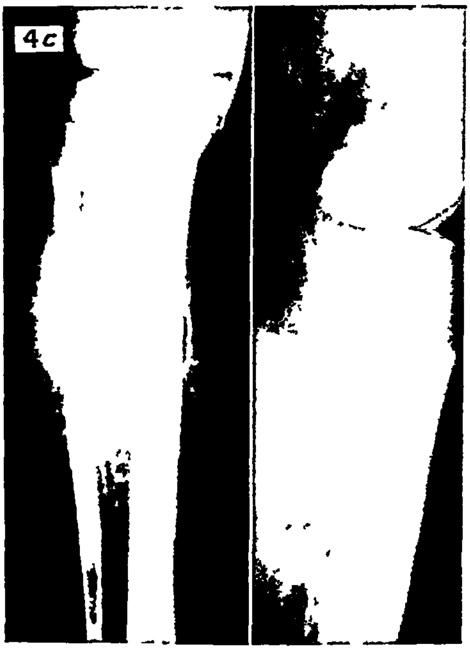
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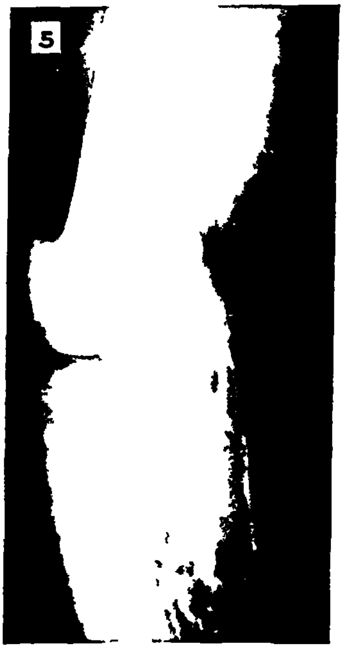
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MR MOORE

LIGATION
OF THE
POPLITEAL
VEIN
FOR
GRAVITATIONAL
SYNDROME

Some Results with Servo Respirator

A careful watch at necropsy has been kept for signs of pulmonary damage, but none has been found in any case save the following:

Baby N, weighing 4 lb. 12 oz., with hydrocephalus and spinal deformity, was stillborn after spinal tapping for the aftercoming head. An endotracheal tube was passed, and the body was at once transferred to the respirator, which was set in action for 2 hours with increasing negative pressures. No respiratory movements were observed at pressures of −40 cm. of water, some were evident at −55 cm. of water, and movements were very pronounced at −80 cm. of water.

At necropsy the lungs were hypoplastic, each weighing only 5 g. All sections floated (although the child was stillborn). Bilateral pneumothorax and mediastinal emphysema were present, and the lungs were extensively damaged by bullous emphysema. There was no visible rupture. Microscopy showed areas of overdistension alternating with atelectasis. Moderate hypoplasia was evident.

These observations on dead and hypoplastic lung encourage one to believe that the safety margin is wide.

Baby D1, weighing 6 lb. 5 oz. (already referred to in the section on secondary atelectasis), was delivered by cæsarean section for antepartum hæmorrhage with fœtal distress. There was difficulty with respiration at first. Signs of atelectasis were very pronounced at 7 hours, and the condition deteriorated, necessitating intubation at $9^1/_2$ hours, and positive oxygen pressures were intermittently applied. At 11 hours its state was critical, and it was transferred to the respirator with the endotracheal tube still in situ to guarantee an airway. Considerable progress was achieved, but the child became cyanosed whenever the machine was switched off, and improvement was never long maintained. Mucus was from time to time copiously produced and had to be sucked out. Negative pressures of up to 65 cm. of water were applied, being possible in the absence of an alginate seal and with the use, instead, of the endotracheal tube. After $6^1/_2$ hours' intermittent treatment some of the apparatus was accidentally smashed. The child's condition being at that time fairly satisfactory it was transferred to an oxygen tent. It died suddenly 20 minutes later. Death was due to extensive hyaline membrane. In spite of the recklessly high pressures used there was no evidence of pulmonary trauma.

Baby Rh was one of twins born at 29 weeks' gestation. In spite of gastric oxygen and routine resuscitative measures, signs of atelectasis persisted. Spirometry confirmed that the baby's condition was much worse than that of its twin sister (birth weight 2 lb. $^1/_4$ oz.). The baby was placed in the respirator, and respiration was amplified, pressures of −30 cm. and +15 cm. of water being used. Later the positive pressures were discarded. After $3^1/_2$ hours' treatment the physical signs of atelectasis had disappeared. Radiography at 8 hours showed normal expansion. On the 6th day the baby weighed 1 lb. 14 oz., and it was discharged fit after 10 weeks, weighing 5 lb. $7^1/_2$ oz. The untreated twin also survived.

Baby Ku was delivered by cæsarean section, because of severe pre-eclamptic toxæmia, at 32 weeks' gestation. It weighed 3 lb. 4 oz., and its condition at birth was very bad. There was no spontaneous respiration. An endotracheal tube was passed, and positive oxygen pressure was applied, but at once collapse became serious. The baby was transferred thereupon to the respirator and, as there were no spontaneous respiratory efforts to amplify, the emergency control was switched on. This was without effect, and the heart stopped in 20 minutes. On removal the tube was found to be blocked. Necropsy revealed gross atelectasis and generalised signs of asphyxia.

This experience illustrates the dangers of intubating premature infants. We now regard gastric oxygen as safer and more effective.

Baby RcM was delivered by cæsarean section, because of severe pre-eclamptic toxæmia, at 31 weeks' gestation. It weighed 3 lb. 3 oz. and gasped at once. Signs of atelectasis were not gross and had fully disappeared after 4 hours in the respirator. The baby was discharged fit on the 69th day, weighing 6 lb. $4^1/_2$ oz. Unfortunately, as the spirometer was not available for this case, proof of benefit is lacking.

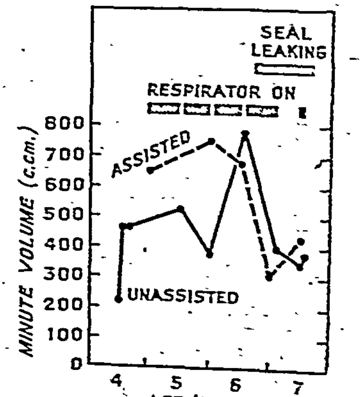

Fig. 16—Baby B. Spirometer readings in respirator.

Baby Su was delivered by abdominal hysterotomy at 26 weeks' gestation because of pre-eclamptic toxæmia and malignant hypertension, which caused the mother's death a few weeks later. It weighed 1 lb. 7 oz. and breathed promptly at birth. After transfer to the respirator it appeared to achieve moderate chest expansion, but a technical fault developed in the photo-electric cell amplifier, after which the

LEGENDS TO ILLUSTRATIONS ON PLATE

MR. COCKETT AND MR. ELGAN JONES

Fig. 1—Pre-ulcerous mesh of dilated subcutaneous veins and venules above, behind, and below interior malleolus in a man, aged 30, who had no demonstrable saphenous incompetence.

Fig. 2—Venogram of ankle region in a young man with chronic ulcers on both sides of ankle. There was so much fibrous tissue round ankle that no veins could be seen or felt.

Fig. 9—Operation on incompetent middle perforating vein, which is connected with mass of thrombosed varices held aside with artery forces. Note great saphenous vein anteriorly. Cf. fig. 10.

Fig. 10—Same operation as in fig. 9. Probe points to hole in deep fascia through which perforating vein penetrates. Note great saphenous vein to right.

Fig. 12—Venogram of lower third of leg of case 1: upper arrow points to incompetent perforating vein responsible for ulcer; lower arrow indicates site of ulcer.

MR. MOORE

Fig. 1 (case 3)—Thin indurated leg with large ulcer and severe equinus deformity. Venogram shows thin veins which have thrombosed and recanalised. Patient was cured by popliteal ligation after other methods had failed.

Fig. 2—" Moth-eaten " appearance of veins which have thrombosed and recanalised.

The patient, a woman aged 48, had had ulcers of the legs for 12 years. History of " white leg " 21 years ago and 12 years ago, but no varicose veins.

Fig. 3—Smooth outline of veins in which no valves can be seen.

The patient, a woman aged 30, was admitted as an emergency with extensive bleeding from a varicose ulcer. Ulcers had been present for 2 years and were getting worse. Varicose veins from the age of 13, becoming worse at 25 after postpartum " white leg." This appearance of the veins can occur either without apparent cause or following thrombosis of the pelvic veins (Moore 1951).

Fig. 4 (case 1)—Venograms of right (*a*) and left (*b*) legs in September, 1950, and of right leg (c) in April, 1951.

(*a*) Right leg in 1950 is normal, showing posterior tibial, peroneal, and anterior tibial veins with numerous valves. Popliteal vein is double, and " fish-tail " appearance of a normal valve can be seen in lateral view. Femoral vein is well outlined and shows, faintly, three valves. Muscular veins are in two groups, best seen in lateral view. There are no connections with superficial veins.

(*b*) Left (affected) leg in 1950 shows partial thrombosis of femoral vein, seen over lower part of femur (entire femoral vein was similar). Popliteal vein is narrow but intact: this was confirmed at operation, at which another large thrombosed vein was found which may have been a second popliteal, as in right leg. Veins of leg are small and muscular veins more prominent than usual but not otherwise affected.

(c) Right leg in April, 1951, about three months after onset of symptoms in this leg. Change from 1950 (*a*) is striking. Partial thrombosis of femoral and popliteal veins is well seen. Veins of the leg, although narrow, as though in spasm, are not obviously abnormal. Long saphenous vein is well filled.

Fig. 5—Old deep venous thrombosis, with complete block at upper end of popliteal vein and collateral channels proceeding up from site of obstruction.

The patient, a woman of 53, had had ulcers of the leg for many years, and varicose veins which had followed postpartum " white leg " 20 years previously. The leg did not improve after ligation of popliteal vein.

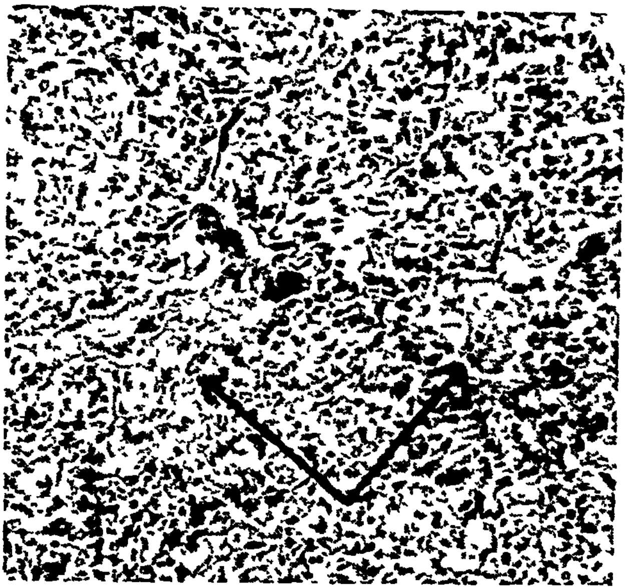

Fig 18—Baby B, post mortem Mucus plugs in bronchioles, without hyaline membrane

signs of rib recession increased The baby was kept alive with the help of the emergency switchgear for a further 2 hours but died at the age of 8 hours At necropsy the lungs were solid, and extensive hyaline membrane was found on microscopy

Baby F1 was aborted at 26 weeks' gestation and weighed 1 lb 11 oz It was immediately placed in the respirator Spirometry was impossible because the respirations were too minute, nevertheless the photo electric mechanism worked well, and respiration was amplified for 8 hours, by which time the baby appeared well enough for transfer to an incubator

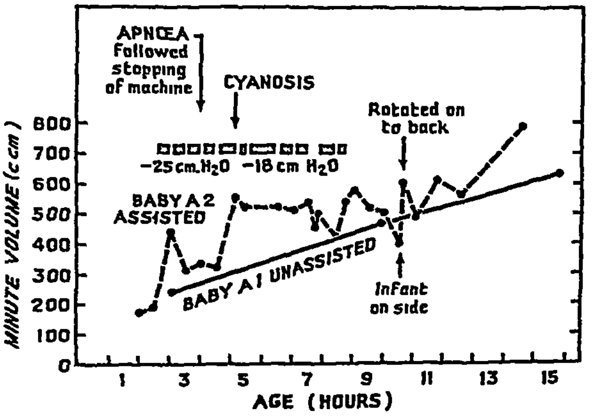

Fig 19—Twin A Spirometer tracing showing improvement in baby A2 while in respirator

Chest radiography at 12 hours showed no evidence of consolidation or deflation Nevertheless death took place at the age of 26 hours At necropsy both cerebral ventricles were full of blood from a ruptured subependymal vessel on the corpus callosum The lungs were moderately well expanded The two lower lobes sank in water, but the remaining lobes floated

Baby B, aged 1½ hours, was admitted from outside in bad condition, having been born at 34 weeks' gestation and weighing 3 lb 11 oz *Mouth to mouth insufflation* had been used Atelectasis was clinically gross, and the minute volume at 4 hours was only 220 ml Fig 16 shows the dramatic improvement obtained in the respirator, but the head seal became incompetent after 2 hours (this is shown by the intersection of the two lines on the chart), and since the child seemed better it was transferred to an incubator instead of setting another seal *This was clearly a mistake* Its condition was satisfactory at 15 hours, but it died at 27 hours after recurrent attacks of cyanosis

Radiography at 4 hours, 8 hours (fig 17), and post mortem showed left basal atelectasis and fine mottling throughout the lung suggesting alveolar atelectasis in increasing degree At necropsy aeration appeared good macroscopically, but histology showed numerous mucus plugs in the bronchioles but no hyaline membrane (fig 18) There was a small intracranial hæmorrhage Good pulmonary ventilation was achieved with the apparatus but diminished after the apparatus was switched off, and the lung pathology persisted

The question arises whether the mucus plugs represented an early stage in *the formation of hyaline* membrane

Twins A1 and A2 were admitted from a nursing home about an hour after premature delivery at 31 weeks' gestation Baby A1 weighed 3 lb 1½ oz, was in fairly good condition, and had a minute volume of 230 ml Baby A2 weighed 3 lb 9½ oz, had a minute volume of only 170 ml, and had a bad colour She stopped breathing shortly after arrival and appeared to be so moribund that it seemed unlikely that transfer to the respirator would be achieved in time Gastric oxygen, however, *revived her, and the tracings in fig* 19 show the improvement achieved with the apparatus A further period of observation having satisfied us that progress was being maintained, the head seal was removed and the child was placed in an incubator Chest radiography at 6 hours *while the baby was still in the respirator* and after 4 hours' treatment, showed satisfactory pulmonary expansion Baby A1 maintained fairly steady spontaneous progress, and the twins are now thriving at the age of 5 weeks

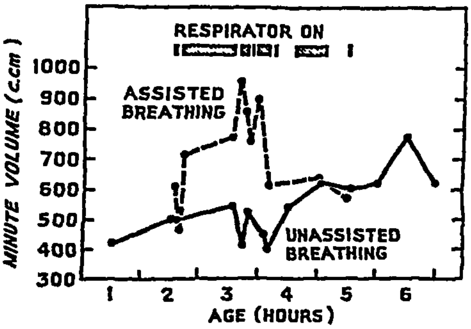

Fig 20—Triplet L2 Spirometer reading showing improvement while in respirator

Triplet L2, born at 33 weeks' gestation of a pre eclamptic mother, was clinically the worst of the three, had a minute volume of 420 ml, and weighed 4 lb 1½ oz Triplet L3 appeared only *a little less fit*, was smaller, *weighing* 3 lb *15 oz*, and had a minute volume of 390 ml Triplet L1, as already mentioned, was reasonably well Triplet L2 was therefore placed in the respirator, and fig 20 traces its progress After 2½ hours' treatment the minute volume appeared fairly stable at about 620 ml, the baby's colour was very good, and only slight rib recession persisted Chest radiography at 6 hours—i e, after treatment—*showed full lung expansion* (fig 21) It is interesting to compare this with the radiograph at the same age of triplet L3, which had not then been treated (fig 22)

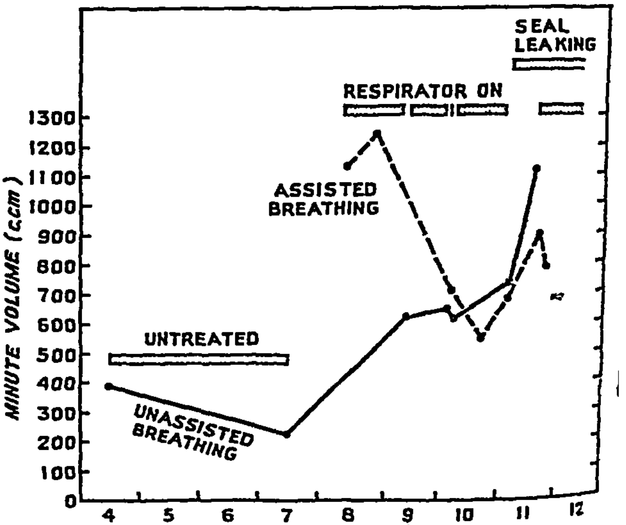

Fig 23—Triplet L3 Spirometer readings in respirator

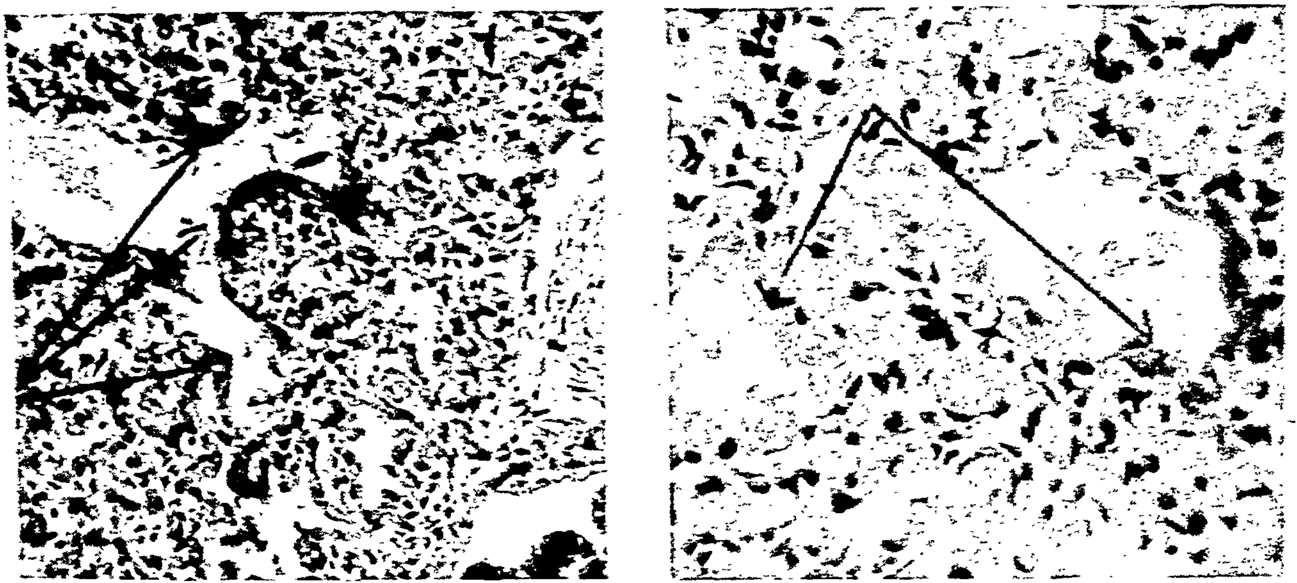
(a) (b)

Fig. 24—Triplet L3; after death aged 20 hours. Hyaline membrane in (a) distended alveolar duct and (b) alveoli.

At 5½ hours triplet L2 had to be removed from the respirator to make way for triplet L3, who was by now very cyanosed in its incubator and whose condition, due to gross atelectasis, appeared to be critical. Triplet L2 after removal made uninterrupted progress and at the age of 4 days had the best minute volume (553 ml.) of the three. It was discharged home weighing 6 lb. at the age of 4½ weeks.

Triplet L3, as already mentioned, deteriorated under routine treatment and at 7 hours the minute volume had dropped from 340 to 230 ml. The baby was placed in the respirator, and at once its colour and general condition improved. Unfortunately after 2½ hours the seal became incompetent. Fig. 23 shows the good progress at first, and then crossing of the assisted and unassisted recording tracings. This occurs with seal leakage owing to the diversion of some of the expired air into the main body chamber as a result of the negative pressures there. The apparatus, to say nothing of the attendants, was showing signs of fatigue and of overheating of some of the working parts. At 12 hours a new seal was applied, but treatment was not persisted with, because the baby was crying vigorously, and at 18 hours it was transferred to the oxygen incubator. Thereafter its condition deteriorated, and even gastric oxygen did not improve its colour. It was thought to have intracranial hæmorrhage and was not disturbed. Death took place at 20 hours, and necropsy revealed solid and œdematous lungs, microscopy showing hyaline membrane (fig. 24). There was no cerebral hæmorrhage.

Summary

An account is given of neonatal atelectasis, and its pathology and diagnosis are discussed.

A simple method of clinical spirometry is described together with its practical applications in differential diagnosis and assessment of pulmonary efficiency.

An interim account is given of a patient-cycled servo respirator designed to treat atelectasis and of our experiences with it. Three cases and possibly a fourth might be claimed as successful results so far as life-saving is concerned, but the disappointment-rate is very high—often because of imperfectly developed technique and sometimes because of complicating conditions such as intracranial hæmorrhage. As an obstacle, hyaline membrane has loomed large, being confirmed at three necropsies. We do not yet know whether this condition is irreversible, but we wonder whether triplet L2 would have succumbed to it in place of triplet L3, which was treated belatedly, had their positions been reversed.

We are indebted to Dr. A. Claireaux for the detailed necropsies and to Dr. R. E. Steiner for the radiological reports. A project of this magnitude could not have been launched without help from sources too numerous to acknowledge, from colleagues both at Hammersmith Hospital and St. Thomas's Hospital, and from friends in the Royal Air Force and Fleet Air Arm who have given much technical advice. We would like also to express our appreciation of the encouragement received from Mr. A. J. Wrigley, Dr. J. Forest Smith, and Professor Moncrieff, and of financial assistance from the endowment fund of St. Thomas's Hospital, where much of the present apparatus was originally developed.

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THE ANKLE BLOW-OUT SYNDROME

A NEW APPROACH TO THE VARICOSE ULCER PROBLEM

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With illustrations on plate

In a paper by H. E. Lockhart-Mummery and J. Hillyer Smitham (1951) the clinical problem of varicose ulcer is clearly stated. They found that their numerous cases fell into three main groups:

1. Those with varicose veins, often large and tortuous, whose skin in the lower third of the leg was perfectly healthy.
2. Those with pigmentation, induration, and ulceration of the lower third of the leg, but with no varicose veins.
3. Those with varicose veins in the thigh and leg, and ulceration.

In this last group, the ulcers were not always cured by dealing with the saphenous incompetence, and often returned when apparently cured in the first instance.

These facts have been repeatedly emphasised by all who have reviewed large numbers of such cases

(Cokkinis 1933, Homans 1939, Wright 1931, Bauer 1942) Hanschell (1949) sums up the problem admirably

> "The great majority of patients with varicose veins, at all ages, have and have had no leg ulcers, while the great majority of patients with leg ulcer, at all ages, have and have had no varicose veins, that in its clinical features, under all conditions, there is no discernible difference between ulcer with, and ulcer without, varicose veins"

Thus it almost seems that there are two separate diseases afflicting the leg—varicose veins and varicose ulcer—and that the two conditions may be quite distinct and separate and may apparently bear little relation to each other

The truth of the foregoing observations has been amply confirmed by our experience in the varicose vein and varicose ulcer clinics at St Thomas's Hospital over the past two years Recently one of us has attempted to analyse and sort out the varieties of ulcer of the leg which present themselves under the ubiquitous title of varicose ulcer (Cockett 1951) After excluding the purely traumatic ulcers, the infective ulcers, the arteriosclerotic ulcers, and the ulcers in erythrocyanoid legs we were left with the group which might for want of a better term be called varicose ulcers Four facts about these ulcers struck us forcibly

(1) These ulcers are situated most commonly in the lower third of the leg, usually on the inner side just behind and above the internal malleolus, and more rarely a similar site on the outer side of the leg They seldom transgress on to the foot or the upper third of the leg One commonly accepted explanation of these facts has been that the ulcer on the inside of the ankle is at the bottom of the column of blood in an incompetent great saphenous vein, and that the ulcer on the outside of the ankle is at the bottom of an incompetent small saphenous vein The treatment of these ulcers by high saphenous ligation and stripping of the veins is based on these supposed facts

(2) Many long-standing cases of gross incompetence of the great and short saphenous veins do not develop ulcers Conversely, many people are seen with ulcers in whom no incompetence of the superficial veins can be demonstrated

(3) Adequately performed ligation or stripping of incompetent superficial veins failed to cure varicose ulcers permanently in a high proportion of our cases

(4) A high proportion of varicose ulcers can be induced to heal with the patient ambulant by the simple expedient of continuous pressure over the ulcer—maintained by a 'Sorbo' or felt pad under a firm elastic-webbing bandage This point was first emphasised by Dickson Wright (1931)

To Homans (1916) and Bauer (1942) we owe the next step in our knowledge of the ætiology of these ulcers They established beyond doubt that some of these ulcers, particularly those not associated with varicose veins, were the result of previous deep-vein thrombosis Moreover the number of patients who got ulcers after deep thrombosis increased with the time elapsing after the deep thrombosis This is shown by the following table based on a long follow-up of 100 cases of deep thrombosis (Bauer 1942)

No of years after thrombosis	*Percentage of cases with indurative lesions of lower leg*	*Percentage of cases with ulceration*
5	45	20
10	72	52
Later	91	79

Studying the material from our own varicose ulcer clinic we found that 27 out of 80 cases of varicose ulcer were obviously related to previous deep vein thrombosis Now, although this is a most important finding it does not explain exactly why so many of these patients should get the typical ulcer in the typical situation just above the internal malleolus

A consideration of all these facts led us to investigate whether there was any local cause in the region of the ulcer to explain its origin This investigation fell naturally into five parts

(1) A clinical investigation to classify ulcers in the lower third of the leg (Cockett 1951) and to observe their natural history

(2) An anatomical study of the venous drainage of the subcutaneous tissues of the lower third of the leg and foot

(3) An anatomical study of the arterial supply of this same region

(4) Operations directed at excising the ulcer locally and investigating directly the condition of the veins in the immediate neighbourhood of the ulcer

(5) Venographic studies of the deep veins and veins of the ulcer-bearing area

This paper is concerned mainly with the results of the first four investigations

CLINICAL OBSERVATIONS

We tried to work out the earliest pathological change in the ulcer-bearing area—to discover the essential pathological change, in the subcutaneous tissues of the lower third of the leg, which predisposed to an ulcer The earliest and most constant pathological change we found was the presence of multiple small tortuous veins directly under the skin of the ankle region, often extending behind and below the malleoli Fig 1 shows such a case the dilated veins were confined to the ankle region, and there was no associated incompetence of the great or small saphenous systems This hæmangioma-like dilatation of all the small subcutaneous veins of the ankle region is a common sight in our varicose vein and varicose ulcer clinic and may be seen both in cases with dilated and incompetent superficial veins and in those without them When the ulcer first appears it seems to sit in the midst of this area of venous dilatation The ulcer itself is usually started by one of four things (1) local trauma followed by infection, (2) local eczema leading to scaling and infection, (3) bursting of one of the dilated varices in the area, leading to a hæmatoma, skin breakdown, and infection, or (4) thrombosis in one or more of these dilated venules

Once ulceration has taken place, local thrombosis, inflammation, and deposition of a plaque of hard fibrous tissue may rapidly hide the multiple subcutaneous venous dilatation in this area At this stage the ulcer appears to be in the midst of a hard plaque of indurated subcutaneous tissue, the classical induration of the lower third of the leg referred to by many authors However, in spite of this it can be seen that many of these ulcers appear to be superimposed on a mass of tortuous dilated veins, some partly thrombosed This has been confirmed many times venographically (fig 2)

Thus on clinical grounds alone there was evidence that some purely local venous incompetence might play a part in the ætiology of these ulcers

ANATOMICAL STUDIES OF VENOUS DRAINAGE

Our anatomical studies yielded some surprising results, confirming our suspicion that it was possible to have purely local venous valvular incompetence in the lower third of the leg Fig 3 shows a dissection of the superficial veins of the leg and foot It will be seen that, in the upper part of the leg just below the knee, the saphenous vein has several large branches (tributaries) draining the subcutaneous tissues of the upper part of the leg From the middle of the leg to just beyond the internal malleolus there are no branches Beyond the internal malleolus in the foot the saphenous vein breaks up into numerous branches draining the subcutaneous tissues of the foot and toes The numerous subcutaneous veins in the lower half of the leg on the inner side—the vital ulcer-bearing area—drain *not into the saphenous vein* but directly into the deep veins of the leg through three easily definable perforating veins

These perforating veins collect the venous drainage of this area, perforate the deep fascia, and empty directly into the posterior tibial venæ comites. They seem to be anatomically constant in position. There may be two, but more usually there are three of them, and usually one is much larger than the other two. Sometimes a small communicating vein passes from the saphenous vein to a branch of the lowest or middle perforating vein, but this is inconstant and may not be present (as in fig. 3). There is almost always a communicating branch between the saphenous and the highest perforating vein.

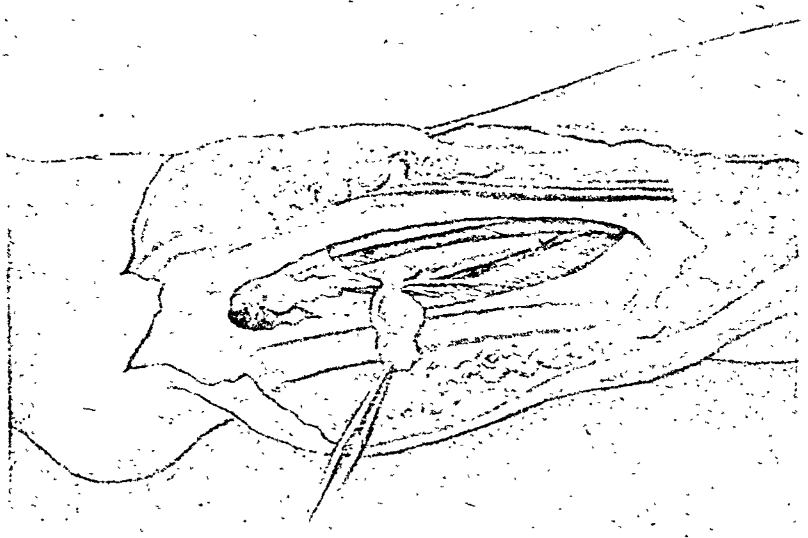

Fig. 4—Dissection of subcutaneous tissues of inner side of lower third of leg of a man who had had chronic varicose eczema of this region, without any saphenous incompetence. Deep fascia has been opened to show junction of large dilated incompetent middle *perforating vein with posterior tibial vein.* Note (1) vein passing from perforating vein, where it penetrates deep fascia, to soleus muscle; (2) great saphenous vein anteriorly; and (3) small dilated tortuous veins in subcutaneous tissues.

The three perforating veins penetrate the deep fascia in a line which corresponds to the space separating the soleus muscle from the deep muscles in the posterior compartment—i.e., a line which corresponds to the course of the posterior tibial vein. They are of such a size that they can easily be dissected out. The holes through which they penetrate the deep fascia have smooth edges easily felt with the dissecting scalpel; each one looks like a small saphenous opening in miniature. Usually one perforating vein enters each hole; this vein is usually formed as the junction of two main tributaries which collect the flow from the subcutaneous venous network. Each perforating vein is provided with a valve at its point of junction with the deep vein. This valve permits a flow of blood from superficial to deep veins, and thence upwards, but prevents reflux of the blood in the reverse direction. The competence of these valves is of supreme importance in the normal venous drainage of the lower part of the leg.

Figs. 3 and 4 show dissections of the whole region of these communicating veins in a normal leg (fig. 3), and in a case of chronic varicose eczema of the lower third of the leg in which the perforating vein was incompetent (fig. 4). A further interesting anatomical fact was shown: at the point where the perforating vein joined the posterior tibial venæ comites the venæ comites themselves communicated with each other, and a vein came directly from the soleus muscle to join the plexus. Thus at this point there was a miniature venous Piccadilly Circus. The possible significance of this muscle vein joining the plexus at this point is evident in cases of deep venous thrombosis, which usually starts in the deep muscle veins of the soleus.

Thus the venous drainage of the inner aspect of the lower third of the leg can be represented diagrammatically as in fig. 5, which shows venous drainage by two routes: (1) straight into the deep veins via the perforating veins; and (2) into tributaries which join the great saphenous vein just below the knee. Venous valvular incompetence may thus affect the lower third of the leg in two ways: (1) by valvular incompetence of either or both of the saphenous systems; and (2) by valvular incompetence of one or more of the perforating veins, the saphenous systems being intact. This latter type of incompetence, we believe, is of greater significance in the production of chronic ulcers and eczema of this region.

One further point must be emphasised. The existence of communicating veins between superficial and deep systems has been known for a long time. Excellent descriptions of the communicators in the lower third of the thigh and just below the knee have been given by Boyd (1948), Kinmonth and Robertson (1949), and

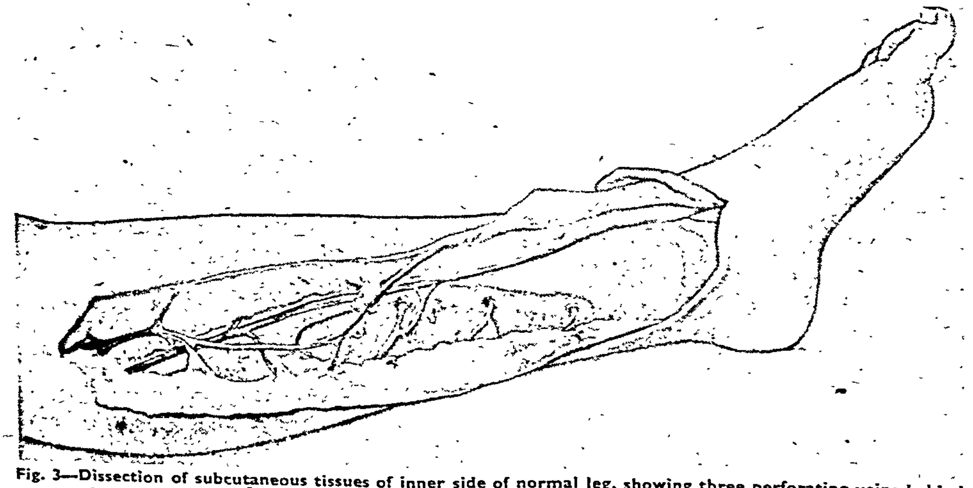

Fig. 3—Dissection of subcutaneous tissues of inner side of normal leg, showing three *perforating veins behind* great saphenous vein. Note (1) communicating branch between highest *perforating vein* and great saphenous vein, and (2) tributaries to great saphenous vein just below knee. Cf. fig. 5.

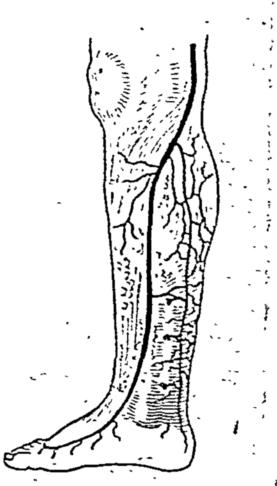

Fig. 5—Main venous drainage of inner aspect of leg.

others Surprisingly enough, little detailed work has been done on the communicating veins below the knee D A W Edwards (unpublished communication), by the injection of indian ink and plasma into amputated legs, has demonstrated that in the upper third of the leg there are numerous small communications between muscular veins and small subcutaneous veins The perforating veins described here differ from these in that they are large and constant in situation and drain directly into a large deep vein Moreover their situation is most significant they are situated just below a powerful muscle pump !

Thus on purely anatomical grounds it is probable that the great saphenous vein normally plays a minor part in the venous drainage of the subcutaneous tissues of the lower and inner part of the leg—the ulcer bearing area It drains the foot the upper part of the leg, and the thigh, and only through tributaries entering it at knee level does it contribute to the venous drainage of the ulcer-bearing area So it is not surprising that operations on this vein should often have little effect on many so called varicose ulcers

ANATOMICAL STUDIES OF ARTERIAL SUPPLY

A study of the arterial supply of the skin and sub cutaneous tissues of the leg and foot has been undertaken in conjunction with D A W Edwards The method has been to inject the arterial system of amputated limbs with bismuth suspension, and next to remove the skin and deep fascia completely in one layer This is then radiographed to give the arterial pattern The results of this investigation will be reported more fully elsewhere, but the main points are of significance in considering varicose ulceration, which is, after all, only a form of localised skin gangrene The arterial supply from knee to ankle comes from perforating arteries arising from the deep arteries directly and from the small muscular arteries These perforating arteries often accompany the perforating veins The density of perforating arteries is greater in the upper part of the leg than in the lower half, falling off considerably both in number and size when the ankle region is reached Below the malleoli the skin of the foot, particularly the heel, is well supplied with numerous large branches directly from the main vessels Thus from purely anatomical studies it is apparent that the skin and subcutaneous tissues in the lower third of the leg have relatively fewer small arteries, and that at the level of the malleoli there is a sort of arterial watershed—the foot below this level having a much more profuse arterial supply

EFFECTS OF INCOMPETENCE OF THE PERFORATING VEINS

The anatomical facts just given suggest that incompetence of the perforating veins draining the ankle would throw a very great strain on the venous mesh in the lower third of the leg which they drain This venous mesh is composed of delicate thin-walled veins which are not designed to stand up to a large venous pressure, unlike the thick muscular trunk of the great saphenous vein itself In the leg the valves are so arranged that the blood-flow is always from superficial to deep veins Every tributary of the deep veins is guarded by a valve at its entry, which ensures that no reflux from

This can be seen on the X-ray screen if 20 ml of 50% 'Pyelosil' is injected slowly into a small vein on the dorsum of the foot of a normal person in the prone position The opaque medium quickly appears in the deep veins of the leg, and within half a minute most of it is in the popliteal vein None can be seen in the superficial veins

The mechanism for returning venous blood from the limb in the erect position is well known The deep fascia of the leg forms a firm investing layer enclosing the large muscles of the calf When these contract within the firm inextensible sheath of deep fascia they squeeze venous blood out of the leg with considerable force Barcroft and Dornhorst (1948) have shown that this calf muscle pump can overcome a resistance greater than 100 mm Hg The valves of the veins are so arranged that the blood can leave this pump only in an upward direction Now, the perforating veins which drain the ankle pass through small holes at the bottom of this powerful pump When the pump contracts, there is, in the veins below the pump, a momentary reflux of blood downwards as far as the valves This can be seen excellently in a post-mortem dissection When the perforating vein has been dissected out, the calf is suddenly squeezed the blood, which is still fluid in the deep veins, is forced towards the perforator but is suddenly held up by its valve

Now, if this valve should become incompetent or be damaged in any way, at every contraction of the calf pump the increase in venous pressure within it would be transmitted downwards and outwards through the incompetent perforating vein to the thin venous mesh above the internal malleolus This would in time lead to dilatation and tortuosity of this mesh, and this would mean stagnation of venous blood in it As we have seen, this is exactly what was seen to happen in ulcer patients from clinical observation alone We have observed every stage from a pre ulcer state, which consists of merely a large mesh of dilated venules round the ankle (fig 1), through thrombosis in this mesh, to a fully developed ulcer sitting on a fibrotic mass or plaque Thus we believe that the genesis of many so called varicose ulcers can be shown diagrammatically as in fig 6

We were fortunate to find at necropsy a man, aged 56, who had had chronic eczema of the lower third of the leg for many years but had not undergone operation, because no varicose veins were visible Fig 4 shows a drawing of the dissected leg The whole of the sub cutaneous tissues in the affected region were full of small tortuous dilated venules, many of which were

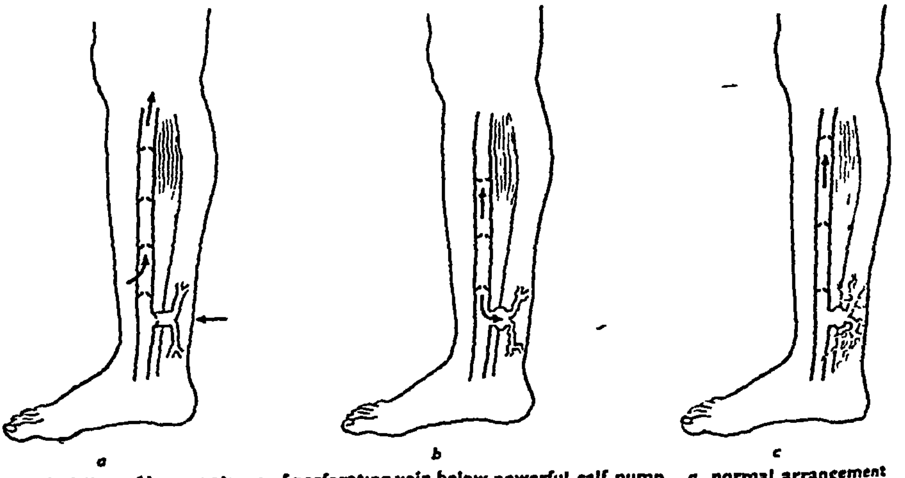

Fig 6—Effect of incompetence of perforating vein below powerful calf pump *a* normal arrangement of valves (arrows indicate direction of blood flow), *b*, effect of incompetence of valve where perforating vein penetrates deep fascia (arrows indicate direction of blood flow on contraction of calf) *c*, final result—dilatation of stump of perforating vein and dilatation and tortuosity of all veins in subcutaneous tissues draining into it.

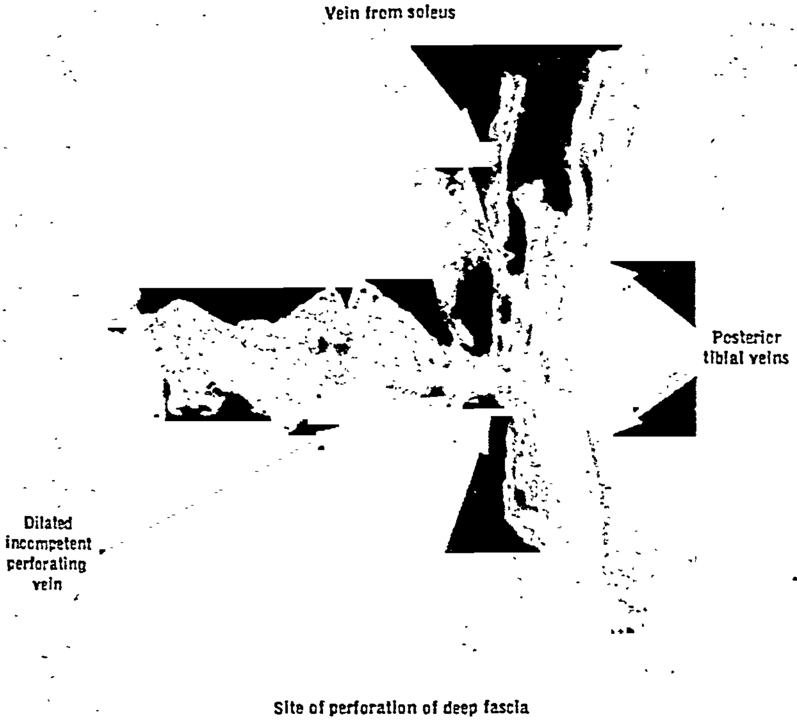
Vein from soleus
Posterior tibial veins
Dilated incompetent perforating vein
Site of perforation of deep fascia

Fig. 7—Dissected and mounted specimen from leg shown in fig. 4. No valve was found where perforating vein joined deep vein. Valves were present in veins of posterior tibial bundle. Cf. fig. 8.

thrombosed, with considerable fibrosis round them, making them feel like an indurated plaque to the examining fingers. This seems to be the essential pathology of the pigmentation and induration so often seen in the stasis syndrome of the lower leg. These dilated vessels were draining directly into one large incompetent perforating vein, which is well shown in the figure and was the middle of the three perforating veins described. The fully dissected and mounted specimen of this incompetent perforating vein is shown in fig. 7. The effect of this local valvular incompetence is well seen on comparing it with the dissected and mounted specimen of a normal perforating vein (fig. 8).

OPERATION FINDINGS AND RESULTS

If this explanation of varicose ulceration is true, it should be possible to find these incompetent perforating veins, and, by tying them at their point of passage through the deep fascia, cut off the source of local venous incompetence, thus applying the principle of the Trendelenburg operation to the lower third of the leg.

The presence of incompetent perforating veins may be suspected in the following circumstances:

(1) A varicose ulcer has not healed, or has recurred, after an efficient surgical obliteration of incompetent veins of the great saphenous system.

(2) Ulceration or induration and pigmentation of the lower third of the leg is present without evidence of saphenous incompetence.

(3) A mass of small dilated varices is present in the lower third of the leg, with or without incompetence of the saphenous vein.

Very occasionally the incompetent perforating vein can be seen as a localised bulge in the lower third of the leg; but this is rare and has been seen and confirmed at operation only twice by us. Most of these local "blow-outs" in the course of a varicose vein are simply local aneurysmal dilatations of the vein wall and do not mark the points at which perforating veins pass through the deep fascia.

In most cases the incompetent perforating vein which is the root of the trouble cannot be seen or felt, because it is very effectively covered by a plaque of indurated tissue consisting of the numerous minute thrombosed venules embedded in fibro-fatty tissue. This is probably why their importance has not been fully appreciated: they are the nigger in the woodpile—the woodpile being the ulcer and plaque of induration.

Figs. 9 and 10 show a typical incompetent perforating vein of the ankle exposed at operation. Fig. 9 shows the site and extent of the incision necessary. Fig. 10 is a close-up of the perforating vein showing the round hole in the deep fascia (exactly comparable to the fossa ovalis) through which it comes, and its relation to the great saphenous vein at the ankle.

This operation involves cutting and dissecting in an area of devitalised skin and one might expect that necrosis and breakdown of the incisions would follow. It has been our practice to excise not only the incompetent perforating vein but also as much as possible of the subcutaneous plaque of thrombosed venules and fibrous tissue, and the ulcer itself if one is present. The resulting defect is left to granulate for a few days and is then grafted with a split-skin graft. There has been no difficulty about these grafts taking. In some of the other cases in which there has been no ulcer but merely a patch of early eczema or pigmentation this has not been necessary, and the skin edges can be brought together quite well and heal. Provided the cause of the poor vitality of the skin—i.e., the incompetent perforating vein—is found and removed at operation, satisfactory

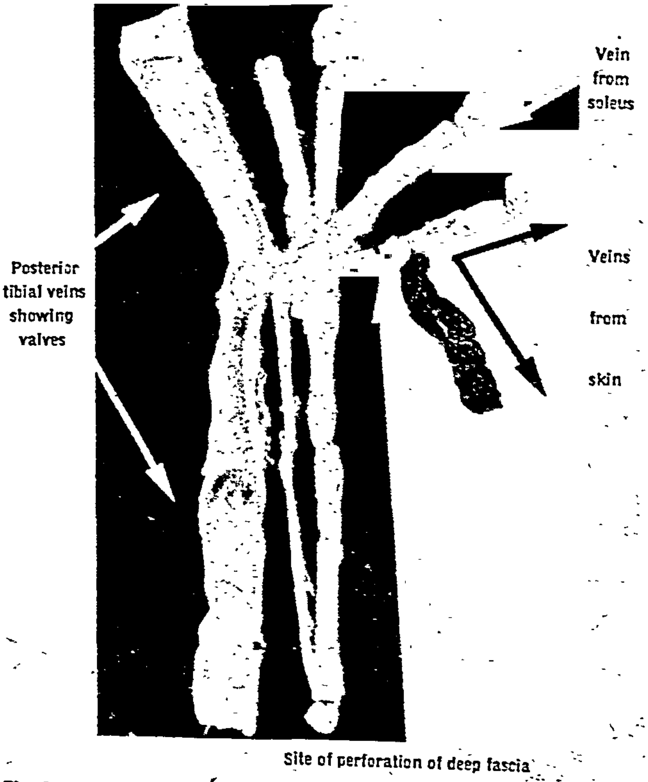
Vein from soleus
Posterior tibial veins showing valves
Veins from skin
Site of perforation of deep fascia

Fig. 8—Dissected and mounted specimen from normal leg (cf. fig. 7). A valve was present where perforating vein joined deep vein, and valves were present in all other veins.

healing will take place However, a good deal of caution must be exercised in dissecting in this area, and we have had one case in which the edges of the incision broke down In general, if an ulcer is present, the indurated plaque, and the incompetent perforating vein should all be excised in one piece, as was done in case 1 (see below), and the area should be grafted If there is no ulcer, as little dissection as possible should be done, but the area of the perforating veins should be approached directly through a longitudinal incision placed slightly behind the internal malleolus (fig 9) The tissues are then divided straight down to the deep fascia, at which plane a gentle search is made for the perforating vein The perforating vein which is most often incompetent, in our short experience so far is the middle one of the three and is situated a hand breadth above the internal malleolus

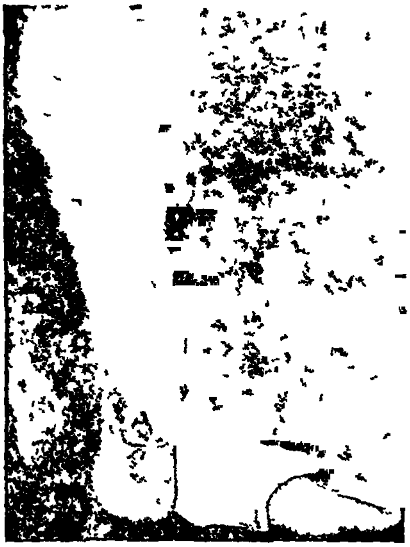

Fig 11—Leg of case 1 before operation note (1) scars of previous operation for tying veins, and (2) great saphenous vein well anterior to ulcer Cf figs 13 and 14

There is considerable variation in the branches (tributaries) of the perforating veins, and in the way in which they communicate with the great saphenous vein But the foramina through which they penetrate the deep fascia are remarkably constant in these positions, and it is for this reason that a standard surgical approach can be made to them

The following is a summary of two cases followed up for nine months and one year respectively

Case 1 —A housewife, aged 57, had had a varicose ulcer of the left leg for fifteen years Fig 11 shows its size and situation There was no definite previous history of deep thrombosis Four years previously she had had a Trendelenburg operation and below knee excision of her varicose veins The ulcer healed for about six months after this operation but then recurred As her below knee veins were still prominent, she was readmitted in October, 1951, and two more fairly large below knee veins were dissected out Again the ulcer healed, but only for a month this time when it recurred again and was as big as ever Venography was then done, and a large perforating vein was seen, connected to a tortuous vein going straight down to the ulcer area (fig 12)

In April she was readmitted to hospital, a lumbar sympathectomy was done to ensure full skin vasodilatation of the ulcer area,

Fig 13—Leg of case 1 three days after opera-

the perforating vein was exposed and divided, and its large tributary leading from the ulcer, and the ulcer itself, were excised in one piece Fig 13 shows the leg two days after this operation The defect was grafted with split skin four days later The skin graft took very well, and fig 14 shows the patient's leg six months later For the first time in fifteen years she can walk about without supporting bandages The area formerly occupied by the ulcer has consolidated and shows no signs of breaking down

Case 2 —A policeman, aged 42, had a small chronic ulcer as large as a shilling about a hand breadth above the internal malleolus It had been present for a year and a half and had resisted all attempts to heal it The venous and arterial systems in the leg were normal, but just underneath the ulcer was a small bunch of dilated veins Venography showed a normal venous system, except that in this region an enlarged and tortuous perforating vein was seen joining the deep vein At operation the ulcer, which had closed in considerably on energetic supportive treatment, was excised, and the underlying dilated perforating vein was found and ligated at its point of penetrating the deep fascia The skin could be brought together easily with a little undermining of the edges Healing was satisfactory, and there was no recurrence nine months later, when the patient was last seen No bandage of any sort has been worn

The follow-up of our cases has so far been too short for us to come to any definite conclusions about the efficiency of the operation in preventing varicose ulceration or in curing established ulceration Since becoming aware of the existence of these incompetent perforating veins in the anatomical situation described we diagnosed them and found them at operation in 10 cases, in 3 other cases we failed to find the incompetent perforating veins we expected to find

The early results have been gratifying, the skin has healed, the spray of dilated veins has disappeared, and the few early ulcers we have treated have not shown any signs of recurrence Only in 1 case, already referred to, did the skin break down This was due to our operating through an area of skin which had been in the active eczematous stage too recently, and the wound became infected

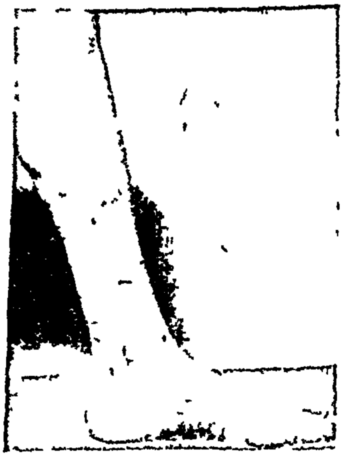

Fig 14—Leg of case 1 six months after operation

DISCUSSION

In the most recent editions of *Gray's Anatomy* (Johnston and Whillis 1951) and *Cunningham's Anatomy* (Brash 1951) the venous drainage of the lower third of the leg is described without any reference to these perforating veins, nor are they shown in any of the illustrations Grant (1951) shows them accurately but does not mention them in the text Thus their anatomical existence and importance do not seem to be widely appreciated

Their importance in the venous drainage of the subcutaneous tissues of the lower third of the leg—the ulcer bearing area—is considerable Many observers—e g, J R Learmonth and L G Higgins (personal communications), Foote (1952), and Dodd (1952)—have noticed the presence of these large perforating veins at operation near ulcers or directly under ulcers, but, so far as we know, these clues have not led to any detailed anatomical study Foote (1952) has advocated operating on them when they are seen, and American workers particularly Linton and Hardy (1948) and Merle Scott (1951), have for some time been convinced that the true cause of many cases of ulcer of the leg lay in incompetence of many communicating veins in the lower leg. Linton's operation of stripping the deep fascia is based on this theory. Merle Scott (1951) has designed an aeropulse legging for fitting on the lower leg, whose design is based on this assumption. However, the fact that the perforating veins usually responsible for the ulcer syndrome are so large, easily accessible, and so anatomically constant in the sites where they pierce the deep fascia has not so far been recognised. Armed with this basic knowledge a planned operation can be performed on them, as accurate as the standard Trendelenburg procedure and based on exactly the same principle.

It now becomes possible to understand why ulcers should develop after a deep thrombosis. For, if there is a block in the deep veins of the leg due to thrombosis, surely the main alternative path for the return of venous blood is outwards through these, and the many other small, perforating veins (the reverse of the normal flow) and up the superficial veins. This means breaking down the resistance or destroying the valves in the perforating veins. Once this thrombosis has settled, and the collateral venous channels have formed and enlarged, the leg is left with the condition which we have shown may lead to ulceration—i.e., incompetent perforating veins below the calf pump. Thus the reason for the development of these ulcers becomes intelligible, and a clue to their early treatment is provided.

Moreover, the anatomical arrangement whereby a vein from the soleus joins the posterior tibial venæ comites at the same point as the perforating vein enters gives the clue to how the valves in the perforating veins may be destroyed. In the man whose leg is depicted in fig. 4 (who died from pulmonary embolism), the large incompetent perforating vein contained an antemortem clot which extended inwards and was continuous with a similar clot in the muscle vein going to the soleus. The veins in the soleus were full of antemortem clot. Thus it seems that here we have an anatomical pathway whereby clot from the deep veins in the soleus may spread out to the superficial veins of the ankle region via the perforating veins. A localised area of induration and redness, apparently a local patch of superficial thrombophlebitis, in the ulcer-bearing area is a common precursor of an ulcer or eczema—and this is probably the mechanism of its occurrence. Such cases usually show calf tenderness as well. It is well known that the organisation of clot in veins will destroy the valves; so here is one possible way in which the valves of the perforating veins may be destroyed after deep thrombosis.

Thus there is reason to believe that incompetence of these perforating veins may be the cause of many post-thrombotic and so-called varicose ulcers. We have therefore called this condition the "ankle blow-out" syndrome to differentiate this particular type of venous incompetence in the lower leg leading to ulceration and eczema from the more generally recognised saphenous incompetence.

SUMMARY

The anatomy of the venous drainage and arterial supply of the inner aspect of the lower third of the leg is described.

The constant anatomical situation of three perforating veins in this area is described, and the effects of valvular incompetence of these veins situated below the calf muscle pump are discussed.

Criteria for the diagnosis of incompetence of these perforating veins are suggested.

An operation aimed at tying these incompetent perforators where they penetrate the deep fascia of the calf is described. The principle of this operation is exactly similar to that of the generally accepted Trendelenburg operation.

The name "ankle blow-out" syndrome is suggested to differentiate this type of venous valvular incompetence from the more generally recognised saphenous incompetence.

We wish to acknowledge the painstaking assistance of Mr. F. R. Scholefield in dissecting and mounting the specimens. The help of Miss J. Dewe with the drawings and of Mr. K. Moreman with the photographs is also gratefully acknowledged, and of Miss F. Hunter with the secretarial work. We should also like to thank the sisters and nursing staff of the Royal Waterloo Hospital for their coöperation and care for the patients.

ADDENDUM

Since this paper was written we have had a further 20 cases in which one or more large incompetent "blow-outs" have been found and tied at operation. In most of these cases the blow-out was either just above or immediately under an early ulcer or area of devitalised skin. The constant anatomical situation of these foramina where the veins perforate the deep fascia has been repeatedly confirmed.

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LIGATION OF THE POPLITEAL VEIN FOR THE GRAVITATIONAL SYNDROME

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With illustrations on plate

Bauer (1948) investigated the deep veins of the legs by venography and by measuring the pressure in the popliteal vein. He found that patients with the gravitational syndrome had no demonstrable valves in the deep veins and no fall of pressure in the popliteal vein when it was occluded below the point of measurement; whereas in patients without leg symptoms the valves were always shown and the pressure always fell. Bauer therefore concluded that the syndrome was the result of an unsupported column of blood in the deep veins extending from the heart to the feet, and that this column should be broken by ligation of the popliteal vein. His results in a large number of cases were excellent (Bauer 1950).

Reports from other surgeons, however, are few and on the whole not impressive. Castagna and Impallomeni (1951) state that ligation of the popliteal vein was first practised by Parona in 1904, but that his results were not good, probably because the cases were ill chosen. The operation was abandoned except by a few surgeons, such as Giordano (1934, 1937), who had success in some cases. Castagna and Impallomeni (1951) reported 20 cases with good results after a month, of which 16 were followed for three months and were still satisfactory. De Takats and Graupner (1951) operated on 10 cases, of which 7 were successful but were only followed for a very short time.

The following cases are therefore reported Though the numbers are small (23 legs in 18 patients), they have been followed long enough to give a reasonable idea of what is likely to happen, and to enable an opinion to be formed on the value of the operation

The gravitational syndrome is characterised by aching of the legs, by a brownish discoloration and induration of the front (sometimes the whole) of the lower leg, with swelling of the ankles towards the end of the day, and by ulceration in the malleolar region or front of the lower third of the limb It may or may not be associated with varicose veins, and there is often, but by no means always, a history or venographic evidence of a previous deep venous thrombosis

The cases described here fall into three groups

Group 1 —Those suffering primarily from ulceration of the lower leg, and only secondarily from discomfort, aching, and swelling

Group 2 —Those in whom the chief complaint was of considerable aching (what has been described as a bursting feeling) and swelling of the ankles and legs, but who complained also of the discoloration and induration already described In this group there were no actual ulcers at the time of operation it was the aching which brought them for advice

Group 3 —Those with swelling of the legs considered to be of venous origin These patients complained of aching and discomfort also, but the swelling was the chief complaint

They had all been given the usual treatment of pressure dressings of one sort or another, from elastic stockings to 'Viscopaste,' without success Many had had superficial veins injected, where visible, but without improvement, and all were a good deal disabled (fig 1)

The method of selection for operation was venographic —i e, patients in whom no valves in the deep veins could be demonstrated by ascending venography (Moore 1949) were considered suitable for ligation of the popliteal vein The venographic appearances, apart from the lack of valves, were of two kinds, the veins being either irregular, "moth eaten" and small, owing to old thrombosis and recanalisation (fig 2), or smooth and often larger than normal (fig 3), an appearance commonly, but by no means always, associated with a history of "white leg" The differences in appearance can more readily be appreciated by comparing them with the normal (fig 4*a*)

RESULTS

Group 1 (13 legs in 11 patients) —The ulcers have completely healed, with no swelling or discomfort, in 9 of the legs (7 patients), the longest time since operation being three years, the shortest nine months, and the average just under two years

One patient, followed for nearly three years, has complete relief from pain and swelling in the legs, although the ulcers did not heal

3 patients, all operated on more than two and a half years ago, have shown no improvement, but they have not been made worse by the operation

Group 2 (7 legs in 5 patients) —There was complete relief of discomfort in all of them and, surprisingly enough, the swelling was less or completely cured The longest time since operation is two and a quarter years, the shortest a year, and the average over eighteen months

Group 3 (3 legs in 2 patients) —I decided to try the effect of popliteal ligation in this type of case, where the swelling seemed to be of venous and not lymphatic origin, because my previous experience had shown that the swelling of the legs usually improved after ligation of the popliteal vein Only 2 cases have so far been operated on, but they are perhaps worth describing

Case 1 —A man, aged 36, complained in October, 1945, of three months and the swelling decreased Three months later the leg was worse again, and he was again in hospital for eleven weeks This swelling and partial recovery had continued since then, making his work as a miner impossible

On examination in September, 1950, the leg was extremely swollen and tight, for which no cause was found except grossly abnormal deep veins of the left leg, shown by venography (fig 4*b*), those of the right being normal (fig 4*a*) Ligation of the deep veins was thought to be justified

At operation in October, 1950, two large veins were found in the popliteal space, one being macroscopically normal and the other thrombosed and adherent to the sciatic nerve An inch of each vein was excised The leg steadily improved after operation

Right Leg —In December, 1950, the same course of events began in the right leg the swelling started in the foot and in about a week spread to most of the right leg Under treatment with anticoagulants it improved rapidly but in January, 1951, it again became severely swollen This time it improved with rest in bed However, in April, 1951, it was once more very swollen The venogram (fig 4*c*) now showed gross abnormality of the deep veins of the right leg The right popliteal vein was tied, and a right Trendelenburg operation was done

The condition gradually improved for two to four months and by February, 1952, there was slight swelling only in the right leg, the left being normal The patient had returned to work as a miner

Case 2 —A woman, aged 46, had two and a half years' history of persistent swelling of both legs without obvious cause The swelling improved with rest in bed In April, 1952, the left popliteal vein was tied It is too soon to say whether there will be any improvement, but the operation has not made the condition worse

DIFFICULTIES ASSOCIATED WITH OPERATION AND REASONS FOR FAILURE

It was not realised at first that (contrary to Bauer's experience) the ulcers were not going to heal spontaneously after ligation of the popliteal vein, but it soon became evident that rest in bed and skin grafting were necessary to achieve this The method now used is to put the patient to bed and to treat the ulcers with streptomycin locally for a few days and then to apply a thin split-skin graft, which takes very well As soon as the ulcer is covered, the popliteal vein is tied, about an inch of it is excised, and the patient is encouraged to be up and about The following two cases illustrate this very well

Case 3 —A woman, aged 56, was seen in December, 1948 She had had ulcers on the lower part of the left leg for fourteen years and on the right leg for four years At the age of 9 she had had a severe injury to the left foot, which became infected, and she was in hospital for a year She had been treated by support (viscopaste, &c) for eighteen months before coming under my care, but without improvement

On examination both legs were thin and without visible veins The lower third of each leg was discoloured, indurated, and ulcerated (fig 1), and there was a severe equinous deformity on each side The arterial supply to the legs seemed normal, but the feet tended to be cold and sweaty Venography showed deep veins which had been thrombosed and recanalised (fig 1)

Treatment —Left lumbar sympathectomy in January, 1949, improved the ulcers on the operated side but did not cause them to heal The ulcers on the right side also improved to some extent In May, 1949, the left popliteal vein was tied and the patient was discharged, with viscopaste support, before the ulcers were healed In January, 1950, the ulcers being still unhealed, the right popliteal vein was tied and skin was grafted on the ulcers on both legs The grafts were successful the ulcers healed on both legs and have remained healed

Case 4 —A woman, aged 67, had recurrent ulceration of the right leg for eight years There was no history of "white leg" and histology of the popliteal vein showed nothing to indicate a past thrombosis No varicose veins were seen On

Trendelenburg operation was done at the same time. The patient was kept in bed for a week and then discharged with supporting dressings, but with the ulcers unhealed. During the rest in bed the ulcers improved, but this improvement ceased as soon as she became ambulant. She remained in bed for a month at home, but still the ulcers did not heal. On Jan. 25, 1950, skin was grafted on the ulcers without preparation and this proved only partly successful. On Jan. 31 local treatment with streptomycin to the ulcers was begun, and on Feb. 8 more skin was grafted. On Feb. 21, 1950, the ulcers had soundly healed, and the patient was discharged. The ulcers have remained healed.

This failure to heal without grafting is probably the cause of the partial failure in the one case which improved but did not heal, for this patient resolutely refused to remain in hospital until the ulcers healed and as resolutely refused to return for further treatment.

The scar in the popliteal fossa has caused some discomfort in 3 patients, with keloid formation, but has proved no real disability. In 1 patient, however, the scar has persistently broken down, although the ulcers, for which the operation was done, have remained healed. This patient has angina pectoris and arterial deficiency in the affected leg; this may be the cause of the trouble with the popliteal scar. It would perhaps be better to make a lateral incision to tie the popliteal vein.

The 3 cases which failed to improve were all in group 1, with ulceration. 2 of them subsequently showed definite arterial deficiency, which was not recognised at the time although looked for, and later healed after sympathectomy; Bauer (1950) has had similar experiences. The 3rd case showed venographically (fig. 5) and at operation a complete block of the upper end of the popliteal vein. It is therefore hardly surprising that no improvement took place—this was a complete error of judgment.

CONCLUSIONS

It seems reasonable to conclude that the operation does no harm, and that in suitably chosen cases it can relieve the patient of symptoms for a considerable length of time.

Most of the patients have continued to wear elastic stockings, but a few have discarded all forms of support and have remained symptom-free.

SUMMARY

23 legs have been treated for the gravitational syndrome by ligation of the popliteal vein.

Complete relief of symptoms has been obtained in 18 and improvement in 1; 3 have shown no change, and 1 is too recently done to judge.

The longest time since operation, in those with a good result, is three years, the shortest time nine months, and the average just under two years.

The patients selected for operation were those in whom no valves could be seen in the deep veins by ascending venography.

The importance of healing the ulcers before discharge from hospital is emphasised.

The value of the operation for œdema of venous origin is discussed.

I wish to thank Mr. D. A. Abernethy, senior surgeon to the Radcliffe Infirmary, Oxford, and the members of the staff of the General Infirmary at Leeds, who very kindly permitted me to treat their cases.

ADDENDUM

Since writing the article, 1 leg in group 1 has broken down after remaining healed for two years and two months. This is the patient referred to later in the article who had had much trouble with the popliteal scar, together with arterial deficency in the legs. Sympathectomy has not improved matters.

In group 3, case 2 has not improved over a period of eight months, but is no worse.

Therefore, of the 23 legs, 17 have complete relief of symptoms and 1 is improved; 1 ulcer was healed for two years and two months but has relapsed; 4 legs are unchanged.

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MELORHEOSTOSIS

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With illustration on plate

Up to 1948 only four cases of true melorheostosis (Léri type of osteopetrosis, or *osteosi eburnizzante monomelica* of Putti) had been reported in this country (Fairbank 1948), and no further case has been recorded here since. Hess and Street (1950) have reported one in America, and Thompson et al. (1951) one in South Africa.

CASE-RECORD

In March, 1952, a healthy male, aged 19, complained of pain in his left knee after pulling on a rope.

History.—On four previous occasions he had had similar sudden pain in one of his other limbs after strenuous activity. In November, 1950, his left arm was the site of pain which subsided after treatment with lead and opium. In March, 1951, while he was playing football, something "went" in his right knee: there was no effusion; movement remained full; the anteromedial compartment was tender; and the condition cleared up in a week under treatment with a U-pad and bandage. In May, 1951, while pulling on a chain at work, he experienced sudden pain at the back of his right shoulder: strain of the serratus posticus muscle was diagnosed and was cured in a week with infra-red therapy. In November, 1951, again while pulling on a chain at work, he felt a sudden pain in his right wrist: the tendon of the extensor pollicis longus was found to be tender and the wrist was strapped with 'Elastoplast' and cured in a week.

At the age of 4 years he had had pneumonia, followed by an operation on his left foot. A subastragaloid arthrodesis had been performed.

On examination the left leg was 2 in. shorter than the right. The left foot was fused at the subastragaloid joint, with the forefoot fixed in inversion, and almost rigid claw toes. The left quadriceps was in good condition. A large hard mass, not attached to the skin, lay posterior to the internal collateral ligament of the knee-joint, and a smaller soft cystic swelling lay medial to the patella. There was no effusion into the joint. Extension 180°, flexion 80°. Slight lateral mobility of the joint, but no laxity of the cruciate ligaments. The skin of the leg was quite normal.

Radiography showed a dense mottled sclerosis of the femur, patella, tibia, and astragalus of the left leg. All the changes were on the medial side of the bone and densest near the hip, knee (see figure), and ankle. There were dense lines of sclerosis along the medial sides of the shafts of the long bones of the left leg. No bony lesions were found in other parts of the skeleton.

The radiological appearances around the joints are typical of melorheostosis, but the straight lines of sclerosis in the shafts of the femur and tibia present a similar appearance to osteopathia striata rather than the candle drippings of melorheostosis. In view of the distribution of the bony changes—which are confined to one side of one lower limb—this must be regarded as a case of melorheostosis.

SUMMARY

A case of melorheostosis in one lower limb of a young male is described

The main complaint was pain, though there was slight limitation of movement There were no skin changes The patient was able to do his job and play football without difficulty

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NECROTIC JEJUNITIS WITH PERFORATION

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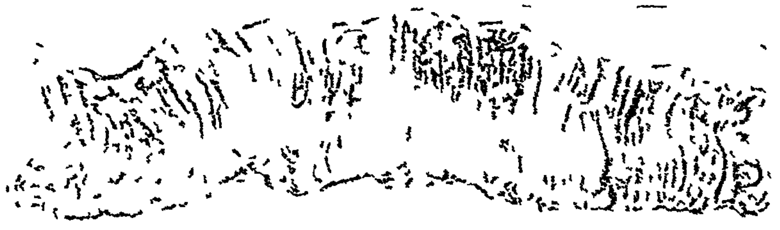
Necrotic jejunitis is a non specific acute inflammation of the upper part of the small intestine, which may proceed to perforation or to hæmorrhage It has been reported in epidemic form in Germany (Fick and Wolken 1949) and, under the name of non-specific ulcer of the small intestine, in isolated cases in the United States (Ebeling 1933, Evert et al 1948)



Operation specimen

The following case, which presented as a general peritonitis, seems to be the second reported in this country The first was described by Young (1949)

CASE-RECORD

A woman, aged 60, was admitted as an emergency on Jan 26, 1952 She had had upper abdominal discomfort after meals for the previous four months, and had lost about a stone in weight Twenty two hours before admission she had been seized with a sudden very severe generalised continuous abdominal pain, and she had vomited several times She had not passed flatus since the onset of the pain

On examination she presented the typical appearance of general peritonitis Her temperature was 100°F and pulse rate 108 Her abdomen was rigid, and bowel sounds could not be heard General peritonitis was diagnosed

Laparotomy —The abdomen was opened through a right paramedian incision The peritoneal cavity contained much foul smelling purulent free fluid A loop of jejunum 9 in long about 4 ft from the duodenojejunal flexure was œdematous and covered with flakes of fibrin The remainder of the jejunum and the ileum was normal, apart from a few jejunal diverticula on the mesenteric border There were no diverticula in the thickened segment of intestine A small hole was found in the mesenteric border of the jejunum through which jejunal contents could be squeezed The affected segment of jejunum was excised, and an end to end anastomosis made

Convalescence —The patient made a good immediate recovery from the operation, but her convalescence was delayed by a pulmonary embolus on the eighth postoperative day, this was treated with anticoagulants She was discharged from hospital on the thirty second postoperative day

Investigations —A swab taken from the peritoneal cavity at operation contained pus cells but no organisms Culture on blood agar was sterile Agglutination was negative to salmonella and brucella groups A fractional test meal gave normal results No pathogens were isolated from the stools. Radiography after a barium meal fourteen days after operation showed that the second part of the duodenum was dilated, and the third part curled on itself Stasis was present, and there was irregularity of the mucosa of the distal duodenum and proximal jejunum, together with some filling defects compatible with ulceration

Operation Specimen —The excised segment consisted of a portion of jejunum 25 cm in length and bearing several ulcers, the largest being 1 3 cm in diameter (see figure) The ulcer bases were occupied by necrotic material infiltrated with many polymorphs and with histiocytes Between the ulcerated areas all layers of the jejunal wall were congested and infiltrated with plasma cells and polymorphs In the areas of ulceration necrosis and inflammation extended down to the serosa and at one point seemed to have perforated the gut wall

COMMENT

The ætiology of necrotic jejunitis is unknown It has been suggested that *Clostridium welchii* type F may be responsible (Zeissler and Rassfeld-Sternberg 1949) but in the present case neither this nor any other pathogen was isolated from the stools Necrotic jejunitis does not seem to be related to Crohn's disease Simple closure of the perforation has been suggested as the best form of treatment, but, in view of the extent of the process, resection and end-to-end anastomosis are preferable

Radiography fourteen days after operation showed well marked changes in the remaining part of the upper small intestine The patient had had symptoms of dyspepsia for some months before her jejunal perforation, so it should probably be possible to diagnose necrotic jejunitis by radiography before perforation or hæmorrhage brings the patient to hospital as an emergency

My thanks are due to Mr A Elliot Smith for allowing me to undertake the care of this case, to Dr *W S Holden for the radiological report, and to Dr H* Kramer for the pathological report

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SUPPURATIVE ARTHRITIS IN THE AGED

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M D Lond, M R C P
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Degenerative disease is so often found in the aged that its presence is apt to be assumed by the physician This assumption leads easily to the further assumption that, if it is possible to explain any symptom in an old person in terms of a degenerative process, that explanation will probably be correct

Though it cannot be denied that these assumptions approach the truth, probability is not certainty, and various diseases masquerade as arteriosclerosis, cerebral thrombosis, cardiac failure, &c

Within a comparatively short time three such cases have come to my notice In each the development of pain and uselessness of an arm led to the diagnosis of a "stroke," and in each the shoulder-joint was eventually found to be full of pus I cannot find any specific reference to this condition in the aged, but it may well be commoner than is imagined and it illustrates the ease with which a large collection of pus can be missed at this time of life

CASE RECORDS

Case 1 —A man, aged 87, had been seized with pain in his right shoulder while sawing wood four days before admission The pain had become worse and was very severe A stroke had been diagnosed

On examination there was a tense effusion in the right shoulder joint, causing great pain on moving the right arm The patient was obviously very ill Radiography of the shoulder showed only an old united fracture through the tip of the right acromion.

Treatment and Death.—The shoulder lesion was thought to be traumatic, and the arm was immobilised, but the patient died three days later.

At necropsy there was about a pint of pus in and around the right shoulder-joint, from which a pneumococcus was grown. No bone abscess was found. Bronchopneumonic changes were found in both lungs.

Case 2.—A man, aged 78, gave four weeks' history of cough, sputum, and pain in the right upper chest. At the same time he had developed weakness of the right arm. His doctor reported that earlier in the illness he had had a temperature of 100°F and signs of bronchitis.

On examination on the day after admission he did not appear very ill. There were signs of consolidation over the upper lobe of the right lung and an effusion into the right shoulder-joint. Pain was not conspicuous, and the first comment on the arm in his hospital notes is "right arm paralysed and spastic." The only other significant finding was extensive dental sepsis. A white-cell count showed 7500 per c.mm. (polymorphs 59%, lymphocytes 26%, monocytes 14%, Türck cells 1%).

Surgical advice was sought, but the patient died suddenly and unexpectedly next day.

At necropsy there was pus, from which no organisms were grown, in and around the right shoulder-joint. The right subclavian vein was thrombosed, and fragments of ante-mortem clot were scattered throughout the branches of the right pulmonary artery, the upper lobe of the right lung being partially consolidated through infarction, without any evidence of suppuration. This condition seemed to have been present for some days. A large recent embolism in the right pulmonary artery was thought to be the cause of death. There was no evidence of pneumonia.

Case 3.—A woman, aged 69, had been diabetic for nine years, and had had a penetrating ulcer on the second right toe for two months. Six weeks before admission she became bedridden through pain and uselessness of her right arm. A stroke was diagnosed.

On examination she was drowsy but conscious, and her urine was loaded with sugar. Her blood-sugar level was 230 mg. per 100 ml. Her knee-jerks and ankle-jerks were absent, and an ulcer on the dorsum of her right second toe had penetrated into the first interphalangeal joint. An effusion into the right shoulder-joint caused considerable pain on movement of the arm. Aspiration of this effusion produced thick pus, from which a coagulase-positive *Staphylococcus aureus* was grown. A white-cell count showed 6000 per c.mm. (polymorphs 87%).

Treatment and Death.—The patient remained afebrile but, despite systemic and intra-articular penicillin, died after eight days

At necropsy the right shoulder-joint was full of pus, which had also tracked among the shoulder muscles. No abscess was found in the bone.

DISCUSSION

Apart from gonococcal disease and penetrating wounds of the joints, suppurative arthritis is usually pneumococcal or associated with osteomyelitis, when it is usually staphylococcal. Of 248 pneumococcal cases 16% were in the shoulder, and of 187 patients 10 were aged more than sixty-five (Bulkley 1914, Keefer et al. 1934, Bloomberg 1935, Eggers 1936, and Blankenhorn and Grupen 1943). Of the cases associated with osteomyelitis the combined figures of Bisgard (1932), Wilensky (1934), and Blaisdell and Harmon (1942) give an incidence of 8·5% in the shoulder. In Blaisdell and Harmon's series, where age is stated, 2 out of 57 patients were aged more than sixty-five, and these workers comment that in adults arthritis tends to appear rather than osteomyelitis. A similar comment is made by Leavitt (1940). These data tend to show that among suppurating joints the shoulder is not a rarity and that it has been observed in the aged (Blankenhorn and Grupen's oldest patient was aged ninety).

As regards the source of infection in the present cases, it seems clear that the toe was responsible in case 3. In case 1 the lungs seem most likely. It is, however, hard to believe that the old man was sawing wood with an established pneumonia. Since the changes found in the lungs post mortem were no more than those expected in one who has spent four days dying, perhaps the primary lesion was a bronchitis. In case 2 there were two possible sources—the teeth and the lungs. Unfortunately the organism is unknown, and further speculation is futile.

CONCLUSION

I do not suggest that joint suppuration is a common cause of uselessness of the arm. My point is that such suppuration can occur in aged people and can be missed; and that, when a swollen painful joint occurs in such a patient, the presence of pus should be seriously considered.

SUMMARY

Three cases of suppurative arthritis of the shoulder-joint in aged persons are described.

In each the first diagnosis was a stroke.

All were fatal.

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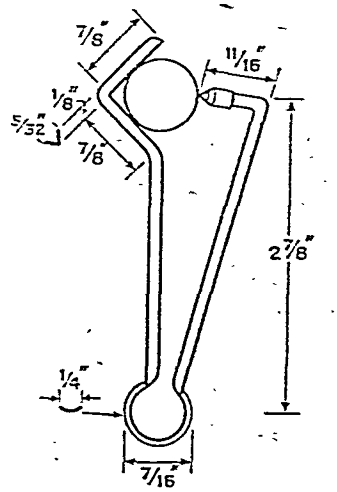
New Inventions

DIAMOND-TIPPED AMPOULE CUTTER

SEALED ampoules containing reagents or medical preparations are generally opened by scratching the glass of the neck with a file and snapping it off. It is often difficult to make a suitable scratch with a file on an ampoule containing liquid, owing to one's natural hesitancy towards applying any force to such a container. In addition, a file scratch often produces a jagged cut which is not only a menace to the operator but also may produce glass splinters which fall into the solution. A file rusts and is difficult to keep clean. A simple ampoule cutter, provided with a diamond point, has been designed to overcome these disadvantages of a file.



The cutter can be readily made at any diamond-tool shop by bending 18-gauge stainless-steel strip into the shape illustrated, and brazing a small diamond on to the point as in making a glass cutter. The diamond need only be ½ carat, and should preferably be a sharp-pointed octahedron. Unlike the glaziers' diamond, it does not require to be polished.

In operation, the neck of the ampoule rests in the crook of the cutter, and with slight pressure of the thumb the diamond is brought in contact with the glass. By rotating the ampoule between the forefinger and thumb of the other hand, while maintaining a steady pressure of the diamond against the glass, an annular scratch is made, and the neck of the ampoule can be broken off cleanly and without effort.

The cutter is inexpensive, compact, light, easy to operate, and rustless, and will accommodate all sizes of ampoules. It should be a useful addition to the equipment of the medical profession.

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Reviews of Books

Prostatectomy A Method and its Management

CHARLES WELLS, professor of surgery, University of Liverpool Edinburgh E & S Livingstone 1952 Pp 103 24s

THIS monograph clearly describes the Wilson Hey operation, its indications, complications, and results As Professor Wells maintains, any competent general surgeon could follow the well-illustrated description readily, whether he had seen the method or not, and could do the operation successfully

The management of the cases, with particular reference to fluid and electrolyte balance, is well described, and there is a short but interesting chapter on the history of the operation The chapter on pathology, however, is somewhat superficial, and the chapter dealing with results is not fully satisfying Professor Wells separates his personal cases from those of his colleagues, which suggests that he has, after all, some doubts whether the operation can be done by any competent general surgeon Some inconsistencies mar the generally good impression Thus he holds to Wilson Hey's retrograde catheterisation, as being necessary to maintain asepsis, but he arranges the towels so as to permit the insertion of a finger into the rectum during the operation Many urologists will disagree with the omission of preoperative cystoscopy, and many more will doubt the wisdom of giving a frail old man 10–11 pints of intravenous fluid in the first 24 hours after prostatectomy

The main teaching is sound, reflecting the modern belief in immediate prostatectomy for acute and chronic retention of urine

Professional People

ROY LEWIS and ANGUS MAUDE, M P London Phoenix House 1952 Pp 284 18s

NOBODY with any responsibility for guiding the affairs of his profession can afford to neglect this masterly account of the present situation of professions in general and the dangers facing them The authors believe that professional people have inherited the leadership in Britain today, but their "tradition of self-examining integrity and self-forgetful service" is in peril Professionalism is all the fashion, and professional status is claimed by technicians, tradesmen, brokers, social workers, administrators, and hairdressers, but these callings are not really based either on instruction in a body of fundamental knowledge or (more important) on a fundamental moral code Indeed "any claim which engineers, scientists, and technologists may have to be regarded as professional from the ethical point of view, derives very largely from their being 'the same sort of people' as doctors, lawyers, teachers, and parsons" Yet the professional tradition is badly needed "to mould, and to civilize, the specialists of the future" Believing that "the basis of professional morality lies in the fiduciary capacity of the man practising his profession," Lewis and Maude conclude that "the standards of any modern profession are ultimately maintained by the example set by private practice," and they implore doctors to retain a proportion of fee-earning practice, both for this reason and to keep in repair for N H S practitioners 'a last citadel of freedom to which all can at need, turn for safety and self-respect" They do not think that the N H S has yet shown clear signs of the insidious dangers which were freely forecast, and they congratulate all concerned, but in endorsing a statement that doctors must "remain the servants of their patients, and personally responsible for their work" they point out that the problem is to translate this into practice One possible means to this end, which they also endorse, is that doctors (like lawyers under the Legal Aid Scheme) should be paid not directly by the State but through a professional body

An independent medical profession, in Lewis and Maude's view, is second in importance only to an independent judiciary and for all their gloom, they recognise that learned institutions, frail as they may appear can simply by their professional standing, develop a strong protective front against State power

and nationally, can be useful In short, members of the true professions

"need to work much harder to strengthen an influence that is already waning, they need to protect themselves and defend their ideals, they need to face the fact that they are an aristocracy, of a sort, and to understand and uphold the personal attainments, as well as the exercise of power, which is implied in that word They certainly need the humility which self knowledge demands, and should discard the dangerous false modesty of pretending to be 'ordinary people—only an expert in this or that'"

Lewis and Maude have much more to say about medicine, and quotations from their opinions have appeared in our leading articles of Dec 20 and again this week They write with an agreeable touch of wickedness, and many will have reason to be grateful both for their perspicacity and for the expository skill already shown in their *English Middle Classes*

A Marriage Manual

HANNAH M STONE, M D, late medical director, Margaret Sanger research bureau and marriage consultation centre at the Community Church, New York, ABRAHAM STONE, M D London Gollancz 1952 Pp 314 12s 6d

THE early editions of this book established it as an outstanding piece of hygiene teaching In its revised and rewritten form it is among the best works on marriage guidance now available The good sense and humanity of its approach are much to be commended The revisions are radical, and include material derived from very recent research The rather unusual question-and-answer presentation, simulating or reproducing a personal interview, has been preserved In the hands of these authors it is highly successful, and makes the book a valuable model for the inexperienced marriage-counsellor It warns him of the type of question to expect (all the recurring decimals of sexual and psychological superstition are here) and provides accurate replies For the patient it is intelligible, reassuring, and explicit The treatment is factual, issues of conduct are dealt with at an adult level, and the style is dignified without being ponderous The book should be read by every medical student

Connective Tissues

Transactions of the Third Conference, February 14–15 1952, New York Editor CHARLES RAGAN, department of medicine, College of Physicians and Surgeons, Columbia University, New York New York Josiah Macy, Jr, Foundation 1952 Pp 166 $3 50

THE report on the first conference on connective tissues was marred by the inconsequentiality which besets impromptu discussion The speakers at the third conference adroitly avoided this, and have produced stimulating debates Perhaps the section most interesting to the general reader is that on hypersensitivity and the hyperadrenal state, which underlines the variability of antibody response among individuals within a species, and discusses much experimental work on the effect of cortisone on antibody production A section on the structure of connective tissue contains some fine electron micrographs of collagen Staining of connective tissue, and the differences between collagen and reticulin, are the subjects of the remaining sections, which give expression to a number of opinions without perhaps adding much to the sum of knowledge on these vexed topics Two coloured plates of an "allochrome" staining method for collagen and reticulin are good, but suffer from a transposition of captions

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Signs and Symptoms (2nd ed London Staples Press 1952 Pp 783 70s)—Prof C M MacBryde, the editor of this book, offers an approach to diagnosis comparable to that of the physician at the bedside In each chapter an important sign or symptom is described, and the mechanism of its production is discussed from the anatomical, physiological and pathological angles This second edition includes some new chapters on pigmentation of the skin, bleeding and vertigo The text is well and fully illustrated This work usefully bridges the gap between standard textbooks and

THE LANCET

LONDON: SATURDAY, JAN. 3, 1953

More Doctors or More Ancillaries?

The behaviour of our generation sometimes recalls that of Stephen Leacock's young man whose distress of mind led him to jump on his horse and gallop off madly in all directions. Traditionally the New Year is a time for reflection—a time for drawing rein so as at least to see what road we are taking. If we knew where we were going we might well prefer to go somewhere else; and we might even be able to direct the horse accordingly. On such hopeful assumptions let us begin the year by considering some present tendencies in our society and profession.

The past quarter of a century has seen a much intensified drive towards social and economic equality. Last week Sir Geoffrey Vickers[1] described how the siege economy of Britain during and since the war has obliged us to share the essentials of existence, and how we have found ourselves paradoxically promoting more and more personal security at a time when its basis in national security grows more and more shaky. The explanation is that during the war we became a far more closely knit community, in which it seemed wrong as well as dangerous that any other member should be allowed to fall below the level of decent subsistence or that his children should lack opportunity to prove their abilities. We also came to believe—and most of us still believe—that good education for everyone, good medical services for everyone, good houses for everyone, good working conditions for everyone, and a degree of security for everyone are all, in the long run, paying propositions, and that a modern industrial nation simply cannot afford ignorance, disease, squalor, and poverty when these can be largely or even entirely prevented by applying modern knowledge. Accordingly, as a nation, we set in motion some major schemes of improvement; and these are now having some interesting incidental consequences. The modern knowledge that has needed application is possessed only by the professional or technical expert; and, in many different ways, direct and indirect, the State has had to pay professional people to perform services that individual members of the public could not possibly afford to buy. As Lewis and Maude point out in the book we review on p. 28, our Governments' programmes since the war have been creating so much new work for the professions, and for experts generally, that everywhere there is a shortage of people trained to do it. The State has in effect been subsidising the professions, which without such subsidy would probably have declined in livelihood and numbers, because the true cost of their services is rapidly becoming too high for even their former clients to meet.

To be in great demand is in some ways an agreeable situation. Bureaucracy may, as Lewis and Maude say, be "a voracious user and spoiler of professional talent," and it will always threaten the professional freedom and responsibility that are essential for really good work; but the medical care of the people of this country is certainly far better at present than it would have been without large Government expenditure on its provision. The danger, as Lewis and Maude see it, lies in a later lowering of standards when the State finds that it has undertaken to do more than it can pay for. Having accepted the principle that, so far as education or medicine is concerned, every citizen has equal rights, the State must try to provide the best for everybody—which is as inconvenient in practice as it is difficult in logic.

> "If you promise to make 'the best available to all,' you cannot pick and choose among priorities. You cannot tot up the figures and say, 'we can afford the best possible treatment to eliminate the scourge of tuberculosis, and we can give a 100 per cent. dental service to children and expectant mothers—because we think these priorities will pay the best dividends on the investment—but we shall have to cut down on hearing aids and massage.' This is to admit that no attempt is to be made to make the best available to those who are neither tubercular nor pregnant, but who do happen to be deaf and suffering from fibrositis. Social justice would be outraged by such arbitrary decisions. The result, of course, is that the best is made available to no one at all."

Actually it is pretty generally understood that, outside utopia, the best of everything cannot be guaranteed for everyone, even in a national service.

> "A modicum of legally enforceable rights may be granted," says Marshall,[2] "but what matters to the citizen is the superstructure of legitimate expectations. . . . It may be possible for every citizen who wishes it to be registered with a doctor. It is much harder to ensure that his ailments will be properly cared for. And so we find that legislation, instead of being the decisive step that puts policy into effect, acquires more and more the character of a declaration of policy that it is hoped to put into effect some day."

Most of us recognise this. Nevertheless, as Marshall adds, in a progressive society the expectations of the public are bound to rise: "the target is perpetually moving forward, and the State may never be able to get quite within range of it." And it is here that Lewis and Maude foresee trouble for the professions which work the social services. When funds prove insufficient to supply all that the public has been led to expect, the State may let the quality of its benefits go down in order that it may still provide them in the promised quantity. This, in their view, has already been happening in the teaching profession, as a result both of the increase in the number of school-children and of "the rash promises" of better education for all. The general average over the whole educational terrain may not have fallen very greatly; but many young men and women are qualifying as teachers who would not have been acceptable before the war, the decline in standards of grammar-school teachers (with its serious implications for the next generation) has become notorious, and unqualified persons are being sought to assist in the control and instruction of over-large classes.

The preservation and improvement of medical standards in the interest of the public is one of our primary duties, and the fact that, mainly for economic reasons, our care of patients is now organised and financed by the State must not be allowed to lead to deterioration of these standards. Lewis and Maude draw attention to one way in which such deterioration might take place when they point out that, in the name of economy, a Government might refuse to adjust the remuneration of doctors to changes in the cost of living and in what can be earned in other occupations. Here we have the unhappy precedent of the recent and continuing deterioration of the medical Civil Service through failure to revise its salary scales; and if the same thing happened in the National Health Service we should eventually see doctors, like teachers, recruited from young men and women of inferior ability and attainments. This financial danger, however, can hardly be regarded as immediate; and we may also dismiss for the moment the possibility that the State will be foolish enough to cease its comparative generosity to the grammar schools of medicine—the teaching hospitals. If a warning parallel is to be drawn between the educational and medical professions, it is the employment of unqualified persons as ancillary school-teachers that seems most nearly comparable to developments in medicine. Indeed the proper use of ancillaries is a major issue on which doctors ought to be clearing their minds and forming a considered opinion.

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[1] *Lancet*, 1952, ii. 1265.

[2] Marshall, T. H. Citizenship and Social Class. London, 1950; p. 58.

It is easy to see that rapid expansion of a profession in response to State subsidy endangers both its quality and status: if the need to expand becomes an excuse for recruiting the second-rate, a vicious spiral is soon in operation. Hence for our own part we should endorse LEWIS and MAUDE's warning against this form of professional dilution or inflation; and it may be remembered that more than a year ago we suggested that the intake of medical students was already too high and should be re-examined.[3] The fact remains, however, that there is a vast amount of work to be done by somebody; and we do not share these authors' apparent objection to the other form of "dilution" which consists in employing people with lower qualifications to do a large proportion of it. Whereas they disapprove of the proposal to allow dental ancillaries to fill and scale children's teeth under the supervision of a dental surgeon, to us this seems a rational and economical way of meeting an admitted need while safeguarding the professional position of the qualified dentist.[4] If there are not enough dentists, or doctors, to do what is required of them, the choice before each profession is between (a) delegating some of its work to ancillaries and (b) enlarging its own membership. If, in choosing enlargement, it makes the mistake of opening its doors too wide, the result will inevitably be a lowering of standards and status; but no such harm need follow judicious delegation of work, which on the contrary can be a means whereby standards and status are maintained and enhanced. Actually, of course, doctors have long made steadily increasing use of ancillaries of every kind, from nurses to chiropodists, from speech therapists to psychiatric social workers; and there are those who feel that, whatever the advantages may have been in the past, the claims of some of these groups of technicians to be members of sister (rather than daughter) professions[5] have now begun to weaken the position of the qualified medical practitioner. SIR HENEAGE OGILVIE, for example, looks on the tendency with foreboding:

> "It is easy," he says, "to see how a ruthless Minister of Health, determined to reduce the cost of the service and to break the cartel of doctors, could set about to dilute labour. An optician would see all cases referred to ophthalmic outpatients, keeping only the unusual ones for the ophthalmologist. A nurse, given a course in the use of specula, could, with the help of a welfare worker, deal with two-thirds of the otolaryngological outpatients. A chiropodist with a box of Scholl's supports would lighten the work of the orthopædic surgeon at outpatients, and a plaster technician would do the same for him in the theatre. In general surgery the meticulous but tedious work of opening and closing wounds could be handed over to an unqualified assistant, allowing the surgeon to do twice as many operations in a session."[6]

Nor is this picture as fanciful as it may sound. We shall shortly be publishing an analysis of the activities of child-welfare clinics from which it is deduced that "the advisory work of the clinic medical officer might now be taken over by the health visitor"; we hear murmurs that much more of the work of radiologists could be just as well done by radiographers; and we see practitioners at experimental health centres provided with clerks to do their paper work and nurses to do their dressings and injections. Is this kind of dilution of medical labour really an insidious peril to the sound practice of medicine? Or is it merely a victory for common sense? Before it goes much further we shall all have to decide whether we approve or deplore it, whether we should welcome or resist it.

With so many different kinds of technician taking part in medicine "the distinction between work which requires and work which does not require a medical qualification is blurred," as FFRANGCON ROBERTS has remarked.[7] Yet it is still perfectly clear that the care of patients, with ultimate responsibility for them, is the function of a medical doctor, who alone is qualified to undertake it. Whatever help we may accept from ancillaries, the task falling on our profession is and must remain immense. There are some 50 million people in this island, all of whom should be equal in our eyes and every one of whom is entitled to expect, whenever he needs it, the attention and care not of an orderly or a laboratory assistant or a photographer but of a fully capable medical practitioner—that is to say a man or woman with courage, energy, understanding, and the wide knowledge required to enable his patients to gain rather than lose by advances in technique. A little knowledge is no less dangerous because its possessor deprecatingly describes himself as a G.P.; and one thing we must certainly resist is the tendency, by depriving him of clinical responsibility, to create an ignorant kind of practitioner who while retaining the title of doctor and the nominal charge of patients is really little more than a contact man prepared to make arrangements with hospitals and specialists. The interests of the public will be ill served by any change that prevents our profession from securing the ablest and most devoted of the young men and women who feel that they have a vocation either for practice or for the more technical side of medicine; and they will be equally ill served by our accepting entrants who are neither able nor devoted. But if in fact we reach the conclusion that the only practicable means of preserving good standards and conditions of work is a closer restriction of our intake of students, surely we must then accept the obvious alternative to more doctors—namely, more ancillaries. The further dilution of medical labour by ancillaries need not be damaging provided everyone acknowledges that the person who is in clinical charge of the patient at any given time, be he consultant or practitioner, is the leader of the team working for that patient—even if all the other members of the team are fellows of the Royal Society. And this position of leadership could scarcely be challenged except for one reason—that the doctor's calibre had been allowed to fall below what is necessary for discharging his supreme responsibility.

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[3] Lancet, 1951, ii, 331.
[4] Ibid, 1952, i, 649; 1952, ii, 814, 972.
[5] Ibid, 1951, i, 895.
[6] Ogilvie, W. H. Ibid, 1952, ii, 820.
[7] Roberts, F. Ibid, 1951, i, 678.

Thus, as happens so often in New Year reflections, we are brought back to ourselves. Though it may be more congenial to try to stop a technological tide from rising, or to put back a social clock, it is probably better in the end to concentrate on keeping, or setting, one's own house in order. The moralists—always so busy at this season—remind us that in the long run a man's status and influence depend on what he is and does; and if our profession proves itself able and willing to give people all the help they ought to get from doctors, it need have no fear of social tendencies or any other threat to its future.

Atelectasis Neonatorum

Prematurity accounts for a large proportion of neonatal deaths, and commonly the cause of death is failure of the respiration for one reason or another. The death of such infants is likely to cause particular distress to the parents, since it seems that prematurity is especially common among older women and those who have already had an abortion or stillbirth. The full-term infant, also, may fail to breathe after birth.

At birth the lungs of the mature infant are structurally not unlike those of an older person, in that the lung alveoli are lined by thin flattened epithelium and have a rich supply of capillaries; there is a considerable amount of elastic, and not much connective, tissue. In other words, the lungs are sufficiently developed to permit the easy exchange of gases as soon as respiration begins. The mature baby also has active reflexes, a responsive respiratory centre, and fairly strong thoracic muscles. Potter [1] believes that immaturity of the respiratory centre is probably never responsible for failure to breathe after birth; but the premature baby has a number of disadvantages whose degree depends on its age since conception. Firstly, the lungs are not only small in relation to its size, but poorly developed; many of the alveoli are lined by cubical epithelium, which forms a relatively solid barrier between any entering air and the inadequate number of capillaries in the alveolar walls. Secondly, the respiratory muscles are weak, and the infant may become exhausted by the efforts demanded of it. In both mature and premature babies respiratory failure often follows atelectasis. On an earlier page of this issue Dr. Donald and Dr. Lord discuss some of the factors responsible for this state of affairs, and describe methods they are pursuing to help the infant struggling for breath. Often asphyxia causes atelectasis, which may, in turn, lead to further asphyxia. Intra-uterine anoxia can initiate respiratory efforts by the fœtus which result in the inhalation of liquor amnii. This is probably not serious to the healthy full-term infant; and, in fact, it may be a normal, though not a regular, feature. In both man and animals movements of a respiratory type have been observed in utero [2]; and 'Thorotrast' injected into the amniotic sac has been identified some hours later deep in the lungs of the fœtus.[3] There is some evidence that these respiratory movements are more readily initiated in the early than in the late fœtus.[4] The healthy mature baby seems to absorb rapidly any amniotic fluid it may have inhaled. Both premature and anoxic infants, however, deal less effectively with such fluid. Anoxia may cause venous and capillary congestion which, particularly in the premature baby, readily leads to hæmorrhages and œdema; these, in turn, disorganise the responses of the central nervous system and prevent absorption of fluid from the lungs. In fact, the œdema will add to the fluid present in the alveoli and render the lungs still more rigid and inexpansible. Anoxia, œdema, and atelectasis form a vicious circle. Secondary atelectasis is more rare than the primary form. Leaving aside cerebral damage and congenital defects, it may follow the formation of hyaline membrane or pre-existing pneumonia. Owing to its elasticity the infant lung contains little residual air; and this may be reabsorbed just before death, giving rise to the appearance of atelectasis.

The obvious requirements for preventing unnecessary deaths due to atelectasis are the avoidance of prenatal or neonatal anoxia—or, failing this, rapid treatment. The simplest treatment is to keep the airways clear and provide oxygen and good nursing. For many infants this is enough; but others need more active help, and for this group Donald and Lord have devised a respirator. The first need, as always in rational treatment, is to determine normal requirements. Neonatal respiration has been investigated for many years, but it cannot be said that our information is yet satisfactory or complete. Donald and Lord describe a spirometer used to measure respiration in normal and premature infants. This is, in essence, a Krogh spirometer into which expired air passes through a simple non-return flap valve. When it is filled to a known extent an electrical device empties the float chamber, which returns to its resting position, and the filling process begins again. The movements of the float are recorded and calibrated. A rubber oxygen mask of United States army pattern, applied upside down, was found to fit the infant face satisfactorily. This apparatus is useful, not only for preliminary determination of normal behaviour, but also for assessing whether a baby needs assisted respiration, and for clarifying diagnosis—for example, to determine whether the respiratory difficulty is due to atelectasis or to the onset of pneumonia. These workers prefer a mask to a plethysmograph [5] since it involves less disturbance of an ill baby in its incubator; and the apparatus can be made cheaply and quickly. Additional information was obtained by means of radiography. The normal values were somewhat higher than those recorded by Cross,[5] whose figures are probably the most accurate yet obtained; for clinical reasons, Donald and Lord could not insist on absolute resting values. Regarding lung expansion, they observed full expansion within 30 minutes of birth. The respirator has been designed for cases in which atelectasis persists or develops secondarily. A Drinker-type apparatus did not prove wholly satisfactory for this purpose, owing to its relative functional inflexibility. Even in healthy premature babies respiration may be very irregular,[4,6] so that one of the dangers of artificial respiration is hyperventilation with consequent alkalosis. Furthermore, newborn infants vary widely in their rate of respiration.[4,5] These difficulties have been avoided by developing a machine that amplifies spontaneous respiratory efforts only. A photo-electric mechanism actuated by a light mirror attached to the flap of the inspiratory valves, is sensitive to the first 0·1–0·2 ml. of attempted respiration; it is effective with breaths too feeble to be measured by spirometer. Either negative or positive pressure, or both, can be applied to the body. With respirators of the plethysmographic type it has proved difficult to find an efficient method of sealing the neck or face from the body-chamber. Neck seals hitherto tried may cause "pistoning" of the whole child or, particularly if it cries or struggles, engorgement of the blood-vessels of the head and neck. Donald and Lord use a rapid-setting alginate which can be injected around the neck, or around the entire head and neck leaving only the face free. The mask is embedded in the alginate. They prefer to leave only the face free as "pistoning" is thus avoided, and should spirometry be needed readings are more likely to be accurate. The alginate can be easily broken and removed by the fingers. This method might be thought to restrict the sick and restless infant, but it appears to give satisfactory results. The alginate remains competent at pressures rather lower than −15–30 cm. water. With regard to safe pressures, Donald and Lord have seen no harm follow the use of −40 cm. water, and once they used −65 cm. with no evidence of pulmonary damage. This agrees with the finding of Smith and Chisholm[7] that mature, and even some premature, babies could exert negative pressures of 40–50 cm. water. It would seem undesirable to use pressure of this degree for more than a short time, and Donald and Lord have found that −15–30 cm. water is sufficient.

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[1] Potter, E. L. Pathology of the Fetus and the Newborn. Chicago, 1952.

[2] Barcroft, J. Researches on Prenatal Life. Springfield, Ill., 1948.

[3] Davis, M. E., Potter, E. *J. Amer. med. Ass.* 1946, 131, 1194.

[4] Smith, C. A. The Physiology of the Newborn Infant. Oxford, 1951.

[5] Cross, K. W. *J. Physiol.* 1949, 109, 459.

These workers follow the usual routine after the infant's birth, and they consider using the respirator only if atelectasis persists. Endotracheal intubation is avoided, especially in premature infants, and gastric oxygen is given instead if the baby needs assistance before it can be put in the respirator. Fortunately the newborn, and especially the premature, infant, seems to withstand pronounced oxygen lack; moreover, the tissues are thin so that a fair amount of oxygen passes into the blood from the stomach, and the hæmoglobin has a greater affinity for oxygen than that of the older baby or adult. This respirator overcomes the serious disability of weak musculature. In the feeble anoxic infant struggling for breath the diaphragm exerts a powerful downwards pull. If the cohering or blocked alveoli do not expand, the intrathoracic subatmospheric pressure is transmitted to the chest wall. This force may be considerable.[8] The soft ribs and weak intercostal muscles are sucked in, with resulting sternal retraction. This makes matters worse, since the pressure on the lungs still further obstructs the entry of air. When negative pressure is applied outside the chest, as in the respirator, sternal retraction is prevented and the subatmospheric intrathoracic pressure is applied where it is most needed—namely, to the lungs. Donald and Lord give a mixture of 50% oxygen and 50% nitrogen. The anoxic infant needs oxygen but not carbon dioxide, which is probably already at a high concentration in its blood. On the other hand, too high a concentration of oxygen is toxic and damages the pulmonary epithelium. Cross and Warner[9] found in infants, as did Dripps and Comroe[10] in adults, that 50–60% oxygen after a short initial depression of respiration stimulated ventilation. One obstacle to assured success is the formation of hyaline membrane. Little is known of the causes of this condition, which may supervene after a period of apparently normal breathing. At necropsy the appearance sometimes suggests that resorption of fluid has caused the deposition of granular material in an increasingly thick layer, which has blocked the alveolar ducts and obstructed the alveoli.[1] Potter[1] has the impression that the incidence of hyaline membrane has been reduced in the Chicago Lying-in Hospital since infants with signs of respiratory distress have been given oxygen in which the humidity is maintained at 90–95%.

Dr. Donald and Dr. Lord describe their account of the new respirator as an interim one; but already they can claim three cases, and perhaps a fourth, as successful results as far as saving life is concerned. They are, with some success, doing their best to treat results; but we greatly need more information about causes, so that fewer newborn infants will have to struggle against anoxia.

Carcinogenic Aromatic Amines

We have lately commented[11] on the research which is being undertaken into the subject of bladder papilloma and carcinoma as an industrial hazard in the chemical industry. Although this danger has been recognised for nearly sixty years, and much has been done to reduce the contact of the workers with noxious chemicals, the progress towards an explanation of the fundamental causes has been slow. The dog was the only species known to be susceptible to these tumours, so that an individual experiment required up to ten years for its completion; for a long time attempts to find a reason for the unusual localisation of the tumours in the bladder epithelium, while all other organs remained apparently normal, failed. It was, therefore, an important step when Bonser, Clayson, and Jull[12] found that the urine of dogs treated with β-naphthylamine contained a carcinogenic metabolite derived from this substance. This metabolite was a water-soluble orthohydroxyamine, 2-amino 1-naphthol, and its tumour-inducing properties were demonstrated by a new technique of implanting a pellet of the chemical suspended in wax into the mouse bladder.[13] A series of experiments has now confirmed that the metabolite is carcinogenic, whereas the parent amine

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6 Cross, K W , Oppé T E *Ibid* 1952, 116, 168
7 Smith, C A , Chisholm T C *J Pediat* 1938 20 338
8 Hermann L *Arch ges Physiol* 1879, 20, 365
9 Cross, K W , Warner, P *J Physiol* 1951, 114 283
10 Dripps R D Comroe J H *Amer J Physiol* 1947, 149, 277
11 *Lancet*, 1951 ii 300 *Ibid* 1952 ii, 73
12 Bonser, G M, Clayson D B Jull, J W *Ibid* 1951, ii 286
13 Jull, J W *Brit J Cancer*, 1951, 5, 328

not.[14] Moreover, an insight was gained into the metabolism of this substance in different species [12] —another important landmark in the chemical investigation of the disease. β-Naphthylamine is only one of a group of some twenty aromatic amines which have been tested for carcinogenic activity in recent years. Although there is no uniformity in the location of the tumours or in species susceptibility, these chemicals all tend to induce distant carcinomas at sites along the routes of excretion. The addition of new carcinogenic members to this group and the collection of more information about their mode of action may lead to the discovery of a common metabolic plan for a diverse, though related, series of compounds, some of which are used in industry.

Scott [15] has produced good evidence to show that the manufacture and handling of benzidine, another aromatic amine, involve a risk of carcinoma to the workmen. His extensive investigation confirms the findings of Billiard-Duchesne [16] and Désoille et al.,[17] and seems to put the carcinogenic action of benzidine beyond doubt. On the experimental side, Spitz et al.[18] had already shown that this chemical induced hepatic, intestinal, and acoustic-gland tumours in rats and (more doubtfully) bladder tumours in dogs. A chemical closely related in structure to benzidine is 4-aminodiphenyl, which has been shown by Walpole et al.[19] to be carcinogenic in the rat. It seems possible that this compound may have been present in distillation residues from aniline in dye factories, though it is probably not so today. In this experiment the commonest tumour was in the large bowel; of 14 rats which survived five hundred days, 7 had epithelial tumours of the large bowel, the exact nature of the growth being uncertain. It may be accepted, however, that the tumours varied in their degree of "progression," [20] and that the most advanced of them had probably reached early malignancy. Methylation is a well-known method of increasing carcinogenicity, and when methyl groups were substituted in both the benzene rings of 4-aminodiphenyl, giving 3 : 2′-dimethyl-4-aminodiphenyl, its carcinogenic power was much greater. Intestinal tumours were commoner and they developed earlier in both large and small intestines. Miller et al.[21] also found that another methylated diphenyl (N : N-dimethyl-4-aminodiphenyl) induced tumours in various organs (but not in the bowel) earlier and more often than 4-aminodiphenyl did in the later experiments of Walpole and his colleagues. The latter concluded that the effective carcinogen in all these cases was a metabolite of the particular amine being tested, and that in the rat these metabolites were excreted in the bile. They suggested that, by analogy with the work of Bonser et al.[12] and others, the effective metabolite is an orthohydroxyamine, and that when *o*-methyl or N : N-dimethyl substitution takes place, metabolic hydroxylation is "steered" into the ortho position relative to the amino group, and carcinogenicity is increased; but these interesting suggestions as yet lack experimental proof.

An American group,[22] led by the Millers, have investigated some aromatic amines and azo compounds in another way. They have done much work on fluorine substitution in various positions in the benzene-ring systems of these compounds. The effect of this substitution is to form a tight bond so that particular positions can be blocked, as it were, against metabolic activity. They concluded that the amino-azo dyes are carcinogenic to the extent that they are methylated in vivo and bound to the liver protein.

The metabolism of the aromatic amines in the widest sense lends itself well to organic chemical analysis; and it would be valuable at this exciting stage of the inquiry into their carcinogenic properties to try to forecast which compounds should most profitably be tested. Each amine requires months of careful study in at least two species (the dog and the rat or rabbit) before the final investigation of the carcinogenic power of its metabolites can be made. Nevertheless, remarkable progress has been made in a few years, and it is reasonable to hope that the problem will be solved before long. The knowledge thus gained may point the way to fruitful investigation of the metabolism of other types of compound. Doctors who see many patients with malignant disease every day are sometimes irritated by the reports of work on this carcinogen or that —work which seems to them to be far away from human disease. But research of this kind is essential to an understanding of the way in which the body is likely to react to carcinogens, and it therefore has an important place in the complete picture of malignant disease.

Annotations

"DISABILITIES"

Our series of articles, written by people disabled by disease or injury, have been widely read; and we may say—without taking credit to ourselves—no wonder. These writers, setting out to show how they have got the better of their handicaps, in great ways or small, unconsciously display so much courage, cunning, and humour that the collected pieces are a testimony to the human spirit. They have now appeared as a book,[23] which should, we think, appeal to laymen as well as doctors.

A CHALLENGE MET

Last summer Denmark was struck by an epidemic of poliomyelitis which was far more severe than any previous one in that country. Professor Lassen, whose account of his experience in Copenhagen during the past six months appears on a later page, is probably right in supposing that "nothing comparable has ever been seen in Europe." Between July 24 and Dec. 3, 866 cases with paralysis were admitted to Blegdam Hospital, Copenhagen; and 316 of these required special measures—such as tracheotomy, artificial respiration, postural drainage, or a combination of these. In four months the hospital dealt with three times as many cases with respiratory insufficiency, paralysis of the ninth, tenth, and twelfth cranial nerves, and involvement of the bulbar respiratory and vasomotor centres as in the preceding ten years

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[14] Bonser, G. M., Clayson, D. B., Jull, J. W., Pyrah, L. N. *Ibid* (in the press).

[15] Scott, T. S. *Brit. J. industr. Med.* 1952, 9, 127.

[16] Billiard-Duchesne, J. L. *Arch. Mal. prof.* 1948, 9, 109.

[17] Désoille, H., Hochfield, M., Aboulker, P. *Ibid*, p. 149.

[18] Spitz, S., Maguigan, W. H., Dobriner, K. *Cancer, N.Y.* 1950, 3, 789.

[19] Walpole, A. L., Williams, M. H. C., Roberts, D. C. *Brit. J. industr. Med.* 1952, 9, 255.

[20] Foulds, L. *J. R. micr. Soc.* 1950, 70, 173.

[21] Miller, E. C., Miller, J. A., Sandin, R. B., Brown, R. K. *Cancer Res.* 1949, 9, 504.

[22] Miller, E. C., Miller, J. A. *Ibid*, 1952, 12, 283. Miller, J. A., Miller, E. C., Sandin, R. B., Rusch, H. P. *Ibid.*

[23] Disabilities. London: The Lancet Ltd. 1952. Pp. 243. 10*s*. 6*d*. (postage 6*d*.).

With rare exceptions death in the acute phase of poliomyelitis is due to respiratory failure or embarrassment, either from involvement of the anterior-horn cells leading to impaired *movement of the diaphragm* and intercostal muscles or from damage to the bulbar area Since the introduction of Drinker's tank-type respirator in 1928, much attention has been given to developing similar but smaller machines, such as the cuirass type Intelligently used, these machines have tided over a crisis many patients who would otherwise have succumbed, less happily, they have created a tragic problem in the invalid who depends permanently on the respirator Respirators, however, will rarely help —and indeed are more likely to harm—patients with respiratory insufficiency from lesions of the lower group of cranial nerves The fatalistic attitude towards severe respiratory paralysis has been countered by the strong advocacy of tracheotomy by American workers, notably Bower [1] and Galloway [2] In Britain this method has only *occasionally* been *practised, though* Kelleher,[3] impressed by the American claims, made a plea for team-work to further its use On this side of the Atlantic, however, it has been left to Professor Lassen and his fellow-workers to apply on a large scale this method in conjunction with others

His figures show that the method has helped to reduce by more than half the mortality from bulbo spinal respiratory paralysis This improvement has been achieved largely by combining tracheotomy with positive-pressure respiration by manual compression of a rubber bag The use of such a device as an accessory to tank-type respirators is commonplace, but complete dependence on it is something new, originating perhaps in Denmark's shortage of mechanical respirators which, despite the ready help of neighbouring countries, have been far too few for all the cases By the Copenhagen scheme a closely fitting inflatable cuff tracheal tube is applied through a tracheotomy, and artificial respiration is maintained indefinitely (in some cases for more than three months) by manual rhythmical compression of the bag, at a rate of 16 to 30 per minute Additional measures—and notably tracheal suction—are applied as need arises 250 tracheotomies have been done in the 316 cases requiring special measures The results varied with the sex and age of the patients, being worst in men (56% mortality) and best in *children It is notable* that of 10 patients with spinal-type respiratory paralysis who were treated exclusively in tank-type respirators, all but 1 survived, which emphasises the value of such apparatus in selected cases Among 11 children treated by respirator and tracheotomy 45% died compared with 38% in a group of 74 children treated by tracheotomy and positive pressure (bag) ventilation

If, as seems possible, this technique marks an advance in the treatment of bulbo-spinal poliomyelitis, it represents a triumph for *enterprise* in the face of an overwhelming outbreak On the human side our Danish colleagues should be congratulated on mustering the large amount of skilled help that the new technique requires To compress a rubber bag at a constant rhythm will tire the most enthusiastic after an hour or two and the operator has also to keep a watchful eye for the restlessness or irritability that is the first token of oxygen lack, and which usually calls for tracheal suction Any who have visited Blegdam Hospital will attest *to the patience* and efficiency with which students are doing this work—and to the remarkable contentment of the patients

A SURGICAL INQUISITION

WOULD the standard of surgery in a particular hosp be raised if a *more searching assessment of the re* was made by independent observers? An experime has been carried out in the United States to see wheth it would [1] In a certain hospital a committee of 7, com posed of 5 general surgeons, an orthopædic surgeon, an a pathologist, held a monthly meeting to scrutin the results of the operations performed and to jud *their value In every large hospital* an unknown sma proportion of operations are performed which are lat proved to be unnecessary Perhaps the preoperativ clinical examination could have been more detailed perhaps the surgeon could have sought a second opinio with advantage, or perhaps further investigations coul have been profitably performed The object of th American committee was to correct these errors b analysing case histories in the light of the pathologic reports and the patient's ultimate condition

To begin with, the committee considered cases wh fell into one of six categories (1) operations involvin the reproductive organs, (2) appendicectomies, (3 operations after which the pathologist reported little o no pathological change in the organ removed, (4 operations which were followed by an abrupt change i the diagnosis, (5) emergency operations, and (6) al operations in which no tissue was removed—e g, uterin suspensions The committee were hard at it, for over month 100 cases came before *them, so each member too* on one of the categories If he had any criticism t make, the whole committee then discussed the particula case Not unexpectedly, each meeting lasted for fou hours or so It was not only the operating surgeons wh had to face this criticism, for the advice of the con sultants was also examined When the work of th *committee got going,* the *number of normal appendic* removed was greatly reduced in a few months Fo example, the records showed a considerable differenc between two surgeons Mr X took out few norma organs whereas Mr Y removed many, a word to Mr Y and his "normal" figures fell The committee though *that too many suspensions* of the uterus were bein performed, so rules were drawn up setting out th conditions that justified this operation A considerabl fall in the number of suspensions followed The wor of the committee is also said to have encouraged mor careful note taking and prompted a search for mor confirmatory evidence before deciding to operate

But there are better *ways of encouraging good work* Probably the best is to train the apprentice surgeon s well that he would never think of operating before h had sought all possible evidence The selection of me for senior surgical appointments is difficult enough o professional qualifications alone, but it should als include an estimate of the candidate's pertinacity i seeking such evidence and his thoroughness in weighing it, for the successful applicant must share the task o training the younger men Moreover, can we be certain that a committee *will judge correctly? Personal* considerations are certainly eliminated by identifying the case-reports by number only, but may not th committee, by laying down rules actually hinder progress or prevent the best being done for the patient? Must we accept the rigid belief that appendicectomy is only justified when pathological changes can be demon strated in the removed organ? Is it not possible that catarrhal appendicitis may resolve completely and th organ return to normal, as the pharyngeal tonsil does? Yet the patient may soon have another attack in whic the appendix may become obstructed and dangerous— not because it is altered structurally but because the immunity of its lymphoid tissue to bacterial attack is paired. If the history, symptoms, and signs strongly ggest an attack of acute appendicitis that has subded, then there are good grounds for removing the ppendix before it can do serious harm—and the decision ould be justified whether it showed pathological changes r not. It certainly seems preferable to concentrate on ethods of training the surgeon rather than to set up a ommittee to censure him after he has been appointed o a responsible position.

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[1] Bower A G *J Amer med Ass* 1949 141 6
[2] Galloway T C *Arch Otolaryng Chicago* 1947, 46 125
[3] Kelleher W H *Lancet* 1951 i 971

[1] Weinert H V, Brill R *J Amer med Ass* 1952 150 992

ALZHEIMER'S AND PICK'S DISEASE

It is easy to understand that gene mutations should cause mental defect or childhood dementia. It is perhaps more remarkable that they should also determine diseases with onset in late middle life. Yet Huntington's chorea, one of the three main types of presenile cerebral degeneration not caused by vascular disease, has long been known to be due to a dominant mutation. This condition is relatively uncommon; but the two other types, Pick's disease and Alzheimer's disease, together account for about one-tenth of all senile and presenile dementia. Individual pedigrees have suggested that Pick's disease and, less certainly, Alzheimer's disease are partly due to genetic factors, though these pedigrees do not show any simple mendelian pattern.

Sjögren and his colleagues [1] in Sweden have made a determined attempt to find out more about these two conditions. Their index cases were 18 patients with Pick's and 18 with Alzheimer's disease. In each of these the diagnosis had been confirmed by necropsy. The cases of Pick's disease showed the characteristic massive but circumscribed atrophy of the frontal and temporal lobes with ballooning of residual neurones and much reactive gliosis; the basal ganglia were rarely affected. The cases of Alzheimer's disease had a less intense but wider atrophy of the cerebral cortex with fibrillar degeneration of the remaining neurones and numerous senile plaques; changes in the basal ganglia were common. In some of these cases the affection was senile rather than presenile, but the average age of onset in each group was close to the 54th year. Clinically the patients with Pick's disease first developed amnesia and then progressive dementia. Those with Alzheimer's disease showed striking disorientation in space, even losing their way about their own homes. A characteristic finding in the patients with Alzheimer's disease was that nearly all showed an increase in muscle tone and an unsteady gait, but not the tremor and pulsion disturbances seen in parkinsonism. Sjögren and his associates regard this abnormality of tone as the best point on which to differentiate clinically the two types of dementia. Their patients with Alzheimer's disease, unlike many others reported, did not show hyperactivity, and most were predominantly apathetic.

In the family study of the two groups of 18 patients it was found impossible to distinguish between senile and presenile dementias among relations, since no necropsy reports were available. In each group 3 of the 36 parents had senile or presenile dementia, and in each group 1 sibling had such a dementia. The incidence of presenile and senile dementia together is estimated to be about 1% in Sweden, and so it seems probable that the frequency of dementias of this kind is increased in the near relations of patients with Pick's and Alzheimer's disease. Family studies of 44 patients in whom either Pick's or Alzheimer's disease was diagnosed clinically agreed closely with those based on the histologically proved index cases; and in the whole sample the risk of parents being affected was 10 ±4% for Alzheimer's disease and 19 ±5% for Pick's disease; the risks for brothers and sisters was 3·8 ±2·1% and 6·8 ±2·9%.

Professor Sjögren tentatively suggests that Pick's disease may be due to a dominant gene of incomplete penetrance, and that Alzheimer's disease is determined by multifactorial inheritance. The next step would seem to be to make post-mortem histological studies of the relations with dementia. One might find, for example, confirmation of Sjögren's hypothesis, in that relations of patients with Pick's disease had Pick's disease, while relations of those with Alzheimer's disease tended to have non-specific dementia with rather early onset.

A surprising feature of the investigation was that the great majority of the patients with Alzheimer's disease came from Gothenburg, while all but 3 of the patients with Pick's disease came from Stockholm.

A NEW KIND OF HOSPITAL FOR DIABETICS

Thanks to the enthusiasm of Dr. Elliott P. Joslin and his colleagues at Boston a new undertaking on behalf of diabetics is projected.[1] Though diabetic patients now live three times as long as their forerunners in the early part of the century, and though coma, tuberculosis, and gangrene are now seen in only about 1% of cases, the fact remains that after 15–20 years of diabetes few patients escape the serious complications of retinitis, neuritis, or nephropathy. Yet, as we have recently noted,[2] the team at the Joslin clinic are confident that if young and hopeful diabetics are taught properly how to manage their disease, such complications need never develop. Instruction of this detailed kind can only be given in hospital; but hospital costs are rising, in America as here. Fortunately the clinic has three funds at its disposal, administered by an advisory committee of which Dr. Joslin is chairman. One of these—the Diabetes Camp, Home and Hospital Fund—can appropriately be used, if supplemented from other sources, to build for this purpose a special hospital of which the running costs would be relatively small. The patients would not be bedfast: on the contrary they would presumably be fit and mobile, more like a class of college students than a group of sick people. Hence they would not need the ward care of nurses, but could very largely be left to their own devices. The hospital, then, could give them meals at a cafeteria, and provide them with "opportunities to do light housekeeping such as is the rule in boarding schools and colleges." Such a plan has long been advocated here, for patients who come to hospital for investigation rather than treatment, and who do not need bed rest or nursing care[3]; but it has not, as far as we know, been tried. The Boston experiment should therefore teach us a good deal.

Land for the new hospital site has been partly given, partly bought by the fund; plans are now being drawn up, and building is to begin this year. The hospital teaching clinic will be on the second floor, and the first floor will be let as consulting-rooms for doctors—an arrangement which should help to cover expenses. Lectures will be given in the adjacent Cancer Research Buildings; and research laboratories for diabetes are also near at hand. Not only diabetics but doctors, medical students, and nurses will be instructed in the prevention of the long-term complications of the disease. The existing fund is insufficient to cover the necessary outlay, but the advisory committee hope to receive enough gifts and subscriptions to meet costs as they arise, even though these are bound to be considerable. They say, simply and sincerely, "We cannot bear to see boys and girls rescued from coma live to have distressing complications later, ending in prolonged illness, suffering and death. If those who read the report saw as we the result of uncontrolled diabetes, the money for the Hospital Teaching Clinic would come soon."

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[1] Sjögren, T., Sjögren, H., Lindgren, A. C. H. *Acta psychiat. Kbh.* 1952, suppl. 82.

[1] Report on the Diabetic Fund, the Permanent Diabetic Fund, and the Diabetes Camp, Home and Hospital Fund. 1952. The Joslin Clinic, Boston, U.S.A.

[2] *Lancet*, 1952, ii, 1073.

[3] Lister, W. A. *Ibid*, 1945, ii, 757.

INFLUENZAL WOOD AND TREES

THOSE engaged in typing influenza viruses have long envied their colleagues concerned with similar problems among bacteria Thus, *salmonellæ* have a more three-hundred-odd serological types, while the pneumococcus and the diphtheria bacillus can boast little more than sixty Compared with these figures, the number of serological subtypes of the influenza-A viruses seems to the investigator as the sands of the sea It is with real gratitude, therefore, that he will turn to a recent account, by Dr George K Hirst,[1] of an attempt to introduce greater order into the serological study of these viruses

Conventional serological methods measure at the same time qualitative and quantitative differences in antigenic composition of influenza viruses Hirst has studied a large number of strains with virus-absorbed sera which indicate qualitative differences only Among influenza virus strains isolated between 1933 and 1947 Hirst finds six main type-specific antigenic components, though there are strong hints of more to come With one exception all the strains studied showed only one type specific component, along with a group specific antigen which is common to most of the strains and confers the influenza A characters The bewildering variety in the antigenic make up of the influenza viruses is accounted for by quantitative variations in these basic components

To those who are not serologically minded it will come as a relief that when the minutiæ of the trees have been explored we get a fascinating picture of the wood The general pattern which emerges is that one type specific antigen at a time is widely distributed throughout the world for a few years until it is replaced by a new antigen, which then dominates the scene for a few more years The occurrence of a new antigen is so rare in comparison with the large numbers of serologically similar strains which have been found during one epidemic period that we have no reasonable alternative to the view that mutation of the virus has occurred on a single occasion, followed by widespread dissemination of the new antigenic subtype The dominance of the new type and the disappearance of the older types is readily explained by widespread immunity to the latter Presumably, therefore, virus bearing a new antigen which is closely related serologically to its predecessors will appear less "virulent" than one which is distantly related

Studies with virus absorbed sera have been few because of the many technical difficulties Hirst's technique illuminates much that has been done by conventional serological methods, although it is unlikely to replace them in general use Like much of Hirst's previous work, this unspectacular study gives a sure enough foundation to bear the weight of much future speculation

CORTISONE IN PREGNANCY

THE effect of cortisone in pregnancy deserves special assessment, and the subject has had relatively little attention Pregnancy is associated with retention of water and sodium, and with an increased urinary output of corticoids[2], and both these changes indicate special activity in the mother's adrenal cortex The case of the patient who becomes pregnant while under treatment with cortisone raises the question of its effects on reproduction and gestation

In rabbits De Costa and Abelman[3] found that cortisone interfered with conception, when given in 15 mg doses daily for several days before mating, but it had little effect on conception when given after mating Preg does were given cortisone daily for various per throughout gestation, and only a third of th gave birth to live young In the rabbit, there cortisone seems to lower the chances of a success pregnancy

In women the effect of cortisone on menstruation variable, but a succession of normal menstrual cyc is common enough during treatment De Costa a Abelman described 5 cases in which cortisone was giv during pregnancy In 2 of these cases (rheumato arthritis and reactivated rheumatic fever) concepti took place during a long period of treatment wit cortisone, 1 woman aborted spontaneously two month after treatment was stopped, and in the second therapeutic abortion became necessary, in both cases the fœtus and placenta were normal In the 3 other pregnancies cortisone given in mid-gestation or later seemed to have no effect on the pregnancy, and live healthy babies were delivered Doerner et al,[4] in an attempt to influence rhesus sensitisation, gave cortisone to 2 women in the later months of pregnancy Neither showed untoward reactions, but there was no appreciable change in antibodies While the published evidence is somewhat scanty, it seems that cortisone is harmless in human pregnancy, at any rate when given after the sixteenth week Possibly cortisone causes a release of œstrogens, and it is known that œstrogens cause abortion in rabbits, but not in women

In conditions complicating pregnancy the possible effect of cortisone on the pregnancy may be a consideration secondary to its effect on the complicating disease In toxæmia the rôle of the adrenal gland is obscure, and it may be argued that the salt-retaining properties of cortisone could precipitate convulsions in a pre eclamptic patient Indeed, fatal convulsions, though rare, are not unknown during cortisone therapy[5] However, the beneficial effects of cortisone on the œdema of nephritis[6] encouraged Moore and his colleagues[7] to give cortisone to 8 patients with toxæmia in whom termination of pregnancy was indicated In all 8 there was considerable clinical improvement, and 7 of the women were delivered of live babies The results in this small series are hopeful, and provide another example of the versatility of cortisone in modifying symptoms Clearly, however, this drug should at present be used warily in early pregnancy—in hyperemesis, for instance

VACANCIES

BEFORE the late war we published each week a list of the vacant appointments for which applications were invited in our advertisement columns In 1940 these lists were discontinued so as to make space for other purposes, but we are now resuming their publication in a different and more useful form In the weekly summary, which in this issue appears on the last three pages of our text, the vacancies will be classified according to the nature of the appointment—e g, obstetrical psychiatric, or casualty In our advertisement columns which remain unchanged, the hospital appointments will, as before, be classified into senior and junior and then be arranged geographically The supplementary summary which is now to be provided should, however, make it far easier for readers to find the items in which they are interested The advantages of the existing classification will remain but the new and separate classification will, we hope, remove its disadvantages

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Special Articles

A PRELIMINARY REPORT ON HE 1952 EPIDEMIC OF POLIOMYELITIS IN COPENHAGEN

ITH SPECIAL REFERENCE TO THE TREATMENT OF ACUTE RESPIRATORY INSUFFICIENCY

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The 1952 epidemic of poliomyelitis in Greater Copenhagen has been the largest and most severe local epidemic ever recorded in Denmark.

ADMISSIONS

The metropolitan area of Copenhagen has a population of 1,200,000 people served by a single hospital for communicable diseases, the Blegdam Hospital. Between July 24 and Dec. 3 2722 patients with poliomyelitis were admitted to this hospital—866 with paralysis and 1856 without. In 316 of the 866 paralytic cases we had to resort to special measures, such as tracheotomy, artificial respiration, postural drainage, or combinations of these. The enormous load of severely ill patients is well illustrated by the fact that in four months we treated three times as many cases with respiratory insufficiency, paralysis of the ninth, tenth, and twelfth cranial nerves, and involvement of the bulbar respiratory and vasomotor centres as in the preceding ten years. At times we had 70 patients requiring artificial respiration, and we still have from 50 to 60 requiring it. To my knowledge nothing comparable has ever been seen in Europe.

The great number of severely ill patients pouring in made therapeutic improvisations necessary. During these months we have in fact been in a state of war, and at the beginning we were not nearly adequately equipped to meet an emergency of such vast proportions.

Fig. 1 shows that the epidemic culminated about Sept. 1. During the week Aug. 28–Sept. 3 our hospital admitted 335 patients or nearly 50 cases daily. The descending branch of the epidemic curve is, as usual, less steep than the ascending branch. At the time of writing, Dec. 7, the epidemic seems to be nearing its end. During the last two months the proportion of paralytic in relation to non-paralytic cases has grown steadily, but as a whole the ratio is 1 : 2. Naturally the number of patients admitted with non-paralytic poliomyelitis does not give an accurate picture of the true incidence of such cases in the epidemic area.

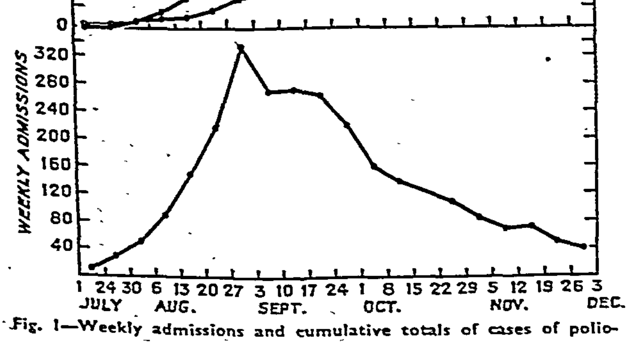

Fig. 1—Weekly admissions and cumulative totals of cases of poliomyelitis in 1952.

TREATMENT OF RESPIRATORY INSUFFICIENCY AND BULBAR DISEASE

In former years our therapeutic results in cases with respiratory insufficiency and involvement of the lower cranial nerves and the bulbar centres have always been very bad.

During the eleven years 1934–44 respirator treatment was used in 76 cases with a mean mortality-rate of 80%. Only cuirass respirators were used.

It is generally agreed that respiratory insufficiency of spinal origin is far easier to treat than respiratory insufficiency due to the involvement of the lower cranial nerves and the bulbar centres. Table I shows clearly the extremely grave prognosis of the pure bulbar and combined forms of respiratory insufficiency. With very few exceptions all our patients belonging to these groups died.

In 1948 we started using tracheotomy in all cases where it proved impossible to maintain an open airway because of pooling of secretions and aspiration into the lungs. In the U.S.A. this procedure seems to have had a beneficial influence on prognosis. In our hands this has not been so.

TABLE I—RESULTS OF RESPIRATOR TREATMENT OF POLIOMYELITIS 1934–44

Type of disease	No. of cases	No. of deaths
Respiratory paralysis without bulbar involvement	17	5 (*29%*)
Respiratory paralysis with bulbar involvement	51	48 (*94%*)
Respiratory paralysis of undetermined type	8	8 (*100%*)

Table II shows that all the patients treated by tracheotomy and with respirators died, whereas treatment with respirators alone had a somewhat better prognosis, 1 man and 4 children surviving. Of these 5 patients 4 had respiratory insufficiency of purely spinal origin, and 1 patient had transient slight impairment of swallowing.

Thus the prognosis of poliomyelitis with respiratory insufficiency was rather gloomy at the outbreak of the present epidemic in Copenhagen. At our disposal we had one tank respirator (Emerson) and six cuirass respirators. This equipment proved wholly insufficient when the epidemic developed into a major catastrophe.

Fig. 2 shows the admission dates of the 316 poliomyelitis patients requiring special treatment—i.e., tracheotomy, artificial respiration, postural drainage, and combinations of these forms of treatment. The chart exclusively comprises patients with respiratory insufficiency, paralysis of the lower cranial nerves, the respiratory or vasomotor bulbar centres or combinations of these forms of paralysis. During the epidemic tracheotomy was performed in about 250 cases. The indication for this operation was invariably stagnation of secretions in the upper airway, leading to inadequate ventilation. By far the greater number of the patients had simultaneously paralysis of the respiratory muscles. The 316 cases did not all come from the metropolitan area, because in recent years we have done much to centralise the treatment of such patients. Consequently fig. 2 includes 75 cases brought in from localities outside our usual area. These admissions account for the three peaks of the curve.

Until the last week of August we used the therapeutic methods practised in 1948–50, but during these terrible weeks the situation became increasingly critical. The

TABLE II—RESULTS OF TREATMENT OF RESPIRATORY PARALYSIS 1948–50

Treatment	Poliomyelitis						Polyradiculitis	
	Men		Women		Children		No	died
	No	Died	No	Died	No	Died		
Tracheotomy and respirator	9	9	4	4	1	1	3	3
Respirator exclusively	6	5	3	3	6	2	2	2

first month of the epidemic brought us 31 patients with respiratory paralysis and/or pharyngeal or laryngeal paralysis Of these 27 died, 19 within three days of admission The mortality rate was thus 85–90% At this point we consulted our anæsthetist colleague, Dr B Ibsen, and on Aug 27 the first patient was treated with the method which soon became our method of choice in patients with impairment of swallowing and reduced ventilation—namely, tracheotomy just below the larynx, with insertion of a rubber cuff-tube into the trachea, and manual positive-pressure ventilation from a rubber bag (bag ventilation)

The main features of the method are

(1) High tracheotomy with excision of a square opening in the anterior wall of the trachea

(2) Insertion of the widest possible rubber tube furnished with an inflatable cuff, so that the cuff closes the trachea, effectively preventing aspiration of stomach contents and secretions from the hypopharynx

(3) Repeated suction of the trachea and the main bronchi, and eventually repeated bronchoscopy, which is easy to do through the tracheotomy opening

(4) Postural drainage, frequent changing of position, and squeezing of the thorax, followed by aspiration through the cuff tube to avoid accumulation of secretions, bronchial plugging, and atelectasis

(5) Positive pressure ventilation (bag ventilation) with insufflation of a mixture of 50% oxygen and 50% nitrogen

Tracheotomy as early as possible is indicated in every patient in whom postural drainage and frequent suction cannot maintain an unobstructed airway and normal ventilation—i e, normal blood values of O_2 and CO_2 Most of these 316 patients had pooling of secretions in the hypopharynx and trachea, and a large majority were at the same time unable to cough or to swallow, and ventilation was inadequate

Quite a large number concurrently presented symptoms conventionally thought to be due to involvement of the bulbar centres Numerous biochemical tests have taught us that it is well nigh impossible to distinguish symptoms *usually attributed to the bulbar centres* from symptoms caused by retention of carbon dioxide, hypoxia, and shock

When manifest hypoxia and/or retention of carbon dioxide is present, eventually in combination with latent or clinical shock, prognosis becomes distinctly worse

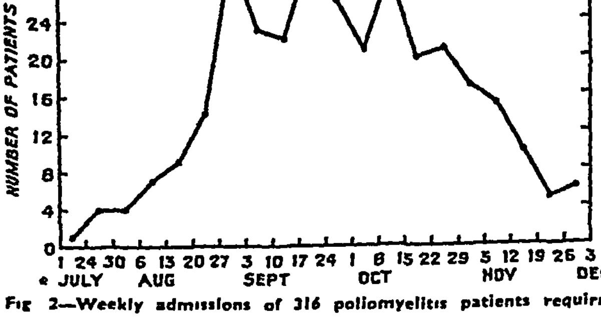

Fig 2—Weekly admissions of 316 poliomyelitis patients requiring special treatment

Early tracheotomy is therefore of decisive importa because hypoxia, retention of carbon dioxide, a vasomotor shock, even of short duration, may hav disastrous effect on nerve cells already damaged b virus infection

The first step of the operation is tracheal intubati through the mouth, thereby securing effective aspirati from the upper airway during the surgical interven and adequate insufflation of oxygen In our cases w have always used cyclopropane If this anæsthetic i not at hand, ether can be recommended Intraveno barbiturates should never be given as an anæsthe and sedatives should not be used, even in irratio and apprehensive patients, before adequate ventilati is secured *After this has been established, sedative* may be beneficial

The operation is done at the highest possible level, with excision of a square opening in the trachea If time permits, a suction catheter is introduced into the trachea and the main bronchi, and aspiration is begun during intermittent manual squeezing and pounding of the thorax to loosen secretions causing plugging and atelectasis of the lungs After this a rubber cuff tube is inserted and the cuff inflated to prevent aspiration of secretions from above At the same time the intubation tube is withdrawn It is important to use a cuff tube with the widest possible inner diameter and to secure the tube so that it does not slide down beyond the

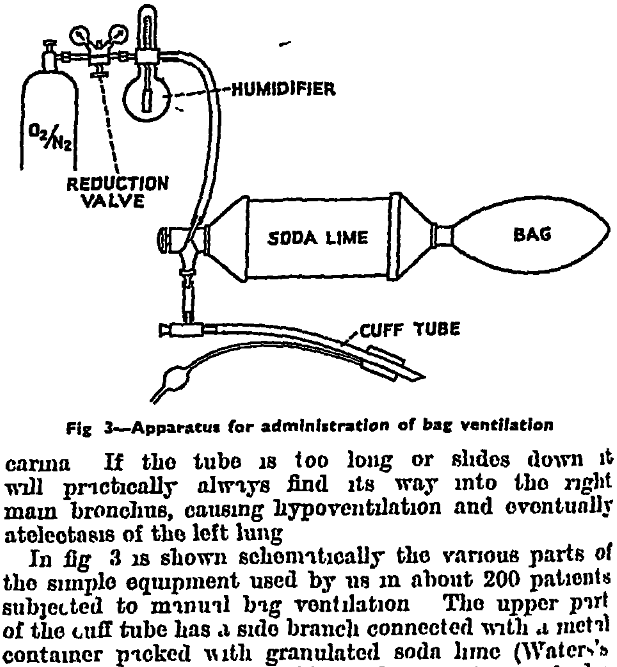

Fig 3—Apparatus for administration of bag ventilation

carina If the tube is too long or slides down it will practically always find its way into the right main bronchus, causing hypoventilation and eventually atelectasis of the left lung

In fig 3 is shown schematically the various parts of the simple equipment used by us in about 200 patients subjected to manual bag ventilation The upper part of the cuff tube has a side branch connected with a metal container packed with granulated soda lime (Waters's canister), from which a rubber tube goes to a cylinder containing equal parts of compressed oxygen and nitrogen A rubber bag is attached to one end of the canister, *and a valve at the other end permits regulation* of the pressure in the system The cuff tube is closed with a rubber stopper If aspiration is needed, the stopper is removed and a Tiemann's catheter is introduced mounted on a jet suctioning apparatus We have mostly used the ejector effect of a cylinder of compressed air, which is very effective and independent of electric power A good humidifier is essential otherwise incrustation of secretions may occur

The canister should be filled evenly with granulated soda lime of the best available quality to avoid insufflation of particles of soda lime into the upper airway causing irritation and increased secretion The canister must therefore be aired thoroughly by blowing a strong current of air through the container before it is used found American soda lime (Wilson) the most suitable the purpose. Unfortunately it is rather expensive, ting about 30s. daily for each patient.

If the precautions mentioned are followed, no ill effects observed. It is necessary to have two canisters for ch patient, and to change them every half hour. ter five hours' use the contents must be changed.

As will be seen from fig. 3, it is a closed to-and-fro stem similar to the one used in modern machines for neral anæsthesia, where carbon dioxide is effectively moved and an adequate supply of oxygen is secured hen the flow-meter registers 5–10 litres per minute. he bag is compressed from sixteen to thirty times per inute according to the patient's condition and age. he amount of oxygen mixture that should be given at ach compression of the bag depends on the thoracic xcursions and the general condition of the patient. The insufflation pressure must be short, and it is essential o release the pressure completely during expiration, so hat the least possible resistance to the passive elastic deflation of the lungs is maintained—i.e., atmospheric pressure. Expiration should therefore be twice as long as the insufflation. This is very important for reasons explained below. At all times the bag should only be partly full of gas. This can be regulated through the flow-meter and the valve at the top of the canister. We have several times measured the insufflation pressure when bag ventilation is administered correctly. It amounts to 20–30 cm. water. But the insufflation phase must be short.

The stomach should be emptied just after the operation, and in many cases it is advisable to insert an indwelling stomach-tube with continuous suction to avoid vomiting. Many of our patients had atonia of the stomach and paralytic ileus.

ADVANTAGES AND DISADVANTAGES OF BAG VENTILATION

Advantages

These are many and in our opinion far outweigh the disadvantages of the method:

(1) The equipment is easily procurable and inexpensive and needs no electric power.

(2) It is especially well suited for emergency treatment of patients before transportation to a treatment centre.

(3) Bag ventilation when correctly administered is superior to all other methods of artificial respiration in securing adequate ventilation. It counteracts the development of œdema of the lungs.

(4) The well-inflated cuff tube makes aspiration of secretions from the hypopharynx impossible.

(5) Aspiration through a catheter or a bronchoscope is easily done and with a minimum of discomfort to the patient.

(6) The respiratory excursions of the thorax produced are readily observable, and the recognition of atelectasis, pneumonia, and lung œdema by direct inspection, palpation, and stethoscopy is easy. X-ray pictures can be taken whenever necessary.

(7) The patient's position can be easily changed, and the thorax can be squeezed to facilitate effective aspiration through the cuff tube.

(8) Insufflation-rates and the volume of air pressed into the lungs by each compression of the bag can be adjusted for each patient. This is especially important when the patient is regaining spontaneous respiration, because at this stage it is possible to follow the often irregular respiratory efforts, assisting spontaneous movements by gently squeezing the bag or, later on, assisting the patient at every second, third, or fourth respiration.

(9) General nursing is greatly facilitated, as are injections, the taking of blood samples, and physiotherapy (hot packs) of peripheral paralysis and counteracting of contractions.

(10) The method has great psychological advantages. The patient is not encased in a cask, the notorious iron lung, with its collar either too tight or too loose to maintain the necessary intra-tank pressures. There is no danger of friction sores, which are so common when the cuirass respirator is used. All the members of the staff and the many visiting colleagues have been greatly impressed by the look of our patients receiving bag ventilation, by their calm, their apparent confidence, and total lack of apprehensiveness. The beneficial psychological influence of the person assisting the patient is often very great; it helps to keep up morale, creating confidence because the patient feels that somebody he knows well is always around, ready to help. This psychological assistance is especially important when the patient is regaining spontaneous respiration, and shortens the often difficult weaning period.

In our experience this new form of positive-pressure ventilation (bag ventilation) can be used continuously for months, at all times maintaining normal oxygen and carbon dioxide levels in the arterial blood. We have used it on some of our patients for more than three months. As the majority of poliomyelitis patients with respiratory insufficiency who do not die in the acute phase of the disease regain within three months sufficient spontaneous respiration to maintain adequate ventilation, it has in many instances been possible totally to avoid the use of mechanical respirators. This we consider a great advantage.

Disadvantages

The method has the following disadvantages:

(1) Particles of soda lime may be carried down into the bronchi and alveoli.

(2) When bag ventilation is administered continuously for weeks, there is a risk of emphysema.

(3) If bag ventilation is not administered correctly, the venous return may be reduced, leading to lowered cardiac output and a state of shock.

(4) Hyperventilation with subnormal carbon dioxide values may occur.

(5) The weaning period from positive-pressure ventilation is not infrequently difficult.

(6) The assistance of well-trained personnel all round the clock is essential and costly.

Provided the best available preparation of soda lime is used, and the canister is packed carefully and thoroughly aired before being used, the danger that particles may be carried down into the lungs seems to be more theoretical than practical. Nevertheless I am aware of the desirability of completely avoiding the use of absorbers and consequently we have experimented with different kinds of valves separating the ingoing and outgoing flow of air, and at the same time securing atmospheric pressure in the lungs during the major part of the respiratory cycle, thus hindering the venous return as little as possible. So far two types of valves seem satisfactory, having been in continuous use for long periods of time. Yet these valves are still in the experimental stage.

Potential dangers 2–4 may become manifest if bag ventilation is not administered correctly—i.e., the insufflation phase must be short. Danger 5 also depends on how the positive-pressure ventilation is done. In the hands of competent persons, well instructed in the inherent psychological aspects as well as in the technique of the method, difficulties in the weaning period can be greatly reduced.

As regards the expense of trained personnel, mechanical respirators also are very expensive—and, parenthetically, it is not at all certain which type should be preferred in the acute stage. Tank respirators of the newest American design equipped with positive intratracheal pressure attachment are hardly more effective in the acute decisive phase of poliomyelitis than the simple method used by us.

During several weeks we had 40–70 patients in our hospital requiring continuous or intermittent bag ventilation. To do this we have employed about 200 medical students daily. Their pay has been about 30s. for eight hours. The daily cost of the gas mixture per patient is about the same.

In the acute phase of bulbocerebral poliomyelitis several competing factors are involved, often difficult to diagnose and difficult to keep apart: these are virus disease of the central nervous system, hypoxia, retention of carbon dioxide, and vasomotor shock In most cases more than one of these syndromes are present, the patients presenting a mixed clinical picture Only careful clinical observation, supplemented by various biochemical tests, can guide us through this jungle of diagnostic difficulties and lead to a rational therapy

RESULTS

The poliomyelitis epidemic in *Copenhagen is only now* nearing its end Obviously it is therefore at the time of writing possible to give only *a brief account* of the therapeutic results

The first patient subjected to tracheotomy with insertion of a cuff tube in the *trachea and manual* insufflation of 50% *oxygen was treated on Aug 27 The method soon became our method of choice in all* cases with impairment of swallowing, pooling of secretions in the upper airway, and respiratory insufficiency This dangerous combination of symptoms occurred with unprecedented frequency and was present in the great majority of the 316 patients requiring the special forms of treatment previously mentioned

The point of reference is Dec 6, and the material presented comprises all patients admitted up to Nov 6 Some patients (31) admitted after this date are thus not included, but, as nearly all the deaths take place during the first few weeks of poliomyelitis, it is important to have at least a month's observation

The material includes five different types of treatment, all reasonably well defined, but it is only fair to emphasise that the patients treated with tracheotomy and bag ventilation included all those who were most severely ill

The five types and their therapeutic indications are

(1) *Tracheotomy and bag ventilation* —Pooling of secretions in the upper airway, impairment of deglutition, and insufficient ventilation

(2) *Tracheotomy and mechanical respirator* —Hypopharynx not entirely free from secretion, swallowing normal, and ventilation insufficient

(3) *Tracheotomy, eventually in combination with postural drainage and stomach tube* —Pooling of secretions in the upper airway, impairment of swallowing, and adequate ventilation

(4) *Mechanical respirator* —Respiratory insufficiency of purely spinal origin

(5) *Postural drainage and stomach tube* —Impairment of swallowing, without respiratory insufficiency

From the beginning of the epidemic up to and including Aug 25, 31 cases (group I) required special treatment as outlined above From Aug 26 to Nov 6, 250 such patients came into our hospital These patients are divided into five consecutive groups (II–VI), each comprising 50 cases in chronological order The composition of these groups regarding sex and age is very nearly equal

Table III shows that the mortality rate for these 250 patients, of whom the great majority were treated by tracheotomy and bag ventilation, was reduced from over 80% to about 40% representing about *100 lives* We are quite convinced that by far the greater part of these patients were saved by early tracheotomy combined with bag ventilation, and *further, that no mechanical respirator* could have taken the place of the bag ventilation with equally good results

TABLE III—MORTALITY-RATES

Group	Period of admission	No of cases	Died	Died within three days
I	July 21–Aug 25	31	27 (87%)	19 (70%)
II	Aug 26–Sept 8	50	26 (52%)	7 (27%)
III	Sept 8–Sept 27	50	24 (48%)	8 (33%)
IV	Sept 28–Oct 5	50	19 (38%)	10 (53%)
V	Oct 6–Oct 21	50	13 (26%)	7 (54%)
VI	Oct 21–Nov 6	50	18 (36%)	10 (55%)
Total II–VI		250	100 (40%)	42 (42%)

The table also shows a continuous drop in mortal rate, from group II to group V, from 52 to 26% Th probably is due to the fact that it naturally took s time before the treatment including adequate instruct of the hundreds of medical students employed—ab 1000 altogether—could be organised so that the b ventilation was correctly administered

Obviously it also took some time to learn the m effective ways of combating pulmonary complicatio and vasomotor shock Observing the decreasing mortality rate during the course of the epidemic, we naturall searched for evidence of decreasing severity of th bulbar cases but could not find any, a clinical impressi which is supported by the somewhat higher mortality rate in group VI The steadily increasing percentage of patients dying before the third day after admissio points the same way. During the month after Nov 6 we *treated 31 patients, who at a later date will be included in this series, with a death rate of 23% up to Dec*

The mean mortality-rate for 150 consecutive patients *(table IV)* treated by tracheotomy and bag ventilation was 47% However, *comparing the three groups shows a tendency towards lower mortality rates*—40%

TABLE IV—THREE GROUPS OF PATIENTS IN CHRONOLOGICAL ORDER TREATED BY TRACHEOTOMY AND BAG VENTILATION

Group	No of patients				No died			
	Male adults	Female adults	Children	Total	Male adults	Female adults	Children	Total
I	17	15	18	50	15	6	10	31 (62%)
II	17	14	19	50	8	5	7	20 (40%)
III	12	12	26	50	6	5	8	19 (38%)
Total	46	41	63	150	29	16	25	70 (47%)

The following data refer solely to the 250 patients *admitted between Aug 26 and Nov 6 after* the introduction of bag ventilation

Of 55 men treated by tracheotomy and bag ventilation 31 (56%) died, *of 43 women* 17 (40%) died, and of 74 children 29 (38%) died The mortality-rate for males thus seems greater than for women and children This is in accordance with our clinical impression that more men than women and children were critically ill, but a great proportion of the patients treated by tracheotomy and bag ventilation were in a very bad state on admission

Only 11 patients were treated by tracheotomy and respirator from the time of the operation Of these 5 died, all of them children

By tracheotomy alone, or in some cases combined with postural drainage and continuous suction through a stomach tube, 33 patients were treated—2 men, 5 women, and 26 children Only 1 of the adults died, whereas 9 children died, in most cases probably owing to severe encephalitis, which seems to have been rather common among the children this year *10 patients* were exclusively treated in respirators None of these patients had impairment of swallowing, and their respiratory insufficiency *was purely spinal* With 1 *exception* all survived Finally 20 patients with impairment of deglutition only and with pooling of secretions in the upper airway but with adequate ventilation were treated by postural drainage and with an indwelling stomach tube They all survived *5 patients* were moribund on admission and died before treatment could be instituted

CONCLUSIONS

I do not think that this method is ideal It certainly needs to be perfected, and we are working at improving it However, in comparison with results formerly obtained in our hospital, it seems fair to regard the results as satisfactory in the circumstances

It should emphasise that the results of treatment of spiratory insufficiency and paralysis of the lower cranial rves in poliomyelitis have been favourably influenced early tracheotomy, with insertion of a tightly fitting bber cuff tube ; repeated aspiration and bronchoscopy ; ostural drainage and stomach-tube ; and bag ventilaon. In our hands this method has reduced the ortality-rate from above 80 to about 40%.

Parliament

Economies in Hospital Staffing

IN the House of Commons on Dec. 19, on the motion for the adjournment for the Christmas recess, Mr. ARTHUR BLENKINSOP called attention to a circular[1] recently sent by the Ministry of Health to hospital boards with regard to economy in man-power. The Opposition, he said, would certainly seek the earliest opportunity of raising the matter much more fully.

The circular would embitter relations between management committees and regional boards. There was no doubt that the proposals in it would affect most unfairly the position of one hospital as against another. The Opposition had no objection to a comprehensive review of hospital staffs ; indeed, that had been going on for some years, and a great deal of progress had been made : but the circular provided for an immediate return of all existing hospital staffs, and for what amounted to a freezing at that wholly arbitrary figure.

Mr. Blenkinsop said that by the operation of this circular hospital management committees were being stripped of some of the last vestiges of their authority. This would cause many who had given most valuable voluntary service to doubt whether they could usefully continue their work. Did this proposal mean that the Ministry was in process of disbanding these committees ? In any case, matters within the competence of the committees would now be transferred to the regional boards, and matters within the competence of the boards would now be subject to the decision of the Ministry. The Ministry was the last authority which should have the power of dealing with these detailed administrative questions. Mr. Blenkinsop had no objection to the fixing of an agreed establishment figure beyond which the staff could not be increased without authority ; but the Ministry was taking an arbitrary figure. Why had it given up the view that proper establishments should be worked out and agreed on, and that these should be made compulsory, if necessary, subject to review by higher authority ? This day-to-day review of a whole host of cases would block up the whole machinery. The regional boards were saying that they would need more staff to provide the information for which the Ministry was asking. There was bound to be delay in this procedure, which might mean the loss of people best qualified for the jobs.

Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the planned programme for dealing with the staffing of the hospital service had been going on for some time. It was essential that progress should be made in this matter, particularly in view of the disparity between the staffing of hospitals. This circular would speed up the process and show where the gaps existed. Far from making the position worse, it would make it better because the staff would be obtained where they were most needed. The Minister had made it quite plain that it was his intention to allow shortages of staff to be made up. Of 435 regional boards, boards of governors, and management committees, 264 had now been visited ; in 180 cases establishments had been determined for administrative and clerical staff, and in all these there had been no engagement of extra staff without previous consent. The Opposition ignored the disparity of staffing. In one of the teaching hospitals there were 102 on the nursing and midwifery staff to every 100 staffed beds : in the average general hospital there were 53 nurses and midwives to every 100 staffed beds ; and in the mental hospitals there were 15 on the nursing staff to every 100.

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[1] See *Lancet*, 1952, ii, 1168, 1175.

In England Now

A Running Commentary by Peripatetic Correspondents

OUR tea club is an old and respected institution. The tea is manufactured from two vast kettles in a picturesque array of teapots in a subterranean cavern in the basement, and is distributed by safe hand on trays to the parched occupants of the periphery of the building. It is our experience, however, that the safer the hand the slower the feet, and by the time the third storey is reached not a few of the original calories have escaped into the circumambient atmosphere. Further, during the vicissitudes of the journey the destination of the cups, originally crystal clear, becomes sullied with uncertainty, so that the member at the end of the round never knows whether he is to receive a cup bearing the inscription "Lab. 5," "Cleaners," or, more simply, "Peggy." The other day we were interested to find ourselves drinking out of a cup with the stark label "Rat linseed."

In 1939 the iron hand of war reached down into our basement and dealt the tea club a blow from which it has never fully recovered. Even now the sugar gives out towards the middle of the third week of the ration period, and those of us who are accustomed to protect our livers from the effects of tannic-acid absorption by the judicious ingestion of sucrose spend an unhappy few days. Our genial and courteous Animal Man is occasionally in a position to alleviate our distress by impounding—without their knowledge or permission—some of the monkeys' sugar. During the Black Days he frequently brings in a lump with the comforting assurance : "It's all right, sir, they'll never miss it."

In the circumstances, however, it is not surprising that there should be mutterings among those who are not placed so fortunately adjacent to the animal house, and a splinter group has actually been formed to drink illicit coffee. They post lookouts in the corridors, and their source of carbohydrate is a jealously guarded secret, but it is suspected that much is due to their foresight in coöpting a visiting American. Once a week we have a departmental tea-party, at which both the orthodox and the seceders partake of cake ; and our conscientious accountant has worked out the fraction of the tea-club subscription which non-members have to pay to qualify for two slices. Even so, unscrupulous dissenters have been observed lingering behind after the party is over to pick up a few crumbs which they have not paid for. Feeling runs high, especially as it has recently been found necessary to raise the subscription, and it is felt that a stand should be taken on the matter. Since the recent cold spell, however, we have lost our confidence that a stand would be successful, for there are indications of disunity in the highest places. Twice in one week our President-Secretary-Treasurer has been discovered guiltily drinking 'Bovril.'

* * *

The African Dingaka Association, composed of witch-doctors from the Union of South Africa with delegates from Rhodesia, Swaziland, Bechuanaland, and Basutoland, has been holding a convention, five hundred strong, in Pretoria. The medicine-men turned out in full ceremonial rig, with head-dresses of beads and feathers, jingling bracelets, and ear-rings, and their garments decorated with bones, shells, and beer-bottle tops. Their president, Lukus Somo, said they had gathered to reaffirm their faith in the traditional methods of their ancestors, and in order to obtain government recognition of their claim to official status. They take a dim view of non-members who practise their profession, and dub them "quacks and illiterates." They have voted £10,000 to start a medical school in Johannesburg at which students of their craft may be trained in genuine witch-doctoring and herbalism.

The South African Government has recently banned the advertising of magic remedies, made from insects, reptiles, and "human ingredients" and guaranteed effective against evil spirits, witchcraft, and supernatural forces. Anyone advertising *muti*, as this sort of medicine is called, may be fined £50 and sent to gaol for six months. The Dingaka Association want this ban removed for genuine practitioners, but they do not explain why they still use this type of remedy, nor how they obtain the "human ingredients"

* * *

"Next please," said the porter John, who had been holding a magazine upside down, rose to his feet, pulled his jacket down, straightened his tie, arranged his handkerchief smoothed his hair, straightened his tie again "Come along, sir," said the porter, "he's waiting" That did it Our *restraint vanished* and we crowded round the door "Is he in a good *mood*? Has he ploughed many? Has he had his afternoon tea?" The porter smiled enigmatically and John was led into the outer darkness We gathered round the table

"Wasn't long with the last one"
"Never is if you're good"
"Long ones are for the doubtful"
"I hate being at the end of the alphabet"
"At least you know what he *asked in the morning*"
"That's the trouble Do you know what he *asked yesterday*? What dose of neostigmine would you use in a myasthenic crisis?"

There was a silence "What *is* the *dose*?" said a strangled voice They say that books should never be brought to an oral examination, but somehow they always seem to appear Glances were cast uneasily in their direction and there was a soft shuffling of feet Suddenly panic seized us, books were flung open, leaves turned, pages sought "Neostigmine 'stigmine," voices intoned in a pagan chant

"Here it is," cried Smith "Neostigmine 0 5 to 1 mg in a 1 2000 solution given intramuscularly The methylsulphate should be used" There was an ominous *silence* "How could anyone remember a dose like that," said Smith at last "It's impossible" "Don't worry He won't pip you on a thing like that You never get pipped on doses" George spoke with authority—this was his third attempt We cheered up

"What about yesterday?" said Smith
"Well," I said coldly, "what about yesterday?"
"He asked Jones the dose of aloin Jones said 5 grains" Smith's voice became a broad impersonation "'With that dose, Mr Jones, the only thing you would fail to pass would be this examination'"

The door opened "Next please" I stood up, straightened my tie, adjusted my handkerchief, smoothed my hair "Come along, sir," said the porter, "he's waiting"

* * *

I have never really forgiven medical *advertisers for* making me buy my *own stamps*, *now they* are all licensees who only pay for returns But their annual bounty in the form of diaries and calendars deserves at least a word of thanks Perhaps they would take it in the form of a few kindly hints

First, don't call me madam, that is no way to address an old rugger blue And you haven't heard of the fellowship I got ten years ago I don't think much of your blotting-paper either One sneeze and it is lodged irretrievably behind the mantelpiece Larger and double-sided, please I'm far too busy *to notice* which side I'm using Nor am I impressed by Continental-looking reprints—e g, *Hodenschmerz on* "Nips for Neurotics" True the language is English, but the typeface is that of the *Zeitschrift fur Bunkwissenschaft* And please make it snappy Do you expect me to read a page or more of single-spaced typing with no headings? And you medical publishers, why so sheepish about the price of your wares? They are far too dear, anyway, and it's the same old wolf whether you say "Price £5," "This costs £5," "This is priced at £5," "This is to be had for £5," or "This sells at £5" (Liars! You know as well as I do that doctors stopped buying books years ago!)

* * *

C G P

O fledgeling college, steered to birth
By Willink slaves and J H Hunt,
Let's hope that you may prove your worth
And earn an R in front

Letters to the Editor

FATAL APPENDICITIS

SIR,—Mr Skyrme Rees's large and interesting ser of cases (Dec 20) was so well documented and examine that one could wish he had gone a little further a listed the causes of death in the fatal cases

His definition of group III (appendix abscess) i difficult to understand Were all these 935 cases reall "among those which were not operated on," and, if so from what strange series of misfortunes did 81 of them di

I am not sure that the *mortality*-rate can be reduced by advocating earlier operation, nor do I believe that the "expectant or conservative" treatment of uncomplicated appendicitis occupies any large place in our minds Delay, when it occurs, is usually the result of sheer neglect or mistaken diagnosis My own efforts at diagnosis have been so humiliating that I have long abandoned any attempt at recognising acute appendicitis and I have confined my endeavours to deciding whether an acute abdomen exists or not, and, if it does and requires operation, I have tried to hazard a guess as to the best place to make an incision This diagnostic humiliation has been somewhat tempered by evidence of a similar fallibility on the part of my associates, and by the fact that of some 500 patients whom I have treated for genuine acute appendicitis, only 2 have died—a mortality rate for all types of case which approaches the "irreducible minimum" to which Mr Rees refers None of my cases died from pulmonary embolism, in spite of a belief in the heresy of putting sick patients to bed and keeping them there until they feel better

I hold that this satisfactory state of affairs is a result of the early inculcation of sound and sensible principles for dealing with this condition, of later association with a surgeon who had strong leanings towards conservatism and of working in areas where the standard of general practice is high If you, Sir, will bear with me, I should like to enunciate the principles which I was taught or have picked up as I went along, because I think their correct application is the only way to reduce the mortality of this condition Needless to say, they should be applied in hospital, not in the home

(1) Forget the diagnosis of appendicitis and concentrate on recognising the presence or absence of an "acute abdomen" If there is doubt in this matter, it is better to wait (a few hours) and see, than to look and see If the patient gets worse, operate If he gets better or develops the measles, then it would be folly to operate

(2) Patients with a tender lump (appendix abscess) do not form one clinical group, but two Those with a slightly tender lump and a long history (7 days or more) must not be operated on—not even if they are children or old people Nowadays, with antibiotics, all these lumps resolve without incision, and it is quite unnecessary to starve the patients or put them on an intravenous drip Those with a very tender lump and a short history—say, 3 days—must be operated on forthwith, and the appendix should be removed

(3) Use a McBurney (or Rutherford Morison) incision when the tenderness is maximal in the flank Use it, if you like, in young males whose symptoms are mild Never be tempted by its cosmetic advantages to use it at any other time In all other cases and *especially* if there is a lump, use a low paramedian incision This will allow adequate exploration and treatment of patients in whom the diagnosis has been at fault, it will allow the uncontaminated areas of the abdomen to be packed off before the exploring finger releases a gush of pus, and it will allow visual and digital contact with the pelvic floor—essential for finding, sucking out and draining an associated pelvic abscess A few patients will develop an incisional hernia, but it is comforting to reflect that this complication is peculiar to the living

(4) Always look for a pelvic collection of pus by retracting the lower end of the wound outwards, introducing the half hand into the depths of the pelvis, and displacing the small

wel medially. This manœuvre often reveals a large and suspected quantity of pus.

(5) Drain all "perforated" cases, and those in which emostasis has been imperfect, and any others if there is oubt in one's mind. A residual abscess in the right iliac ssa will always find its way out along a drainage track, but a clean stitched case it will probably require a second peration, or may even find a path of lesser resistance leading o the general peritoneal cavity. Drains do not carry infection nto wounds made to expose the gall-bladder, the thyroid—r the appendix.

(6) Distinguish very clearly between postoperative patients with soft distension of the abdomen and a satisfactory general ondition, and ill-looking patients with firm abdominal distension. Give parenteral fluid to the latter, never to the former; and this will achieve a great saving of salt and water.

(7) If the patient develops early mechanical obstruction, a considerable degree of surgical skill is about to be required. Be very wary of the "modern" advice to perform ileo-transverse colostomy through a separate incision. The distended small bowel pushes the transverse colon up into the epigastrium, and it is impossible to identify individual loops of small bowel. Reopen and extend the wound, and at once eviscerate as much small bowel as is required to obtain adequate exposure. This evisceration will not kill the patient and, if it is to be done at all, it is best done quickly. Whether the bowel can be returned or not is a matter for earnest discussion between surgeon and anæsthetist. It can be kept in place, while the abdominal wall is sutured, by a large piece of corrugated rubber. Through and through sutures may be required.

I hope that Mr. Rees will agree with my expansion of his brief comments on the minutiæ of operative technique, and with the bearing I suggest they have on his subject.

Barnet General Hospital. V. J. DOWNIE.

SIR,—Of the 7 fatalities in Mr. Skyrme Rees's group I, where inflammation was limited to the appendix, no less than 6 were due to pulmonary embolism. Out of the total of 1958 cases this gives the very high proportion of one death from this cause in every 326 patients. Possibly in the earlier cases in the series the importance of some form of support to the heels was not realised? It is now recognised that thrombosis usually originates in the veins of the calves, which must be kept off the table during any operation which might be followed by a pulmonary infarct or embolism. I have recently described[1] a simple support which serves as a constant reminder to the theatre staff that a heel support is imperative.

The treatment of cases in group III, in which an abscess was present, leaves the reader in doubt as to the precise nature of the treatment, for it is stated that "most abscesses were treated by drainage only," and subsequently we are told "these cases are among those which were not operated on." The crux of the matter is whether cases of appendicular abscess were submitted to operation or treated conservatively. The fact that out of 935 cases no less than 81 died—a mortality of 8·7%—suggests immediate operation, because with expectant treatment and removal of the appendix some three months later, the mortality is in the region of 1%. A typical example is to be found in the figures of Sworn and Fitzgibbon,[2] who analysed 2126 cases admitted to St. Thomas's Hospital, and found that the mortality of immediate operation in cases of appendix abscess to be 7·9%, as compared to 0·68% in cases treated expectantly. These figures, and many others which indicate similar results, point to one of the measures which will reduce deaths from appendicitis—namely, discrimination in dealing with cases of localised infection, as opposed to what the late Sir James Berry called "the hard and fast rule, adopted by so many, of operating at any stage—a rule so easy to follow, but often so disastrous to the patient."[3]

I agree that Mr. Skyrme Rees is technically correct in stating that the term "conservative treatment" should not apply to cases of appendicitis as opposed to those of peritonitis, in case doctors may be misled into treating on expectant lines inflammation which is limited to the appendix. However, during some thirty years of consulting practice I have never met a practitioner who deliberately "cooked" a diagnosed case of acute appendicitis when surgical measures were available, in the hope that resolution might occur.

London, W.1. MCNEILL LOVE.

RESECTION FOR PULMONARY TUBERCULOSIS

SIR,—It appears to me that both your leading article (Dec. 6) and Dr. Brailsford's letter (Dec. 27) over-simplify the problem of treating pulmonary tuberculosis. You refer to a paper by Ryan et al.[1] which proposes an interesting conception, but which is unlikely to prove to be of universal application. It is of course possible that the course of the disease is different in the U.S.A., but in any event the observations quoted are based on a small series of 30 patients treated surgically. In this country we are not so often able to reduce the disease to a purely nodular condition.

However this may be, surely Dr. Brailsford misses the point when he says (as in effect he does) that surgery cannot be expected to help the sufferer from pulmonary tuberculosis, or that patients can overcome the disease more easily without surgery than with it?

No-one, Sir, will deny that many small and some extensive tuberculous lesions will heal either spontaneously or with simple medical treatment. But neither can it be denied that many tuberculous lesions lapse into a chronic state, with healing in some places and extension in others. Chemotherapy will not then make any appreciable difference to the course of the infection, which may be expected to result in the death of the patient sooner or later.

Surgery is not indicated in pulmonary tuberculosis (or, indeed, in any other condition) until it is seen that healing is unlikely by less drastic means. I take it that Ryan and his colleagues, in common with other workers in this country and elsewhere, are attempting to prevent the breakdown which is so distressing a feature of this disease by removing the lesions which appear unlikely to heal permanently after a considerable period of sanatorium treatment. It is just here that resection of the affected areas of the lung is proving to be of greatest worth as a technical method, but it is a matter of experience that the patients do best when they have been made as fit as possible before operation by medical treatment on the commonly accepted lines. The patients will usually only remain fit in the sheltered conditions of a strictly ordered sanatorium routine. If they would be fit for normal life without danger, there would be no indication for operation. Working on these lines, the question of infectivity of the sputum becomes of secondary importance, for although the persistence of tubercle bacilli means that the patient is a danger both to himself and to others, their absence is a less important prognostic point than the demonstration of instability of the lesion by observation, or of some other indication of the unlikelihood of healing—e.g., size (a diameter of 2 cm. or more) or persistent cavitation.

If Dr. Brailsford is upset by the report of "30 wedge or subsegmental resections," I am afraid that he will be profoundly shocked if he hears that Mr. F. Ronald Edwards, myself, and our colleagues in Liverpool can report a series of more than 700 lung resection operations for tuberculosis. We feel convinced, nevertheless, that the extended use of this method has resulted in a great change for the better in the patients' prospects, and that

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1. McNeill Love, R. J. *Brit. J. Surg.* 1952, 40, 214.
2. Sworn, B. R., Fitzgibbon, G. M. *Ibid.* 1932, 19, 410.
3. Berry, Sir James. *Lancet*, 1932, i, 1027.

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1. Ryan, B. J., Medlar, E. M., Welles, E. S. *J. thorac. Surg.* 1952, 23, 327.

there are fewer patients needing repeated admissions to hospital as a result

Chemotherapy is extremely valuable, but its place is still limited, when and if a sufficiently potent antibiotic becomes available to arrest tuberculosis medically, thoracic surgeons will be pleased to be able to rest a little! There is no panacea, and if surgery is needed, neither resection nor thoracoplasty is universally applicable I am sure that Dr Brailsford would agree with me that the object of treatment is to restore the patient as nearly as possible to a state of good health by the safest and quickest means Ryan and his colleagues, and those with whom I have the pleasure of being associated in Liverpool, believe that it is an advance to resect the lesion which is unlikely to heal while it is still possible to do so, although we here have no great faith in the technique of multiple wedge resections

I hope that Dr Brailsford will believe me when I say that surgery (including lung resection) is often beneficial in pulmonary tuberculosis, that it has a logical basis, and that it often produces a dramatic improvement in the general health, and I can assure him that surgery is not undertaken unless it appears necessary for the reasons I have given The healed lesion is of no concern to the surgeon, but the failure to treat adequately the unhealed localised lesion is of the utmost concern to the patient because of the tragic consequences of the development, sooner or later, of chronic cavitation which may be difficult or impossible to cure

Liverpool B J BICKFORD

SPLENOMEGALY IN SCARLET FEVER

SIR,—Dr O'Reilly asks (Dec 20) whether others have had the same experience as he in finding splenic enlargement in scarlet fever

While in charge of an isolation block in a military hospital in Egypt during the late war, I recorded the prevalence of splenic enlargement in various infectious diseases The prevalence in three of these infections was as follows

	Total cases	Splenomegaly	
		No	%
Scarlet fever	42	3	7 1
Tonsillitis	81	5	6 2
Diphtheria	221	14	6 3

In all cases malaria was excluded by blood films and in all cases the spleen was no longer palpable on discharge

Department of Child Health,
University of Sheffield R S ILLINGWORTH

PRECISION IN DIAGNOSIS

SIR,—I agree with Dr Todd (Dec 27) that it is often quite impossible to attach a precise textbook diagnosis to a patient's disability and at the same time maintain one's professional intellectual integrity, and I find myself in sympathy with his plea for a less rigid system of *nomenclature in medical documents*

I would suggest, however, that a cause of error, confusion, and misunderstanding more fundamental and *more serious than the mere attaching of officially accept*able disease labels to patients, lies in the assumption that behind these labels there are disease entities each possessing a genuine, intrinsic, if vague, reality The belief that diseases have independent existence is implanted in us by the teaching we receive as students and is encouraged by our textbooks, our journals, and all forms of professional communication so that the whole pattern of our thought and speech is influenced by it, and that the belief is accepted without question is implicit in the way we talk about "discovering" or "describing" diseases (diseases which by the way, we have not defined) or in the way we pass over without comment such phrases as "the biological properties" *of this or that disease—phrases which imply that the* diseases in question have existence in their own right

The problems raised by this hypostatisation of diseases are not purely abstract theoretical or linguistic, for example, he is a singularly fortunate or forgetful doctor *who cannot recall that any of his patients have suffered* as a result of his preoccupation with diagnostic labels and his misconception of their significance—or lack of *significance To some extent, too, the failure to appreci*ate that disease names do not represent real *things* causes disease statistics *to* be less accurate than they *might be, though probably the search for names as* such has a more serious effect in this way, as Dr Todd seems to imply

It is difficult to see what cure there can be for this state of affairs unless it be in an increasing awareness of the extent and danger of this fundamental misconception

Falkirk RONALD G HENDERSON

COUGH MIXTURES

SIR,—I was interested to see in an annotation[1] a reference to the use of inhalations of carbon dioxide (in a 5% mixture with oxygen), and to Banyai's description of this inhalation as an "effective expectorant, which not *only* stimulates respiration and increases bronchial peristalsis but 'liquefies mucopurulent inflammatory exudates'"

Dr Herxheimer and *Dr McAllen* mentioned carbon dioxide favourably in their subsequent letter,[2] in which they were good enough to refer to my work on expectoration I would only add that in my view it is unlikely that bronchial peristalsis plays any part in expectoration Anatomically it is improbable that a peristaltic mechanism exists in the alveolar musculature (the myoelastic tissue of Macklin) Many investigators have postulated a kind of reflex by which expectoration is always associated with peristalsis, but I have been unable to demonstrate any such mechanism radiologically I found instead that the expulsive force came from reinforcement of the normal respiratory effort, *rather than from* added peristalsis It follows that carbon dioxide increases expectoration simply by stimulating respiration

University of Berne,
Switzerland T GORDONOFF

RESEARCH INTO INTESTINAL POLYPOSIS

SIR,—For more than twenty five years the research department of St Mark's *Hospital*, assisted by an annual grant from the British Empire Cancer Campaign, has been collecting information about the inheritance, pathology, and *treatment of familial intestinal polyposis* (polyposis intestini)

More than fifty families have been investigated, and in each case a complete family pedigree has been constructed A special follow-up department has been organised to keep in touch with all these polyposis cases and *their relatives, of whom more than one thousand are* now included in the hospital records It would be of great assistance to the further development of this work *if doctors who know of other cases of generalised intestinal* polyposis would be good enough to send me the names and clinical details of such patients, having obtained their permission to do so This would enable me to trace linkages between new cases and families already investigated If any such linkage could be discovered *either now or at a later date, I should inform the doctor* at once but should not of course communicate with the patient unless the doctor wished me to do so

I am signing this letter because I am responsible for organising this research, but I should like it to be understood that all the surgical staff of St Mark's Hospital are actively cooperating in this investigation

Research Department
St Mark's Hospital
City Road London E C 1 CUTHBERT DUKES

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[1] *Lancet*, 1952 i, 939

[2] *Ibid* p 1213

COLLEGE OF GENERAL PRACTITIONERS

SIR,—For many general practitioners Christmas will ave been brighter this year than any since the war, nd this not only because some of us have larger bank alances than for many years past.

It can have been no accident that the announcement f the completion of the spadework by the steering ommittee was made before the New Year but after 'Danckwerts." So let us all respond to the good news f the birth of the new college by joining at once as foundation members, by paying our joining subscription promptly, and—one more thing—by making a gift to the college of a substantial amount of money to raise a foundation endowment fund.

Money is power, and we all want the new college to be powerful for our good. Money given now is more valuable than money given in six months' or a year's time. Money given by members of the profession who are not general practitioners will be an especial encouragement to the college, and it would be into such an endowment fund that these donations could best be paid.

I have sent a cheque for what is to me "a substantial amount of money" to the secretary of the new college, asking him to pay it into, or use it to start, such a foundation endowment fund; and I appeal to every member of the profession to consider whether he can also do this as a birthday present to the new college. I enclose my card, but you will appreciate that I would prefer to sign myself as

ONE OF MANY ?

PAROTID TUMOURS

SIR,—Mr. Payne will probably like to be reminded in reply to his query (Dec. 20) about the operative diagnosis of parotid swellings that Dr. Redon is coming over from Paris in May to open a discussion on the treatment of tumours of the parotid gland at the surgical section of the Royal Society of Medicine. British surgeons will look forward with great interest to an authoritative account of parotidectomy by a speaker whose experience of the subject is almost certainly unrivalled.

With regard to the value of histology, our article was not concerned with the subleties of histological subdivision of the mixed parotid tumour group. We merely indicated that histology might be necessary to separate such widely different pathological entities as, for example, mixed parotid tumour, adenolymphoma, inflammatory swellings, and carcinoma, which clinically at the moment of presentation might be indistinguishable.

London, W.1.

DAVID PATEY
BERNARD H. HAND.

CHEMOTHERAPY OF TUBERCULOSIS

SIR,—May we correct an erroneous impression which may have been given by your account last week of the Royal Society of Medicine symposium on the chemotherapy of tuberculosis.

Referring to our interim statement on the Medical Research Council trials of isoniazid, you state that "Preliminary results . . . suggest that on the whole isoniazid plus streptomycin will prove the most valuable combination" (when compared with streptomycin plus P.A.S. and with isoniazid alone); "it has shown itself strikingly superior to streptomycin plus P.A.S. or to isoniazid alone in the type of case where chemotherapy is expected to give little benefit."

Our actual report was that clinically "there is a suggestion that streptomycin plus isoniazid is somewhat more effective than either streptomycin plus P.A.S. or isoniazid alone, but that the difference is not striking." There was no suggestion of "striking" superiority. We stressed that the correct placing of the combination of isoniazid plus streptomycin in chemotherapy will depend largely on the bacteriological results, which are not yet available. Until this information is forthcoming it would be unwise to regard streptomycin plus isoniazid as superior to other treatments.

Tuberculosis Research Unit,
Medical Research Council Laboratories,
Holly Hill, London, N.W.3.

MARC DANIELS
WALLACE FOX.

PARTIAL THORACIC STOMACH IN CHILDHOOD

SIR,—I feel sure there will be many engaged in children's medicine who will feel grateful to Professor Smellie and his colleagues (Dec. 13) for affording us the information about these 112 small children whose main symptom was vomiting and who were shown to have a short œsophagus or so-called partial thoracic stomach.

During the twenty-five years which have elapsed since Sheldon and Ogilvie [1] published their cases of œsophageal obstruction in early life many such cases have been reported, but it would seem that we are still in doubt about the causation of this so-called partial thoracic stomach. I believe with Professor Smellie that the condition in its early stages is much more frequent than the records of the more advanced condition, when obstruction and ulceration are present, would suggest.

I wonder whether Professor Smellie can tell us whether this common and interesting condition is still considered to be a congenital defect, and whether it has ever been found post mortem in a neonate. Is this a condition which may lie latent from birth without causing vomiting ? I should have thought that were it a congenital abnormality its presence would have been occasionally reported by our radiological colleagues when carrying out barium-swallows and follow-through examinations for conditions other than vomiting. Also can we be told whether any of these children were re-examined radiologically after the cessation of vomiting, and if so do the results disclose a disappearance of the partial thoracic stomach ?

Meanwhile, even at the risk of being told that this is undoubtedly a congenital abnormality, I would like to ask whether Professor Smellie thinks it at all likely that the condition may after all be due to some of the causes of vomiting which have been discussed by Dr. B. S. B. Wood,[2] of which persistent underfeeding is an important one. For some time now I have wondered whether the condition has any connection with a hungry infant's persistent efforts to return its food and try and enjoy it again while waiting for the ending of the four-hour interval laid down by child-health authorities. Such efforts might over a period of weeks tend to pull, push, or balloon the stomach into the thoracic cavity via the hiatus and thus produce the partial thoracic stomach. This possibly may be thought to be an over-simplification. At any rate it might be worth while to feed these small infants so that they are fully satisfied and, if partly or completely artificially fed, can obtain the food easily by sucking from a boat-shaped bottle with a very easy teat, to prevent them being waked from sleep for a feed, and to make sure the child is fully satisfied within ten or twelve minutes. The still-prevalent teaching of the mother by midwife, maternity unit, and teaching centre that the neonate should take twenty minutes over a feed is certainly asking for trouble.

Leeds.

WILFRED VINING.

⁂ This letter has been shown to Professor Smellie and his colleagues, who reply:

"Professor Vining raises a number of important and pertinent points to only some of which definite answers can be given.

"As symptoms referable to the anomaly frequently arise within twenty-four hours of birth it is difficult to avoid the conclusion that the disease is congenital. In so far as our own records go, a partial thoracic stomach has not been encountered in a neonate post mortem We have some evidence, however, which suggests that the condition can remain symptomatically latent from birth

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[1] Sheldon, W., Ogilvie, A. T., *Arch. Dis. Childh.* 1929, 4, 347.

[2] *Lancet*, 1952, i, 28.

"It is understandable that unsuspected cases are not likely to be accidentally discovered on routine barium-meal examination Experience has taught that, even when the disorder is definitely suspected and when special attention is directed to the lower œsophagus, radiological confirmation of the lesion may be far from easy If during the screening no œsophageal reflux occurs, visualisation of the supradiaphragmatic portion of the stomach may not be possible A number of our children have been re-submitted to radiological study when symptoms have abated, some have retained the anatomical abnormality, but in others it has become difficult to be certain of this once reflux has ceased to occur

"Professor Vining's suggestion that the herniation of the stomach through the diaphragm might be caused by the regurgitating efforts of the starved and hungry infant is ingenious and thought-provoking In our view, with which Dr Wood concurs, there is no evidence to suggest that under-feeding is a factor in the production of a partial thoracic stomach From further analysis of infantile vomiting, Dr Wood[1] considers that in a number of his infants with 'persistent vomiting of uncertain origin' the cause is gastro œsophageal incompetence"

CONGENITAL DEFECTS FROM MATERNAL RUBELLA

Sir,—Having recently seen a fatal case of encephalitis complicating rubella in a child aged 6 years, I view with mixed feelings the suggestion by Mr Robin (Nov 22) that there is every justification for recommending that all girls should be exposed to rubella before leaving school

Bulawayo Southern Rhodesia J Charles Shee

VITAMIN B_{12} IN PRACTICE

Sir,—In your leading article of Dec 13 you state that "at the moment there is no way of distinguishing before treatment the patient who has a vitamin-B_{12} deficiency from one who has a folic acid deficiency" This unqualified statement is untrue Though it is not possible to distinguish between these two deficiencies by hæmatological methods, this can be done by microbiological assay of vitamin B_{12} in serum using *Euglena gracilis* var *bacillaris*[2] With this method it is found that in patients with vitamin B_{12} deficiency the serum B_{12} concentration is very low—usually less than 50 μμg per ml In normal subjects and in patients with megaloblastic anæmia due to folic acid deficiency, the serum B_{12} concentration is always above 100 μμg per ml[3]

In all patients with untreated pernicious anæmia low serum B_{12} concentrations have been found In patients with megaloblastic anæmias other than pernicious anæmia (associated with gastro-intestinal conditions or pregnancy) the pre-treatment serum B_{12} concentrations were variable, being either as low as in pernicious anæmia or within the normal range Patients with low serum B_{12} concentrations all responded to treatment with vitamin B_{12} those with normal concentrations failed to respond to vitamin B_{12} but responded to either folic acid or folinic acid Occasionally, deficiency of both factors has been present, in these patients the serum B_{12} level was low but the response to vitamin B_{12} alone was incomplete

Though the method is at present a research technique, these results indicate that microbiological assay of vitamin B_{12} is of value in the differentiation of megaloblastic anæmias It must be noted, however, that occasional samples of serum (about 6%) contain some substance not considered to be vitamin B_{12} or to be hæmopoietically active, but with growth-promoting action for the test organism Such sera may give falsely high results If more than one pre treatment serum sample is tested, however, the method becomes very reliable and a definitely low serum B_{12} concentration can be confidently accepted as proof of severe vitamin B_{12} deficiency in the body

Postgraduate Medical School
of London, W 12

D L Mollin
G I M Ross

TERRAMYCIN

Sir,—A recent experience demonstrated the effectiveness of terramycin in salmonella infections—a subject discussed by Mr Ritchie and Dr Phillips (Dec 13) Two children, now aged 5 months and 9 months, passed stools containing *Salmonella typhi-murium* for 10 and 12 weeks respectively Repeated courses of succinyl sulphathiazole, penicillin aureomycin and chloramphenicol failed to produce more than an odd negative stool even during actual treatment

It was found that a 4 μg tablet of terramycin in the culture-plate medium inhibited the growth of the organism *On giving an elixir of* terramycin (125 mg t d s for the younger child and q d s for the older child), their stools were negative 36 hours after treatment began, and remained negative for the week of treatment and for the week following They were then discharged from hospital No change in feeding or environment was made during this time

This exclusive and striking in vitro and in-vivo action suggests that terramycin may be the drug of choice in this type of infection

Ingham Infirmary,
South Shields

A J Watson

SHORTAGE OF JUNIOR HOSPITAL STAFF

Sir,—I read with interest the letters and your annotation on this subject in the issue of Dec 20

The whole object of doing house jobs is to gain clinical experience, either as the first rung in the specialist ladder or as a prelude to general practice It is quite obvious that the numbers available should bear an ascertainable mathematical relationship to the number of general practitioners and specialists

It is also apparent that unless the present position materially alters there will not be enough juniors to undertake those duties not requiring specialist training Surely the answer is the permanent appointment of general duties officers to fill the gap, with pay and emoluments comparable with those obtainable in general practice

London W 1

Guy Rigby-Jones

THE AFFERENT-LOOP DISTENSION SYNDRO

Sir—Professor Wells and Mr MacPhee (Dec 20) point out that great care should be taken to distinguish between the afferent and efferent loop syndromes The distinction is important, but the time to recognise unduly sensitive bowel is before the operation of partial gastrectomy

They also write "When a patient has typical jejunal symptoms but does not show the patterns of efferent loop hypermotility as described by Glazebrook, *the afferent* loop syndrome in a *forme fruste* should be suspected I am sure however, that many, if not the majority, of cases of efferent loop hypermotility are caused by (*a*) the powerful stimulus of a distended afferent loop, and (*b*) the damming back of pH regulators and digestive ferments in a distended afferent loop

Lessening, or virtual disappearance, of afferent loop syndromes with the passage of time does not me that the condition has righted itself These sad ar ndernourished individuals can make adjustments by estricting their diet and taking light work, while their pathetic bowels, once vigorous, lose the power to make ffective protest.

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[1] Wood B S B Astley R (in the press)
[2] Ross G I M *J clin Path* 1952 5, 250
[3] Mollin D L Ross, G I M *Ibid* p 129

Professor Wells and Mr. MacPhee, by focussing attenion on the afferent loop, have made a substantial ontribution. It is to be hoped that the conception of 'neurotic attacks"[1] will now cease to bedevil the erious and growing problem of the post-gastrectomy syndrome.

Harrogate. A. J. GLAZEBROOK.

PITUITARY EXTRACT IN OBSTETRICS

SIR,—The report of the Emergency Obstetrical Service in the Manchester area[2] is disturbing since it reveals that whole posterior pituitary extract (the preparation mentioned was 'Pituitrin') is still being used in domiciliary obstetric practice.

We firmly believe that whole posterior pituitary extract should not be used in obstetrics since it contains not only the oxytocic but also the toxic vasopressor factor. *Admittedly the purified oxytocic fraction* (injectio oxytocini, *B.P.*) contains some vasopressor substance, but its vasopressin content per unit activity is not more than 1/20 of whole extract (injectio pituitarii posterioris, *B.P.*); hence the latter is much more toxic. Vasopressin constricts the coronary vessels and produces impairment of the action of the heart. In a woman who has already lost blood this may produce shock or even death.

Obstetric Unit, University College Hospital Medical School. W. C. W. NIXON.
Department of Pharmacology, University College, London, W.C.1. H. O. SCHILD.

BUTAZOLIDINE

SIR,—To the reports of toxic effects following the administration of butazolidine I would like to add two observations which I have not seen described in publications in this country. They seem noteworthy among others I have seen, which include the usual digestive, cutaneous, purpuric, and hæmaturic incidents, and three cases of jaundice, apparently obstructive. I cannot at present give their proportional incidence, as they have occurred in three hospitals and in private practice.

One patient went into left ventricular failure complicating generalised œdema. This complication was mentioned by Stephens et al.[3] and Steinbrocker et al.[4]

Another patient had characteristic œdema with extensive patches of œdematous erythema on limbs and trunk, progressing to peeling of the face and limbs and maculate purpura on the trunk, after taking one tablet only. There was no evidence that this patient had had the drug before.

I may add that I am taking the drug myself with much relief of the pain of my rheumatoid arthritis.

Hove, Sussex. W. A. BOURNE.

SUFFERING FROM PERNICIOUS ANÆMIA

SIR,—Patients with pernicious anæmia suffer more at the hands of doctors than the failure to reassure them mentioned by Dr. Todd (Dec. 20).

Recently an applicant for entry to the teaching profession was medically examined and found physically fit in all respects. She gave a history of pernicious anæmia, successfully treated; and this was entered on the official form as a minor condition not likely to interfere with the performance of her duties. Her application for entry to two teachers' training colleges has been rejected on medical grounds, because of pernicious anæmia.

Had she not told the examining doctor about her anæmia it would not have been diagnosed clinically; so she is being penalised for giving an honest history, and her whole career is jeopardised unfairly. What remedy has she?

If I had to be ill I should rather have "pernicious" anæmia than "benign" tertian malaria or a "benign" adenoma. Would it not be better to give up the adjective "pernicious" and talk about addisonian anæmia, as many already do?

Giggleswick,
Settle, Yorks. D. P. LAMBERT.

Public Health

Deaths During the Fog

THERE were 4703 deaths registered in Greater London in the week ended Dec. 13 when, during the first half of the week, smoke-laden fog covered most of the area.[1] The figures for the preceding two weeks were 1902 and 2062, and deaths in the corresponding week of 1951 were less than a third of this year's total. Deaths from influenza and pneumonia increased from 89 in the week ended Dec. 6 to 380 in the week of the fog: and many more deaths from respiratory or cardiac disease were referred to coroners than in normal weeks.

First reports on the chemical content of the fog indicate that there was more sulphur dioxide and carbon in it than usual. The Ministry of Health suggests that "these increases are for the present better regarded as a measure of fuel consumption, principally coal, rather than as an index of 'atmospheric vitriol.'" The Ministry says that an analysis of the information given on the death certificates is being made, pathologists' reports are being examined, and further investigation of the constituents of the fog and smoke is in hand. No conclusions can be reached until this work is completed.

Saving Fuel in Hospitals

The Northern Ireland Hospitals Authority, examining the reasons for the rising cost of the hospital and specialist services, has been paying particular attention to means of reducing fuel consumption in its hospitals. The authority's report for the year ended March 31, 1952, says that an engineer and a stoker-demonstrator have been visiting some of the hospitals in Northern Ireland to test the fuel-burning plant, and to make recommendations for improving efficiency. It is estimated from their reports that expenditure on fuel in the general hospitals visited (1740 beds in all) can be cut from £29·3 per bed per annum to £23·6—an annual saving of £9900. The changes needed to save this sum are being made wherever possible. All the hospitals in Northern Ireland will eventually be dealt with.

Appointments

BOOTH, R. W., M.R.C.S.: appointed factory doctor, Cinderford district, Gloucester.
BRENTNALL, T. D., M.R.C.S.: appointed factory doctor, Oakham district, Rutland.
LOVE, S. H. S., M.B. Belf., D.A.: consultant in anæsthetics, hospitals of Belfast H.M.C.
MILLAR, J. H. D., M.D. Belf., M.R.C.P.: part-time consultant neurologist, Royal Victoria and Claremont Street Hospital, Belfast.
O'RIORDAN, J. P., M.B. Dubl., D.P.H.: port M.O., Dublin.

Colonial Medical Service:

BEDELL, F. E., L.M.S.S.A.: district M.O., Windward Islands.
EASMON, C. O., F.R.C.S.: surgical specialist, Gold Coast.
GORROD, C. E., M.B. Aberd., D.P.H.: M.O.H., Federation of Malaya.
HALL, C. L., B.M. Oxfd: senior M.O., Tanganyika.
JOHNSTON, H. M., M.B., M.P.H.: senior M.O.H., Jamaica.
LUNKING, F., M.B.: M.O., Federation of Malaya.
McDONALD, W. H. B., M.B. Lond., D.T.M. & H.: senior M.O., South Pacific Health Service.
McGREGOR, ALAN, M.B. Durh.: senior M.O., Tanganyika.
MAXWELL, R. W. D., M.B., D.P.H.: deputy director of medical services, South Pacific Health Service.
MURCOTT, E. H., M.D. Edin., D.P.H.: deputy director of medical services, Nyasaland.
REECE, A. A., M.D.: M.O. (grade A), Trinidad.
SPICER, J. R. C., M.B. Lond., D.O.M.S., D.T.M. & H.: specialist (ophthalmology), Gold Coast.
SUTHERLAND, E. S., L.R.C.P.E., D.P.H.: senior M.O.H., Jamaica.
SWISTERSKI, K. P., MED. DIP. Lwow: anæsthetist, Barbados General Hospital, Barbados.

North East Metropolitan Regional Hospital Board:

DOW, J. R., M.R.C.P., D.M.R.D.: consultant radiologist, Hackney Hospital.
HAMILTON, MARGARET, M.B. Leeds, D.A.: part-time consultant anæsthetist, Eastern Hospital.
MORGAN, J. A. U., M.R.C.P.: consultant pathologist, Hackney Hospital.

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1. Any Questions. *Brit. med. J.* 1952, ii, 1006.
2. *Lancet*, 1952, ii, 746.
3. Stephens, C. A. L. jun., Yeoman, E. E., Holbrook, W. P., Hill, D. F., Goodin, W. L. *J. Amer. med. Ass.* 1952, 150, 1084.
4. Steinbrocker, O., Berkowitz, S., Eholich, M., Elkind, M., Carp, S. *Ibid*, p. 1087.

1. See *Lancet*, 1952, ii, 1222.

Obituary

CHARLES PORTER

M D, B Sc Edin, M R C P E

Dr Porter who died on Dec 15 at the age of 79, was medical officer of health of St Marylebone from 1910 until his retirement in 1939.

He was educated at the Royal High School, Edinburgh, and in the Universities of Edinburgh and Freiburg He graduated M B in 1896, and took the M D (with high commendation) in 1902 From 1902 to 1906 he was lecturer on bacteriology in the University of Sheffield

During his long term of office in St Marylebone he was closely concerned with the preparation and supervision of many of the borough's plans for improving the health of its people, and he contributed especially to the plans for slum clearance, housing, and maternity and child-welfare services (several of which were the first of their kind under municipal schemes)

His work, however, was not restricted to local public-health matters He was president of the Society of Medical Officers of Health and chairman of the council of the Royal Sanitary Institute, of which he was also vice-president He served upon many departmental committees and at the invitation of the Minister of Health, took part in international health conferences in other countries He was an honorary fellow of the American Public Health Association, and among other bodies of which he was for many years a member were the General Nursing Council for England and Wales, the Council of the Queen's Institute of District Nursing the Royal Sanitary Institute and the Sanitary Inspectors' Examination Joint Board, and the Worshipful Company of Plumbers, whose Master he was for the current year

Dr Porter was a well-known writer on public health and preventive medicine For ten years he was honorary editor of *Public Health* the official organ of the Society of Medical Officers of Health and, apart from works on many different aspects of hygiene, he was joint author of a standard textbook on sanitary law

He leaves a widow, and a son and three daughters by a former marriage

H A B writes

'Charles Porter, with his short, stocky, monocled figure and inexhaustible energy, was a great personality An outstanding authority on preventive medicine, his reputation and influence extended far beyond St Marylebone which he served as medical officer of health with such distinction for nearly 30 years He took a foremost part in grappling with the many public health problems of his day, and he was inevitably to be found in the midst of controversies ranging from epidemiological research to the severely practical and revolutionary 'one pipe' system of drainage for buildings

"He possessed a keen journalistic sense and was a prolific writer—indeed, his only hobbies were reading and writing Apart from being author, editor, commentator, and reviewer, he contributed a weekly page to a public health journal for many years, never missing an issue even though he might be in America for three or four months taking part in an international health officers' course or reporting abroad to a world health organisation Most of his work was set to type from his own neat handwriting, and he had an uncanny knack of writing just enough to fill the space allotted to him

'In addition to his work for D P H students, he was keenly interested in the training of sanitary inspectors and health visitors, and his name was familiar to a host of these officers who studied under him and eventually found him a lively and sympathetic, but searching examiner He excelled as an after dinner speaker, and was greatly sought after for the aptness of his comments and the brilliance of his wit

Charles Porter did not suffer fools gladly, but for those prepared to work hard with him he was an inspiring and fearless leader, and a delightful and helpful friend"

ARTHUR CANT

M B Birm

Dr Arthur Cant who died on Nov 30 when he was within a few days of his 80th birthday, was a well-known Midland general practitioner

Educated at King Edward's School, Birmingham, he studied medicine at Mason's College, Birmingham, and qualified M R C S in 1895 He graduated M B at Birmingham when the university was granted its charter in 1901 After house-appointments in Birmingham and Kidderminster he settled, more than fifty years ago, in Coleshill Warwickshire He soon became not only the doctor but the trusted friend of the widespread rural community and, working to the end of his long life, he retained to the last the affection of his patients

GEORGE GRANT

M A, M B Aberd

Dr Grant, who died on Dec 19 at his home in Dunbar was in practice in Cardiff for the first thirty years of the century Born at Grantown-on-Spey in 1867, he was educated at Fordyce Academy and at the University of Aberdeen where he graduated in arts and medicine The five years after qualification were spent in assistantships in various parts of England, and he settled in Cardiff in 1900 A friend writes

"He set his face against all innovations in principle, though he was usually delighted with any which he was persuaded to accept Thus he ran his large practice without benefit of motor car or telephone, and till he retired he made all his visits on a bicycle He knew his patients through several generations I remember him greeting a woman in 1930 in Crewe station with great affability, and afterwards saying 'I don t remember her name, but her son had pneumonia in 1919 when he was six' He refused to join the National Health Insurance scheme in 1911, and, perhaps partly because of this much of his work was done among mothers and children he became especially successful in advising on the rearing of delicate babies His Welsh patients accepted his plain speaking, for he was, after all, a Scot, and they valued his honesty conscientious care, and infinite patience He was never in a bad temper and seldom—and then justly—angered He was ready to enjoy everything and to see good in everyone In his retirement he made new friends, who were no longer also his patients, and many people in Dunbar would say 'It always does you good to meet Dr Grant'"

Mrs Grant survives him with three daughters

Births, Marriages, and Deaths

BIRTHS

BUTCHER—On Dec 16 at Durban South Africa to Nancy (née Cowan), wife of Mr Nigel Butcher F R C S E—a daughter

ELLIS—On Dec 28 at Newcastle General Hospital to Alysoun (née Benson) wife of Dr Errington Ellis—a daughter

KRAMER—On Dec 28, at Queen Charlotte's Hospital to Elisabeth (née Dalley), M R C S wife of Mr Ivor R H Kramer L D S—a son

MARSH—On Dec 16 at Pembury Hospital Tunbridge Wells, to Molly (née Moon) wife of Dr S A Marsh—a son

OWENS—On Dec 6 at Pretoria South Africa to Joan wife of Dr W J Owens—a son

SAXTON—On Dec 18 at Moreton in Marsh Hospital to Anne wife of Dr Arthur Saxton—a son

SLOWE—On Dec 21 to Dorothea (née Jolly) wife of Dr J J Slowe of Rectory Cottage Shincliffe Durham—a daughter

TUCKER—On Monday Dec 22 to Helen (née Rennie) wife of Dr Hugh M Tucker, Urquhart Villa Lossiemouth Moray—a daughter

MARRIAGES

[illegible]—On D[illegible] 20 in Fanwood New Jersey USA [illegible] M D to Margaret Slocum LL B [illegible] in London Peter Gray M B, of Newport [illegible] of Golders Green London

DEATHS

BEAVER—On Dec 21 at Cockburnspath Berwickshire Robert Atwood Beaver O B E M D Victoria major R A M C retd

COLE MARSHALL—On Dec 24 at Rickmansworth, James C[illegible] Marshall M D Lond, F R C S

FERGUSON—On Dec 27 at Rotherwick Basingstoke, Hampshire Henry Arnot Ferguson M B Dubl D P H, colonel, R A M C retd

HICKLING—On Dec 21 at Fenham Newcastle upon Tyne Gertrude Hermine Hickling M D Manc D P H aged 69

HICKS—On Dec 2[illegible] at 56 Friar Gate Derby Henry Thomas Hicks F R C S aged 81

MEDLOCK—On Dec 27 at Hertford Charles Harold Medlock F R C S

REID—On Dec 21 at Willesden Lane, Brondesbury N W 6 John Reid M D R U I D P H aged 81

REYNOLDS—On Dec 22 at the London Clinic, Frank Ne[illegible] Reynolds F R C S E, F I C O[illegible]

SCOTLAND—On Dec 23 at Bowden, Cheshire, Douglas Ch[illegible] Scotland F R C I F aged 57

SCOTT—On Dec 8 at the National Hospital Queen Square W C 1 Philip Dennis Scott M B Lond of 78, Clifton Hill N W [illegible]

WOOD—On Dec 18, at Yatton Som William Vincent We[illegible] M C M R C S, aged 77

Notes and News

THE WORLD'S CHILDREN

THE 20th century, Arnold Toynbee said last year in the *New York Times*, "will be chiefly remembered not as an age of political conflicts or technical inventions, but as an age in which human society dared to think of the welfare of the whole human race as a practical objective." Let us hope he is right. It is, at all events, a more encouraging appraisal of our century than most. And at least the United Nations International Children's Emergency Fund can claim to have attended strictly to this practical objective. Its life story is briefly outlined in a pictorial record [1] of some of the children it has helped. Born in December, 1946, it started work immediately—bringing food, clothing, and medicine to children in devastated parts of Europe. In recent years it has gone farther afield, to poor and undeveloped countries in Africa, Asia, Latin America, and the Eastern Mediterranean. Here its task has been to teach, at the very simplest level, something of the proper care of infants and children, and of childbearing women. And since so much of a child's welfare depends on what goes into his belly, UNICEF has played the part of a benevolent milch-cow in these many countries, providing fresh milk when it is possible, dried milk when it is not, supplying dairy equipment and milk-drying plants, and encouraging people to increase their own milk-supply. In Yugoslavia, for instance, UNICEF collaborated with the government in a comprehensive milk conservation plan, providing much of the equipment while the government supplied buildings, transport, and labour. Much of the labour was provided, in Sarajevo, by volunteers who helped to dig the foundations and put up the buildings for the milk plant. The same kind of help has been given by UNICEF in eight other European countries, and to peoples in Central and South America and the Eastern Mediterranean. Some populations are so sick from endemic diseases that they have not the heart or strength to grow themselves adequate food. UNICEF has supplied the D.D.T. for antimalarial campaigns in some 26 countries. Teams go through the countryside spraying the houses, protecting millions from the disease, and making it possible for vast areas to be brought under cultivation. This means there is more for the family to eat, because the men are better able to work in the fields. Mass-scale B.C.G. vaccination has also been begun in some parts of the world, and UNICEF has provided penicillin for government-administered campaigns in countries where yaws is rife. Maternity and child-welfare clinics have been started in many countries; and UNICEF helps to start midwifery training centres, and provides midwifery kit—which gives status—for those midwives who complete their training.

UNICEF believes it has already helped some 60 million children, but estimates that some 500 million are in need of help. The size of the problem is therefore much greater than our recent verse [2] suggested. The income of UNICEF comes voluntarily from governments, peoples, and individuals throughout the world. In its six years of life it has helped children in 76 countries, giving only such supplies and equipment as the country itself cannot provide; and its contribution is in every case matched or more than matched by the government of the assisted country. Thus a contribution to UNICEF is at least doubled in value by the time it reaches the children; and in addition, of course, *bis dat qui cito dat*. Not many investments, nowadays, give such good returns. The address is UNICEF, United Nations, New York.

GEOGRAPHICAL PATHOLOGY

THE International Society of Geographical Pathology has for its object the systematic study of diseases and their distribution and characteristics throughout the world, and it investigates pathological problems upon a common plan, with the aim of throwing light upon the pathogenesis of disease conditions by comparing observations made in widely different regions. The inquiries cover morbid anatomy and histology, clinical manifestations, biochemistry, bacteriology, virology, serology, and epidemiology, and include the diseases of wild and domestic animals. At its first meeting in Geneva in 1931 the society discussed cirrhosis of the liver; at Utrecht in 1934, arteriosclerosis; at Stockholm in 1937, the anæmias. During the war the activities of the society were interrupted, but through the enterprise of Prof. F. Henschen (Stockholm) representing morbid anatomy, Prof. L. Michaud (Lausanne) representing clinical medicine, and Prof. F. C. Roulet (Basle) also a morbid anatomist, the society met again in Liège last July, under the presidency of Prof. J. de Josselin de Jongh and the chairmanship of Prof. J. Firket (The Hague) to discuss hepatitis. The proceedings of the meeting are to be published in *Documenta de Medicina Geographica et Tropica*, of Amsterdam.

A VIGOROUS CENTENARIAN

IN the 19th century, when there were still plenty of innominate diseases about, the great natural historians of medicine had their sharp eyes open for symptoms, and their inquisitive minds in a ferment of analysis and synthesis. *Guy's Hospital Reports*, which completed its hundredth volume in 1951, might almost be called the nature notebook of many of these brilliant observers. In an article now reprinted, Mr. R. C. Brock [1] recalls some of the long list of clinical triumphs recorded in it. Astley Cooper described here the necropsy findings in two cases of aneurysm, in one of which he had ligated, eighteen years before, the common carotid, and in the other, thirteen years before, the external iliac artery; Thomas Williamson King first ascribed to the thyroid an internal secretion; Bright gave his most extensive (though not his first) account of his disease in these pages; Addison's disease was generally accepted as an entity largely because Sir Samuel Wilks, one of the editors, repeatedly wrote up cases in the *Reports*. Addisonian anæmia, too, was given much attention in the journal; and Babington, in 1841, recorded there, for the first time, the relation between chorea and heart-disease, quoting observations by Addison. Hodgkin discovered his disease in 1832, before the *Reports* had begun; but the eponym was conferred in its pages in 1865. Taylor, author of the *Manual of Medical Jurisprudence*, contributed his classical articles on poisoning, and on tattoo marks as evidence of personal identity; Gull provided the first account of anorexia nervosa, discussed the significance of fatty stools and mesenteric gland disease, and described the condition we now call myxœdema. Wilks noted in its pages the association between aneurysm and syphilis, and showed that this infection produced other internal lesions; and this remarkable man also described for the first time lymphatic leukæmia (under the name "leucocythæmia"), bacterial endocarditis, and alcoholic peripheral neuritis. Chevers (anticipating Pick) published the first clear clinical account of constrictive pericarditis in the *Reports*, and Cooper Foster described the first gastrostomy done in Great Britain. The long record runs on into this century, when Hurst, one of the most dynamic of editors, published in the *Reports* 75 articles between 1908 and 1939, many of them on his work on the alimentary canal. Ryle, too, described his studies of the digestive system, made with Izod Bennett; and Ryle's tube appeared in these pages in 1921.

A few odd gaps in publication explain the fact that the *Reports* is older than its century of volumes suggest; but like all the truly mature it is not ashamed of its age—which is in fact a green 116. Mr. Brock has roused the echoes of the thundering *Reports* of the past; and we may reasonably expect the bombardment to continue. Meanwhile a modest salvo, in congratulation, seems in order.

HOSPITAL LIBRARIES

PATIENTS' libraries were discussed at a meeting of the medical section of the Library Association on Dec. 12, at which Mr. A. Lee, chairman of the section and librarian of the Liverpool Medical Institution, presided.

Miss Sheila Moore described the evolution of hospital libraries, whose purpose, she thought, was to provide a means of escape from the monotony of ward routine, to distract from pain, and to act as a link with the outside world. The St. John and Red Cross Library took a large part in the story; but the resolution of the Library Association in 1930, recommending hospital authorities to provide libraries under the control of trained professional librarians, had not been widely adopted. However, the Ministry of Health memorandum of 1950 suggested that "a library service should gradually be developed to a high standard in all hospitals." During recent years a few hospitals, mainly large mental hospitals, had appointed professional librarians to their staffs. Sometimes the librarian was expected to organise social events and other activities; and, while Miss Moore did not see how one person could do the two jobs and provide a really efficient library service, these appointments were a step in the right direction She thought that these dual appointments were made simply because the money could not be stretched to meet the need for two people to do two different jobs. Describing the library of which she is in charge at St Thomas's Hospital, London, Miss Moore said they were hoping to see what results could be achieved by a full-time hospital library They had had a great deal of help from public, university, and special libraries for example, they had borrowed from the School of Oriental and African Studies books in Urdu, Hindu, Turkish, and Arabic, and a request from a patient for a life of Bonnie Prince Charlie in Gaelic was met within four days from Inverness Public Library The St Thomas's library now had 8000 volumes and was still growing A new trolley had been designed to take the books to the wards, similar in principle to the picture postcard turn tables used by stationers

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[1] United Nations Publication, no. 1952.1.20. UNICEF, United Nations, New York. Pp. 30. $0.15 or the equivalent in other currencies.

[2] *Lancet*, 1952, ii, 1138.

[1] *Guy's Hosp. Rep.* 1952, 101, 235.

Mr Gilbert Barker, librarian of the St John and Red Cross Hospital Library, said that all who took up this work found inspiration and satisfaction in it The essentials were a love of people and books and the toughness of an ox, for the combination of mental and physical work was tremendous

Mr W J Bishop, of the Wellcome Historical Medical Library, pointed out that Soranus of Ephesus, a first century physician, had encouraged patients to acquire varied reading matter that was easy to hold By the 18th century many large hospitals had libraries for patients and by the 19th century it was exceptional, particularly for mental hospitals, not to have them Crichton Royal, founded in 1842, soon had 5000 books, and Edinburgh Royal Infirmary had 3000 volumes in the 1890s Of course the libraries did not compare with the modern ones, among other things, patients used to complain that the books were almost entirely of an uplifting and devotional character

DANGEROUS DRUGS ACT

On Dec 8 3-methoxy-N-methylmorphinan came under the terms of part III of the Dangerous Drugs Act, 1951 It is now therefore illegal to import or export this drug except under licence, and the Home Office has power to make regulations designed to prevent its improper use The provisions apply to the three forms of the drug (dextromethorphan, levomethorphan, and racemethorphan), to its salts, and to any preparation, mixture, extract, or other substance containing the drug

University of Cambridge

The following associate lecturers have been appointed Mr Christopher Parish (thoracic surgery), Mr L M Rouillard (plastic surgery), Dr Brian Donnelly (radiology), and Dr W Paton Philip (diseases of the chest)

On Dec 13 the degree of M CHIR was conferred on R N Ticehurst, and the degrees of M B, B CHIR were conferred by proxy on Hamish Nicol

University of London

The title of professor of dental surgery has been conferred on Dr F C Wilkinson, director of the Institute of Dental Surgery, British Postgraduate Medical Federation

At a recent examination for the academic postgraduate diploma in medical radiology (diagnosis), J M Lockie and Edward Mercieca were successful

University of Sheffield

Dr D R Wood has been appointed to the senior lectureship in pharmacology, Dr T M Abbas to the senior lectureship in obstetrics and gynæcology, and Mr J S D Bacon, PH D, to the senior lectureship in biochemistry

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Dudley Stourbridge and Dist Sr H O and H O	46
Edgware General H O	46
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iversity of Bristol

At recent examinations the following were successful:

M.B., Ch.B.—K. J. Barker, Marjorie E. Barton, N. G. Blackwell, R. Bollen, Ann E. Booker, J. C. Causton, Anne W. Christie, an M. Claremont, Barnett Ginsberg, Alan Moore, I. W. Palmer, N. Prichard, P. H. Sherwood, H. S. Smith, D. W. G. Stone, E. Tovey, H. A. P. Walker.

niversity of Liverpool

At recent examinations the following were successful:

M.D.—H. G. Frank, D. R. W. Haddock, A. Jolleys, R. S. ones, P. P. Newman.

M.Ch.Orth.—C. J. R. Conacher, W. C. Lawrence, M. Lunz, Page, A. Rahim, E. H. Strach, J. G. Stubbs, K. J. M. Watson.

D.M.R.T.—R. V. Samapurnavanitya.

D.P.H.—R. Muscat.

University of Edinburgh

On Dec. 19 the following degrees were conferred:

M.D.—*Alick Cameron.

Ph.D. (in the faculty of medicine).—*S. W. Bibile.

M.B., Ch.B.—F. E. Adderley, Jean M. Bell, George Beveridge, eean Bheenick, D. A. Brown, J. D. Cormack, J. T. Dixon, A. G. Fraser, A. H. French, A. K. Fulton, Alice B. E. Gray, Ann S. Haig, R. W. Hall, D. L. N. Haultain, P. A. Hood, Isabel J. Huggan, A. D. L. Hunter, J. L. Hunter, R. D. Jones, P. L. Kennedy, D. S. Lyon, R. B. Macpherson, R. S. Maini, D. J. B. Makins, N. E. L. Margetson, A. R. Mather, Q. S. Moore, Elizabeth M. Munro, W. S. Munro, G. M. Ogilvie, T. G. Paterson, W. B. Paterson, J. M. Robertson, Ian Shaw, Catherine J. Tulloch, R. P. M. Urquhart, Bryan Willis, F. F. Wilson, W. M. Wilson, Elizabeth J. Q. Wood, J. C. Yellowley.

*In absentia.

The following diplomas have also been awarded:

D.M.R.-D.—F. G. T. Beetham, D. A. E. Dewar, R. K. McFarlane, D. A. R. Ritchie.

D.M.R.-T.—A. R. Lyons, K. S. Preston, J. B. McEwan.

The Crichton research scholarship has been awarded to Dr. Evelyn A. C. Skinner, and the Hastilow research scholarship in rheumatism to Dr. W. R. M. Alexander.

University of Durham

On Dec. 19 the following degrees were conferred:

M.B., B.S.—B. T. M. Aboko-Cole, Kathleen D. Blackett, Q. A. Bynoe, Robert Chambers, Dorothy H. Cooper, Ann E. Crabbe, E. P. Daniels, C. C. Day, G. MacA. Dowson, K. W. H. Fenwick, F. M. Fyfe, Edith P. Gilbertson, J. C. Gilbertson, J. C. Gilmour, H. E. Harper, A. G. Larson, Moira Lickley, C. R. Markham, Jean A. Rosenstein, I. M. Telfer, Archibald Turner, I. A. R. Watson, Alan White.

University of St. Andrews

In recent examinations the following were successful:

M.D.—R. A. B. Rorie.

M.B., Ch.B.—Keith Davies, Colin Gunn, Julia C. Izzard, R. M. Kelly, Eileen M. Key, E. D. McEwan, H. R. Simpson, Elizabeth M. Stephen.

University of Glasgow

On Dec. 19 the following degrees were conferred:

Ch.M.—R. B. Wright (with high commendation).

Ph.D.—T. W. Wikramanayake.

M.B., Ch.B.—G. J. Addis, J. C. Baird, A. T. Bowie, Mavis J. Bowyer, Z. D. Brodie-Mends, D. B. Campbell, G. R. Carroll, Nathaniel Chazan, Joan A. Cree, G. L. W. Cunningham, A. F. Davidson, J. McK. Davie, J. A. Docherty, Angus Dodds, T. E. S. Fergusson, Morag B. P. Fernie, H. F. Frame, D. A. S. Fraser, Annice H. G. Gillespie, A. K. Gillies, Joyce E. J. Hassan, Hugh Hatrick Thomas Hetherington, W. E. I. Healy, D. E. Jardine, J. S. Kennedy (with commendation), W. McG. Kirk, S. J. Lepper, Mrs. David G. Lindsay, Eileen M. MacColl, Francis McCormack, Alasdair Macdonald, Jean Y. MacDougall, A. G. R. McFadyen, James McGlone, S. W. McGowan, Barbara S. Maclean, Donald Macmillan, T. E. Macnamara, A. S. MacPhail, Ian Macpherson, Ferguson McRae, Robert Meldrum, C. M. Morton, R. O. Nkeaka, A. R. Pate, Robert Reid, H. G. Robinson, E. D. T. Ross, George Ross, G. B. Ross, Joyce W. Russell, J. H. Shearer, W. M. Shovlin, Allan Sinclair, J. D. Stevenson, Sheena G. MacD. Stuart, John Sutherland, A. S. Taylor, A. S. Thomson, Dorothy E. Walby, Ethna A. Walshe, Doris M. White, J. G. Young, Jean McI. Young.

The diploma in public health was awarded to James McGovern.

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(continued overleaf)

Royal College of Surgeons of Edinburgh

At a meeting of the college on Dec 17, with Prof Walter Mercer, the president, in the chair, the *following were admitted* to the fellowship

W A Anderson, M I Anwar, Mohammad Anwer, Agnes U Campbell, B M Corkill C M Couves R M Gaitonde *G B Gibson*, R W. L Heddle J H Hofmeyr Y M Kim I C S Knight, G B Ong, *J N* Ravalia, John White

W D MacLennan was admitted a fellow in dental surgery

Fellowships in Clinical Research

The Medical Research Council invite applications for a third series of *fellowships in clinical* research, tenable at centres in the United Kingdom during the academic year 1953–54 (see *Lancet*, 1951, i, 536) The awards will be made for one year in the *first instance, and* will be renewable annually in approved cases up to a maximum of three years in all Candidates must be medically qualified and clinically experienced, and should preferably have worked in a department where clinical research was in progress They will be invited to submit their proposals about the type and place of work, but the council will be *glad to help successful* candidates to find suitable departments or *laboratories* Applications must be sponsored by the head of the appropriate department in the candidate's university or medical school Forms of application may be had from the secretary, Medical Research Council, 38, Old Queen Street, London, S W 1, to whom they must be returned not later than March 1

South African Research Fellowship

Applications are invited from doctors registered in South Africa for the 1953 award of the Eli Lilly medical research fellowship The value is $250 a month for 12 months, plus travelling expenses to and from the U S.A The closing date for applications is May 15 Further details can be had from Dr L Eales, hon- secretary of the selection committee, Cape Town Post-Graduate Medical Association, P O *Box* 2980, Cape Town

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Emergency Bed Service—*In the week ended last Monday*, applications for general acute cases numbered 1379 The proportion admitted was 93 03%

Dr Macdonald Critchley has been elected corresponding foreign member of the Academie de Médecine of France

Diary of the Week

JAN 4 TO 10

Monday, 5th

Royal Eye Hospital *St George's Circus Southwark S E*
5 P.M Dr T H Whittington Convergence Heterop
Introduction to Orthoptics

Tuesday, 6th

Postgraduate Medical School of London
5 30 P M (London School of Hygiene and Tropical Med
Keppel Street, W C 1) Sir James Spence Method
of Clinical Science

Institute of Dermatology, St John s Hospital, Lisle Street
5 30 P M Dr H Haber Cutaneous Manifestations of S
and their Differential Diagnoses

Wednesday, 7th

Institute of Dermatology
5 30 P M Dr J O Oliver Serological Diagnosis of Sy

Medico Chirurgical Society of Edinburgh
8 30 P M (Royal College of Surgeons 18 Nicolson St
Dr T M Galloway, Mr R M Hill *Hypertension*

Thursday, 8th

Postgraduate Medical School of London
5 30 P M Dr S J Folley, D SC, F R S *Pituitary Hor*
in Reproduction and Lactation

Royal Eye Hospital
5 P M Dr S Nevin *Diagnosis of Cerebral Tumour*

Institute of *Child Health, The Hospital for Sick Chi*
Great Ormond Street W C 1
5 P M *Dr C Worster Drought Speech Disorders in Chi*
of School Age

Institute of [illegible]
5 30 P M [illegible] ratum Diutinum G
loma [illegible] ions

St George's [illegible] Hyde Park Corner, S
5 P M Dr [illegible] ical demonstration

Alfred Adler Medical Society
8 P M [illegible] Chandos Street W 1) Dr J D Wyndham Pe

Liverp [illegible] 114, Mount Pleasant Liverp
8 P [illegible] Diagnosis and Treatme
and Larynx

Friday, 9th

Royal Eye Hospital
5 30 P M Mr Howard Reed Visual Fields

Institute of *Dermatology*
5 30 P M Dr Brian Russell Clinical demonstration

Society of Chemical Industry
7 P M (London School of Hygiene and Tropical Medi
Prof E R H Jones, F R S *New Routes to Cortiso*

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Newcastle R H B Sr Reg	49
Nottingham City Sr H O	50
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Poole Gen H O	50
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Sheffield R H B Locum Cons or S H M O	
Shrewsbury Royal Salop Infy H O s	
Southampton General H O	
Southampton Royal S Hants H O	
St Albans City H O	
St Helen s H O	
Stockport Infy H O s	
Stoke-on Trent City Gen H O 's or Pre reg H O 's	
Swindon Hosp Group H O	
Taunton H M C H O or Pre reg H O	
Truro Royal Cornwall Infy H O	
Wakefield Clayton Sr H O	
Wakefield Gen Sr H O	
Weston-super-Mare Gen H O s	
Whiston County H O	
Winchester Royal Hants Cty H O	
Wolverhampton H M C H O 's	
W*orksop* Victoria H O	
Worthing Group H M C H O	
Wrexham Maelor Gen H O	
Yorkshire East Riding H M C H O	
Northern Ireland Hosp Authority Sr H O	
UROLOGY	
Hastings and St Leonards Buchanan Sr H O	
Salford Royal Sr *H* O	
GENERAL	
New York Albany *Internships* & Residencies	
New York Rochester Gen Interns and Res	
PUBLIC APPOINTMENTS	
GENERAL PRACTICE	
HOSPITAL SERVICES—NON MEDICAL	
MISCELLANEOUS	

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EOGRAPHIC VARIATION IN NATURALLY ACQUIRED TUBERCULIN SENSITIVITY*

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ALMOST all proponents of B.C.G. vaccination agree that c.g. need not (or should not) be given to persons already fected with tuberculosis. B.C.G. infection is believed be effective only if it precedes infection with virulent ibercle bacilli. This doctrine governing the use of c.g. seemingly involves no serious theoretical problem: tuberculin test is made; if the tuberculin reaction is egative B.C.G. is given, if positive, B.C.G. is not given; nd few would challenge the view that tuberculin testing hould be a reasonably efficient way to separate previously ifected from non-infected persons in a population.

Turning from theory to practice, however, one finds an mazing variety of recommended tests, dosages of tuberulin, kinds of tuberculin, criteria for distinguishing ositive from negative reactions, and so on. From the tandpoint of vaccinating or not vaccinating with B.C.G. hese differences may or may not be important. But they ust affect the validity of daily decisions in practical uberculosis work regarding the identification of persons reviously infected with tuberculosis.

The present paper deals very broadly with the problem f using the tuberculin test to obtain information on aturally acquired tuberculin allergy and the use of such aterial as an index of the prevalence of tuberculosis nfection in a population. The report is based on pre-accination Mantoux tests made by the field staff of he Tuberculosis Research Office of the World Health rganization, Copenhagen, in connection with large-cale studies on B.C.G. vaccine and vaccination carried ut during the past several years. It is the third in a eries of papers illustrating how routine health-service rogrammes can contribute to the solution of fundaental problems in medical science, if the work is carefully planned and done with at least reasonable accuracy.

In the course of selecting children to receive B.C.G. n this series of studies, pre-vaccination Mantoux tests ave been made on about 40,000 children in Denmark, exico, Egypt, and a rural part of South India. All of he tests were given with the same lot of P.P.D. tuberculin RT XIX-XX-XXI),† and the work, though carried out in idely separated countries, was performed with a high egree of uniformity by personnel who had had intensive raining in field techniques and procedures. Most of hem have, at some time, worked under close supervision n the research programmes in Denmark. Both a weak nd a strong dose of tuberculin were used, thus providing unique and fairly large body of data for the study and omparison of the pattern of natural tuberculin sensitivity f children living in four different parts of the world.

TUBERCULIN SENSITIVITY IN DIFFERENT COUNTRIES

From this material we present here only the results of pre-vaccination tests with 10 and 100 T.U. for about 10,000 children in Denmark, 1700 in Mexico, 3000 in Egypt, and the results of 5 and 100 T.U. tests for 2500 children in South India. The criterion for giving the 100 T.U. test, and B.C.G. vaccination as well, was failure to react with at least 6 mm. of induration to the initial 10 T.U. test (5 mm. to the 5 T.U. test). The 100 T.U. test played no part in the selection of children for vaccination: it was given only to obtain additional information on tuberculin sensitivity before vaccination.

The tuberculin sensitivity of these children is probably fairly representative of each of the four different areas; B.C.G.-induced allergy had not yet distorted the pattern of natural allergy in any of the populations, and the few who had been vaccinated were identified and excluded from the material. The Danish children attended 225 municipal schools in a rural part of Jutland; the Egyptian group comprised pupils in 10 municipal schools in the Delta area and 3 schools in Luxor in the Upper Nile; the Mexican children attended 3 schools for working mothers in Mexico City; and in South India the children were part of a general population surveyed in several villages in the Madanapalle area. The ages of the children ranged from 7 to 14 years, though the groups in Egypt and India included some up to 20.

The results of the pre-vaccination tests are not expressed in terms of the percentage of positive reactors, as is customarily done. Instead, simple histograms are given to describe graphically the frequency distributions of the tranverse diameter of the indurated area of the tuberculin reactions. This form of presentation brings out features which would have been completely obscured by arbitrarily classifying reactions simply as positive or negative. In fact, it provides the basis for a much better understanding of the nature of tuberculin sensitivity.

The four histograms shown in fig. 1 describe the pattern of pre-vaccination tuberculin sensitivity of the children tested with a weak dose of tuberculin in the four countries. General inspection of the histograms discloses one important feature common to all but the one for India: the distributions are clearly divided into two

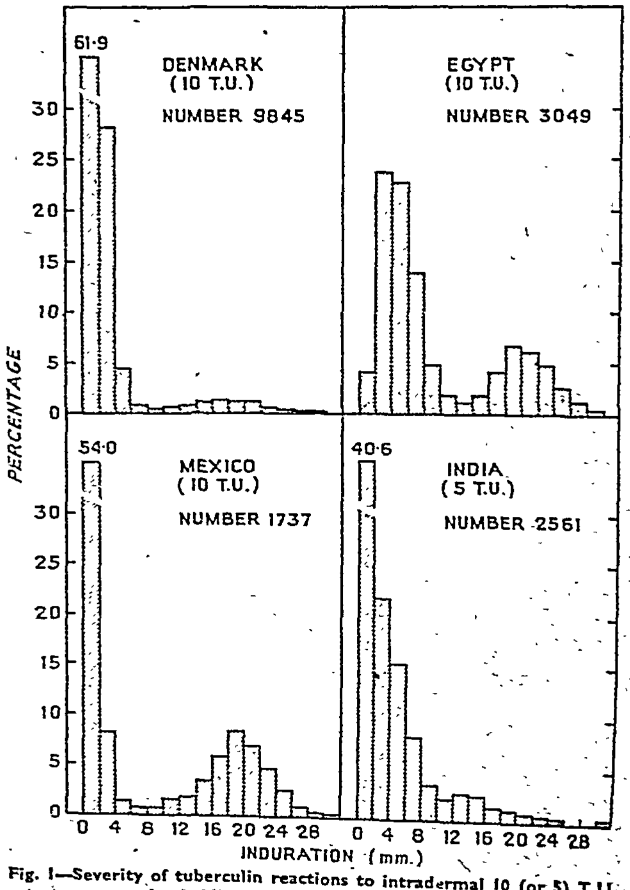

Fig. 1—Severity of tuberculin reactions to intradermal 10 (or 5) T.U. test among school-children in Denmark, Mexico, Egypt, and India.

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* This is the third of a series of papers entitled Research Contributions of B.C.G. Vaccination Programmes. The first two papers appeared in *Public Health Reports*, 1951, 66, 259, 1427.

† One Tuberculin Unit (1 T.U.) of RT XIX-XX-XXI is prepared to contain 0·00002 mg. in 0·1 ml. of solution.

tuberculosis infection is the only or necessarily the principal cause of tuberculin sensitivity in man Evidence presented here and elsewhere demands, we believe, the recognition of at least two kinds of tuberculin sensitivity. The kind designated here as *high grade sensitivity* (fairly strong reactions to a weak dose of tuberculin, about 5–10 T U) constitutes the specific response to tuberculous infection in the classical sense, as accepted by tuberculosis workers since Koch first discovered that normal animals infected with tubercle bacilli become sensitive to tuberculin The kind designated here as *low-grade sensitivity* (small reactions to a weak dose of tuberculin which appear as large reactions to a strong dose) constitutes a "non specific" response—i e, a response to tuberculin the cause of which is still unknown

According to this interpretation high-grade tuberculin sensitivity should be found wherever human tuberculosis is found, and variations in the proportion of children with this kind of sensitivity ought to correspond roughly to variations in the prevalence of tuberculosis Such was in fact the case in the material presented here Tuberculosis is known to exist in all four localities, and high-grade sensitivity is also found in all four

Moreover, we can accept as an established fact that children are rarely exposed to tuberculosis in Denmark, where the prevalence of the disease is one of the lowest in the world Knowledge of the prevalence of the disease in Mexico and Egypt is much less precise, but it is undoubtedly very much higher than in Denmark As regards the village children tested in India, we know from the results of a careful X ray survey of the general population that only a very low frequency of active cases of tuberculosis was found § From what we know, the prevalence of tuberculosis in each locality corresponds reasonably well to the proportion of children having high-grade tuberculin sensitivity, and these proportions may be estimated from the histograms (cf fig 1) as being roughly 0% in Denmark, 35% in Mexico City and Egypt, and 10% in the village children in South India

The proportion of children having the low-grade kind of tuberculin sensitivity in the four countries corresponds neither with the proportion having high grade sensitivity nor with the prevalence of tuberculosis On purely epidemiological statistical evidence we are forced to postulate that this kind of sensitivity is the result of something other than infection with *Mycobacterium tuberculosis* (of the human or bovine type) We know as yet very little about the cause, but from this and other recently published studies it appears to be related to geographic factors A large and geographically extensive study of tuberculin sensitivity of student nurses in the U.S A has shown the low grade kind of sensitivity to be highly prevalent in the south-eastern states but relatively rare throughout the rest of the country (Palmer et al 1950) In that study, as in the present one, there was a lack of correlation between the prevalence of low-grade sensitivity, on the one hand, and both high grade sensitivity and other signs of tuberculosis, on the other Further, it was pointed out that the low-grade sensitivity is more prevalent in rural than in urban areas while the reverse is true for the high-grade The other study dealing directly with this subject was made in the mountainous area around Darjeeling, north of Calcutta (Bates et al 1951) Children living on tea plantations situated at high altitudes (6000 ft above sea level) had a pattern of tuberculin sensitivity resembling that found in Denmark, children living in the low-lying valleys less than 3 air miles away had a pattern somewhat like that described here for South India So far as was known, the prevalence of tuberculosis was about the same throughout the entire area (Incidentally, it m mentioned that the children in Mexico City l altitude of over 7000 ft) In both the stud United States and the one in Darjeeling the kind of sensitivity was designated as "non spe the hypothesis was offered that it is due to infec an organism antigenically related to *Myco*

Practical Significance

In applying the present results to tuberculo it is of interest to inspect fig 1 a little more note how currently accepted criteria for selecting for vaccination actually operate in different co In most B C G programmes today pre vac Mantoux reactions to a weak dose of tuberc separated at 6 mm (or 5 mm) In Denmark and 6 mm falls at a place on the scale where the reactions is low, with the significant consequen errors in the measurement of reactions will have small effect on the selection of children for vacc We may note, also, that in these countries 8 10 mm would give about the same result In Eg India the frequency of reactions at or near 6 relatively high which means that even small e systematic differences in the measurement of r will make large differences in the proportion of given B C G For example, changing the criter 6 to 10 mm in Egypt means changing the pro vaccinated from 50 to 70%

It is also of interest to consider to what ext proportion of children excluded from vaccinati similar "% positive" figures from tuberculin may be used as valid measures of the frequ tuberculous infection in a population Curves the percentage of "positive reactors" by age in a like Denmark are probably reasonably correct as of tuberculosis infection, because of the relative of low-grade sensitivity But corresponding age in countries where low grade sensitivity is preval be very misleading and subject to even greater both a weak and a strong dose of tuberculin are u the proportion of reactors combined to give "% positive" figure If our hypothesis is confirm low-grade sensitivity is unrelated to tuberculosis in it will be necessary to re-examine the results o tuberculin-testing surveys, since the presence grade sensitivity increases the frequency of the sidered positive reactors in a population It m be that current estimates of the prevalence of tub in many countries have been unduly magnified

Finally, at least on theoretical grounds the and prevalence of low grade sensitivity have im implications as regards B C G vaccination I countries—e g, Denmark—B C G is being given to children who are non sensitive to tuberculin time of vaccination They have neither been pr infected by the tubercle bacillus nor subjected factor that produces the low-grade or non spec of allergy. The B C G -induced allergy later appe these children is therefore uncomplicated by any allergising influences In some other countrie Egypt—B C G is being given mainly to childr already exhibit some sensitivity to tuberculin, bu we have no knowledge of how this complica production and interpretation of B C G -induced

SUMMARY

This paper contains a simple visual analysis patterns of tuberculin sensitivity found before va of children in Denmark, Mexico City, Egypt, an India Histograms of weak dose reactions (5 or on sizable samples of children in these four c bring out the fact that tuberculin sensitivity is separated into three main kinds high-grade se

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§ Personal communication from Dr Johannes Frimodt Moller, Chief Madanapalle Field Research Station World Health Organization Tuberculosis Research Office and Medical Superintendent Union Mission Tuberculosis Sanatorium, Arogyavaram South India reactions), low-grade sensitivity (small reactions), itive non-sensitivity. The findings are interpreted cating that high-grade sensitivity represents the response to contact and infection with human ulosis in the classical sense. Low-grade sensitivity, other hand, seems to be independent of true ulous infection but closely associated with geo- c factors. The third kind represents children ave neither had a tuberculous infection nor have subjected to the influence of the unknown factor causes low-grade sensitivity. The material shows here are wide variations in different countries in the rtion of children having each of the three different of sensitivity.

e present system of selecting children for vaccination rding to the size of the reaction to a weak dose of rculin) seems to be fairly satisfactory for assuring those with a high level of allergy will not be vacci- d. But it is entirely inadequate for separating children low-grade sensitivity either from those with high- e sensitivity or from those who are non-sensitive to rculin. By the present scheme some children with grade sensitivity are vaccinated and some are not. seems wholly illogical and emphasises the need to y the pattern of tuberculin sensitivity on an inter- onal basis. It also emphasises the unexpected pitfalls n techniques and procedures are directly transplanted 1 one country to another without prior knowledge of differences that may exist in different parts of the ld.

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UT, LEUKÆMIA, AND POLYCYTHÆMIA

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OUT occurs very rarely in patients with typical onic myeloid leukæmia and rarely in patients with ical primary polycythæmia; but it does occur not ommonly in patients who have a disorder of the od-forming tissues apparently related both to myeloid æmia and to polycythæmia. In these patients the eloid metaplasia of the spleen and other tissues is posed of cells of the erythroblastic and leucoblastic es, in various proportions and especially of mega- yocytes. The changes in the bone-marrow are either se of hyperplasia involving erythroblasts, leucoblasts, megakaryocytes; or of fibrosis, with various nbers of bone-marrow cells among the fibrous tissue, gakaryocytes being the most conspicuous. Histo- ically, therefore, these cases differ from typical cases myeloid leukæmia in showing myeloid metaplasia olving all bone-marrow elements and not pre- ninantly leucoblastic cells. They are related, histo- ically, more closely to primary polycythæmia, in ich hyperplasia of all bone-marrow elements, in ious proportions, has been recognised for many years eber 1921).

MYELOID LEUKÆMIA

Many workers have stated that gout might be expected occur commonly in cases of chronic myeloid leukæmia, ing to the increased production of uric acid, but that fact it occurs very rarely: a probable case of chronic eloid leukæmia is mentioned in Duckworth's (1889) atise on gout; Roberts and Rose Bradford (1907) only 1 case of gout and myeloid leukæmia, and in at the patient had had gout for many years before the leen became enlarged and the blood leukæmic; and Wintrobe's (1951) textbook only one reference to gout and leukæmia is given, and that is to an atypical case of leukæmia (Brunner 1932). Forkner (1938) says that the simultaneous occurrence of gout and leukæmia is so rare that any real relationship seems doubtful. In a recently published case attacks of gout occurred soon after the beginning of a course of X-ray treatment in a patient with typical chronic myeloid leukæmia (Shorvon 1946).

POLYCYTHÆMIA

Gout occurs in a small proportion of patients with polycythæmia. Of 168 cases of polycythæmia reviewed by Tinney et al. (1945), gout occurred in 8, and of 125 cases of polycythæmia reviewed by Videbæk (1950) gout occurred in 11. In 8 cases gout began from two months to three years before polycythæmia was recognised (Weber 1921, 1934, Rosenthal and Bassen 1938, Tinney et al. 1945), and in 7 cases gout began from three months to four years after polycythæmia was recognised (Weber 1921, Avery 1930, Rosenthal and Bassen 1938, Reifenstein 1939, 1945, Tinney et al. 1945).

It is known that in some patients with polycythæmia who survive many years the disorder gradually changes, the polycythæmia diminishing, the spleen enlarging, and increased leucoblastic and megakaryocytic hyperplasia of the spleen and other tissues developing, with increased leucocytosis and with immature leucocytes in the circulating blood (Rosenthal and Bassen 1938, Stone and Woodman 1938, Tinney et al. 1945, Videbæk 1945).

When polycythæmia is seen at that stage, a fairly characteristic picture is presented. The patient is elderly and complains of abdominal pain, discomfort, or swelling due to the large spleen; of hæmorrhages into the tissues or from the alimentary tract; of tiredness and weakness; and of cramps in the legs at night. The patient may have had attacks of gout, or may have chronic gout. There may be acne rosacea, a slightly yellowish complexion, no enlarged lymphatic glands, a large hard spleen, and a large soft liver. Examination of the blood shows a slight anæmia, a moderate leucocytosis, and a few immature leucocytes and nucleated red cells. Examination of the bone-marrow shows either large numbers of megakaryocytes in an active marrow or sclerosis of the marrow, often with megakaryocytes among the fibrous tissue.

In some patients who present these features no history suggesting preceding polycythæmia can be obtained, though "chlorotic polycythæmia" (Rosenthal and Bassen 1938) could not be recognised from the history. When there is no evidence of preceding polycythæmia, "megakaryocytic myelosis" or "myelosclerosis" may be diagnosed, but many different names have been used to describe such cases, and there is disagreement about the nature of the disorder and its relationship to chronic myeloid leukæmia. Gout may precede the finding of the enlarged spleen and other features, or may occur while the patient is under observation. For example, in 6 cases gout occurred from seven to thirty-two years before recognition of the disorder of the blood-forming tissues (Hagedorn 1926, Hoffmann 1926, Coste et al. 1948, Merskey 1949), and in 1 case five years after the disorder was recognised (Brunner 1932). Of 30 patients with "chronic marrow failure, myelosclerosis, and extra-medullary hæmatopoiesis" 2 had gout (Wyatt and Sommers 1950).

I have had under my care 9 patients with gout, splenomegaly, and immature cells in the circulating blood; 5 of these had polycythæmia at some stage of the disorder, but in the other 4 there was no history suggesting preceding polycythæmia, nor did this develop under observation.

The presenting symptoms which led to the discovery of splenomegaly and the other features were abdominal pains or discomfort in 3 cases, hæmorrhage per rectum in 2, diarrhœa and hæmorrhage per rectum in 1, epistaxis in 1, weakness and tiredness in 1, and gout in 1.

Of these 9 patients 4 had gout before any other symptoms of the disorder of the blood-forming system , attacks of gout began one, three, eight, and forty-one years before the splenomegaly was discovered The 5 other patients began to have attacks of gout one, two, four, five, and eleven years after splenomegaly was discovered

These 9 patients were observed for from four years and four months to seventeen years, 7 having been observed for more than six years Three patients developed *chronic gout, and this was their chief disability* towards the end of their lives Six patients had courses of X-ray treatment to the enlarged spleen, which in 4 produced considerable improvement in the patient's feeling of well-being and decreased the size of the spleen Courses subsequent to the first had diminishingly favourable effects In 1 patient an attack of gout was precipitated by each course of treatment

Severe anæmia occurred as a terminal event, with cachexia, in 2 patients Otherwise severe anæmia occurred only after intestinal hæmorrhages, and in 1 patient for a short time without evident cause, recovery taking place later

Of the 5 patients who had polycythæmia 2 had it when first seen, one for abnormal tiredness, and the other for a hæmorrhage per rectum The 3 other patients developed polycythæmia under observation, either spontaneously or as an effect of treatment with iron, liver extract, or X-ray treatment to the enlarged spleen In all 5 patients polycythæmia disappeared later

Necropsies were made of 8 of the 9 patients who had gout In 6 of these the bone-marrow was hyperplastic, megakaryocytes were the predominant cells, and there was no sign of sclerosis In 1 patient the bone-marrow was sclerotic, but large numbers of megakaryocytes were present in the fibrous tissue, and in the remaining patient the bone-marrow was sclerotic, without megakaryocytic activity, though megakaryocytes were prominent in the myeloid metaplasia of the spleen

Case 1 —A man, aged 71, died in March, 1945, of cachexia and chronic gout, after seven years' observation The presenting symptom, gout, had been present in attacks since 1897 When he was first seen for gout in 1938, a large spleen was found There was no anæmia, there had been no polycythæmia, and there was moderate leucocytosis, about 25,000 per c mm , with a few immature leucocytes Severe anæmia developed at the end of 1938, and by the middle of 1939 the patient was polycythæmic He had moderate anæmia and abnormal bruising from then till death His blood uric acid level was constantly above 7 mg per 100 ml in 1938–45 He became bedridden from chronic gout in 1944

Necropsy showed bone marrow hyperplastic, megakaryocytes very numerous, no fibrosis, spleen affected with myeloid metaplasia and fibrosis, with malpighian bodies preserved in some sections and absent in others and the liver with slight myeloid metaplasia

Case 2 —A man, aged 66, died in June, 1947, of congestive heart failure, after six years' observation The presenting symptoms were weakness and tiredness in 1941, and a large spleen and polycythæmia were found Gout began in 1938, and chronic gout developed in the last four years of life The patient had never had severe anæmia, but he had polycythæmia in 1941 and 1945, with leucocytes normal or slightly increased immature leucocytes being constantly present in very small numbers His serum uric acid level was 6 8–12 9 mg per 100 ml *in 1944–47 X ray treatment in* 1944 and 1946 had little effect on the size of the spleen

Necropsy showed bone marrow hyperplastic, with very large numbers of megakaryocytes and no fibrosis , the spleen with slight myeloid metaplasia , liver with cirrhosis and no myeloid metaplasia and small areas of myeloid metaplasia in the kidneys

Case 3 —A man, aged 49, died in June, 1945, of weakness, wasting, and anæmia, after six and a half years' observation The presenting symptom was abdominal discomfort due to a large spleen in January, 1939 The patient had had attacks of gout in the feet since 1931 , these recurred often, and chronic gout developed towards the end of his life He had never had polycythæmia He had slight anæmia at first leucocytosis (38,000 per c mm) with a few immature , and nucleated red cells constantly This leucocytosis d appeared under X ray treatment In 1943 and 1944 th number of nucleated red cells greatly increased and surpass the leucocytes in number The serum uric acid level w constantly high, above 7 0 mg per 100 ml in 1939–45

Necropsy showed bone marrow replaced by fine fibro tissue containing endothelial lined spaces packed with myelo cells with large numbers of megakaryocytes , the spleen wit intense myeloid metaplasia, large numbers of megakaryocyt and some *increased fibrosis , and intense myeloid* metapla of the liver

Case 4 —A man, aged 61, died in April, 1945, of weakne and wasting, after nine years' observation The presentin symptom was hæmorrhage per rectum in November, 193 *when a large spleen was found Attacks of gout began* i 1929 The first hæmorrhage per rectum took place in 1930 when the patient was found to be plethoric, but his sple was not felt at that time He was subject to abnorm bruising from 1930 to his death He had never had seve anæmia , the polycythæmia disappeared in 1941 and nev reappeared Moderate leucocytosis was present, nev exceeding 15,000 per c mm , and there were a few immatur leucocytes, never exceeding 3% Four courses of X ra treatment were given—one in 1938, two in 1939, and one i 1940, the first two courses producing considerable improvemen in health

Necropsy showed bone marrow hyperplastic, with ve large numbers of megakaryocytes and some slight fibrosis the spleen with fibrosis, myeloid metaplasia, and very fe and small malpighian bodies , and the liver with no myeloi *metaplasia*

Case 5 —A man, aged 58, died in February, 1950, o cachexia, anæmia, and heart failure, after seventeen years observation The presenting symptom was abdominal pain since 1920, later found to be due to repeated hæmorrhages into th *perinephric tissues, producing a large hæmatoma, which was* opened in 1933 The patient had a large spleen and a large liver, slight anæmia, and leucocytosis of 20,000–38,000 per c mm in 1933–40 Leucopenia followed X ray treatment in 1940, 1941, and 1942 The patient had never had polycythæmia or any past history suggesting this A few immature leucocytes (2–4%), and a few nucleated red cells were alwa found The patient had gout in his great toes in 1944 and 1947 His blood uric acid level was constantly high in 1930–50, being nearly always above 7 mg per 100 ml

Necropsy showed bone marrow active with very numerous *megakaryocytes and slight fibrosis , the spleen with localised* areas of myeloid tissue with large numbers of megakaryocyt and some generalised myeloid metaplasia, but with malpighia bodies preserved , and the liver with very slight myeloid metaplasia

Case 6 —A *woman, aged 63, died in March, 1936, after* a operation for ligature of the splenic vessels, after five an a half years' observation The presenting symptom wa epistaxis in 1930, when a large spleen was found The patie had been subject to abnormal bruising since 1920, and achi in the left side of her abdomen since 1923 She had attacks gout in her hands and feet in 1934–36, and moderate anæm in 1930–36, never polycythæmia, and moderate leucocyto usually about 20,000 per c mm , with a few immature leucocytes, never exceeding 3% Her blood uric acid level 12 5–16 0 mg per 100 ml in 1936

Necropsy showed bone marrow hyperplastic with very lar numbers of megakaryocytes and no fibrosis , the spleen wi intense myeloid metaplasia with large numbers of me karyocytes and no malpighian bodies and the liver wi moderately intense myeloid metaplasia with large numb of megakaryocytes

Case 7 —A man, aged 63 died in June, 1942, after a operation for ligature of the splenic vessels, after six and a half years' observation The presenting symptom was pa in the left side of his abdomen in 1936, when a large sple was found The patient was subject to abnormal bruis from 1935 to his death He had repeated hæmorrhages in his gastro intestinal tract from 1939 to his death He had attacks of gout in his great toes in 1940–42 His blo uric acid level was 6 5–8 0 mg per 100 ml in 1939–42 He had moderate polycythæmia at times, anæmia after th *severe gastro intestinal hæmorrhages, and moderate* leu cytosis, 20,000–30,000 per c mm , a few immature leucocyte from the occluded hepatic-vein pressure to obtain the effective portal-vein pressure.

These theoretical considerations do not detract from the practical value of the method for assessing portal hypertension. It is a useful preliminary to vascular surgery in cirrhosis both to confirm the diagnosis of portal venous hypertension and to distinguish the site of the portal venous obstruction. It may also be useful, after portacaval anastomosis for cirrhosis, to repeat hepatic-vein catheterisation; a continued low pressure reading confirms that the shunt is still patent.

SUMMARY

The pressure obtained with a catheter occluding a hepatic vein does not differ significantly from that obtained directly from a portal-vein radicle, unless there is extrahepatic portal venous obstruction.

The mean occluded hepatic venous pressure in 24 patients without liver disease was 6·8 mm. Hg. In 11 patients with portal cirrhosis the mean pressure was 22·0 mm. Hg. Raised values were also obtained in 2 patients with subacute hepatitis and in four patients with congestive heart-failure. Normal values were found in 3 patients with extrahepatic portal venous hypertension and in 12 patients with obstructive jaundice (9 extrahepatic and 3 intrahepatic).

Theoretical objections to the method do not invalidate its use in the clinical assessment of portal hypertension.

We are indebted to Mr. Sol Cohen for kindly referring one patient; to our surgical colleagues for their coöperation: and to the Lund Fund of the Diabetic Association for an expenses grant.

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HEREDITARY SPASTIC PARAPLEGIA

REPORT OF A FAMILY WITH ASSOCIATED EXTRAPYRAMIDAL SIGNS

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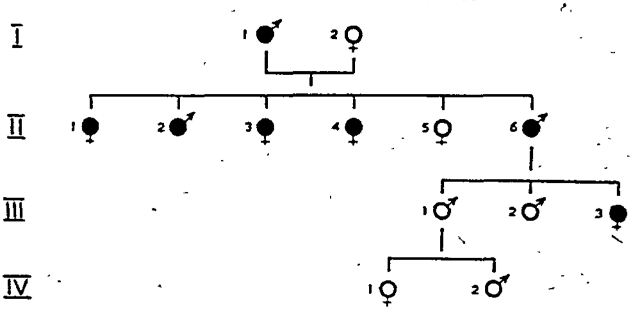
HEREDITARY spastic paraplegia is a well recognised though rare disorder. Few affected families have been described in this country, until recently, apart from those recorded by Gee (1889), Holmes (1905), and Ogilvie (1908). In America Rhein (1916) published an extensive review of the subject, as did Paskind and Stone (1933), the latter with a necropsy report. Bell and Carmichael (1939) were only able to find one family with this disease in the previous twenty-five years' records of the two major hospitals for nervous diseases in London, and their comprehensive review, concerned chiefly with the genetic aspects, is based largely on families recorded in the Continental literature. Garland and Astley (1950) report a further family, and Bickerstaff (1950) records the largest number of cases so far found in one family in this country.



Family with hereditary spastic paraplegia: affected members shown in black. No known consanguinity in marriages.

The criteria of differentiation of this condition from other heredofamilial disorders of the nervous system, such as the hereditary ataxias and hereditary ataxia with paraplegia, are usually accepted as being the absence of ataxia and of cerebellar signs other than nystagmus. Whether any genetic relationship exists between spastic paraplegia and the hereditary ataxias is uncertain, but examples of hereditary spastic paraplegia occurring in the same stock as the hereditary ataxias have not been observed (Bell and Carmichael 1939). The post-mortem findings in these diseases are so diverse, and often apparently lacking in correlation with the previous clinical manifestations, that they do not provide a firm basis on which to form a classification in our present state of knowledge.

The essential features of hereditary spastic paraplegia are increasing spasticity of the lower limbs with relatively little loss of power, often associated with nocturnal flexion spasms of the feet, the upper limbs being slightly or not at all affected. The symptoms tend to appear at the same age in a particular family in which several members are affected in one or more generations, a fact which has been emphasised by Garland and Astley (1950). Various associated abnormalities have been described in some families; these include pes cavus reducible on standing (Bickerstaff 1950), amyotrophy, mental deterioration, speech disturbances, optic atrophy, and extrapyramidal lesions.

PRESENT FAMILY

The present family, inhabitants for several generations of a village adjacent to the Cambridgeshire Fens, is described partly because of the rarity of the condition in this country, and partly because of the presence in several members of extrapyramidal disorders, an association which has not been noted in any of the families so far reported in this country.

The pedigree is shown in the accompanying diagram. Nos. II 2, II 4, II 5, II 6, III 1, III 2, and III 3 have been examined. Information about the other members of the family has been derived from questioning all the members interviewed. The father of I 1 was a strong active man who lived to an old age and, so far as is known, had no disability. His wife was also healthy.

I 1.—Male. Died at 74. Said to have had a slight tremor of the right arm and of the toes of both feet, coming on when he was a young man. During middle age, soon after dislocating a shoulder, he developed difficulty in walking and a tendency to a shuffling gait. Disabilities were insufficient to prevent his working as a farm labourer.

I 2.—Wife of I 1. Said to be healthy and died aged 75.

II 1.—Female. Severely crippled; never able to walk, owing to paralysis of legs and arms. Died at 20. Said to have had "cancer on the chest."

II 2.—Male, aged 65. At age of 10 progressive weakness of the left leg, with foot-drop, gradually came on. At 20 he noticed slight weakness of the right leg, and both legs tended to shake, especially when he was tired. Contractures had developed in the left leg, and permanent foot-drop necessitated a surgical boot. At 30 uncontrollable movements of head, arms, and legs, worse when he was unoccupied, came on gradually. Weakness of his legs progressed very slowly and insidiously, with increasing contractures in the legs, particularly the left. He could get about with difficulty, using crutches, until the age of 60, when he had to give up work, having hitherto run a small shop. Since his retirement his difficulty in walking has steadily increased, and he is now

TABLE II—SERUM CHLORAMPHENICOL LEVELS AFTER RECTAL ADMINISTRATION OF 17 MG PER KG BODY-WEIGHT

Case no	Serum-chloramphenicol (µg per ml)				
	1st hour	2nd hour	4th hour	8th hour	12th hour
1			20	20	20
2	40	20	20	—	—
3	40	20	20	40	30
Mean	40	20	20	20	17

= No sample available — = Non inhibitory concentrations

When a dose of 17 mg per kg was given per rectum, the antibiotic serum level behaved in a similar way, but the concentration at a given time was always less than with the bigger dose (table II and the figure)

On a previous occasion, I estimated the serum-chloramphenicol in a few patients after oral doses of 50 and of 25 mg per kg (El Borolossy 1951) The figure compares the levels recorded then with those now obtained after rectal administration It will be seen that, with a dose of 25 mg per kg given by rectum, the serum-chloramphenicol attains a high level rapidly, and then declines rapidly during the second to the fourth hours When the same dose is given by mouth, the serum level rises slowly to reach its maximum at the fourth hour Between the fourth and the twelfth hours the two curves lie close to one another A possible explanation of the differences in absorption during the first four hours is that when given by rectum the antibiotic is immediately brought into contact with an absorbing surface, whereas when it is given by mouth it has to pass the stomach barrier before reaching the absorbing surface of the intestines It should, however, be noted that all the serum levels obtained, whether administration was oral or rectal, were above that required for inhibition of the majority of sensitive bacterial strains

CONCLUSIONS

Rectal administration of chloramphenicol in doses of 17 mg, or more, per kg body-weight produces an effective concentration of the antibiotic in the blood for the following twelve hours Given per rectum a dosage of 17–25 mg per kg should be adequate in the treatment of most cases of typhoid fever

Addendum —After this investigation was completed I received a letter from Dr P Moggi of Milan indicating that "the hæmatic concentration of chloramphenicol given per rectum is nearly equivalent to that obtained when this antibiotic is administered per os "

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Preliminary Communication

DERIVATIVE OF p-AMINOSALICYLIC ACID WITH ENHANCED ANTITUBERCULOUS ACTIVITY

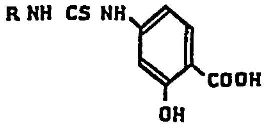
The many attempts that have been made to prepare derivatives of p aminosalicylic acid with enhanced antituberculous activity have so far failed in their object, all alterations in chemical structure so far tried having resulted in products of unaltered or diminished activity with the possible exception of the synthesis of the phenyl ester[1] The present work represents a new line of attack on this problem, of which the preliminary results appear to offer some promise

The powerful antituberculous activity of derivatives of p aminobenzaldehyde thiosemicarbazone, discovered by Domagk and his collaborators,[2] is well known, and it has also been found that considerable variations in this activity result from altering the substituents in the amino group In addition, it has been found in this institute[3] that some in-vitro antituberculous activity is exhibited by certain cyclic compounds (thiouracil derivatives) which contain the thiocarbamido grouping The object of our experiments was to explore the possibility of obtaining enhanced antituberculous activity by combining thiocarbamido and/or p-aminobenzaldehyde thiosemicarbazone groupings with p aminosalicylic acid in one molecule

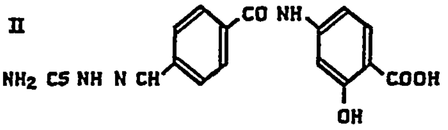
With this purpose in mind the following four types of compound have been synthesised (*a*) 4-thiocarbamido derivatives of salicylic acid (I, R = H, Me, *n*-Pr, Ph), (*b*) the thiosemicarbazone of 4-(4′ aldehydo)benzamidosalicylic acid (II), (*c*) the thiosemicarbazone of 4-(4′-aldehydo)phenylcarbamidosalicylic acid (III), and (*d*) the thiosemicarbazone of 4 (4′-aldehydo)phenylthiocarbamidosalicylic acid (IV)

The results of in-vitro biological tests are shown in the accompanying table It will be seen (table, A) that with a small inoculum and prolonged incubation compound IV is rather less active than p aminosalicylic acid, whilst the other compounds are all much less active It was observed, however, that compound IV was somewhat unstable in solution, and the tests were therefore repeated with a larger inoculum and shorter period of incubation, under these conditions (table, B) compound IV is considerably more active than p-aminosalicylic acid

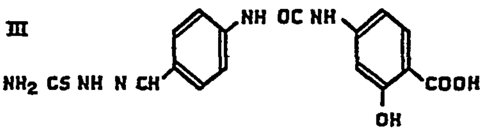
I



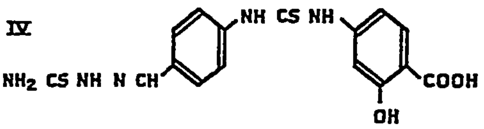
II



III



IV



This observation made it desirable to carry out an in-vivo test of the antituberculous activity of compound IV Mice were injected intravenously with 0 1 mg (moist weight) *Mycobacterium tuberculosis*, strain H37RV, and compound IV was administered at 0 5% in the diet (approx 30 mg daily) for 28 days from the day of infection No toxic effects were observed, and the median survival-time of the treated mice was 30 days as compared with 21 days for an untreated control group

Compound IV is more active in vivo than p aminosalicylic acid but less so than streptomycin, assessed by similar chemotherapeutic tests in mice, its activity is probably more of the order of the thiosemicarbazones The sharpness of the end-point obtained with compound

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[1] Freire, S A Rist N Grumbach, F *Ann Inst Pasteur* 1951, 81 407

[2] Domagk, G Behnisch R. Mietzsch F, Schmidt H *Naturwissenschaften* 1946 33 315

[3] Cornforth J W, Hart, P D Arcy Rees R. J W Unpublished data.

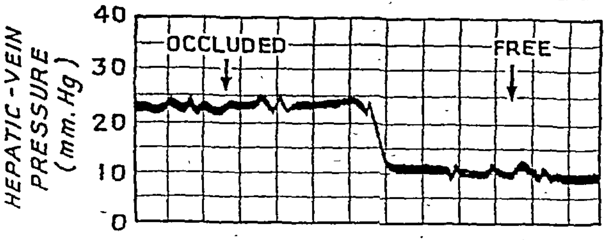

Fig. 3—Fall in pressure as catheter is withdrawn from occluded to free hepatic vein in portal cirrhosis (case 1).

hypertension. This is an interesting finding in view of the reported development of intrahepatic portal hypertension in such patients (Ahrens et al. 1950).

Infective Hepatitis

The mean occluded hepatic-vein pressure was normal in the 4 patients in this group, though 2 had pressures outside the upper range of normal. These 2 patients both had subacute hepatitis, and it seems possible that they already had some distortion of lobules, fibrosis, and portal venous obstruction. The finding of normal pressures in the acute stage of infective hepatitis suggests that the splenomegaly which may accompany this disease is not due to portal hypertension.

Congestive Cardiac Failure

The occluded hepatic-vein pressure in 2 patients with congestive heart-failure due to rheumatism and in 2 with cor pulmonale was raised, and there was only a slight gradient between the occluded and the free pressures (table III). This reflects the rise in pressure in the right side of the heart. The finding of a high occluded hepatic-vein pressure can result from long-continued congestive heart-failure.

Case 5.—A housewife, aged 41, with cor pulmonale, had had asthma since adolescence, and in the last year had developed increasing dyspnœa, œdema of the ankles, and swelling of the abdomen. On admission she showed the classical features of severe cor pulmonale, and the spleen was found to be enlarged. The occluded hepatic-vein pressure was 21·7 mm. Hg, and the free pressure 21·4 mm. Hg.

DISCUSSION

The present results are in agreement with those of Myers and Taylor (1951) using the same technique in normal and cirrhotic persons. Values in the same range are recorded directly in the portal vein exposed at operation (Walker 1952, Blakemore 1952). Pressures taken from fine plastic tubes inserted into a portal-vein radicle at operation also agree well with the occluded hepatic-vein pressures (table I). The findings of Myers and Taylor (1951) and Friedman and Weiner (1951) in laboratory animals are further confirmatory evidence. It therefore seems probable that the pressure measured in an occluded hepatic vein indicates the height of the portal venous pressure, although it is difficult to provide a satisfactory theoretical basis for this assumption.

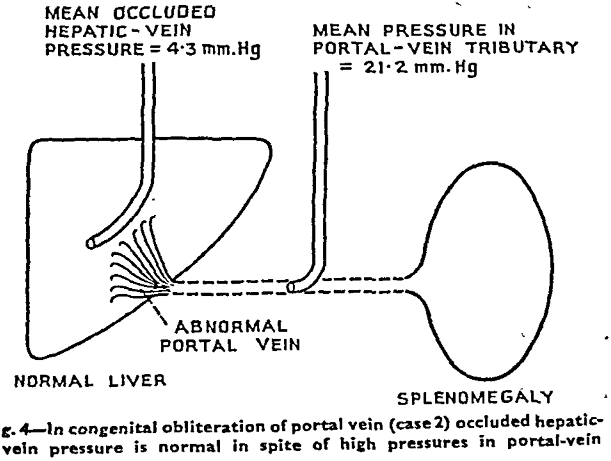
MEAN OCCLUDED HEPATIC-VEIN PRESSURE = 4·3 mm.Hg
MEAN PRESSURE IN PORTAL-VEIN TRIBUTARY = 21·2 mm.Hg
ABNORMAL PORTAL VEIN
NORMAL LIVER
SPLENOMEGALY

Fig. 4—In congenital obliteration of portal vein (case 2) occluded hepatic-vein pressure is normal in spite of high pressures in portal-vein tributary.

A pressure gradient exists from the portal vein to the hepatic veins. This pressure head is dissipated in the hepatic sinusoidal bed in overcoming vascular resistance. The occluding catheter stops blood-flow through a hepatic-vein radicle and the portal-hepatic vein pressure gradient in that radicle is lost. The static column of blood built up in this way is a measure of the pressure in the hepatic sinusoidal bed. It may in fact be more correct to call the pressure measured by the occluding catheter the intrasinusoidal pressure rather than the portal venous pressure. The intrasinusoidal pressure may be produced not only by the portal vein but also by the hepatic arterioles which open into the sinusoids. The agreement between values for portal venous pressure and the occluded hepatic-vein pressure suggests that the hepatic arterial component must play little part in the genesis of the intrasinusoidal pressure in normal man. This may not be true in hepatic cirrhosis, where direct portal venous-hepatic arterial shunts have been postulated (Herrick 1907, Epplen 1922, Dock 1942), though not universally accepted (Wilson 1951, Popper et al. 1952). It is unfortunate that it has not been possible to compare simultaneously the pressures in the occluded hepatic vein and those in the portal vein, but in one patient the pressure taken from an abdominal portal collateral was within 1 mm. Hg of that obtained simultaneously from the occluded hepatic vein. Direct shunting of arterial blood at high pressure into the portal vein in cirrhosis seems unlikely. Shunts between the hepatic artery and the hepatic veins in cirrhosis might cause a rise in hepatic venous pressure without there necessarily being a rise in portal-vein pressure. However, the oxygen unsaturation of the hepatic-vein blood did not differ from that in patients without liver disease. Shunts of any magnitude between hepatic artery and hepatic veins do not seem likely in cirrhosis, and intrahepatic shunting of blood therefore does not interfere with the practical application of this technique in normal subjects or in cirrhosis.

TABLE III—SUMMARY OF RESULTS

Type of case	No. of cases	Mean hepatic-vein pressures (mm. Hg)	
		Occluded	Free
Without liver disease ..	24	6·8 ±0·49† (2·6 – 11·2)‡	4·9 ±0·46 (0·6 – 10·6)
Portal cirrhosis *	11	22·0 ±1·94 (15·6 – 35·2)	8·9 ±1·02 (3·9 – 15·6)
Extrahepatic portal hypertension	3	8·0	5·2
Obstructive jaundice:			
Extrahepatic	9	6·7 ±1·32 (0·9 – 12·3)	3·4 ±1·16 (–2·5 – +8·8)
Intrahepatic	3	9·6	6·7
Infective hepatitis	4	10·5	5·8
Congestive heart-failure ..	4	13·5	13·2

* Includes one patient with hæmochromatosis.
† Standard error of the mean.
‡ Range.

Differences in the position of the catheter tip produce slight and insignificant changes in the occluded hepatic-vein pressure. There is always a small fluctuation in pressure with the phases of respiration, and the height of the pressure varies somewhat with the type of respiration. Forced inspiration causes a marked rise in pressure. A rise in intra-abdominal pressure, due for example to ascites or to gaseous distension, will produce a conspicuous increase in intrahepatic vascular pressures. This will be reflected in both occluded and free hepatic-vein pressure and may be responsible for the higher mean free hepatic-vein pressure in the cirrhotic group. If abdominal distension from any cause is present, the intra-abdominal pressure must be measured and subtracted

RESULTS OF IN-VITRO TESTS

—	Compound	Inhibitory concentration * (mg per 100 ml)
		14 days incubation inoculum 0 0008 mg per ml †
A	I (R = H)	10 0
	II	2 5
	III	2 5
	IV	0 625
	P A S (Na salt)	0 156
		7 days' incubation, inoculum 0 008 mg per ml †
B	I	10 0
	II	10 0
	III	2 5
	IV	0 625
	P A S (Na salt)	> 20 0

* In a synthetic medium containing albumin 0 25 %
† Moist weight, *Myco tuberculosis*, strain H37RV

IV in the in-vitro tests, and its relative independence of inoculum size, also suggest a similarity in action to the thiosemicarbazones rather than to *p* aminosalicylic acid On the other hand, the tolerance of the mice in the above-described experiment to large doses of the compound indicates that its toxicity is lower than that of the thiosemicarbazones

More detailed pharmacological and chemotherapeutic studies of compound IV are now in progress

It is of interest that since the chemical part of this work was completed, two papers [4 5] have appeared dealing with the preparation of *p*-thiocarbamido derivatives of salicylic acid (cf series I above), the authors of these papers agree with our conclusion that this series shows no enhancement of antituberculous activity as compared with *p* aminosalicylic acid

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Unusual Manifestations of Bronchial Carcinoma

THE section of medicine of the society met on April 28, under the chairmanship of Sir ALUN ROWLANDS, president of the section, to discuss Unusual Manifestations of Bronchial Carcinoma

Dr PHILIP ELLMAN reviewed the common manifestations of bronchial carcinoma, a disease that caused more deaths in 1951 than respiratory tuberculosis More cases were now being discovered by means of miniature fluorography in the silent stage when the chances of successful surgical treatment were greatest He described 6 examples of joint manifestations, in some of which the joint changes preceded the symptoms directly due to the lung lesion The patients had polyarthritis of rheumatoid type or pulmonary osteoarthropathy with gross clubbing of the fingers and toes and enlargement of the nose The most striking and important feature was the very rapid reversal of the condition after pulmonary resection, dramatic improvement sometimes being noticed within a few hours of operation The conjunction of bronchial carcinoma and pulmonary tuberculosis was not very rare now that carcinoma had become so common and the prevalence of tuberculosis in middle-aged men had risen Certain pneumoconioses, especially asbestosis, were sometimes associated with carcinoma and it was possible that there was a causal relationship He described a patient with generalised "honeycomb lungs" and bronchial carcinoma, it was suggested that the prolonged inhalation of chrome dust might have produced both conditions Dr Ellman referred to carcinoma of the lung presenting as a general medical disorder—e g, "pyrexia of unknown origin," influenza, cardiac conditions, Addison's disease, abdominal conditions, and low back pain

Mr T HOLMES SELLORS said that it was impossible to estimate what proportion of patients had operable tumours when diagnosed, it was probably of the order of 15% Although routine radiography did bring to light some truly symptomless cases, this was less common than many believed, patients hid their symptoms and preferred to visit a mass miniature radiography unit rather than admit their ailments to their doctors Of 200 consecutive cases at Harefield Hospital, 67% presented with respiratory symptoms, 11% with general symptoms, and the remainder with symptoms directing attention to other systems General constitutional symptoms might predominate and the clinical picture might be one of "pyrexia of unknown origin" or unexplained loss of weight The first symptoms and signs might be due to metastases in the cervical nodes, skin, adrenals, liver, or bone, and a particularly misleading symptom was persistent back pain On occasion this had been wrongly diagnosed and treated by manipulation A very difficult manifestation in the nervous system was vague personality changes due to metastases in the frontal lobe He had seen intussusception due to secondaries in the small intestine that were only discovered after operation The diagnosis of unresolved pneumonia could be the cause of unnecessary delay, and the term should be abolished. Mr Holmes Sellors emphasised the need to investigate fully all cases of repeated bloodstaining of the sputum Pleural involvement by the tumour might lead to referred pain in the abdomen Mediastinal involvement might cause loss of voice, dysphagia, or obstruction of the superior vena cava The deep chest pain that was so common a complaint might also arise from invasion of mediastinal structures Among the cardiac manifestations were heart block, pericarditis, and auricular fibrillation

Dr R A HENSON discussed the neurological manifestations of bronchial carcinoma and described 15 cases seen at the London Hospital In none of them was there evidence of metastases in the nervous system Subacute cerebellar degeneration, sensory neuropathy—and polyneuritis had already been described, and he gave 8 examples of motor neuropathy, a condition not previously recorded in this disease In 7 the nervous symptoms preceded those directly due to the carcinoma, and in 1 they began nine months after an apparently successful pneumonectomy All these patients had an atrophic paresis, limited at first to the limb girdles In some there was also bulbar palsy, ptosis, diplopia, and depression or absence of the tendon reflexes Only 1 had any sensory loss, although 6 had paræsthesiæ and pain, sometimes very severe 4 had extensor plantar responses and 1 had cerebellar signs In 1 there were no abnormal signs in the nervous system, the condition appearing as a pure myopathy Some degree of myopathy may have been present in all the cases In 1 there was a remission after pneumonectomy, and another patient improved after neostigmine had been given because of an erroneous diagnosis of myasthenia gravis, but 2 others had similar remissions although they received no treatment at all 1 had a remission after multiple vitamin therapy, but it was unlikely that the treatment was responsible The cause of the lesions in the nervous system was unknown It had been suggested that they were due to metabolic disorders or to a virus infection In 2 of Dr. Henson's cases, the post-mortem changes in the spinal cord were apparently inflammatory It was probable that the cancer and the neuropathy were linked by a common cause, rather than that one was directly caused by the other

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[4] Aumuller W Horner, L, Kimmig, J, Meyer Rohn, J *Chem Ber* 1952, 85 760

[5] Tietze, E, *Petersen* S Domagk, G *Ibid*, 1953 86 312

from the occluded hepatic-vein pressure to obtain the effective portal-vein pressure.

These theoretical considerations do not detract from the practical value of the method for assessing portal hypertension. It is a useful preliminary to vascular surgery in cirrhosis both to confirm the diagnosis of portal venous hypertension and to distinguish the site of the portal venous obstruction. It may also be useful, after portacaval anastomosis for cirrhosis, to repeat hepatic-vein catheterisation; a continued low pressure reading confirms that the shunt is still patent.

SUMMARY

The pressure obtained with a catheter occluding a hepatic vein does not differ significantly from that obtained directly from a portal-vein radicle, unless there is extrahepatic portal venous obstruction.

The mean occluded hepatic venous pressure in 24 patients without liver disease was 6·8 mm. Hg. In 11 patients with portal cirrhosis the mean pressure was 22·0 mm. Hg. Raised values were also obtained in 2 patients with subacute hepatitis and in four patients with congestive heart-failure. Normal values were found in 3 patients with extrahepatic portal venous hypertension and in 12 patients with obstructive jaundice (9 extrahepatic and 3 intrahepatic).

Theoretical objections to the method do not invalidate its use in the clinical assessment of portal hypertension.

We are indebted to Mr. Sol Cohen for kindly referring one patient; to our surgical colleagues for their coöperation; and to the Lund Fund of the Diabetic Association for an expenses grant.

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HEREDITARY SPASTIC PARAPLEGIA

REPORT OF A FAMILY WITH ASSOCIATED EXTRAPYRAMIDAL SIGNS

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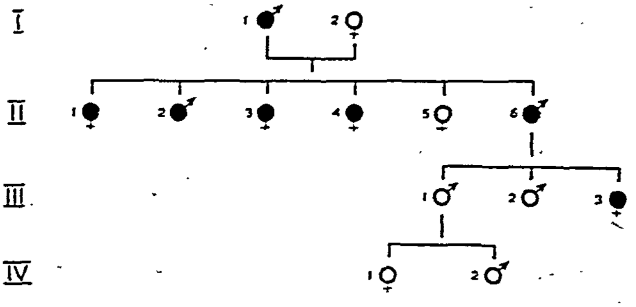
Hereditary spastic paraplegia is a well recognised though rare disorder. Few affected families have been described in this country, until recently, apart from those recorded by Gee (1889), Holmes (1905), and Ogilvie (1908). In America Rhein (1916) published an extensive review of the subject, as did Paskind and Stone (1933), the latter with a necropsy report. Bell and Carmichael (1939) were only able to find one family with this disease in the previous twenty-five years' records of the two major hospitals for nervous diseases in London, and their comprehensive review, concerned chiefly with the genetic aspects, is based largely on families recorded in the Continental literature. Garland and Astley (1950) report a further family, and Bickerstaff (1950) records the largest number of cases so far found in one family in this country.

The criteria of differentiation of this condition from other heredofamilial disorders of the nervous system, such as the hereditary ataxias and hereditary ataxia with paraplegia, are usually accepted as being the absence of ataxia and of cerebellar signs other than nystagmus. Whether any genetic relationship exists between spastic paraplegia and the hereditary ataxias is uncertain, but examples of hereditary spastic paraplegia occurring in the same stock as the hereditary ataxias have not been observed (Bell and Carmichael 1939). The post-mortem findings in these diseases are so diverse, and often apparently lacking in correlation with the previous clinical manifestations, that they do not provide a firm basis on which to form a classification in our present state of knowledge.



Family with hereditary spastic paraplegia: affected members shown in black. No known consanguinity in marriages.

The essential features of hereditary spastic paraplegia are increasing spasticity of the lower limbs with relatively little loss of power, often associated with nocturnal flexion spasms of the feet, the upper limbs being slightly or not at all affected. The symptoms tend to appear at the same age in a particular family in which several members are affected in one or more generations, a fact which has been emphasised by Garland and Astley (1950). Various associated abnormalities have been described in some families; these include pes cavus reducible on standing (Bickerstaff 1950), amyotrophy, mental deterioration, speech disturbances, optic atrophy, and extrapyramidal lesions.

PRESENT FAMILY

The present family, inhabitants for several generations of a village adjacent to the Cambridgeshire Fens, is described partly because of the rarity of the condition in this country, and partly because of the presence in several members of extrapyramidal disorders, an association which has not been noted in any of the families so far reported in this country.

The pedigree is shown in the accompanying diagram. Nos. II 2, II 4, II 5, II 6, III 1, III 2, and III 3 have been examined. Information about the other members of the family has been derived from questioning all the members interviewed. The father of I 1 was a strong active man who lived to an old age and, so far as is known, had no disability. His wife was also healthy.

I 1.—Male. Died at 74. Said to have had a slight tremor of the right arm and of the toes of both feet, coming on when he was a young man. During middle age, soon after dislocating a shoulder, he developed difficulty in walking and a tendency to a shuffling gait. Disabilities were insufficient to prevent his working as a farm labourer.

I 2.—Wife of I 1. Said to be healthy and died aged 75.

II 1.—Female. Severely crippled; never able to walk, owing to paralysis of legs and arms. Died at 20. Said to have had "cancer on the chest."

II 2.—Male, aged 65. At age of 10 progressive weakness of the left leg, with foot-drop, gradually came on. At 20 he noticed slight weakness of the right leg, and both legs tended to shake, especially when he was tired. Contractures had developed in the left leg, and permanent foot-drop necessitated a surgical boot. At 30 uncontrollable movements of head, arms, and legs, worse when he was unoccupied, came on gradually. Weakness of his legs progressed very slowly and insidiously, with increasing contractures in the legs, particularly the left. He could get about with difficulty, using crutches, until the age of 60, when he had to give up work, having hitherto run a small shop. Since his retirement his difficulty in walking has steadily increased, and he is now

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

THE society's 73rd annual congress was held in London, under the presidency of Mr ALEXANDER MACRAE (Newcastle) on April 23–25 Over 200 members were present

After a short opening speech by the PRESIDENT on Prognosis in Malignant Melanoma of Choroid and Ciliary Body, in which he reviewed the progress of over 60 consecutive cases papers were read on an interesting diversity of subjects Mr E F KING reported 2 cases of thyrotoxicosis after keratoconus and discussed the significance of their association Mr P L BLAXTER described and discussed a new provocative test for glaucoma (the bulbar pressure test) Mr A G CROSS gave a humane account of the liberal ideal in the exercise of ophthalmology Mr ARTHUR LISTER and Mr F B ZWINK followed the course of central retinal vein thrombosis with different treatments concluding that no essential benefit accrued from these Mr FREDERICK RIDLEY surveyed 600 contact-lens cases treated at the Westminster branch of the Moorfields, Westminster and Central Eye Hospital Mr T KEITH LYLE discussed some pitfalls in the diagnosis of plerocephalic œdema Mr A L MCCURRY reported some cases of the Stevens-Johnson syndrome, and Mr J H DOGGART gave an engaging account of the occasions in which calcium is deposited in the cornea

The Bowman lecture was delivered by Sir GEOFFREY JEFFERSON, F.R.S, who spoke on the Syndromes of the Cavernous Sinus

Chemotherapeutic Agents in Opthalmology

Opening the main discussion, Prof ROBERT CRUICKSHANK emphasised that the variations in the sensitivity of bacteria, and the possibility of otherwise sensitive-organisms developing resistant variants, made it essential that antibiotics should be used for the treatment of specific infections and not of clinical syndromes If this was to be done there must be close collaboration between clinician and bacteriologist It was essential never to forget possible toxic manifestations of antibiotics and chemotherapeutic agents allergic reactions, blood dyscrasias, and secondary effects resulting from elimination of normal flora were among the most important Local irritation or necrotic action was especially important in ophthalmology, and might be assessed by the effect of antibiotics on tissue culture Drug resistance might sometimes be overcome or prevented by the combination of two chemotherapeutic agents, and synergistic effect might be obtained by combining two bactericidal substances There was a possibility, however, of antagonistic action when a bactericidal drug was used in combination with a bacteriostatic substance

Prof ARNOLD SORSBY pointed out that the eye was pharmacologically a double organ Diseases of the external eye responded to antibiotics in the same way as diseases of other tissues of the body However, drugs given systemically were prevented by the blood-aqueous barrier from entering the intra ocular fluids and cornea freely Consequently the treatment of infections of the interior of the globe and cornea involved special problems Small concentrations of antibiotics could be found in the aqueous after enormous systemic doses, but only penicillin was sufficiently non-toxic to allow such dosage Subconjunctival injection was required if high intra ocular concentration was to be obtained Antibiotics suitable for this method of administration were penicillin and streptomycin in solution, and chloramphenicol in micronised suspension Of the relatively non toxic members of the sulphonamides, sulphamerazine was the most likely to be effective in intra-ocular infection as it penetrated the blood-aqueous barrier the most readily

Mr DEREK AINSLIE discussed the use of polymyxin, which has a powerful bactericidal effect against the gram-negative bacillary organisms He had found it suitable for subconjunctival injection, and, when given in this way, it was effective against both experimental and clinical infections of the cornea due to the destructive *Pseudomonas pyocyanea*

In the discussion Dr. G SAUBERMANN (Switzerland) said that intra ocular infections could be treated with aureomycin given intravenously, and Dr HENRI MILLER (France) stated that he had found that the application of antibiotics to a scarified area of the sclera induced intra ocular penetration

Other Topics

Mr C DEE SHAPLAND described changes in the refraction of the eye following the operation of lamellar scleral resection Mr R A WEALE discussed some aspects of total colour-blindness, concluding that cone-monochromatism was a defect which must be located not in the retinal receptor layer but in a more central zone Mr F R NEUBERT showed a large number of excellent photographs of vascular patterns on the eye and discussed their significance

Mr E S PERKINS described a simple applanation tonometer, and Dr ALEXANDER E MACDONALD dealt with the practical application of topical cortisone

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Reviews of Books

Lectures on the Scientific Basis of Medicine

Vol. I 1951–52 Delivered to the British Postgraduate Medical Federation London University of London, The Athlone Press 1953 Pp 396 30*s*

NO medical man, however specialised, could fail to find something to interest him in this book, and many, because of their specialisation perhaps, will want to read it from cover to cover For here are 18 lectures drawn from the first series of 39 given during the winter of 1951–52, on the scientific basis of medicine The title of the whole series may not have been too happily chosen, for it could alienate those who look on medicine as an art, with some scientific accretions, but in spite of the title, it is to those that we would specially recommend this book, for its demonstration that the actual contributors to the scientific aspects of medicine are so often themselves informed by values not "scientific" in any narrow sense Here Adrian, Dodds, Jefferson, Mackintosh, and Macfarlane are perhaps outstanding Both title and book should make their own appeal to the medical scientist, of whatever seniority, the beginner will find perspective and inspiration, the labourer in a narrow field will be refreshed by wider vistas, and even the doyen of medical science can read the other man's contribution, and be redeemed from narrow pride in his own achievements Those of the idler sort may be gratified by what seems to be a negative correlation between the excellence of individual articles and the number of references at their tail, after corrections have been applied for the length of the article itself and the volume of literature "at risk" in the field covered, for it seems a proper saying of Bacon that "books must follow sciences, and not sciences books."

Psychoanalysis Evolution and Development

CLARA THOMPSON, M.D, with the collaboration of PATRICK MULLAHY London Allen & Unwin. 1952 Pp 252 18*s*

IN the United States deviations from Freudian psychoanalysis have been numerous and influential Their sponsors have mostly tried to introduce more regard for social and cultural factors than Freud displayed or conceded; consequently less weight is given to innate instinctual forces bedridden. He is a frail thin old man, blind in his left eye, which was injured in childhood. Moderate dorsal kyphosis and signs of chronic bronchitis. No other relevant findings except in the nervous system. Grimacing movements of face and head, and slight athetoid movements of all four limbs, worse when he is unoccupied. Cranial nerves normal apart from moderate bilateral nerve deafness. No nystagmus. Slight increase in tone in arms. Abdominal reflexes present. Flexion contracture of left hip with internal rotation, flexion contracture of left knee, left talipes equinovarus, right leg held in extension with permanent equinus deformity of foot. Much wasting of legs with almost complete absence of left calf muscles. Continual writhing movements of legs, especially toes. Tone very spastic. Power diminished generally, movements of feet restricted by contractures. Knee-jerks very brisk and equal, sustained right ankle clonus; owing to contracture absent left ankle-jerk. Both plantar responses extensor. No sensory loss.

II 3.—Female. Said to have been severely crippled. Never able to walk, but could crawl as a child. Developed pulmonary tuberculosis. Died at 23.

II 4.—Female, aged 61. First had pain in legs at age of 9. Used to fall and could not get up. Remembers having to be helped to school. Legs became stiff and weak soon afterwards, and condition became gradually worse; by the age of 18 she was unable to walk or stand. She could crawl for a further two or three years, but has been bedridden since, and has spent the past fifteen years in various institutions. Has had pain in the legs and thighs, which have gradually become immobile and fixed. Manipulation under anæsthesia eleven years ago caused a fracture of the left femur, which has not united. Her arms have remained unaffected, and she has been in good health otherwise. No urinary symptoms. She is thin and pale. Blood-pressure 260/160 mm. Hg. No other abnormality in the heart, lungs, or abdomen. Cranial nerves normal. The muscles of the upper limbs are thin, but there is no localised weakness or wasting. Deep reflexes brisk and equal. Trunk and abdominal muscles apparently in spasm, abdominal reflexes absent. Gross generalised wasting of all lower-limb muscles, with fixation of knees in full extension, and ankles in plantar flexion, there being some subluxation backwards of the left ankle. Shortening of left thigh from ununited fracture. Slight movement only of both hip-joints. There is spastic paralysis of lower limbs with contractures, and no deep reflexes or plantar responses can be elicited. No sensory loss. No tremor or movements.

II 5.—Female, aged 59, healthy. Blood-pressure 180/90 mm. Hg. No neurological abnormality or other abnormal physical signs found on examination. Married but childless.

II 6.—Male, aged 53. First had stiffness of both legs at age of 10. At 14 arms similarly affected to a slight degree and painful after manual work. He was in Papworth Sanatorium with a left pleural effusion at the age of 20. Stiffness of the legs has become gradually worse, but he can still proceed at a reasonable speed with the aid of a stick. He has noticed slight unsteadiness on his feet in the past eight years, which he associates with the weakness, particularly when he tries to do anything quickly. About five years ago he noticed a tremor of both lower limbs and of right hand, and to a slight extent of left hand. Slight frequency of micturition during the past few years, but no difficulty in controlling his bladder.

A healthy-looking well-nourished man. No abnormality except in the nervous system. Fundi and cranial nerves normal. Immobile expressionless face. No nystagmus. Slightly increased tone in the right upper limb, but tendon-reflexes equal. Slight intermittent tremor of parkinsonian type of right thumb and index finger. Abdominal reflexes present but sluggish, and trunk muscles appear normal. Very slight symmetrical wasting of whole of both lower limbs. Bilateral pes-cavus deformity reversible by pressure on soles of feet. Slight involuntary irregular non-repetitive writhing movements of athetoid type of feet and toes. Gross spasticity of both lower limbs. Exaggerated knee and ankle jerks and extensor plantar responses. No sensory loss. Treatment with 'Artane' has enabled him to walk more rapidly and without the aid of a stick, and on examination there is considerable reduction in the stiffness of his lower limbs, which was presumably in part due to extrapyramidal rigidity.

III 1.—Male, aged 26, healthy. Good physique; no abnormal signs found on examination. Police officer.

III 2.—Male, aged 22. Good physique; no abnormal signs found on examination. Serving in Forces.

III 3.—Female, aged 18. A relation noticed that she walked awkwardly, dragging her right foot, at the age of 5. Shortly afterwards dragging of left foot appeared, but less severe. These symptoms have got slowly and progressively worse; she now walks slowly with a shuffling gait and cannot walk for more than half a mile. She can cycle for long distances and runs a small sweet-shop. About a year ago she noticed that her right foot "draws up" at night. This consists of the foot becoming dorsiflexed at the ankle, also assuming the cavus position, causing discomfort; these spasms last several minutes and wake her from sleep. Recently she noticed writhing movements of the toes of both feet, similar to those of her father. General health good, and she has had no other illnesses of note.

A healthy-looking girl with no abnormalities other than in the nervous system. Her cranial nerves, upper limbs, and abdominal reflexes are normal, but she does not swing her right arm freely when walking. The lower limbs show an unusual position at rest, the right foot being involuntarily dorsiflexed and curled up in the cavus position. The left foot is held in the neutral or slightly plantar-flexed position with some pes cavus. There is slight spasticity of the muscles above, but extreme spasticity of the muscles below, the knee and considerable force has to be used to move the ankle-joints at all, and to straighten out the pes cavus, which does, however, disappear completely when the action of the muscles is opposed. There is slight wasting of the whole of both lower limbs, with very slight weakness on movement at both hips and knees, worse on the left side than the right, and moderate weakness of movement at the ankles. Both knee-jerks very brisk and equal, but the ankle-jerks can only just be obtained, and the plantar responses cannot be elicited at all. Slight writhing movements of the toes of both feet. There is no sensory loss. The lower part of both legs, round the whole circumference, and the whole of both feet are bluish purple and always cold.

Treatment with artane enabled her to walk a mile without undue fatigue, whereas previously she could only walk a quarter of a mile with difficulty.

IV 1.—Female, aged 5 years, said to be healthy.

IV 2.—Male, aged 13 months, said to be healthy.

DISCUSSION

The chief interest of this family lies in the presence of associated extrapyramidal abnormalities. III 3 was the first to be seen and presented an unusual clinical picture. There was slight generalised weakness of the lower limbs, and the tone of the thigh muscles and the knee-jerks were only slightly increased, while on passive movement of the ankle-joint the impression was of lead-pipe rigidity. The ankle-jerks could barely be elicited, and the plantar responses could not be obtained. The writhing movements of the toes did not appear until later and, until the other members of the family were seen, it was not realised that the signs were due to a combination of spasticity and extrapyramidal rigidity. Three other members of the family had evidence of extrapyramidal lesions. I 1 was said to have a tremor of his right arm and "constant movements" of his great toes. II 2 showed grimacing movements of his face and also movements of his head which were usually non-repetitive and had an athetoid quality. He also had slight athetoid movements of all four limbs. II 6 had a somewhat expressionless face, a parkinsonian tremor of his right hand, and writhing movements of his toes and feet.

We have been unable to discover reports of any family in this country with extrapyramidal signs, although several examples have been recorded in France, America, and Germany. Ballet and Rose (1905) report one case, in a family with this disorder, who had choreiform movements and a tremor of the hands accompanying the spastic paraplegia. Mason and Reinhoff (1920) mention four cases with a coarse tremor affecting the jaw, tongue, arms, or hands. In a family reported by Bremer (1922) two members had grimacing tics; and of two cousins described by Guillan and Bize (1933) one had incessant choreiform movements of the head and hands. A further example of this association is a case (Jackson

Dr Thompson is most in sympathy with the teachings of Erich Fromm, Karen Horney, and Harry Stack Sullivan. Her contacts with Sandor Ferenczi, by whom she was evidently psycho analysed in Budapest, have also influenced her outlook. The first seven chapters of the book are devoted to a respectfully critical review of psycho analytic theory as developed by Freud, chapter eight is about "Deviants around 1912, Adler and Jung," and the ninth and tenth chapters deal with Rank, Ferenczi, Reich, Horney, Fromm, and Sullivan For the latest phase Dr Thompson has concentrated on developments in the United States, where psycho analysis has been more affected than elsewhere by social psychology and cultural anthropology the European scene and particularly English modifications and variants, are ignored Her account is clear, tolerant, and well-informed, though not penetrating it is a useful guide to the chief mutations which psycho analysis has undergone in America under the impact of criticism and external influences

Pharmacology in Clinical Practice

Harry Beckman, M.D, director, department of pharmacology, Marquette University Schools of Medicine and Dentistry Philadelphia and London W B Saunders 1952 Pp 839 63*s*

This valuable book will be welcomed by those who find difficulty in fusing the pure pharmacologist's version of his subject with the excessively empirical presentation found in many textbooks of therapeutics Dr Beckman's new publication is essentially a manual for clinicians, and his long experience as a practising physician and as a teacher have equipped him for the task Thus his frequent references to the limitations of drug therapy are realistic "I think," he says, "in terms of specific diseases and the opportunities they present to the pharmacologist, in terms of symptoms and not of anatomical groupings of organs or chemical groupings of drugs" He emphasises, too, that the practitioner does not "reason forward from the drug to the patient but from the patient and his malady to the drug" He has stripped the subject of any discussion of historical development and of the relations between chemical composition and biological activity, feeling that there is room for at least one book of this kind

The style is informal and makes for easy reading, though some may find the fairly common use of the imperative mood a little disconcerting The language is often vivid thus the section on cardiac arrhythmias begins "The heart, that amazing organ, begins whamming away before we are born and continues faithfully to do so until we wander out of this vale of tears" The segregation of the old fashioned materia medica (obstinately indispensable even for the most modern drugs) in a compendium enables him to avoid cluttering up the text with references to physical and chemical properties Perhaps he is over generous to research workers who have published rather vague conjectures, but he does not always take them seriously "speculation is fun and sometimes harmless" The book is lavishly illustrated, and the lengthy index has evidently been compiled with great care and with an eye on the needs of the practitioner

Twins

A Study of Three Pairs of Identical Twins Dorothy Burlingham London Imago Publishing Co 1952 Pp 94 35*s*

Most books on twins deal with the biological aspects of twinning and use the differences between identical and fraternal twins to study the part played by inheritance in the development of various qualities Miss Burlingham, however, is chiefly interested in the direct effect of being an identical twin on child development

The three pairs she studied in a war time residential nursery were unusual in that they had no normal family care The first two pairs entered at 4 months and were studied in detail till they were 3, the third pair spent most of their lives in another residential nursery and came under observation from $3\tfrac{1}{2}$ till 5 A residential nursery is no substitute for a home, but making allowance for this handicap to emotional development these studies show clearly that identical twins have special difficulties to overcome The most obvious is jealousy Rivalry between twins starts earlier and is more intense than that between an older and a younger child. This complicates the development of a happy relationship with each other and with the parents One pair were quarrelling so much towards the end of the study that they were separated Another difficulty is that these identical twins tended to turn to each other in all their troubles and to develop as a team withdrawn from their surroundings The chief temperamental differences between the twins was a tendency for one to become the active and aggressive member and the other the passive member of the pair But this rélationship was unstable and was reversed in one pair when the illness of the aggressive member allowed the other to take over this rôle

Miss Burlingham's study shows that one must be cautious in basing conclusions on the greater resemblance of identical than fraternal twins It is possible that the identical-twin relationship itself may be an environmental factor differing from the fraternal-twin relationship in ways important to emotional development

Pédiatrie

Robert Debré, Marcel Lelong Paris Flammarion. 1953 Pp 2234 Fr 14,500 2 volumes

This is probably the only European textbook of pædiatrics published in loose-leaf form, with annual revision It covers all the common diseases of infants and children likely to be met in temperate climates, but it does not touch on general subjects such as growth and development, nor the various aspects of child health

Infectious diseases are omitted, because they form the subject of another volume in the series, but there are good sections on vitamins and on the treatment of poisoning Short œsophagus and hiatus hernia are treated as distinct conditions, and it is surprising to read that pink disease has its maximum incidence between 3 and 4 years of age, but in general the authors are in agreement with current British teaching The book is beautifully printed and illustrated, and the short sentences and frequent subheadings make it readable

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Frazer's Manual of Embryology (3rd ed Baillière Tindall, & Cox 1953 Pp 488 42*s*)—This was always the book of an individualist, and, in preparing the new edition, Prof J S Baxter has been at pains to preserve the character the late Prof J E Frazer conferred on it It is, as he says in his preface, "largely a record of the personal observations of one man extending over many years—and, indeed, is the only complete record of those observations that is available" The second part of the book, which deals with the development of separate organs and regions, is thus much as Frazer set it down The first part, which covers early and general development, Professor Baxter has rewritten to include the important advances which have been made in the past twenty years This is an improvement, for it was a former weakness of the book that its author sometimes ignored current work in his field Under the new hand the book maintains its distinction

Magicians, Theologians, and Doctors (London Edward Goldston 1952 Pp 293 21*s*)—The author of this work is Mr H J Zimmels, PH D, lecturer in Jewish history at Jews' College, London, and his studies in folk medicine and folk law are gathered from the Rabbinical *Responsa* of the 12th to 19th centuries Being decisions on cases taken from daily life, the *Responsa* serve two purposes for later generations to the rabbi, presumably, they are—or were—a guide for decisions in similar cases, to the historian they constitute a rich mine of raw material for research, since they deal with actual experience and are very careful in their presentation of facts The author has arranged his excerpts under various headings the education of doctors, theories on the causation and character of disease, therapeutics, remedies, surgery, and so forth The following quotation is an example of folk lore "Long nails cause sorrow Nails grow on the third day after being pared Therefore one should not cut them on Thursday in order to avoid their growing on the Sabbath" Treatment is largely of the magical kind, thus the liver of a mad dog is recommended as a cure for a man suffering from the dog's bite, and a patient with a bone stuck in the throat should have a similar bone laid on the nape of his neck The text, which is rather scrappy, is largely composed of this kind of material Nearly half the volume is occupied by bibliographic notes and references

1934) with a mask-like expression and a tremor of the head and right arm, three other members of this family with spastic paraplegia having no extrapyramidal abnormality.

Several workers have commented on the tendency for hereditary spastic paraplegia to appear at the same age in members of a particular family. Other families, however, have shown a wide diversity of the age of onset. In the second generation of the family reported here three of the five affected members were aware of the disease at the age of 9 or 10 years, whereas in the two more severely affected members it became apparent in early childhood. III 3 was also under the impression that her disease began at the age of 9. although her relations noticed its onset earlier. III 3 and II 5 had pes-cavus deformities which could be reversed with counter pressure as described by Garland and Astley (1950). Nocturnal flexion spasms, so typical of hereditary spastic paraplegia, only occurred in III 3 and were in dorsiflexion, not plantar flexion as is usual.

In generation II a striking facial resemblance was noticed among surviving affected members, conforming with a similar observation by Bickerstaff (1950). The only unaffected sibling, II 5, in this generation bore no resemblance to them in appearance or temperament, and was said to take after her mother. In certain families mental deficiency or progressive mental deterioration has been recorded. This family appeared to have average intelligence.

In view of the diffuse nature of the pathological process in those cases which have come to necropsy, it is not surprising that the clinical manifestations are often more widespread than the name of the disease suggests.

SUMMARY

A family is described in which there were seven cases of hereditary spastic paraplegia. In four of these there were associated extrapyramidal signs.

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CORTISONE AS AN ADJUNCT TO SURGERY IN THE TREATMENT OF KELOIDS*

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THE work of Ragan et al. (1949), Spain et al. (1950), and Baxter et al. (1951) has shown that in experimental incised wounds cortisone and corticotrophin (A.C.T.H.) can suppress all the elements of healing. Partly or completely they will suppress the exudative and cellular reactions of the first twenty-four hours and the capillary formation, fibroplasia, collagen deposit, and epithelial growth, usually seen between the fifth and twentieth days. Such granulations as are formed in the cortisone-treated wound lack the compactness of the normal granulation scar. These effects of cortisone are not influenced by the administration of vitamin C.

On the ground that a keloid is primarily a disorder of healing characterised by an excess deposit of intercellular substances, it seemed to me reasonable to try cortisone in the treatment of keloids. Conway and Stark (1952) had already reported promising results.

Keloids

There is difficulty about every aspect of keloids—definition, ætiology, and treatment.

DEFINITION AND HISTOLOGY

Alibert in 1810 is said to have been the first to use the term keloid to describe the clinical condition which we recognise by this name. He likened the extensions of the mass of scar tissue into the dermis and subcutaneous tissues to claws. To him a keloid was like a crayfish with legs implanted into and through the skin. It is not possible today to be much more precise than this loose descriptive definition. Although a major keloid may be distinguished easily enough from a typical hypertrophic scar, and both almost always from a fibroma, it is often impossible to distinguish with general agreement a hypertrophic scar from a keloid.

In all these three states collagen is an important constituent. In a typical keloid the collagen fibres are arranged in nodular masses which extend and grow irregularly into the surrounding dermis and subcutaneous tissues, where they blend into the surrounding normal collagen. In a fibroma the growth of collagen fibres is uniform and a capsule is created at the boundary with the surrounding tissues; there is no blending at the periphery between the collagen fibres of the tumour and the normal collagen bundles. Histologically as well as clinically a hypertrophic scar resembles a keloid more closely, but in it the collagen fibres grow more uniformly and tend to lie parallel to the lines of force across the scar. As in the keloid, however, these fibres blend with the surrounding normal collagen fibres at the periphery.

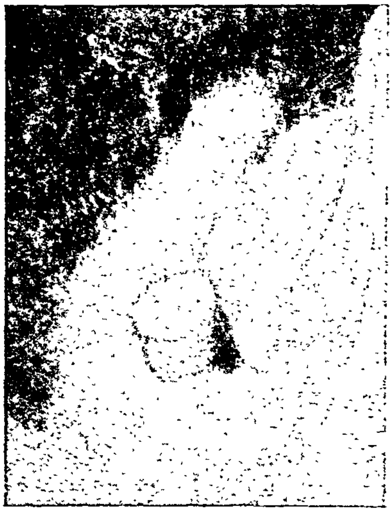

Fig. 1—Bulky keloid in lower part of mastoid scar developed in spite of irradiation in boy who had several normal scars elsewhere.

These descriptions of the three related states, and the distinctions between them, have been oversimplified here. They are true only of extreme examples of each, but the nodular arrangement of the collagen fibres and their peripheral blending seem to be useful in the histological definition of a keloid. Important constituents of both keloids and hypertrophic scars, in addition to the collagen which constitutes most of their bulk, are the fibroblasts and blood-vessels, which vary with the age of the lesions and contribute to their symptoms.

ÆTIOLOGY

Many clinical factors are known to be important to various degrees in the ætiology of keloids. They include pigmentation of the skin; infection; original cause of injury; site, direction, and depth of the scar; the age, and the metabolic and endocrine balance of the patient at the time of the injury.

Origin of Collagen

Collagen is the critical constituent of a keloid and accounts for most of its bulk. It has two possible origins.

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* Read at the annual meeting of the British Association of Plastic Surgeons, London, September, 1952.

THE LANCET

LONDON SATURDAY, MAY 9, 1953

Diet and Immunity

A DEFICIENT diet might be expected to impair resistance to infection, but undisputed immunological evidence of this is hard to come by

During the 1914–18 war vitamin-A deficiency was blamed for xerophthalmia among Danish children[1] Vitamin A was also found to be of value in puerperal fever,[2] but this has been disputed[3] In mice vitamin A has been reported[4] to increase resistance to mouse-typhoid infection, but no significant effect was detected by other workers[5] Results with members of the vitamin-B complex are equally conflicting There is some evidence that biotin deficiency may lower resistance[6] other experiments[7] show that vitamin-B deficiency has little effect, whilst some workers conclude that aneurine-deficient[8] and undernourished[9] animals are more resistant to virus infections, and pantothenic-acid deficiency increases resistance to pneumococcal infection[10] Again, with vitamin C it is difficult to assess the effect on immunity Guineapigs given cabbage daily respond better to active immunisation than those given mangolds,[11] but vitamin-C deficiency appeared to have no effect on the sickness-rates of Negroes[12] There is no conclusive evidence, either, that vitamin D has any effect on immunity Severe and long-continued protein depletion has been reported to have adverse effects on antibody production,[13] but the responses to immunisation of half-starved German civilians and of well fed British soldiers were remarkably alike[14] Diphtheria antitoxin production has been found to be as high in nutritionally deficient patients who had lost up to 40% of their body-weight as in well-nourished people[15] It is interesting to find, however, that pulmonary infections are relatively prevalent among the predominantly vegetarian Kikuyu, whilst arthritis is commoner in the meat-eating Masai tribe[16]

On the whole, therefore, the evidence suggests that most other physiological functions of the body are affected by diet before distinct effects on immunological response become apparent Some precision is given to this conclusion by the work of HOWIE, BARR, and GLENNY[17] on pregnant Scottish blackface ewes which were given two injections of diphtheria alum-precipitated toxoid (A P T) One group of ewes received a supplement of oats and linseed cake, whilst the controls were grazed on the same pasture but without dietary supplement Both body-weight and fleece-weight were higher in the ewes receiving the dietary supplement, and when the interval between the A P T injections was one month the serum-antibody titre was twice as high in the better fed group When, however, the interval between injections was two months the immune response was better, and it was not possible to detect any beneficial effect of the dietary supplement on the immunisation The serum-antitoxin content was followed for a year after immunisation In the first six weeks there was a rapid fall, this was followed by a slower decline, and a year later the antitoxin content had fallen to about 0 3% of the peak value when the interval between the injections had been one month, and to about 1 4% of the peak value when the interval had been two months

Newborn animals possess passive immunity, due to antitoxins obtained from the mother partly by antenatal placental transmission from the maternal blood-stream and partly by neonatal absorption by the suckling of colostrum The antitoxin titre of the colostrum at the time of birth is commonly much higher than that of the maternal blood-serum, presumably owing to selective antenatal accumulation of antitoxic globulins from the blood-stream, but a few hours after suckling has started the antitoxin concentration in the colostrum falls rapidly It has long been customary not to attempt the immunisation of infants during the first few months of life, in order to avoid the possible inhibiting effect of maternally transmitted antibodies on the development of active immunity in the offspring Unsatisfactory development of immunity has been observed in lambs given two injections of diphtheria A P T two weeks and six weeks after birth, when the amount of maternally transmitted antitoxin present was sufficient to combine with too high a proportion of the injected antigen[18] A third injection of A P T two months later resulted in satisfactory immunity

The Delphic oracle is no longer available for consultation, and the herd of goats which first drew attention to the magic of Delphi is dispersed, but we can learn from the Scottish blackface ewes and their lambs that for active immunisation the most effective interval between injections of the antigen is two months, that under these conditions diet has little effect on the development of immunity, and that routine immunisation with A P T should not be applied to infants during the first few months of life

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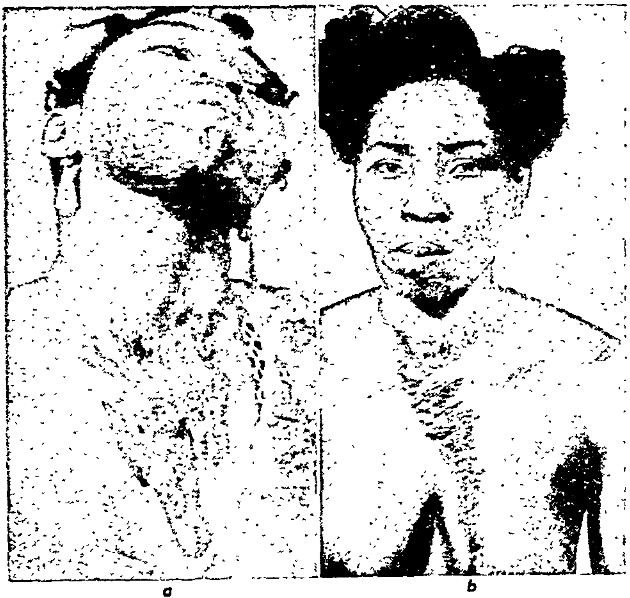

a b

Fig. 2—Keloids due to vitriol before (a) and after (b) standard method of treatment by excision plus irradiation.

(1) It may be formed by fibrillation or shedding of the cytoplasm of the fibroblast. This implies a limit to the amount of collagen produced by each fibroblast. The treatment of a keloid should therefore rationally be directed towards suppressing fibroplasia during its most active period in wound healing—say, from the fifth to the twentieth days. But this hypothesis is not in accord with the growth of keloids, which continues for weeks or months after primary healing. The pathological healing seen in keloids suggests that collagen is being formed in some other way.

(2) An alternative hypothesis is that collagen is produced by a chemical and enzymic process: the fibroblast secretes into the surrounding intercellular matrix enzymes which react with other substances there to form the adult collagen fibres. One possible mechanism, postulated by Meyer (1947), is as follows:

> "The young fibroblast secretes into the surrounding tissue spaces hyaluronic acid, a precursor of collagen, and chondroitin sulfate. By local acidification in the immediate neighbourhood of the cells the first fibres are produced by the polysaccharides from the native soluble collagen which denature into the insoluble fibre, on the surface of which lies a sheet of polysaccharide. With aging of fibres the polysaccharide layer becomes thinner and the hyaluronate is replaced more and more by chondroitin sulfate. Only in metabolically very active connective tissue like that of skin, hyaluronic acid production continues in considerable quantities. The role of ascorbic acid in the production of fibre formation may be that it is actually a component of chondroitin sulfate, replacing in the chain some of the glucuronic acid molecules."

The value of this hypothesis is that it conforms to the clinical course of most keloids. It implies that one fibroblast may be responsible for an indefinite amount of collagen. Further, cortisone is thought to act chemically, and we may reasonably suppose that the suppression of wound healing mentioned above is due at least in part, to a chemical inhibition by cortisone of some process similar to that postulated by Meyer. If this were so it would be necessary to give cortisone at any rate in maintenance doses, for a considerable period. But I must emphasise that I know of no direct chemical evidence that cortisone can react in any way with hyaluronate, native collagen, or chondroitin sulphate.

UNPREDICTABILITY

Fig. 1 shows a mastoid scar whose lower part is occupied by a bulky keloid which appeared and persisted in spite of early irradiation and recurred after I had excised it. The boy had other scars, none of which were keloid. Although keloids are without question more common in patients under 30, and in some types of patient (e.g., coloured patients), and although certain sites are more prone than others (e.g., outer shoulder and front of upper sternum), and although certain injuries are more likely to cause a keloid (e.g. acid burns), there is great variability between different people and in different scars on the same person. One patient, like this boy, may show a single keloid among normal scars. Another will develop keloids in several incisions, and then a later incision may heal quietly and cleanly to give a hair-line scar. This makes it very hard to assess any new therapy.

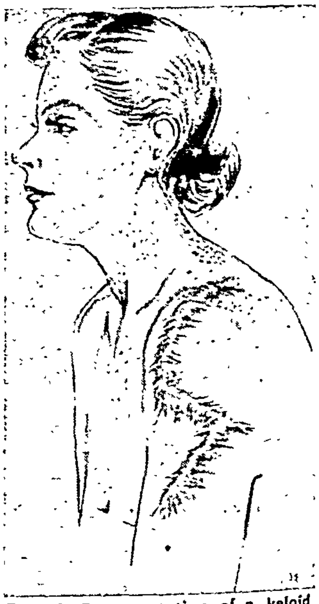

Fig. 4—Representation of a keloid following Z-plastic correction of vertical scar on shoulder. This keloid persisted two years in spite of irradiation.

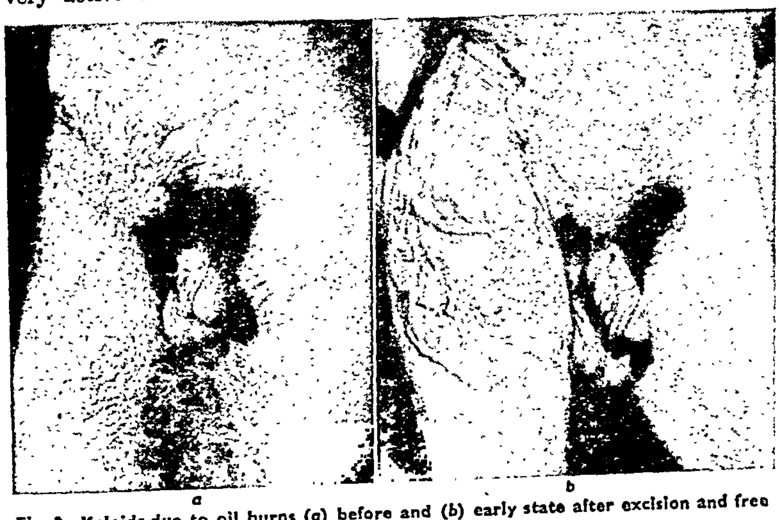

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Fig. 3—Keloids due to oil burns (a) before and (b) early state after excision and free graft cover.

Limitations of Standard Methods of Treatment

Fig. 2 shows a massive keloid, caused by vitriol from a rejected suitor, before and after treatment by surgery plus irradiation. The results cannot be called ideal The girl has a deeply pigmented line over her chest (the price of the otherwise beneficial X rays) and a flat, supple, and rather broad scar where the keloid was ; but this is nothing like so unsightly as it was before, and is symptomless.

Fig. 3 shows oil burns before and after treatment. The massive carapace of keloid left across the groin, thigh, base of penis, and scrotum was tender and itched constantly. It was excised, grafted at one operation, and completely healed a month after operation. The grafts are free from tenderness and itching. The patient has full extension at the hip; but

Symposium on the Thyroid

On Feb 25 the Society for Endocrinology combined with the section of endocrinology of the Royal Society of Medicine to hold an all-day discussion on the thyroid gland Meetings of this type serve a useful purpose in summarising the state of knowledge in a particular field, and perhaps even more by bringing together clinicians and workers in the fundamental sciences These two groups were about evenly represented in the symposium, but it was evident that nearly all the active research on this gland is at present coming from the biochemists They had a particular triumph to celebrate in the isolation and chemical and physiological characterisation of 3,5,3′-triiodothyronine

The credit for this biochemical feat of arms belongs to GROSS and PITT-RIVERS,[1] whose accounts of it began to appear towards the end of 1951 At the same time ROCHE and his colleagues across the Channel were pursuing independently a similar line of inquiry, and would no doubt have soon reached the same conclusions This piece of research illustrates so well the effectiveness of modern techniques in able hands that the salient points are worth restating The key technique in this instance was the combination of paper chromatography with the use of the radioactive isotope I^{131} Material from an animal which has received this isotope can be simultaneously analysed for all its iodine-containing compounds The starting-point was serum from a patient who had received a therapeutic dose of I^{131} Chromatograms made a few days after the dose revealed not only the expected thyroxine, but also another iodine-containing substance which was quite clearly different This unknown substance was eventually proved to be 3,5,3′-triiodothyronine, by synthesis and comparison of the natural and synthetic products by means of crystallography Interest now centred on the physiological properties of this substance When tested in rats by the goitre-prevention method it proved not only to have thyroxine-like properties, but to be about five times as active as thyroxine Several further comparisons between thyroxine and triiodothyronine were described at the meeting Triiodothyronine has been shown to be the more potent of the two in increasing the metabolic rate of mice, in promoting growth in thyroidectomised rats, in preventing the appearance of thyroidectomy cells in the pituitaries of rats on thiouracil, and in preventing the escape of radio-iodine from chick thyroids In addition, it is now known to be more potent in the treatment of human myxœdema (although in this respect it has no particular practical advantages) FOLEY, on the other hand, has observed that triiodothyronine is less effective than thyroxine in promoting milk flow in cattle

Biochemists now have an enormous amount of information about how the thyroid hormone is made, quite a lot about how it is released from the gland and transported in the blood, and almost none about its fate after it has disappeared into the peripheral haze, and even the form of the substance which acts on the peripheral tissues is in doubt PITT-RIVERS inclines to the view that thyroxine loses an iodine atom somewhere in the periphery, and that the triiodothyronine thus formed is the agent promoting the changes that we have come to regard as characteristic of the thyroid hormone ROCHE, on the other hand, has found that the two substances are formed at an approximately equal rate in the thyroid, suggesting that either or both may influence tissue metabolism MACLAGAN, in an admirably lucid paper, put forward some odd observations on the effect of thyroxine antagonists of the type of *n* butyl 3 5 diiodo 4-hydroxybenzoate (B D H B) In suitable doses this substance abolishes the effect of exogenous thyroxine on the oxygen consumption of mice, and given by itself it produces a small but significant depression of oxygen consumption When given with triiodothyronine, B D H B not only fails to reduce the rise in oxygen consumption, but actually increases it slightly The fact that B D H B counteracts the action of thyroxine, but not of triiodothyronine, suggests that it prevents the conversion of the former substance into the latter, thus endorsing PITT-RIVERS's view that triiodothyronine is the substance which acts on the tissues B D H B can thus be pictured as a competitive antagonist which interferes with the action of whatever enzyme is concerned in removing an iodine atom from the molecule of thyroxine It is, however, much more difficult to explain the apparent enhancement of the efficacy of triiodothyronine by B D H B MACLAGAN's suggestion that B D H B prevents the de iodination of triiodothyronine (as well as that of thyroxine) involves the assumption that triiodothyronine is de-iodinated after it has acted on the tissues, de-iodination is thus pictured as a step in the process of getting rid of used hormone, rather than as an essential part of hormone action This may be true, though the fact that de-iodination and hormone action occur more or less concurrently has probably led most people to suppose that the loss of iodine atoms is an essential part of the action of the hormone Clearly the de-iodination in vivo of organic iodine containing compounds deserves greater attention from biochemists than it has so far received So far, the only de-iodinating enzyme whose properties have been defined is that found by ROCHE and his colleagues in the thyroid itself This acts only on mono and di-iodotyrosine, and has no action on thyronine derivatives ROCHE has sought other enzymes in extra-thyroid tissues, but so far without conspicuous success

It was evident at the meeting that biochemists are fully aware of this and other obscurities, as problems become defined the appropriate techniques will be brought into action, and before long there will be further advances in knowledge to record But it was difficult to feel equally optimistic about the solution of clinical and pathological problems, the outstanding example of which is the ætiology of Graves's disease The solution of this problem could scarcely fail to throw light on other examples of endocrine overactivity Indeed it might also help to elucidate other diseases whose ætiology is at present equally obscure, such as rheumatoid arthritis and ulcerative colitis Yet progress in the investigation of Graves's disease has been negligible, and it is hard to discern any vigorous effort in this direction One cause is the lack of a satisfactory method of

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[1] Gross J , Pitt Rivers R *Lancet*, 1951 ii 766 *Ibid*, 1952 i 439, *Ibid* p 593 Gross, J Pitt Rivers, R , Trotter, W R *Ibid*, p 1044

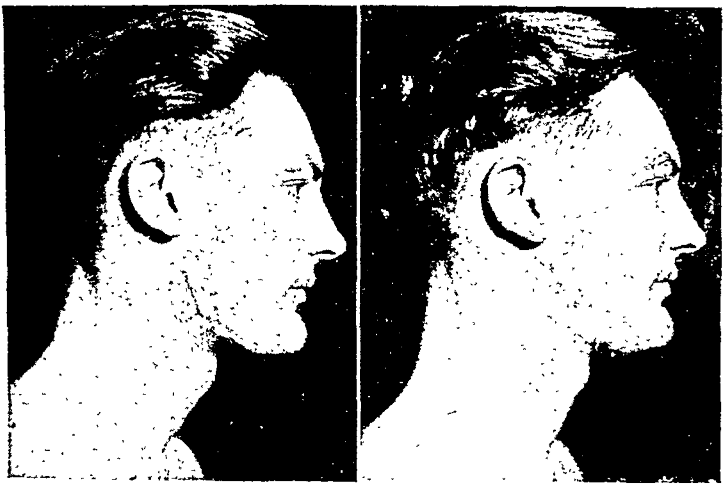

Fig. 5—(a) Result (in spite of preoperative and postoperative irradiation) of excision of keloid, due to acne and repair with Wolffe graft, and after (b) re-excision and cortisone therapy. The patient can now shave over the scar.

the appearance especially of the border scars, is not that of a normal thigh and groin.

Fig. 4 shows the sort of disaster which can follow radical surgery, even when it is supported by intensive irradiation, if the patient is one with a definite keloid tendency in the region of the scar. The massive unsightly tender itching scar which followed my Z-plastic correction of a vertical scar over the deltoid muscle persisted in this state for over two years.

Treatment with Cortisone

In any plan of treatment based on the use of cortisone the importance of the observation of Spain et al. (1950) that it has no effect on established granulation tissue must be emphasised. There are no theoretical grounds for the belief that systemic or local cortisone, or A.C.T.H. with or without hyaluronidase, can remove the mass of the keloid. Published reports (Conway and Stark 1952) confirm this, although relief from symptoms of tenderness and itching has been claimed. It therefore follows that the first stage in treatment with cortisone is removal of the mass of keloid plus an appropriate plastic repair of the defect. It is the subsequent healing which is controlled with cortisone. What is attractive about this plan of attack is that a critical feature of the result must always be the quality of the surgery, both of plan and of technique.

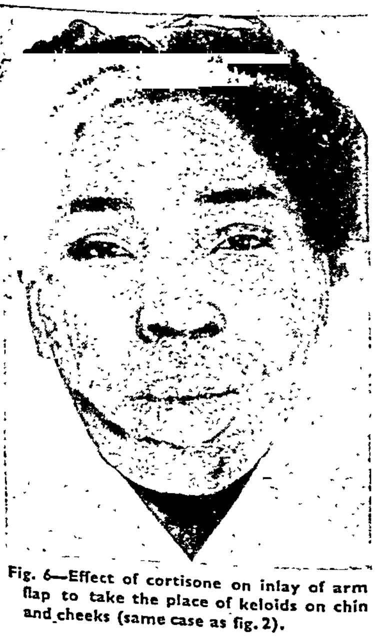

Fig. 6—Effect of cortisone on inlay of arm flap to take the place of keloids on chin and cheeks (same case as fig. 2).

Conway and Stark (1952) report two successes by this combination and one at least of those depicted in their photographs is a very considerable therapeutic triumph. Their experience of local injection of A.C.T.H. with hyaluronidase showed that only symptomatic, not structural, relief could be obtained. Polson and Pattee (1951) report a complete failure in a sternal keloid treated by excision plus large doses of cortisone.

Of my own 8 cases only 3 could be classified as major keloids. The others might be better called hypertrophic scars. 3 of the 8 were due to burns, 3 to acne, and 2 to trauma of the outer upper arm. The age of these keloids at the time of treatment varied from five years to six months. 4 of the 8 had resisted previous surgery plus irradiation. The longest any case has been followed up after my treatment is eighteen months, and the shortest twelve months. 5 cases were treated with systemic cortisone 100 mg. daily from the fifth to the fifteenth or the twentieth days. This late and moderate dosage of cortisone was chosen to avoid the risk of wound disruption and general symptoms. 3 cases were treated with local cortisone—cortisone acetate about 25 mg. daily from the fifth to the fifteenth days. One of these cases treated locally had to have the viscous cortisone acetate evacuated from under the wounds. All 8 cases had full penicillin cover for six days or more. Whenever possible, undermining was restricted to the very minimum necessary for closure. Serum-proof silk was used for skin closure.

Of the 5 treated with systemic cortisone plus surgery 1 is a good result, or at least eminently satisfactory to me (fig. 5). The scars of the cases treated systemically were undoubtedly smaller, of better appearance, and without symptoms after surgery; but it is impossible to attribute this effect with certainty to the cortisone. Of the 3 scars treated with local cortisone 2 gave good results in that the scars were flat, pale, supple, and inconspicuous, and caused no symptoms, but the 3rd gave a poor result, the scars being still easily noticeable on the face.

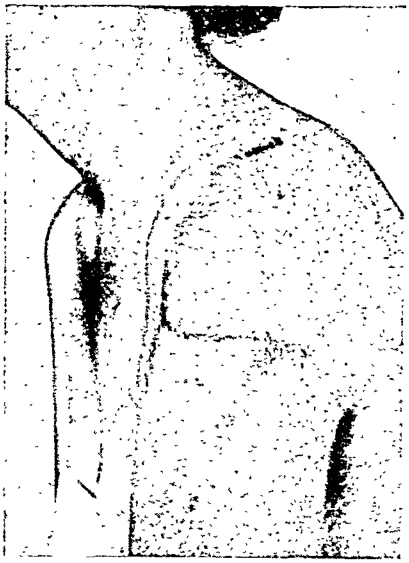

Fig. 7—Effect of cortisone therapy after excision of keloid shown in fig. 4. The scar is smaller; there is less itching and tenderness.

In 2 of the patients treated, euphoria and retention of water were observed. These toxic effects were temporary and ceased on withdrawal of the cortisone. In all the cases the relative lack of reaction round the skin sutures and of suture marking was noted.

Fig. 6 shows the result of cortisone therapy in the keloid due to vitriol (cf. fig. 2), and fig. 7 in the scar over the deltoid muscle (cf. fig. 4).

Conclusions

The only reliable evidence remains the reported effects of cortisone on experimental incised wounds. No unequivocal evidence has been published, and none is presented here, that cortisone has any consistent effect on keloids; but in the present short series it does inducing thyrotoxicosis in animals This condition can of course be produced by giving thyroid or pituitary extracts, but such a procedure tells us nothing useful about the cause of Graves's disease The only claim to have produced a convincing replica of Graves's disease in animals comes from BANSI and his collaborators,[2] who state that wild rabbits, when freshly caught and caged, regularly develop a condition resembling thyrotoxicosis They show tachycardia and exophthalmos, waste rapidly despite a good intake of food, and usually die within a few weeks Both the uptake of radio-iodine and its subsequent discharge are much greater than in tame rabbits Microscopically the animals' thyroids show distinct hyperplasia The syndrome can be prevented by the administration of anti-thyroid drugs The case for regarding this syndrome as comparable to Graves's disease in man is substantial, and it is therefore all the more regrettable that no attempt seems to have been made to repeat the observations outside Germany The experimental procedure—which demands, it would seem, some acquaintance with the poacher's art—can scarcely be described as a convenient laboratory technique, and it is perhaps for this reason that it has aroused so little interest in this country

The failure of clinicians to investigate vigorously the ætiology of Graves's disease can largely be ascribed to the efficiency of modern methods of treatment The prime stimulus to research comes from dissatisfaction with the status quo, and it is not easy to feel dissatisfied when a disease can be readily controlled by various methods of treatment All these methods are essentially empirical and none is radical, but their only major failing, from the practical point of view, is their relative inability to control the ophthalmic symptoms Nevertheless no-one should feel content with these methods, which achieve their object only by battering the overactive thyroid into submission—whether the weapon employed is surgical, pharmacological, or radiological The manic can be kept quiet with leg-irons and handcuffs, but such contraptions are not regarded as instruments of therapy We need to know what makes the overactive thyroid go wild, only with this knowledge can we hope to evolve a method of treatment deserving the name of "cure"

The Ghost in the Machine

AN intelligent member of our profession once had the opportunity, with his family, of watching from his Hampshire home a display of the aurora borealis His family quickly identified the phenomenon, but the doctor, feeling too scientific for that, attributed the glow in the sky to a fire down Portsmouth way, and shortly afterwards was able to smell the smoke He used to say that this illustrated the effect of a hypothesis on the scientific mind

His was an erroneous hypothesis, but even a hypothesis which turns out to be largely correct, and illuminating—like the theory of evolution—can lead us into extravagances It is as though, having seen an inch or two into the millstone, we feel obliged to declare we have seen through the whole thing This characteristic of the scientific mind, so irritating to laymen, has justifiably annoyed Dr F M R WALSHE[1] as well In his Hughlings Jackson lecture to the Royal Society of Medicine, last December, he complained of some notions derived from cybernetics now infecting neurophysiology, which can be summed up (in his phrase) as "nerve nets can know universals" He quoted the statement of PITTS and MCCULLOCH[2] that

> "The basic premise of philosophical idealists and realists and of scientific naturalists and mechanists to the effect that natural and biological systems can have neither knowledge of universals nor normatively defined and behaviour-controlling purposes must be rejected A teleological system can be, and in human nervous systems it is, a mechanical system in which the behaviour of the system is controlled by a negative feedback over the goal"

But, as WALSHE points out, the term "universal" has a long and striking history in the grammar of metaphysics "Expressed in its simplest form the Universal is *one thing common to many*" To know universals, he says, is to know two things it is (1) to know the nature, essence, or being of things—i e, to know that which is the essence of a thing without which it would not be what it is—and (2) to be able to recognise and predicate common qualities of singular things In the light of this definition he criticises another quotation from *Perspectives in Neuropsychiatry*, which states

> "A self-re-exciting loop of neurones, sharing neurones with other loops in which reverberation can be set up by the entry of afferent impulses from different sense receptors, gives and preserves the association between particular events and allows the recognition of a universal to be sparked by the receipt of a particular"

But, WALSHE argues, the mental recognition of a universal is the recognition of a reality which is not individual However complex the activities of the neuronal circuits, their stimuli are and remain individual and even material "No amount of 'sparking' in the circuits can produce a concept of something which of its nature transcends the individual" The late C E M JOAD made the same point in his last book[3] It is extremely difficult, he said, to see how what is commonly called an abstract thought could depend, even at several removes, on a sense object, "for how could an historical generalisation be the result of a physical stimulus?"

There is another difficulty not mentioned by WALSHE or JOAD which seems to us of interest What do we mean when we speak of "knowing" universals? A man when he "knows" a universal is consciously aware of it, or can become consciously aware of it by directing his attention to it, moreover, unless he is *consciously* aware of it—or, at any rate conscious—he cannot act upon it in the second of WALSHE's senses that is, he cannot use it to recognise and predicate common qualities of singular things A machine working on the principle of negative feedback can act on the resultants of past experience without consciousness (though, as WALSHE points out, the computations of even the most able machine remain meaningless without a human intelligence to read off the symbols) Without consciousness, appear to have helped considerably in preventing the recurrence of keloids. It is also quite clear that, at some levels of dosage and length of administration, cortisone has little or no effect.

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[1] *Brain*, 1953 76 1

[2] Perspectives in Neuropsychiatry London 1950

[3] The Recovery of Belief London Faber & Faber 1952 Pp 250 15*s*

Further trials should, I believe, be directed towards the investigation of what is the best dosage and best type of extract—cortisone or A.C.T.H., local application or pellet implantation, administration by mouth or by injection. Almost certainly longer treatment than that given to these cases will be necessary. Perhaps consistent local effects in the treatment of keloids can be obtained only with toxic amounts of cortisone. Whatever permanent rôle may be found for cortisone, we must suppose that its use will have to be preceded by a surgical excision of the keloid and a properly planned repair.

Of my 8 patients the first 4 were treated at the Queen Alexandra Hospital, Millbank, where it was possible, through the courtesy of the Officer Commanding, Colonel J. O'Meara, to obtain cortisone for this work. At Millbank the cortisone treatment was administered and supervised by Captain Ian Cran, R.A.M.C. Others of these patients were treated at Guy's Hospital in conjunction with Dr. Kenneth MacLean, on whose advice I have relied for control of the systemic effects; and in a further case I have been aided in the same way by Dr. Desmond MacManus. I take this opportunity of expressing my appreciation of this help, and to Dr. S. de Navasquez, morbid histologist to Guy's Hospital, who has constantly guided me on the pathological aspects of the problems.

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KELOID, A HAZARD OF PIERCING FOR EAR-RINGS

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THE conventional pattern of surgery is occasionally relieved by some bizarre condition which surprises even the most seasoned practitioner. Relying on his experience he considers the case unique until medical literature reveals, to his chagrin, that the nonesuch is almost a commonplace.

CASE-RECORD

Early in 1949 Mrs. A, who is now 28, had her ears pierced by a layman, and plain gold rings were inserted. No significant inflammation arose, and three months later the same rings were used by a friend, who has noticed no subsequent abnormality.

In 1950 the patient was found to have pulmonary tuberculosis, and thoracoplasty was performed by Mr. Dillwyn Thomas. Whilst she was in hospital, the lobes of both her ears became tense, and painless nodules increased so rapidly in size that she could no longer wear her ear-rings.

Photographs taken after my first examination, on Oct. 14, 1952, showed sessile tumours resembling button mushrooms in front of and behind both lobules, the condition being worse on the left side. Radiographs of the lungs did not disclose any active tuberculous focus, and the sputum was negative. The long and soundly healed scar over the thorax was, however, distinctly keloid.

On Oct. 28 the tumours were removed from both ears under general anæsthesia. Because each of the nodules was densely hard, none of the overlying skin could be preserved to repair the resulting defects, and suturing was therefore done secundum artem. Healing took place without incident, and today the cosmetic appearance is surprisingly normal.

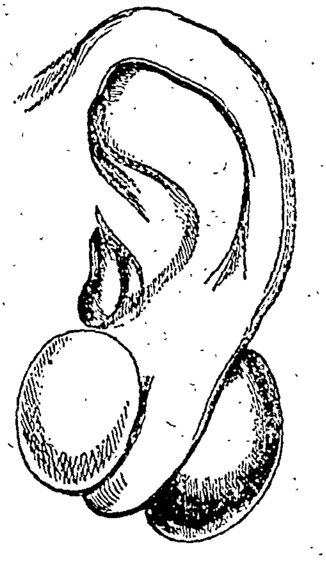

Fig. 1—Hilton's case.

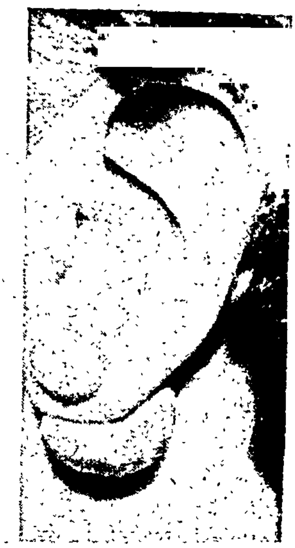

Fig. 2—Present case.

Dr. A. F. Sladden reported on the tumours as follows: "The tumours have a fibromatous structure with good vascular supply. The central portion of each lobule contains areas of densely packed fibres surrounded by a zone of looser texture. Between this and the overlying epithelium there is a narrow zone showing few hair follicles and sebaceous glands and containing small foci of inflammatory cells. The appearance suggests compression of the skin layers by the actively growing central tissues. No nerve structures are present, and there are no neoplastic cells and no signs of tuberculosis. The general structure corresponds closely with the textbook description of keloid, and it therefore seems probable that the tumours are true keloids rather than simple fibromata."

DISCUSSION

It appears from published reports that such tumours were commonest during the middle and later years of the 19th century. One author of that period accounts for its prevalence by a suggestion that "when trade is good factory-hands seem to delight in the barbarism of irritating their ears with cheap and bad jewellery." Knapp (1876) also felt that the danger lies in the rings themselves, for he emphasised "the harmful galvanic action of the alloyed metals." The fallacy of this exploded theory is demonstrated by my patient, since the ear-rings which appeared to cause tumour formation in one person produced no harmful effect in another.

Fig. 1, reproduced from an article describing a case under the care of John Hilton (*Lancet* 1860), resembles quite strikingly the photograph of my patient (fig. 2) and supports the generally accepted view that these tumours are bigger behind the auricle. Hilton's treatment was excision of the lobes, because of a common belief that the condition was "semi-malignant." No pathologist has yet found evidence of malignancy, however, and recurrence after local resection of the tumours probably results from their incomplete removal.

With the passage of time it has become evident that these tumours, formerly regarded as fibromata, are in fact typical manifestations of keloid scar tissue, and my case strongly supports that view. I was particularly impressed by Brennan's (1929) description of a Negress with enormous keloid masses springing from tribal markings on the lobes of both ears. His patient also had a pronounced keloid scar on her upper arm.

Keloid scars are known to arise more commonly in tuberculous patients. In view of the history of tuberculosis in my patient it would be interesting to know then, the mind is less efficient than a machine, even though all the mechanical structures of the brain and nervous system remain intact These considerations are so striking that no mechanical analogy seems to us equipped to explain them fully

WALSHE cautioned his hearers not to be intimidated by the current of authoritative opinion now setting in favour of a physical and statistical account of mind, since we may easily take the evidence too seriously and allow the frailty of the logic to escape our notice. This is harsh criticism of a sincere body of thought, nevertheless it does seem possible that the determinists have not noticed quite where their argument is taking them For if we are all determined together it is hard to imagine what critical value attaches to any of our opinions Given a correctly selected set of facts a calculating machine can give the right answer to a problem But the facts supplied to the human machine, we must (if we are determinists) assume, are selected only by the random circumstances of the environment Moreover, the machines are fallible a man may see a mirage and take it for a lake, or hear an owl's screech and take it for a human cry, he may also be supplied with inaccurate data by other fallible machines in his circle We must therefore expect an extremely wide range of answers to his problem, all of them "right" and some of them conflicting The determinists may, indeed, be "right" in some more absolute sense than this, but if they are it can only be by accident, as it were—much as the prophecy which comes out of a fortune-telling machine may occasionally hit the truth And again, if they are right, they leave us nothing to do but sit back, like old-fashioned Marxists, and wait for history to take its course All this might not matter very much, but should they in fact be wrong, and yet succeed in convincing us that they are right, then we might easily—by an act of free-will—give up doing anything useful at all, on the erroneous assumption that we could leave everything to the machine

The picture WALSHE draws of scientists anxiously trying to cram Nature into too small a portmanteau, and refusing to believe that it cannot be made to shut, could not have been imagined before the middle of the last century Before that, philosophers regarded all knowledge as their province, and were willing to go where truth led, even if it took them to the boundaries of metaphysics The natural scientist of today, WALSHE says, "tends to shrink back in his quest for truth when the possibility dawns on his mind that perhaps after all the ancient concept of the soul is not yet dead, and may once again have to be evoked to account for the activities of the human mind " He himself boldly, even defiantly, declares for the soul Defiance, however, seems hardly necessary The mind considering the religious view of the universe is not faced with a choice between what is clearly true and what is clearly false, or obliged, by a painful and crippling leap, to achieve belief in the incredible Rather it is faced with two descriptions of Nature, both all but impossible of belief Is it any harder—or any easier—to believe there is a primary cause for the continuous creation of worlds than that there is no cause at all? (Incidentally, it is surely interesting that determinists, those sticklers for causation, should prefer no cause at all to a first one) The more scrupulous the mind the less readily will it be able to choose between these hypotheses, and after long weighing of both the most it may be able to affirm is that one belief seems slightly less improbable than the other

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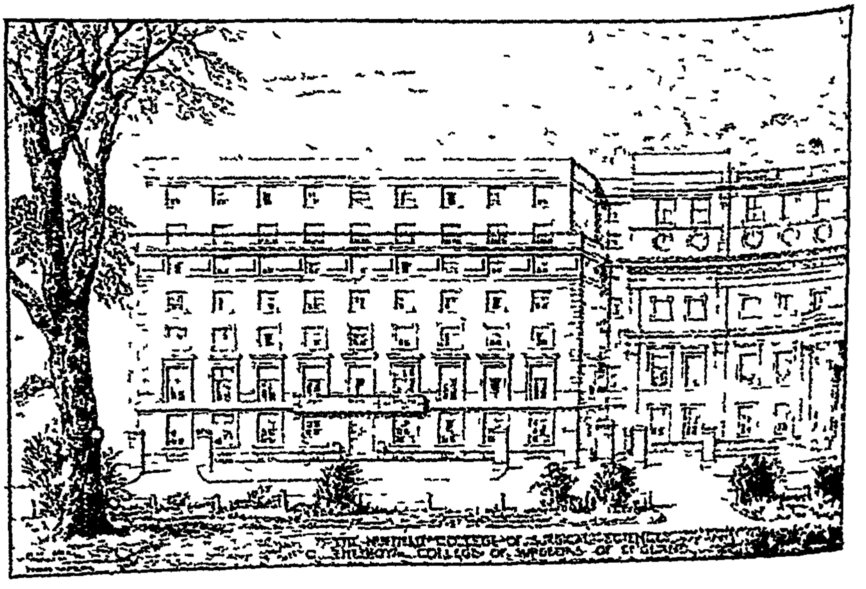
Annotations

THE SURGEONS BUILD

GREAT disasters should be followed by great recoveries The Fire of London gave us St Paul's and many another fine thing, and it is for us to ensure that the eventual result of the bombing will be to enrich our city The Royal College of Surgeons suffered heavily in the war, but like a well-pruned tree may yet be the better for it When the Queen laid the memorial stone last Tuesday, the new buildings were springing up around her, and above the blue and white marquee we could imagine the ceiling of the great hall already closing over her head The building programme will not only make good the war time losses, but will provide noble quarters for all the scientific and educational duties of the college

The great hall seats 700 people, and in its austere and dignified design will be a fit centre for surgical congresses, lectures of the college, and receptions and other social occasions Three floors of museums will lie above it, given by the Wellcome Trustees, and these will be matched by three floors of laboratories, lying above a new council chamber The library is to be enlarged, and an exhibition hall will connect the old and new buildings Later the Nuffield College of Surgical Sciences, the gift of Viscount Nuffield, will rise facing Lincoln's Inn Fields, in which there will be all the amenities of college life for 90 resident postgraduate students from Great Britain, the Commonwealth, and abroad A department of



whether an appreciable percentage of those who develop tumours after ear-piercing have a tuberculous diathesis.

My sincere thanks are due to Mr. Tal Jones for his excellent photographs, and to Miss Wade, of the Royal Society of Medicine, for her help in preparing this article.

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CHLORAMPHENICOL IN TYPHOID AND PARATYPHOID FEVERS

NEW LINES OF TREATMENT

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I HAVE previously reported on the curative effect of chloramphenicol in 200 cases of typhoid fever (El Ramli 1950). The recommended scheme of treatment was to give 50 mg. per kg. body-weight in the first two hours (loading dose), followed by 25 mg. per kg. twelve-hourly until the temperature became normal, and half that dose for fourteen days in convalescence.

Since then some further investigations have been made. (1) A new régime has been tried in which the initial loading dose was omitted and a smaller daily dose of chloramphenicol was given twelve-hourly. (2) The relation between treatment in convalescence and the incidence of relapse has again been studied. (3) The therapeutic value of chloramphenicol produced by different pharmaceutical firms has been compared. And (4) the therapeutic response to rectal administration of chloramphenicol in the form of suppositories has been assessed.

TABLE I—AGE-INCIDENCE OF ENTERIC FEVER IN PRESENT SERIES

Age (yr.)	No. of patients
0–5	*181 (*45·5%*)
6–10	75 (*18·8%*)
11–15	55 (*13·8%*)
More than 15	87 (*21·8%*)

*Of these patients only 4 were aged less than 2 years.

These observations were made in 398 cases of typhoid or paratyphoid fever admitted to the Abbassia Fever Hospital between February and September, 1952. Of these cases 81% were diagnosed as typhoid fever, 17·5% as paratyphoid A, and 1·5% as paratyphoid B. The diagnoses were based on the clinical picture, the isolation of the organisms from the blood, urine, or stools, and a rising Widal titre.

TABLE II—TREATMENT OF ENTERIC FEVER WITH DIFFERENT MAKES OF CHLORAMPHENICOL 12·5 MG. PER KG. OF BODY-WEIGHT TWELVE-HOURLY

Make of chloramphenicol	No. of cases	Average duration of fever (days)	
		Before treatment	After treatment
‘Chloromycetin’ (Parke Davis)	90	13·7	3·3
‘Synthomycetine’ (Le Petit) ...	108	13·6	3·7
‘Kémicétine’ (Carlo Erba) ..	200	13·8	3·9
Total	398	13·7	3·7

A few other cases have since been treated with ‘Microchlorina’ and ‘Alficetyn,’ other brands of chloramphenicol; results are similar to those recorded above.

The age-incidence of enteric fever in the present series is shown in table I. Of the 398 patients 45·5% were under 5 years of age, mainly between 2 and 5; 64·3% were under the age of 10; and only 21·8% were over 15.

FINDINGS

New Régime of Treatment

The dose used in the present series was 12·5 mg. per kg. twelve-hourly without any initial loading dose. This dosage gave a satisfactory response (see table II). The average duration of fever after the start of treatment was 3·7 days, compared with 3·5 days in the previous series (El Ramli 1950). All the patients received the daily dose in two equal doses. I now regard it as preferable to give the chloramphenicol twelve-hourly, for the following reasons:

(1) There is less interference with the patients' rest.

(2) The serum-chloramphenicol level is maintained higher than it would be if the daily dose (25 mg. per kg.) were given at shorter intervals, because each dose would then be smaller.

(3) The therapeutic response is the same whether the daily dose is given two-hourly, four-hourly, or twelve-hourly (El Ramli 1950).

Duration of Treatment in Convalescence

The patients in the present series were given chloramphenicol, after the temperature became normal, on three different lines:

Group I included 289 patients in whom chloramphenicol was given for 0–3 days after normal temperature had been reached; of these patients 26·3% relapsed (see table III).

Group II included 58 patients in whom treatment was stopped when the temperature became normal, to be resumed throughout the second week of convalescence, when relapses are expected; 13·8% of them relapsed. Smadel (1950) and John and Vinayagam (1952) favour this scheme of interrupted treatment in convalescence and report favourable effects on the incidence of relapses.

Group III included 51 patients whose treatment was continued for twelve consecutive days after their temperatures had become normal; 3·9% of them relapsed.

The results obtained show that the relapse-rate is much less where treatment is continued for twelve days in convalescence (group III). The reason why there were

TABLE III—RELATION BETWEEN DURATION OF TREATMENT IN CONVALESCENCE AND INCIDENCE OF RELAPSE

Drug used	Duration of treatment in convalescence (days)						Total	
	0–3 (group I)		7 after 7 days' rest (group II)		12 (group III)			
	No. of cases	No. of relapses	No. of cases	No. of relapses	No. of cases	No. of relapses	No. of cases	No. of relapses
Chloromycetin	51	16	19	4	20	1	90	21 (*23·3%*)
Synthomycetin	78	18	17	2	13	0	108	20 (*18·5%*)
Kemecetin	160	42	22	2	18	1	200	45 (*22·5%*)
Total	289	76 (*26·3%*)	58	8 (*13·8%*)	51	2 (*3·9%*)	398	86 (*29·7%*)

All the cases were observed for an average of 3 weeks after the temperature became normal, which it did in 2–5 weeks. Relapse took place after 10 days on the average (range 1–21 days).

anæsthesia will lie above it. Finally the south-western part of the existing college is to be reconstructed, to provide a fellows' common-room ground-floor lecture-rooms, and a department of dental surgery

In his address of welcome Sir Cecil Wakeley, president of the college, thanked Her Majesty, herself an honorary fellow of the college, for "thus recognising our endeavours to raise from the ruins of our old college a new home of English surgery" He mentioned the many donors whose generosity has made it possible for the work of rebuilding to go forward.

FARMER'S LUNG

In rural areas with a high rainfall, farmer's lung is commoner than is generally supposed and causes a good deal of minor illness among agricultural workers Fuller[1] has been able to collect 32 cases in eight years from the Devonshire area The disease appears in those who are exposed to dust from mouldy hay and straw Hay becomes mouldy when it has lain wet in the field after cutting The extra moisture encourages the growth of various moulds, and when the hay is handled large amounts of spore-bearing dust may be inhaled The cowman puts out fresh hay for the cattle each day, and when this is being done, says Fuller, it is impossible to see across the cowshed for dust The same thing happens during the threshing of ricks of oats wheat and barley which have been harvested in bad weather The greatest risk is to members of mobile threshing teams, who may be repeatedly exposed The risk is greatly reduced by the use of a combine harvester, when the corn is threshed as soon as it is cut

The disease is divided by Fuller into three stages In the isolated acute attack there is a sudden onset of fever at the end of the day of exposure The fever lasts only two or three days, and is accompanied by a cough with a little mucopurulent sputum which may be blood-stained Anorexia, lassitude, and frontal headache may last for several days after the acute symptoms have subsided. Moist sounds may be heard in the chest but there is no radiographic abnormality. The acute illness is so short that the patient does not always consult a doctor

The subacute phase, however, is more incapacitating and often brings the patient to hospital or chest clinic The majority of Fuller's cases were in this group They gave a history of repeated exposure to mouldy hay or corn during the previous two or three months They complained of increasing breathlessness with a short dry cough and bouts of fever in the evenings after exposure These patients were often cyanosed, but there was no bronchospasm or other evidence of asthma X-ray examination of the chest showed a fine alveolar mottling with evidence of compensatory emphysema. The symptoms cleared up in a month or two after the patient had been removed from contact with the dust, but the radiographic appearances remained abnormal for three or four months

The third stage is fortunately rare and develops only when the pulmonary changes have become irreversible The final picture of pulmonary fibrosis, emphysema, and bronchiectasis is indistinguishable from that of the other non-silicotic pneumoconioses, such as those found in cotton-spinners and bagasse workers

It is not clear how the fungus-laden dust gives rise to farmer's lung, and little is known about the morbid anatomy in the earlier stages Fawcitt[2] and Törnell[3] regarded the disease as a specific fungus infection of the lung, but, as Duncan[4] points out, the rapid recovery which follows removal from exposure does not suggest a progressive mycosis, and there is no good evidence that any of the fungi found in mouldy hay are capable of invasive spread within the lung The mere presence of fungi in the sputum means nothing for they are common contaminants Fuller found that 15% of unselected sputum samples contained moulds, including those commonly found in mouldy hay—a reminder of the importance of Koch's postulates Perhaps the mould spores and dust act as allergens, or as chemical or mechanical irritants, giving rise to a foreign-body reaction and miliary fungal granulomata This possibility is supported by the work of Zettergren,[5] who showed that when rabbits inhaled sterile threshing dust, mixed with the spores of *Candida albicans* one of the commoner fungi found in sputum and in mouldy hay, a characteristic lesion, the miliary fungal granuloma, was produced. This lesion was larger and took longer to resolve than the lesion produced by dust alone There was no evidence of invasion of the lung by fungi in those animals which had been exposed to candida But this explanation is by no means established

A LIVELY SOCIETY

It is often said that the general practitioner and the consultant do not see enough of each other they regularly read each other's letters but they rarely meet And if, as another saying puts it, the art of letter-writing went out with the quill pen, it is not surprising that there is, on both sides a wish for closer contact to colour these formal exchanges The gap is being closed in several ways and one of the strongest bridges is formed by the clinical society, whose meetings draw together general practitioners and hospital staff in a very helpful way—helpful to both doctor and patient Though the plan is excellent, it must be backed by much administrative care and dexterity if it is to succeed For one thing general practitioners are not as a rule enthusiastic over meetings of any kind, in the past few years important issues of medical politics have taken them to many more than usual, and some no doubt feel that, though clinical meetings are just the thing once in a while, a monthly meeting is a little too much for a crowded calendar A great deal therefore depends on the attractiveness of what a particular society can offer and hence on the ingenuity of its officers, themselves busy doctors for whom these extra duties reduce already meagre leisure hours

In this respect a clinical society which we saw at this bridge-building last week has been splendidly served by its architects For 64 years the doctors of Ipswich and thereabouts have had their clinical society as a convenient and agreeable means of telling each other about their interesting professional experiences. Like many good things, the Ipswich and District Clinical Society was subdued by the late war, but happily a prompt postwar resuscitation by the then secretary, Mr. F. R Stansfield, obstetrician and gynæcologist to the Ipswich group, soon restored its vigour, and today it is as lively as ever. The society's members include most of the doctors and many of the dentists in East Suffolk, and this year the president is a dental surgeon, Mr. J C. Rowbotham On the average, rather more than half the members attend each meeting On May 2 a new idea, admirably put into execution by the present secretary, Dr R M Mayon-White, pædiatrician in the Ipswich area, turned out to be a winner The society invited the section of general practice of the Royal Society of Medicine down for the weekend The main purpose of the invitation was to encourage doctors from other districts to talk shop in Ipswich homes, but the quality of the afternoon's clinical demonstrations and short papers (four by general practitioners), which formed the introduction to this hospitable plan, was more than enough to make a notable day for those visitors who were unable to stay as long as they wished Dr Mayon-White and his colleagues had fewer patients in groups II and III than in group I is that chloramphenicol was scarce and large quantities were required for treatment in the last two groups.

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[1] Fuller C J *Thorax* 1953 8 59
[2] Fawcitt R. *Brit J Radiol* 1936 9 354 *Ibid*, 1938, 11 378
[3] Törnell E. *Acta med scand* 1946 125 191
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These findings confirm those obtained in the previous series (El Ramli 1950), when the relapse-rate was less in cases treated for 11–15 days in convalescence (7·7% in 26 cases).

Chloramphenicol of Different Makes

Owing to the increasing number of pharmaceutical firms synthesising chloramphenicol, I felt it necessary to assess the relative therapeutic values of the different makes in typhoid and paratyphoid fever. The results recorded in tables II and III show no significant difference in their therapeutic values.

Rectal Chloramphenicol

Rectal administration is useful in infants and young children, patients vomiting or unable to swallow, and patients unable to coöperate. Chloramphenicol suppositories were used in 22 cases of typhoid or paratyphoid fever, and the response in these cases was identical with the classical response of enteric fever to chloramphenicol (see table IV), the average duration of fever after the start of treatment being 2·8 days. The daily dosage was 50 mg. per kg. divided into two, three, or four doses. This high dosage was instituted because it was my first experience with rectal chloramphenicol, and I thought that absorption through the rectum might be less than after oral administration.

A. W. El Borolossy estimated serum-chloramphenicol levels after the rectal administration of 25 and 17 mg. per kg. and reports his results in an accompanying paper (El Borolossy 1953). With both doses he could detect chloramphenicol in the serum twelve hours after its rectal administration. This result is in accordance with the clinical response obtained and encourages the trial of small dosage of rectal chloramphenicol.

TABLE IV—RESULTS OF TREATMENT OF ENTERIC FEVER WITH RECTAL CHLORAMPHENICOL 50 MG. PER KG. OF BODY-WEIGHT GIVEN IN TWO, THREE, OR FOUR DOSES

Age-group (yr.)	No. of cases	Average duration of fever (days)		No. of relapses
		Before treatment	After treatment	
0–5	12	16·8	2·8	2
6–10	3	9·3	3·3	0
11–15	1	14·0	2·0	0
More than 15	6	11·2	3·2	0
Total ..	22	14·1	2·8	2

16 cases were treated with synthomycetin suppositories and 6 with kemecetin suppositories; there was no difference in response between the two groups.

SUMMARY

398 cases of typhoid or paratyphoid fever were treated with chloramphenicol produced by different firms, and the results were analysed.

The dose used was 12·5 mg. per kg. body-weight twelve-hourly.

The relapse-rate was reduced when treatment was continued for twelve days after the temperature became normal.

22 cases were treated with chloramphenicol suppositories in daily dosage of 50 mg. per kg. divided into two, three, or four doses. The clinical response was the same as to oral chloramphenicol.

I am very grateful to my colleagues Dr. A. Hamid Omar and Dr. A. W. El Borolossy for their unfailing efforts and enthusiasm in this work and for help in the preparation of this paper.

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CHLORAMPHENICOL LEVELS IN SERUM AFTER RECTAL ADMINISTRATION

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Chloramphenicol is effective when given by mouth; but oral administration is sometimes difficult or even impossible—e.g., in cases of coma, persistent vomiting, or mental confusion. Rectal administration, in the form of suppositories, suggests itself as an alternative, and the clinical findings of El Ramli (1953) suggest that, given by this route, the antibiotic attains therapeutic levels in the blood.

TABLE I—SERUM-CHLORAMPHENICOL LEVELS AFTER RECTAL ADMINISTRATION OF 25 MG. PER KG. BODY-WEIGHT

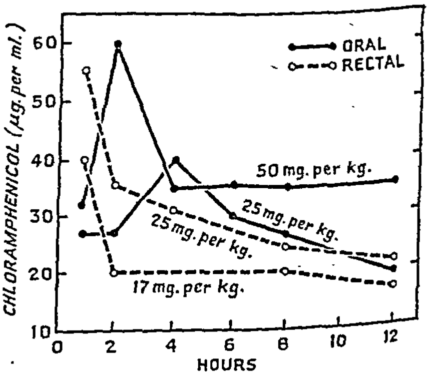
Case no.	Serum-chloramphenicol (µg. per ml.)						
	1st hour	2nd hour	4th hour	8th hour	12th hour	18th hour	24th hour
1	10	20	20	20	10	...	...
2	40	20	30	40	40	...	...
3	20	20	40	40	40	...	...
4				40	20	...	...
5	80	80	40	20		...	...
6	80	80	40	20	40	...	...
7		40		30		...	...
8	60	20	20	—	—	...	...
9	80	40	30	40	20	...	...
10	80			40		...	...
11		20		20	20	—	—
12		20		10	20	—	—
13				20	—	—	—
Mean	56	36	31	26	21	—	—

... = No sample available. — = Non-inhibitory concentrations.

To confirm this, I estimated the serum-chloramphenicol after rectal doses of 25 and of 17 mg. per kg. body-weight. The sera were obtained from typhoid cases treated at the Abbassia Fever Hospital by Dr. A. H. El Ramli. For the assay of the antibiotic, the turbidimetric method was used, employing a sensitive strain of *Bacterium coli* as the test organism.

RESULTS

Table I and the figure show that a high concentration (average 56 µg. per ml.) was obtained one hour after the rectal administration of 25 mg. per kg. This rapidly declined during the second hour, but was then maintained at an almost constant, moderately high level (between 36 and 26 µg.) between the second and eighth hours. Twelve hours after administration there was still an average concentration of 21 µg. per ml. which in most cases will inhibit enteric organisms. Only in 2 out of 13 cases were inhibitory concentrations not obtained at the twelfth hour. The last 3 samples (table I, nos. 11–13) were examined for antibiotic concentrations eighteen and twenty-four hours after administration; but inhibitory serum concentrations were not found at that time.



Serum-chloramphenicol levels after oral or rectal administration (mean of readings obtained).

assembled at the East Suffolk and Ipswich Hospital a splendid collection of pædiatric cases, medical, surgical, and orthopædic As a visitor remarked, the presentation was up to the best teaching hospital standards The welcome opportunity for an exchange of views and the interest of this model meeting were an example of a combination which we commend to other societies who would like to travel The practice of medicine, and especially general practice, has a habit of taking up weekends and interfering with excursions of this kind, but Ipswich's clinical society has shown that there are considerable advantages in resisting such interference

RECTAL ABSORPTION OF CHLORAMPHENICOL

IN this issue Dr El Ramli, of Cairo, describes the treatment of typhoid and paratyphoid fevers with chloramphenicol, which he administered rectally to some of the patients The antibiotic was given by this route to infants, young children, patients who were vomiting or unable to swallow, and those who were uncooperative The dosage was 50 mg per kg body-weight daily, divided into two, three, or four doses According to El Ramli, chloramphenicol was as effective when given rectally as when given orally, the average duration of fever with administration by either route was about 3 days Dr El Borolossy, also working in Cairo, examined the blood levels of chloramphenicol 12 hours after rectal administration of the drug He states that with a dose of 25 mg per kg body-weight the serum chloramphenicol level reached a high level within an hour and then declined rapidly in the 2nd to the 4th hours Between the 4th and 12th hours the serum chloramphenicol curves after rectal and after oral administration were close together According to El Borolossy, concentrations inhibitory to susceptible organisms were obtained in the serum up to 12 hours after oral or rectal administration of 17–25 mg of chloramphenicol per kg body-weight

These observations do not agree with those of Roy and his colleagues,[1] of Toronto These workers administered perforated capsules of chloramphenicol rectally to convalescent infants and children In some cases the capsules were not retained, but when they were retained the blood levels were disappointing With doses of 55 mg per kg body-weight the absorption of the antibiotic was irregular, and sometimes none could be detected in the serum 4 hours after administration, and even when it was given 4-hourly, the blood levels did not rise above 7 μg per ml After oral administration the blood levels ranged from 10 to 420 μg per ml The rectal dosage, already large, could not be increased, owing to the difficulty of retention Because rectal absorption was so irregular and produced such low levels, Roy and his colleagues concluded that this method of administration is of dubious value Kelly et al,[2] of Philadelphia, report similar experiences They found that the blood level after rectal administration was only about a fifth of that after oral administration of the same dose (22–24 mg per kg body-weight) The blood levels were more consistent after oral administration Absorption from the rectum appeared to take longer than absorption from the upper part of the gut, after rectal administration there was little change in the blood level for as long as 6 hours

Thus it seems that there is little to recommend the rectal use of chloramphenicol Absorption is uncertain, a larger dose of this expensive drug is needed, and possibly proctitis and perineal dermatitis may result If for any reason the antibiotic cannot be given by mouth, it can be administered by intramuscular injection dissolved in acetyl dimethylamine

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COMMITTEE ON N H S COSTS

Mr Iain Macleod has now chosen the people who are to meet under the chairmanship of Mr C W Guillebaud, the Cambridge economist,

> "to review the present and prospective cost of the National Health Service, to suggest means whether by modification in organisation or otherwise, of ensuring the most effective control and efficient use of such Exchequer funds as may be made available, to advise how, in view of the burdens on the Exchequer, a rising charge upon it can be avoided, while providing for the maintenance of an adequate Service, and to make recommendations"

Invitations to serve on the committee have been accepted by Mr J W Cook, D SC, F R S, regius professor of chemistry in the University of Glasgow, Sir Geoffrey Vickers, V C, a member of the National Coal Board and of the Medical Research Council, and Sir John Maude, secretary to the Ministry of Health from 1940 to 1945 and later deputy chairman of the Local Government Boundary Commission Mr Macleod also invited the Trades Union Congress to nominate a member, and the T U C have chosen Miss B A Godwin, a member of their council and assistant general secretary of the Clerical and Administrative Workers Union

FOOD-POISONING DUE TO CLOSTRIDIUM WELCHII

BACTERIAL food-poisoning may arise by multiplication of bacteria—usually of the salmonella group—in the intestine, or by ingestion of toxic bacterial products, such as those produced by certain staphylococci Among the organisms which have been suspected, but not convicted, of causing food poisoning is *Clostridium welchii* This was isolated from the fæces of patients in outbreaks described by Klein[1] Many years later McClung[2] described three outbreaks in which *Cl welchii* was isolated from the food, and a volunteer who ate a sample of the food contaminated with this organism developed typical symptoms The important study by Hobbs et al[3] makes it clear that we must now include *Cl welchii* among the proven causes of food poisoning

The outbreaks studied by Hobbs and by previous workers have shown that the usual foods infected with this organism are dishes containing meat which has been cooked, allowed to cool, then eaten either cold or reheated on the following day Stewed, braised, or boiled meats are particularly liable to cause the disease The clinical picture is fairly definite Diarrhœa and abdominal pain begin after an incubation period of 8–20 hours, the patient rarely complains of nausea and vomiting, in contrast with staphylococcal food-poisoning Salmonella food-poisoning almost invariably produces a rise in temperature, whereas *Cl welchii* never causes pyrexia The disease is usually mild, with recovery in about 24 hours, but some old people have succumbed to it

The *Cl welchii* responsible for this disorder shows certain peculiarities On primary isolation the colony is small and is non-hæmolytic, though faint hæmolysis may develop after some days' incubation The organisms are relatively heat-resistant, the spores have withstood boiling in foods for 2–3 hours, and in laboratory experiments for 5 hours Experimental work by Oakley and Warrack[4] has shown that these heat resistant strains of *Cl welchii* produce only small amounts of the recognised clostridial toxins, and these workers believe that the strains should be classified as heat resistant strains of *Cl welchii* type A The organism can be isolated from the fæces of most of the patients affected Hobbs

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g constantly found. Nucleated red cells were numerous
r the hæmorrhages.

'ecropsy showed bone-marrow hyperplastic with very
ıerous megakaryocytes, some with ingested cells; the
en with myeloid metaplasia, megakaryocytes not con-
ıuous, some fibrosis, and malpighian bodies few and
ıll; and the liver with very slight myeloid metaplasia.

'ase 8.—A man, aged 51, died in July, 1950, of weakness
ı wasting, after four a half years' observation. The
senting symptom was intestinal hæmorrhage in March,
6, when a large spleen was found. The first intestinal
morrhage took place in 1942, and these were repeated until
8. The patient was subject to abnormal bruising in 1949
l 1950. He had no polycythæmia while under observation,
any history suggesting it. He had never had severe
emia except after intestinal hæmorrhages. His leucocytes
re normal in 1946–48 but later increased to 20,000 per
m., and in 1949–50 he had leucopenia. Immature
cocytes were 8–12% before the first course of X-ray treat-
nt in November and December, 1948, which improved his
alth considerably. A second course, in 1949, also had a
od effect, but a third course, in 1950, had no effect. The
tient had gout in his great toes in 1948–49. His serum-
ic-acid level was 6·6–8·3 mg. per 100 ml. in 1948–50.

Necropsy showed fibrosis throughout all parts of the bone-
arrow examined, very dense in places; but in most areas
e bone-marrow cells, especially the megakaryocytes, were
cognisable; the spleen with myeloid metaplasia and very
ıall and scanty malpighian bodies; and the liver with very
ght myeloid metaplasia only.

Case 9.—A woman, aged 74, died in January, 1946, of
art-failure, after six and three-quarters years' observation.
ıe presenting symptoms were diarrhœa and the passage of
ood per rectum in April, 1939, when a large spleen and a
ge liver were found. The patient was subject to abnormal
uising from 1937 onwards. She had "chlorotic poly-
thæmia" in 1939, with more than 7,000,000 red cells per
nm., but her Hb was 70%. After having iron by mouth she
veloped typical polycythæmia, which later disappeared.
ıe had high leucocytosis (40,000–60,000 per c.mm. with
ss than 1% immature leucocytes); later the number
leucocytes became normal, but a few immature leucocytes
rsisted. The patient had gout in her hands and feet in
40–41. Her blood-uric-acid level was above 7 mg. per
0 ml. in 1939–41. She died of congestive heart-failure.
o necropsy was done.

DISCUSSION

Gout occurs fairly often in patients who have myeloid
ıetaplasia involving all three main bone-marrow
ements—erythroblasts, leucoblasts, and especially mega-
aryocytes—but it does not occur commonly in patients
ho have mainly leucoblastic myeloid metaplasia or
ıainly erythroblastic myeloid metaplasia. The blood-
ric-acid level is usually normal in typical cases of
rimary polycythæmia (Wintrobe 1951), and most cases
f typical chronic myeloid leukæmia under my care
ave had a normal blood-uric-acid level. The most
triking fact is that myeloid metaplasia occurs in some
atients who have had gout for many years, and this
ıust be of great importance in considering the causes of
ıyeloid metaplasia, and may throw light on the cause of
hronic myeloid leukæmia. In most of the published
ases in which gout occurred years before the myeloid
plenomegaly was discovered there is no means of knowing
hen the disorder of the blood-forming tissues began;
ut 1 patient was seen with gout three years before
plenomegaly was found (Coste et al. 1948). In the type
f case under discussion gout may occur more commonly
han is generally believed, for the descriptions of several
atients suggest that they had gout, though not diagnosed
s such (Rosenthal and Bassen 1938, Vaughan and
Harrison 1939, Dustin 1947).

Several other patients under my care, with "megakaryo-
ytic myelosis" or "myelosclerosis," had constantly high
lood-uric-acid levels, though they did not develop gout.

Rarely gout may occur in acute myeloid leukæmia;
and a patient with chronic gout may have an acute fatal
illness closely simulating acute myeloid leukæmia.

SUMMARY

The relationships between gout, myeloid leukæmia, and primary polycythæmia are stated.

Gout occurs much more commonly in patients with myeloid metaplasia involving erythroblasts, leucoblasts and megakaryocytes than in patients with typical myeloid leukæmia or with typical primary polycythæmia.

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SUPPORTIVE THERAPY

AN IMPROVED TYPE OF DEXTRAN

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INTENSIVE investigation into the causes, prevention, and treatment of shock was made necessary by two wars. But in a world of increasing mechanisation, with its heavy toll of accidents, shock is far from being a purely war-time problem. Collaborative research has resulted in a clearer understanding of supportive therapy, and the importance of maintaining the circulating blood volume has been firmly established. The wide use of blood-transfusion and plasma infusion means that surgical shock, as formerly known, is no longer seen.

The expense and potential shortage of stored blood and the danger of virus hepatitis after infusion of plasma have stimulated a revival of the search for alternative substances for supportive therapy. These substances have been termed "plasma substitutes," but with the development of materials which in many respects are preferable to plasma it is felt that a new designation is required. Since the primary use of these substances is to restore or to maintain the circulating blood volume, the term "blood-volume restorer" is suggested.

CRITERIA FOR BLOOD-VOLUME RESTORERS

Ease of infusion.—The viscosity of the material should be such that it is easily infusable in all climates.

Freedom from undesirable effects.—The substance must not be toxic or antigenic. It must not produce hæmolysis. It must be easily sterilisable and free from pyrogens.

Maintenance of manufacturing standards.—The material must be capable of rapid and economic manufacture on a large scale, with exactly reproducible composition. It must be storable, without alteration, for long periods under varying conditions of temperature.

Elimination from the body—The material should eventually be excreted or metabolised Any storage in the body should be brief, and there should be no adverse effect, either immediate or delayed, on any organs or at the site of injection

Retention in circulation—A satisfactory blood-volume restorer should remain in the blood-stream with levels of not less than 50% of the amount infused at the end of twenty-four hours This implies that the material should not be rapidly katabolised, excreted, or readily diffusible through the capillary wall The retained material must also have an adequate water-holding capacity

The mechanism by which macromolecular colloids hold water in the circulation is complex There are two main factors involved (1) the osmotic pressure of the solution, which depends on the molecular concentration and hence decreases with increase in molecular weight, and (2) the water-binding capacity of the colloid, which increases with increase in molecular weight The combined effect of these two factors, which tend to balance one another may be termed the water-holding capacity of the colloid

TYPES OF MATERIAL

During the last few years interest has been focused on three polymers polygelatin, polyvinylpyrrolidone, and dextran Because these substances are polymers they can be produced in various ranges of molecular size, and it is possible to obtain samples of the same polymer having widely differing properties It is shown below that molecular size is of the utmost importance

In the form which has been used for infusion gelatin produces a highly viscous solution which does not flow easily at room-temperature in this country In our experience it is necessary to warm this material before infusion Injudicious heating may cause denaturation, this may also happen with prolonged storage Evidence has also been produced of tissue changes after the infusion of gelatin (Skinsnes 1947) A derivative, oxypolygelatin, has been produced which is less viscous in solution and stable to storage The advantage, however, has only been achieved at the expense of a high excretion-rate and a correspondingly low blood level

Polyvinylpyrrolidone cannot be broken down in the body and tends to be accumulated in the liver and reticulo-endothelial system (Nelson and Lusky 1951) The German army used a form of polyvinylpyrrolidone during the war 1939–45, and Müller (1946) reported that the appearance of the spleen and lymph-nodes at necropsy after the infusion of this material was comparable to that seen in the storage diseases The use of the material was given up after army pathologists had found widespread liver and kidney damage More recently a type of polyvinylpyrrolidone has been prepared with a much smaller molecular size than that used by the Germans It is claimed that this does not give rise to organic changes, but the excretion-rate is so high that the effect on the circulation volume can only be transient

Dextran, which is a polymerised form of glucose, does not seem to be stored in the body in significant amounts, and is probably eliminated by being broken down to a molecular size small enough to be excreted by the kidneys, or glucose elements may be broken off and utilised as such A few reactions of an anaphylactic type were reported with some of the earlier kinds of dextran, these were considered to be due to the presence of large molecules, but the possibility of contamination cannot be completely excluded More complete hydrolysis of the crude dextran produced a material virtually free from reactions but at the cost of a high excretion-rate and a low twenty-four-hour blood level

Because of its basic advantages it was decided to investigate the possibility of preparing an effective blood-volume restorer from dextran The problem was to determine the best molecular range and to find out if the material could be produced on an economic scale

DETERMINATION OF BEST MOLECULAR RANGE

Dextran is prepared biosynthetically from sucrose by t action of *Leuconostoc mesenteroides*, which polymeris the glucose half of the molecule Before it can be us the crude dextran must be hydrolysed, the result product containing molecules of molecular weight rang from a few thousand to several million in a proporti depending on the time and conditions of hydrolysis.

From a physiological point of view the molecul spectrum may be divided *arbitrarily into four range*

(1) The highest range consists of those molecules wh are so large that they may produce undesirable reactions

(2) The lowest range consists of those molecules which p through the glomeruli and are excreted

(3) Above this is the range of molecules which are to large to be excreted but small enough to diffuse through th capillary wall and thus be lost from the circulation into th tissue fluid *These molecules are undesirable because, apa from any effect on the intracellular-extracellular fluid balanc they have a certain water-holding capacity, and this associate water is lost from the circulation*

(4) The next highest range contains those molecules whi are too large to diffuse through the capillary wall but n large enough to produce reactions

It therefore seems logical that the ideal form *dextran should be that containing the largest amou* possible in the last-mentioned range

To estimate the transition values between the vario ranges it was necessary to obtain a distribution curve the molecular spectrum for each of the types of dextra involved *This was done by obtaining samples of a ve* small part of each range by repeated fractionation from suitable solvent, and by measuring the intrinsic viscosit of each sample For the sake of clarity the charac teristics of each type of dextran used are described he *in terms of molecular weight* Since the values of th molecular weight have been derived from intrin viscosity measurements, the figures given must b regarded as approximations until they can be confirme by ultracentrifuge studies on the type of dextran use

From studies of excretion rate and blood levels in th rabbit and man with various types of dextran, describe in more detail below, the glomerular threshold seems t correspond to a molecular weight of 60,000, and th capillary threshold appears to be about 130,000 in ma and a little higher in the rabbit It must be borne i mind, if tempted to compare these figures with that o albumin, that diffusion depends on other factors beside molecular weight—e g, charge and shape It is impractic able to produce anaphylaxis in man and it was impossib to demonstrate it in the rabbit with any form of hydr lysed dextran free from pyrogens and other contaminant It is therefore thought that an upper limit at a molecul weight of 250,000 leaves an adequate margin of safety

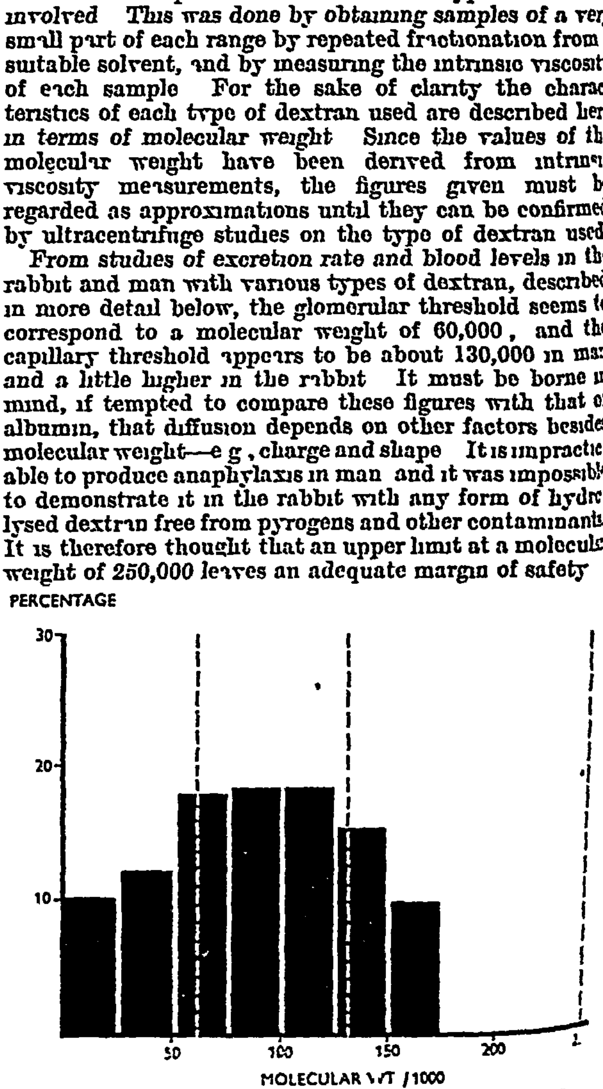

Fig 1—Distribution of molecular weight of standard dextran

isolated them from 89·9% of these patients, but from only 2·2% of normal persons. In a study of animal fæces the organism was rarely isolated from bovines but not uncommonly from pigs, rats, and mice. It was also isolated from fresh meat (except lamb) and from blowflies. Volunteers developed mild food-poisoning after eating cultures of *Cl. welchii* which had been isolated from contaminated meat, but it was uncertain whether the disease was due to a toxin alone, or to the ingestion of vegetative organisms.

There seems little doubt that this type of food-poisoning, like others, could be eliminated by good hygiene. Once more the dangers of eating precooked foods, kept a long time in conditions suitable for bacterial multiplication, have been demonstrated.

TEN NUFFIELD YEARS

TEN years ago Lord Nuffield, having set up and munificently endowed the foundation which bears his name, charged it with the task of advancing health and social well-being. Its work is thus one in which we should all like to take a hand and an interest. In its progress report[1] the foundation describes itself as "a private fund serving the community," and it has certainly made good use of the opportunities offered by its amateur status. As a discerning pioneer it has been quick to foster schemes likely to be of public benefit but not yet sufficiently established to have won official support, and it has generously backed workers engaged in promising but admittedly speculative research.

Over the ten years, 1943–53, the foundation's total income has been £5¼ million, of which it has spent nearly £4¼ million. £786,000 has been given to medical work (including £229,000 for rheumatism); £347,000 to biological research; £560,000 to research in physics; £463,000 to the social sciences; £32,000 to agriculture; £925,000 to the care of old people; and £831,000 to fellowships and scholarships.

During the second half of the period the emphasis of the programmes for medical work shifted from particular specific diseases (with the exception of rheumatism) to normal health. Thus it has made grants of £167,220 to promote teaching and research in child health. The largest grant (£100,000) was spent on the establishment of an institute of child health in the University of London. Industrial health has also claimed its support, and £150,000 was given to establish departments of industrial health in the universities of Durham, Glasgow, and Manchester, and over £15,000 to set up a working model for an industrial health service on the Slough trading-estate. Disquieted by the Teviot report on the unsatisfactory state of the nation's teeth, the foundation also decided to encourage postgraduate teaching and research in dental health, and it has made grants totalling £90,000 to the dental schools in the universities of Durham, Leeds, and Manchester and at Guy's Hospital.

The chronic rheumatic diseases cost the community so dearly in health and distress that the foundation felt justified in singling out this group of diseases for special attention. Accordingly in 1947 it financed a pioneer centre at Manchester for the study of rheumatic diseases. The following year the management of the Oliver Bird Fund of £450,000 for the study and alleviation of rheumatism was entrusted to the foundation. Since 1947 it has financed much chemical work aimed at the total synthesis of cortisone and corticotropin (A.C.T.H.). The foundation's keen eye for the future has also ranged purposefully over the biological sciences, and its eclectic help has been offered to workers studying such diverse topics as cellular biology, micro-organisms, comparative endocrinology, immunology, and neurophysiology. A second part of the report, which is to appear shortly, will describe the allocation of grants and fellowships in more detail.

THE SMALL-LIST DOCTOR

DISSATISFIED with the prospects for the small-list general practitioner under the distribution scheme which came into operation on April 1, a group of members of the British Medical Association made requisition in March for an extraordinary general meeting of the association; and this meeting was held on May 5. The resolution before the meeting was:

> That the Association being concerned by the modification of the present method of remuneration by capitation fees agreed in the Working Party's report requires the Council forthwith to approach the Minister of Health with proposals for the better protection (financial and otherwise) of the small-list doctor and of the doctor newly seeking entry into practice, and requests the Minister of Health not to implement the Working Party's report until the scheme for distribution of remuneration has been considered in the light of such proposals, and meanwhile to continue the present method of payment.

In proposing this resolution, Dr. W. J. Grant claimed that for the small-list man and the newly entered practitioner the Working Party's distribution scheme was tantamount to direction of labour by economic pressure—a device which no Government would have dreamed of using against the humblest member of a trade union. A practitioner's inescapable expenses were identical whether his list was 500 or 1500; and in Dr. Grant's view the present scheme paid little regard to this fact. He suggested loading the capitation fee for the first 1500 patients—say, 8s. a head for the first 500 and 6s. for the next 1000—as a means of remedying this "inexcusable injustice."

The chairman of the General Medical Services Committee, Dr. A. Talbot Rogers, explained that his committee had found it impossible to propose an immediate plan to offset the difficulties of the small practice, because they would know neither the size of the problem nor the amount of money available to solve it until the effects of the new distribution scheme had been observed. It was simple enough to find out which doctors had small lists, but the reasons for the small lists were much more complicated. To enable the facts to be collected and the results of the new scheme to be analysed, the Working Party had been recalled and had already begun its discussions. Preliminary figures for March and April indicated that the number of principals in general practice was increasing in the way that the Working Party had hoped, and that the consequent gain to the central pool would be more than enough to provide for cases of hardship among small-list and newly established practitioners. Dr. Talbot Rogers thought that hardship was not so widespread as many people believed, but he assured the meeting that now the necessary information was becoming available a satisfactory answer would be found. The meeting readily accepted this assurance and confirmed by a very large majority the approval given to the Working Party's plan by the association's Representative Body in Dublin last July.

It is easy to understand the impatience of those doctors who may be in real difficulties under the new method of distribution; but it is equally clear that any changes based on uncertain evidence would lead only to further dissatisfaction. At all events, the meeting made it clear that these difficulties are certainly being tackled—and in a sensible way—which is no doubt what those who asked for the meeting wanted to know.

Sir ROBERT ARCHIBALD, professor of bacteriology and parasitology in the Farouk University, Alexandria, and a former director of Wellcome Tropical Research Laboratory in Khartoum and the Stack Medical Laboratory, died on May 2 at the age of 73.

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[1] Nuffield Foundation: Review of the First Ten Years, 1943–53. Copies are obtainable from Nuffield Lodge, Regent's Park, London, N.W.1.

The suggestion of Dr Frankel and Dr Ellis Moore (April 18) that pancreatic enzyme action is deficient because of the rapid passage of food in the bowel is interesting. One of the investigators in this department has shown[1] that in dogs the external pancreatic secretion in response to a meal is markedly reduced after gastrectomy. This may be an additional factor in the deficiency syndrome. In the four cases I have described, however, no improvement has been observed after giving sodium bicarbonate by mouth. In three of the cases, a reduction in the severity of the deficiency symptoms has been noted after supplying pancreatic enzymes in addition to alkali, but in none has the griping abdominal pain been relieved.

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IAN MACPHEE

INFLUENCE OF LANGUAGE ON MEDICINE

SIR,—In his letter published in your issue of April 11, Dr Penman inquires whether any of your readers knows who adopted the motto *Nullius in verba* for the Royal Society. John Evelyn proposed this motto among several others, but Dr Penman might like to read pp. 142–144 in volume 1 of *A History of the Royal Society* by C. R. Weld (London, 1848).

The Royal Society,
Burlington House,
London, W. 1

D. C. MARTIN
Assistant secretary

HAZARDS OF LUMBAR PUNCTURE

SIR,—In your leading article of April 11 you say that "the occurrence of headaches in 40% of ambulant patients in Sciarra's series confirms the idea that twenty-four hours' rest in bed is advisable after lumbar puncture." If this suggestion is accepted, it follows that every patient who is to have lumbar puncture must be admitted to hospital. Even if this were practicable, the necessity for it would be debatable. The experience of Williams[2] in military hospitals suggested that headache was commoner among patients who were confined to bed after lumbar puncture than among those who were returned to duty.

In a clinic such as this, where many cases of syphilis are investigated and treated, lumbar puncture is a routine procedure. The number of patients involved is such that, if they were all to be admitted, the delays would be considerable. Most of them are working men and women who are free from symptoms and many would strongly object to the idea of entering hospital, either because to do so would be inconvenient or, in some cases, because it would involve disclosure of some of the facts of their illness to relatives and friends. In these circumstances it is more satisfactory to perform routine lumbar punctures in the outpatient department, and to allow patients to return to their homes or their work immediately afterwards. To do so has been the practice in this clinic for some years. Arrangements for admission to hospital are made only for elderly patients, for pregnant women, or for patients with some serious disability.

Recently during an investigation undertaken to assess the value of the Dattner needle in reducing the incidence of headache following lumbar puncture, we made a survey of the case records of 258 patients (168 male and 90 female). All of these had lumbar puncture performed in the outpatient department, and were then allowed to return to their ordinary occupations. At the next visit they were asked whether they had noticed any reactions, and if so, what was the nature, duration, and severity of their symptoms. Many who had suffered slight or moderate symptoms made no spontaneous complaint. The frequency and severity of symptoms were as follows:

54 patients (21%) complained of severe headache, 28 (11%) of moderate headache, and 36 (14%) of mild headache.

22 patients (9%) had noticed some stiffness or soreness of the back.

118 patients (46%) had noticed no ill effects.

In assessing the results it can be seen that 118 patients (46%) had had some degree of headache, but in many cases this had been so mild and transient as to cause them little or no inconvenience. Of the 54 patients (21%) who complained of severe headache, the majority recovered completely after a few days' rest in bed with no special treatment.

In the absence of any conclusive evidence that enforced rest in bed for twenty-four hours will appreciably reduce the risk of severe headache, we submit that the practice of performing lumbar puncture on ambulant patients is justifiable. It seems hardly necessary to add that in these, as in any, circumstances lumbar puncture should be carried out with strict aseptic precautions and all possible care and skill.

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E. GALLAGHER
C. G. H. CAMPBELL

SIR,—May I support most strongly the remarks by Dr Jackson (April 25) regarding general anæsthesia during pneumo encephalography.

Though it may be said that general anæsthesia adds another risk to a procedure itself not free from hazard, the advantages of its use in children, or even in an adult if one has reason to believe he will coöperate badly, to my mind far outweigh this risk. It is kinder to the child; vomiting does not occur; the required position is more easily maintained; better films are obtained; and the procedure is accelerated. In addition, as Dr Jackson says, both in children and in adults there is a striking reduction in the subsequent headache and vomiting.[1]

This is not easy to explain, however; for the degree of meningeal irritation, as shown by the polymorphonuclear pleocytosis in the cerebrospinal fluid is the same with or without anæsthesia. It is not due to prolonged unconsciousness, for the patients have usually come round by the time they return to the ward. Whatever may be the reason for this difference, so striking is it that patients who have been unfortunate enough to have to undergo this unpleasant but valuable procedure twice, and who have experienced both methods, leave no doubt in the minds of their doctors and their fellow patients which they prefer.

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EDWIN R. BICKERSTAFF

TRAINING OF PHYSIOTHERAPISTS

SIR,—Dr Cawadias, in your last issue, expresses himself as being at a loss to understand the tendency of the Chartered Society of Physiotherapy to monopolise physical treatment in this country. As one who has availed himself a great deal of the help of its members the answer seems to me plain.

This body was formed nearly sixty years ago, its members pledging themselves (unasked) to work only under medical direction. Their three-year course of training is at officially recognised schools, usually associated with teaching hospitals. By 1920 their status was such that a Royal Charter was conferred upon them, and Queen Mary became their Patron. In this way their members have become, in Dr. Cawadias's words, "accepted members of a medical team, receiving alike the support of the medical profession and the confidence of the public."

The Government-sponsored Cope Committee which reported last year, after examining all the available evidence, stated that the Chartered Society of Physiotherapy's standard of training appeared to be the only one acceptable for universal adoption in the National Health Service. It has surprised many that this report

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[1] Annis, D., Hallenbeck, G. A. *Surgery*, 1952, 31, 517.
[2] Williams, D. I. Personal communication, 1946.

[1] Bickerstaff, E. R. *Lancet*, 1951, i, 1209.

Special Articles

CONFERENCE ON POLIOMYELITIS

A MEETING, under the chairmanship of Sir JOHN CHARLES, the chief medical officer, was held at the Ministry of Health on April 15, to discuss the implications of the recent Danish outbreak of poliomyelitis in which there were a large number of cases with respiratory paralysis of the bulbar and bulbospinal forms for which an unusual method for maintaining respiration was adopted. This method, which has been described by Lassen,[1] consists in the performance of a tracheotomy and insertion of a cuffed endotracheal tube; through this tube intermittent positive-pressure ventilation with a nitrogen-oxygen mixture is maintained by means of manual compression of a rubber bag.

The meeting was attended by representatives, including specialists in infectious diseases and anæsthetists, from all regions and was addressed by Dr. W. H. Kelleher, Dr. B. A. Sellick, Dr. A. B. Christie, Dr. J. R. Esplen, and Dr. G. E. Breen, all of whom had visited the Blegdams Hospital, Copenhagen, where they had seen this method of treatment employed.

Dr. KELLEHER said he had reached the conclusion that Lassen's method should be studied carefully and, perhaps with certain modifications, should be used for suitable cases in this country. The Danes had found that in certain bulbar forms of poliomyelitis treatment by postural drainage alone was not always enough; and their method, which aims at the clearance of the upper air-passages and prevention of flow of secretions into the lower air-passages, is claimed to have brought about a considerable fall in the mortality. As regards points of detail, Dr. Kelleher questioned the need for a closed-circuit apparatus with the danger of inhalation of soda-lime particles; he also thought that consideration should be given to the use of silver tubes wherever possible in place of rubber tubes, with a view to minimising the risk of producing stenosis of the trachea.

Dr. SELLICK said he felt that in this country we should concentrate on the good points of Lassen's method but consider whether any improvements are desirable. He had the impression that more cases than necessary were subjected to tracheotomy and suggested that instead of immediate tracheotomy an endotracheal tube should be passed through the mouth (when the upper air-passages have been cleared) and allowed to remain there for 8–12 hours, during which time the patient's condition could be assessed and the causes of respiratory embarrassment more accurately defined. He mentioned the practice of Nielsen, of Sweden, who leaves an endotracheal tube in place for as long as 3 days in the treatment of barbiturate poisoning (though it is not easy to keep an endotracheal tube in position in a conscious patient). Dr. Sellick wondered why so much stress had been laid on the use of a mixture of 50% oxygen and 50% nitrogen, and thought that at any rate in the more chronic cases mixtures of air and oxygen or compressed air alone should be satisfactory. Dr. Sellick emphasised the importance of *adequate* postural drainage and the value of introducing drugs to prevent bronchospasm and reduce sputum viscosity.

Dr. CHRISTIE and Dr. ESPLEN discussed the types of case for which Lassen's method was suitable. Dr. CHRISTIE pointed out that postural drainage is difficult when the patient is being nursed in a tank respirator but could easily be employed in conjunction with the Copenhagen method. He was impressed by the amount of secretion which could be aspirated through the endotracheal tube in the Copenhagen method. Dr. ESPLEN supported Dr. Sellick's suggestion for the use of an endotracheal tube passed through the mouth for a few hours while the patient's condition is being assessed.

Dr. BREEN, whose visit to Copenhagen was more recent than those of the previous speakers, said that the Danes were now inclined to think that cuffed tubes were not always necessary and that well-fitted silver canulæ were quite satisfactory in some cases. He said that they had completely abandoned the use of tank respirators and were relying on bag ventilation. Dr. Breen suggested that in order to overcome the disadvantages of manual compression consideration should be given to the use of the Bang respirator,[2] the use of compressed air with a Kifa motor, and the Spiropulsator. He said that a Bang respirator could be made for £40–50 and that a spiropulsator costs about £150.

Mr. T. HOLMES SELLORS said that he thought that the chief need in dealing with this problem was proper coördination between the various branches of the profession, and emphasised the valuable part which can be played by anæsthetists with experience in chest surgery. These anæsthetists are skilled at treating "wet lungs," and their services should be employed in the early stages when they could best advise on the method of treatment to be used. Mr. Holmes Sellors thought it was important to avoid unnecessary tracheotomies, and underlined the value of postural drainage when this is properly carried out.

Dr. W. RITCHIE RUSSELL agreed with Mr. Holmes Sellors about the important part which anæsthetists can play, and endorsed his references to the value of adequate postural drainage. In this connection he mentioned the need for the proper training of the nursing staff. He said that pure spinal cases should be treated in tank respirators but that such respirators were not of course suitable for pure pharyngeal cases. For such cases postural drainage was the treatment of choice; tracheotomy had been advocated in the United States but was becoming less common. He was somewhat sceptical about the claims put forward for the Copenhagen method and thought that it was only likely to be useful for combined bulbar and spinal cases.

Mr. TERENCE CAWTHORNE reminded the meeting that tracheotomy can be a mutilating procedure, and when employed should be carried out below the first ring of the trachea so as to avoid the risk of subsequent laryngeal stenosis. He suggested the use of an expiratory valve so as to enable the patient to cough and use his voice; the valve should be removable, to allow aspiration of secretions. Mr. Cawthorne said that tracheotomies should be performed by persons experienced in this procedure; a circular hole was best as it was least likely to give rise to stenosis.

Dr. A. CRAMPTON-SMITH, who referred to his experiences as anæsthetist to a unit for head injuries, described his practice of emptying the stomach and bronchi in patients whose cough reflex has been lost. He referred to the danger of ulceration of the glottis and trachea if endotracheal tubes are left in place for too long. He also referred to a hand inflator, developed by Prof. R. R. Macintosh, which is useful as a pure emergency measure.

Dr. T. D. CULBERT said that he was of opinion that analysis of blood gases frequently gave helpful information in the management of patients being treated by artificial respiration.

Dr. T. ANDERSON, who had also visited Copenhagen, emphasised the value of team-work in dealing with these cases, but said that the team must have a leader. He also referred to the importance of an adequately trained nursing staff.

Dr. E. C. BENN thought it important that a modified tank respirator should be designed to allow the nursing of a patient in the prone position with a view to ensuring adequate postural drainage. Dr. J. G. JOHNSTONE, on of the Cope Committee should apparently have been pigeon-holed, and the reasons for this are a matter of which more should be heard

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[1] Lassen, H. C. A. *Lancet*, Jan. 3, 1953, p. 37.

[2] Bang, C. *Ibid*, April 11, 1953, p. 723.

London, W 1 W S C COPEMAN

RENAL DUCTS OF BELLINI

SIR,—I see by Dr Duran-Jorda's letter last week that he is not satisfied with the anatomical and clinical data I presented (April 18) to show that the ducts of Bellini communicate with the renal calyces I hope that some histologist will soon furnish us with an authoritative statement on this subject

Dr Duran-Jorda, referring to comparative anatomy in support of his views, informs us that the kidney of the cat has no Bellini ducts at all Following his example it may be of interest to note that the kidney of the elephant—judging by the specimen in the Royal (Dick) Veterinary College, Edinburgh—has very nice ones

Edinburgh. JAMES A ROSS

HOSPITAL COSTING

SIR,—May I reply to your comment on my letter of April 25?

Your quotation from the Nuffield Trust report on the subject of "dramatic economy" and "dramatic waste" does not by any means convince me that you were right in saying that "it is generally agreed that there is no large-scale extravagance to be exposed" Rather am I confirmed in my previous statement that "no authoritative pronouncement has been made to this effect" and my doubts that the Ministry of Health would subscribe to it Indeed, as previously stated, the Ministry's actions have long indicated entirely opposite views If further support is wanted for my contention about extravagance, it will be found in the report of the Comptroller and Auditor-General on the National Health Service accounts, published only a few days ago The following are only some of the items "Losses of bedding and linen included sums of £6963 and £8150 at two large hospitals" "At some other hospitals it is still not possible to discover the deficiencies" "Farms and gardens run by the hospitals showed a deficit of £614,033 (without taking into account rent and depreciation), as compared with £569,087 in the previous year"

I note that you accept as sound my example, taken at random, of the hopelessness of the alternatives to costing suggested in your annotation of March 28—with the reservation that you had in mind other fields in which financial cost figures may be relatively uninformative compared with staff numbers I think we can rest assured that no administrator would consider cost figures as in a vacuum, whether in providing medical, nursing, or any other services, including catering Cost figures are only a guide—a steady platform from which to survey the field of action and not a diving-board! It may well be that from such a vantage-point it may be useful to count heads, and to allow for those wearing the laurel wreath of a merit award But let the platform first be erected

Moreover one must be selective in the innumerable comparative indices which can be thought up Your reference to a "battery of indices" must surely send a chill through those who by experience know that many a so called index is a misnomer in that it does not point significantly in any direction These words accord ill with the views of modern management, and, indeed, are difficult to relate to the view expressed in your annotation that "the figures which are of most use, to laymen and executive officers alike, are the simplest figures—the figures behind which lies little calculation and 'treatment'"

When you ask in your final sentence "for common-sense adaptations to the special problems, not merely conventional systems applied wholesale," it is obvious that you approve of the systems outlined in the costing reports of the Nuffield Trust and King Edward's Hospital Fund, both of which have taken the most appropriate principles and practice from industrial accounting and adapted them to hospital requirements No-one suggests that a costing system for the production of the "Comet" is suitable for assessing costs incurred in treating a hospital patient, and, conversely, no-one would suggest the use of a hospital system for industrial purposes Nothing conventional will do—industrial systems are tailored to individual requirements, and the conventional method of costing in hospitals is a proved failure But if by a "conventional" system you have in mind to decry a business-like system developed to the point of actual comprehensive usefulness, then I can assure you that "half measures" will only serve to add to the present confusion, no matter how much they are buttressed about by indices

ADMINISTRATOR

SIR,—Nearly seventeen years ago, Dr Andrew Topping drew attention [1] to the futility of attempting to compare maintenance costs in hospitals He wrote "Few, if any, hospitals are exactly alike as regards construction lay-out, type of work done, staffing arrangements, occupation rates, and financial commitments" Those who are now attempting to draw comparisons would do well to read Dr Topping's article

Whittington Hospital
London N 19

D J McCARTHY
Hospital secretary

AN UNUSUAL TYPE OF HERNIA

SIR,—The unusual herniæ described by Mr Howard (Feb 21) and by Mr Rose (May 2) seem to be examples of an uncommon type of direct inguinal hernia that I described in 1937 [2] I have since found it perhaps a dozen times, and several of my friends and colleagues have told me that they have encountered instances, but I have *not seen any references to it in the literature*

The hole may be anywhere in the tendinous lower part of the fused internal oblique and transversalis, but I have never seen it as far out as it seems to have been in Mr Howard's case I have always assumed that these herniæ come through congenital defects because the margins of the hole are sharp and tendinous, quite unlike the diffuse bulge of a structure that has yielded to prolonged presures

London, W 1 HENEAGE OGILVIE

SIR,—I have read with interest the case reported by Mr Howard Soon after this account appeared I came across a similar case

A woman, aged 50, was admitted on March 6, complaining of a painful lump in the left groin with pain in the abdomen She had noticed this lump, which she took to be a hernia for the past six months, and was able to reduce it herself Lately it had become more painful, and it had become difficult to reduce it, although she had always succeeded in doing this up to the time of admission During the day of admission she had severe colicky pain in the abdomen, but she did not vomit The lump in the groin was very tender, and the patient could not reduce it She then came to hospital and was admitted At no time could muscular effort be related to the appearance of the lump

The lump was more or less at the site of the left internal ring There was a suspicion that it was slightly higher than one would expect, but because of the patient's obesity it was impossible to ascertain its position accurately

At operation an incision was made parallel to and about 1 in above the left inguinal ligament The external oblique aponeurosis was cut through, and, as in Mr Howard's case, a lump of fat was noticed over the fibres of the internal oblique muscle and apparently attached to it On exploring this lump of fat, which was about 2 in above and lateral to the internal ring, a small hernial sac was found which was about the size of a plum stone It was now empty, the hernia apparently having reduced itself as soon as the general behalf of the Ministry, said that specifications will shortly be circulated for the modification of the Both respirator, but that such modifications will not, for the moment, facilitate the use of postural drainage for patients being nursed in these respirators.

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[1] *Lancet* 1936 ii 807

[2] *In* Post-Graduate Surgery, edited by R Maingot London, 1937, vol 3, part 18 chapter 2, p 3620

At the conclusion of the meeting Dr. R. A. **Beaver** demonstrated a machine which he has developed to provide automatic compression and which can be used in conjunction with bag ventilation (the "artificial student"). He said that such a machine could be produced for £16 complete, but that at present it was not possible to purchase the electric motors, as there is a delay of three months in delivery from the manufacturers.

THE WORLD'S FOOD-SUPPLY

On March 25 the food group nutrition panel of the Society of Chemical Industry held the third of a series of four meetings[1] on Food and the Future. On this occasion it considered New Natural Sources of Foodstuffs.

FOOD AND FODDER YEAST

Mr. A. C. **Thaysen**, ph.d. (Colonial Microbiological Research Institute), whose paper was read by Mr. H. J. **Bunker**, pointed out that the value of yeast lies in its ability to convert about 80% of the inorganic nitrogen of the medium into protein. The rate of conversion, compared with more orthodox methods, is enormous. For example, a fully grown bullock, weighing half a ton, produces protein at the rate of 0·9 lb. per day; half a ton of soya bean yields at the rate of 82 lb. per day; while half a ton of torulopsis yields 51 tons of protein in twenty-four hours.

Food yeast is at present being produced both in Jamaica and in South Africa. The cost—at 1*s*. 2*d*. per lb.—corresponds to 0·069*d*. per lb. of protein, compared with 0·8*d*. per lb. of protein from beef. Very little yeast, however, is at present consumed by man. In Germany and Finland it is used solely as animal feed. Compared with other sources of animal feed, yeast is expensive; for it sells at £130 per long ton, compared with soya-bean meal at £30.

Yeast contains an appreciable concentration of vitamins. As a supplement to human dietaries, apart from its protein content, yeast would supply much-needed members of the vitamin-B complex, and used in this way it is certainly economical.

Dr. Thaysen emphasised that yeast is recommended only as a supplement and not as the sole source of protein. Yeast itself is deficient in methionine, and as a sole source of protein would therefore be inadequate; but in combination with other foods which compensate for this deficiency, yeast would be a valuable addition.

He pointed out that the very fact that waste materials were being used as media for growing food yeast was a measure of our shortage of food. Mr. Bunker emphasised the future possibilities of food yeast, when present economics could be considered irrelevant. He pointed out that dried brewer's yeast sells at £90 per ton, and when debittered, but not extracted, at £130.

The value of torulopsis as a food converter, compared with saccharomyces, lies in its ability to ferment pentoses as well as hexoses. This is valid only when waste sulphite liquor is used as a medium: when grown on molasses both these organisms are equally valuable. Vast quantities of raw material are available—for example, as much as a quarter of a million tons of waste sulphite liquor, which really is a waste material, is available annually in the United States and Canada, as well as hydrolysed wood, banana skins, bracken, and peat. *Rhodotorula gracilis* could provide a valuable addition to fat resources, since the organism contains 42% fat and 23% protein.

EFFICIENT USE OF SUNLIGHT

Mr. N. W. **Pirie**, f.r.s. (Rothamsted Experimental Station), outlined the measures generally proposed for increasing the world's food-supply. On the question of increased irrigation, when the water-supply is limited this may involve diverting water from hydro-electric schemes, and the settlement must depend on quantitative considerations. On low-lying land the water can be run through the turbine and then used for irrigation. On high land it is necessary to compare the energy obtained from the water when converted (*a*) via the turbine and (*b*) via the extra plant growth.

As to an increase in cultivable area, this implies that we have decided that agriculture is the most profitable method of using sunlight. Mr. Pirie pointed out that photosynthesis is extremely inefficient, and the advocates of unicellular photosynthetic organisms, such as chlorella, dispute that farming is the best way to produce food. Algæ have no greater efficiency in trapping sunlight but can be more readily made to work at maximum efficiency by provision of optimum temperature, carbon dioxide, and nutrients. These conditions would render chlorella culture as costly as glass-house cultivation.

Since the green plant will be our main source of food for a long time to come, the best use must be made of it. Only a small part of the crop is eaten directly by man; most is fed to animals or used as a fertiliser, or even wasted. Crops grown primarily as animal food are wasteful, despite the high esteem in which their products are held, because the over-all conversion is usually only 5–10%. Economies in the use of soil can be made both here and by replacing textile fibres by synthetic fibres.

Direct consumption of crops by man is desirable. Plants are, however, relatively poor sources of protein, with the exception of legume seeds and most young leaves. Young, vigorously growing leaves contain up to 30–40% of protein and little fibre, but only a few plant species will stand up to continuous cropping of very young leaves. The alternative is to separate the fibre from the proteins, fats, and carbohydrates of lower-quality leaves.

The advantage of fractionating leafy crops lies in the fact that the products are more valuable when separated than when combined. The proteins are suitable for non-ruminants and perhaps man; the fluid extract could be used for feed or as a medium for micro-organisms; and the fibrous residue still containing some proteins and starches is suitable for ruminants or even for fuel.

In many parts of the world there are abundant leafy wastes, such as potato haulms, sugar-beet leaves, and sweet-potato leaves. When, however, satisfactory techniques have been developed our choice of domesticated plants might well be reconsidered. Plants that use sunlight most efficiently might be chosen rather than those grown merely because a use has been found for them.

On the question of economics, leaf protein, even extracted from crops grown specially for the purpose, would cost less than existing protein foods, and about the same as estimates for yeast and chlorella.

DISCUSSION

Mr. A. L. **Bacharach** pointed out that the successful use of industrial by-products, including leaf-protein filtrate, for the cultivation of micro-organisms depended on a balance between carbohydrate and nitrogen in the medium, and asked whether either would need to be added to these media. Mr. **Pirie** replied that carbohydrates are the limiting factor in many plant juices, and in the case of most waste materials little extra ammonium sulphate is required.

Mr. G. E. **Fogg**, ph.d., agreed that algæ culture is unlikely ever to replace ordinary crops, but suggested that algæ have special features which may make them important as auxiliary sources of food. While their anæsthetic was administered The opening in the fibres, about $^{1}/_{2}$ in in diameter, had a definite firm edge The sac was removed as well as the fat surrounding it, and the hole was repaired with silk

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[1] See *Lancet*, 1952, ii, 1269; *Ibid*, March 14, 1953, p. 538.

The patient made a good recovery and was discharged two weeks after admission When seen later she was quite fit

My thanks are due to Mr S W Holmes, surgeon to Mile End Hospital, for permission to publish this case

Mile End Hospital,
London, E 1

P W HATTINGH

TUBERCULOSIS IN GLASGOW

SIR,—In his letter last week, Dr Horace Joules has committed himself to a statement for which, clearly, he sought no verification Since it is contrary to fact he would not wish it to pass unnoticed

It is not the case that, within the area of South-West Scotland—the territory, that is, of the Western Regional Hospital Board—no consultant in tuberculosis has yet been appointed On the contrary, there are in this specialty fourteen consultants, of whom six are within the City of Glasgow itself At present, three additional appointments of similar grading are in process of being made as a first contribution towards five new appointments, all of which are to be related directly to the re-development of the chest-clinic service in Glasgow which is being carried out as a major capital scheme

Western Regional Hospital Board,
64, West Regent Street,
Glasgow, C 2

A K BOWMAN
Senior administrative medical officer

SIR,—Dr Joules, in your last issue, does well to recall attention to the dangerous breeding-grounds of tuberculosis which explain its continued existence The housing conditions and standard of living today are much better than they were when the late Sir John Robertson launched his attack against tuberculosis in Birmingham over forty years ago We then had four times as many deaths in the slums as in the better housing areas of the city, and having seen the slums and watched their gradual disappearance I can understand why the number of deaths from tuberculosis has fallen steadily from 53,858 in 1916 to less than 14,000 in 1951 This is a public health triumph, as are most of the chief items in the decline in the death-rate

With the terrible conditions such as Dr Joules describes in Glasgow, and such as I have seen in this and many other countries, why do we waste our slender resources on the less profitable specialist propaganda and activity? It is little less than humbug to take, at great expense, infected persons from these breeding-grounds to elaborate chest hospitals (there are few sanatoria in the sense that these treat the general rather than the local condition of the patient) to "profit" by the skill of specialists and nurses and then return them to these breeding grounds for further infection As demonstrated by Sir John Robertson so many years ago, the home could be the best place for the treatment of tuberculosis Home treatment is the least expensive, the most pleasant and stimulating for the patient, and the most expeditious and lasting In the hands of the general practitioner, now provided with more effective medication, success would be achieved But the homes must be improved to permit such treatment The evidence is that good housing and a good standard of living will eradicate the disease and leave the people contented with their desirable happy homes, yet the modern specialist propaganda demands the use of many of our slender resources for an ever-increasing build-up of an elaborate chest-hospital system with its ever-increasing staffs In them there is little indication of achieving or even wishing to achieve the desired eradication, for, as the death-rate diminishes, the propaganda increases and the techniques for treatment are elaborated, and these call for more and more personnel, and the concerted demands of these exhibit a group selfishness[1] which would not be tolerated in any voluntary organisation with limited funds

I am at a loss to see how Dr Joules can reconcile his account of the home conditions with the measures he recommends What value would a consultant in tuberculosis be? Glasgow has medical men quite capable of giving the necessary essential advice Dr Joules's statement that "there has been little or no secondment of nurses from general hospitals to sanatoria or other hospitals where tuberculosis is treated" exhibits one of the selfish demands of the specialist, with such behaviour I am in full agreement with the "doctor prominent on administrative committees" Dr Joules's "intelligent approach to the nursing problem of tuberculosis" would risk the sacrifice unnecessarily of anyone's daughter to tuberculosis True the nurse who is unfortunate enough to become a victim of infection now gets compensation, but I do not regard this as adequate or even justifiable when other better methods should be made possible Such threat of secondment will do more harm to the recruitment of nurses than the "good" its adoption would achieve

His final statement is that "the facts should receive the widest publicity in the national press and on the air, in order that there may be quickening of response to this tremendous human need" He surely has not overlooked the possibility of television! This would permit of the demonstration of magnificent chest hospitals with all their attractive surroundings and their spectacular laboratories with elaborate and expensive equipment Personally I have not appreciated that the specialists are a "tremendous human need" I prefer the general practitioner every time

Birmingham

JAMES F BRAILSFORD

COMPARISON OF PHENYLBUTAZONE AND TAB CODEIN CO

SIR,—The recent statements concerning the efficacy and toxicity of phenylbutazone ('Butazolidin') in the treatment of rheumatoid arthritis led us to devise a small trial to compare its analgesic properties with those of Tab Codein Co *B P C*

Thirty outpatients with established active rheumatoid arthritis were given 2 Tab Codein Co t d s for fortnightly periods During this time they were also given a fixed number of tablets of a distinctive colour, containing codeine phosphate (gr $^{1}/_{8}$) and aspirin (gr 8), and they were told to take as many as they needed of the coloured tablets (up to 8 a day) to obtain relief of pain At the end of the period the number of coloured tablets taken was calculated from the number the patient had left

In the next fortnightly period the patient was given phenylbutazone in a dosage of 200 mg t d s in place of Tab Codein Co, and a similar proviso made regarding use of the codeine aspirin tablets This process was repeated for varying periods up to three months The nature of the tablets was unknown to the patients By this means it was thought possible to assess the efficacy of phenylbutazone as an analgesic, compared with Tab Codein Co, by the number of coloured tablets taken additionally during each period At the end of each trial period the patient was asked if he felt "better," "worse," or "the same", the power of his hand grip was estimated by means of a mercury sphygmomanometer, and evidence of toxicity was sought by interrogation and examination

The results were as follows

	Average no of codeine-aspirin tablets per fortnight	*No of patients claiming*	
		Subjective improvement	*No difference between two drugs*
Phenylbutazone	8	21	6
Tab Codein Co	30	3	

At first sight the hand grips appeared to provide evidence of greater power while patients were on phenyl-maximum efficiency is not greater than that of higher plants, it is easier to achieve higher efficiencies with algæ without elaborate conditions. For example, Prof. E. C. Wassink has obtained efficiencies up to 20% in tank cultures of chlorella in the open: this compares with 2–3% in ordinary crops at their best. The plasticity of metabolism of chlorella allows production of food material of any desired composition—for example, 60% protein and 5% fat, or 10% protein and 80% fat, can be produced by varying the conditions. The ability of certain species to fix free nitrogen of the atmosphere as well as to photosynthesise may have great possibilities.

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[1] Brailsford J F *Brit med J* 1950 ii 1493

Miss D. F. HOLLINGSWORTH asked whether any research had been done on the use of food yeast. Mr. BUNKER said that this was not very popular as human food in Germany, and was produced there solely as animal fodder. Formerly it was said that only about 15 g. per day could be consumed without causing digestive disorders; this indigestibility was probably due to contamination with defrothing agents. As prepared at present, food yeast is quite palatable.

Mr. F. E. WARNER pointed out various disadvantages in the new foods from the viewpoint of an engineer. If the production of micro-organisms requires the addition of extra nitrogen it might be more economical to feed the nitrogen—say, as synthetic urea—directly to the ruminant. The economy of production of micro-organisms must take account of the vast amount of equipment and power required for aeration and sterilisation, the possible efficiency of sugar recovery from the molasses medium by ion-exchange, and the possible use of fossil fuels for organic synthesis rather than production of natural materials. He questioned Mr. Pirie's statement that straw has a fuel value three times that of the the power required to produce the fertiliser for it, on the grounds of costs and difficulties of transporting straw, its low calorific value, and the lower thermal efficiency of its slow combustion.

Mr. F. WOKES, PH.D., asked whether the biological value of leaf protein had been measured, and whether it would be an adequate protein in the absence of animal protein. Mr. A. E. BENDER, PH.D., pointed out that the published figures for the amino-acid content of gramineæ leaf protein showed only 50% of the requirements of four of the essential amino-acids, and work at Bangor University indicated that the biological value of two fractions of the proteins from cocksfoot grass were 60 and 46. He said that the apparently small quantity—only 2–5%—of yeast recommended for addition to human diets was nevertheless highly effective judging by an animal experiment by Sure (1946). Sure reported that 1% yeast, when added to a diet in which all the protein was supplied by corn, increased body-weight by 50% and biological value by 25%, while 3% yeast increased growth by 250% and biological value by 100%.

Mr. A. L. GREEN, PH.D., likened present attempts to produce new foods to man's early attempts to produce fire, and suggested that present work should be restricted to orthodox methods of food production, which would see us through this century, after which new ideas might present themselves.

Mr. W. E. LE GROS CLARK said that food yeast had been originated as a food primarily for children to increase their protein intake and was used as such in East Africa and the West Indies. He suggested that the taste for food yeast could be developed in a population by feeding it to young children.

The trend of the discussion suggested that present drawbacks to these new foods are largely due to lack of information, and that further investigation is most desirable. Although orthodox agriculture will see us through this century, all methods of increasing the world's food-supply must be pursued, for they are complementary rather than conflicting.

REGIONAL HOSPITAL BOARDS

THE Minister of Health has made the following appoin ments to fill vacancies caused by the retirement of a thir of the members of the 14 boards in England and Wale Out of 124 appointments, 89 are reappointments o retiring members; 6 appointments are still outstandin Those now appointed will hold office until March 31, 195 The names of medical members are shown in bold typ

NEWCASTLE REGION

Reappointed: Edward Crowther, O.B.E.; **S. Whatel Davidson**, F.R.C.P., F.F.R.; Prof. **R. Bramble Green**, F.R.C.S. Arthur Kay; **J. R. Murray**, M.D.; John Lisle, J.P.; Vi countess Ridley; **R. Gordon Russell**, M.B.

New members: James Thomas Fletcher; Miss Barbar Carmichael.

LEEDS REGION

Reappointed: Alderman D. Beevers, O.B.E., LL.D., J.P. H. J. Edwards; B. Hazell, M.B.E., J.P.; W. Louis Lawton O.B.E., J.P.; C. R. Morris, LL.D.; F. Watkinson, J.P.

New member: **R. Watson**, M.B.; one appointment outstanding.

SHEFFIELD REGION

Reappointed: **Hugh Barber**, F.R.C.P.; A. R. Martin; Alderman A. E. McVie, J.P.; T. Pearson, J.P.; Prof. **G. L. Roberts**, M.B., F.D.S. R.C.S.; E. W. Scorer, O.B.E.; Councillor J. S. Worrall.

New members: **R. Lodge**, F.R.C.O.G.; **D. Macmillan**, A. H. Whiteley, M.B.E.

OXFORD REGION

Reappointed: **A. R. Banham**, F.R.C.S.; J. W. W. Cripps; Capt. F. Gardiner, M.B.E., M.C., J.P.; Colonel C. B. Krabbe, O.B.E.; Prof. **T. Pomfret Kilner**, C.B.E., F.R.C.S.; Miss Rosemary Spooner; **J. A. Stallworthy**, F.R.C.S.; one appointment outstanding.

SOUTH-WESTERN REGION

Reappointed: Mrs. Margaret Ball; Mrs. K. A. Goddard, J.P.; Alderman V. J. Ross; Colonel H. Bland Stokes, M.B.E., J.P.

New members: E. C. F. Bird; Prof. J. A. Coutts, M.A., LL.B.; H. M. Scott, J.P.; P. N. Washbourn; **L. W. Hale**, F.R.C.P.; Miss M. H. Cordiner, S.R.N. (until March 31, 1955).

EAST ANGLIAN REGION

Reappointed: **M. W. B. Bulman**, F.R.C.O.G.; J. Grantham, M.A., H. S. Matthes, J.P.; G. T. Vawser.

New members: Sir Stephen Green, J.P.; **Stephen Mackeith**, O.B.E., M.R.C.S.; Captain E. Murray-Harvey, O.B.E., M.C., F.R.G.S.; one appointment outstanding.

NORTH-WEST METROPOLITAN REGION

Reappointed: Prof. **S. J. Cowell**, F.R.C.P.; Alder Lieut.-Colonel G. B. Gond; **A. Staveley Gough**, F.R.C.S.; **D. F. Hutchinson**, O.B.E., M.R.C.S.; H. Lesser, C.B.E., LL.B.; Miss M. Marriott, S.R.N.; J. M. Oakey, M.C., J.P.; Miss **Esther Rickards**, F.R.C.S.

New members: Lord Hacking, B.A.; Prof. A. Bradford Hill, O.B.E., D.SC.

NORTH-EAST METROPOLITAN REGION

Reappointed: **Louis Comyns**, L.R.C.P., J.P.; Lieut.-Commander H. Denton, O.B.E., R.N. retd; Prof. **Victor W. Dix**, F.R.C.S.; Thomas R. Haggarty, L.D.S.; Mrs. Ruth Rees-Thomas, O.B.E.; Major R. P. Woodhouse.

SOUTH-EAST METROPOLITAN REGION

Reappointed: **E. R. Boland**, C.B.E., F.R.C.P.; Lord Cunliffe; R. J. Mellish, M.P.; **A. Talbot Rogers**, M.B.

New members: Miss D. M. Smith, O.B.E., S.R.N.; Mr. H. J. Lester, J.P.; one appointment outstanding.

SOUTH-WEST METROPOLITAN REGION

Reappointed: Mrs. E. Hailstone, J.P.; **Louis Minski**, F.R.C.P.; **M. F. Nicholls**, O.B.E., M.CHIR.; S. R. Thorrowgood; Mrs. H. Feiling.

butazone, but on a "t" test this was not statistically significant

In computing the incidence of side effects, an additional 15 inpatients were included and given the same dosage of phenylbutazone—i e , 600 mg daily Side effects ranging from slight to severe were noted in 34 patients, in 7 of whom it was decided to discontinue the drug These were

Œdema of minimal degree in 6 patients , and gross œdema necessitating withdrawal of the drug in 1 patient
Indigestion (excluding peptic ulceration) in 6 patients (drug withdrawn in 1)
Vomiting (3)
Diarrhœa (4)
Peptic ulceration (2—drug withdrawn)
Ulceration in mouth and throat (3)
Purpuric reactions (3)
Granulocytopenia (2—drug withdrawn)
Dizziness, hyperacusis, and vertigo (1)
Ulceration of vagina (1)
Pyrexia (104°) (1—drug withdrawn)

A complication of phenylbutazone therapy not to our knowledge previously reported is "pink vision," which was observed by patients, not included in the above trial, who were on a dosage of 800–1200 mg daily

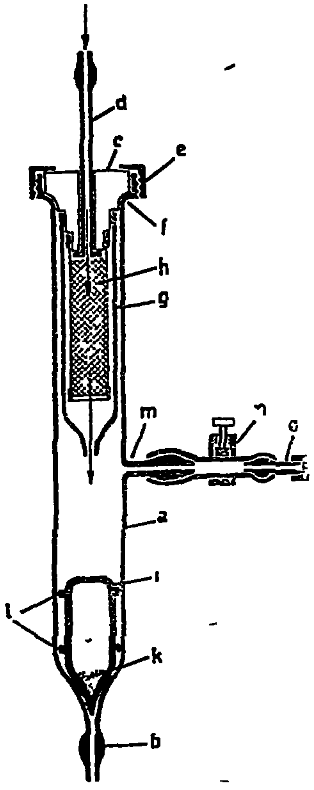
These results confirm the general impression that phenylbutazone is a more potent analgesic than Tab Codein Co in the usual dosage given in rheumatoid arthritis

Department of Medicine, Postgraduate Medical School of London, and Special Unit for Juvenile Rheumatism, Canadian Red Cross Memorial Hospital, Taplow

B M **Ansell**
G R **Fearnley**
E G L **Bywaters**
I **Meanock**

INTRA-ARTERIAL TRANSFUSIONS

Sir,—The articles by Mr Haxton (March 28), Professor Bingham,[1] and others reveal the increasing interest in intra arterial transfusions Therefore I feel that an apparatus that I designed last year to avoid air-embolism in intra arterial transfusion under air pressure might be of interest



This replaces the simple drip chamber and forms a combination of a filter, a drip chamber, and, as an essential part, a floating valve Details are shown in the accompanying figure

The cylindrical glass container (*a*) narrows conically into the tube (*b*) bearing the tubing to the artery Its upper end is closed by the rubber stopper (*c*) with the glass tube (*d*) passing through its centre Hermetic sealing is assured by the metal ring screw (*e*) pressing the upper part of the rubber stopper against the flange (*f*) of the glass container The rubber stopper also bears the cylindrical drip chamber (*g*) and the filter (metal or silk) (*h*) The lower part of the apparatus contains the hollow glass float (*i*), the point of which is ground to fit hermetically into the conical part of the glass container When blood enters the apparatus, passing through glass tube (*d*), filter (*h*), and drip chamber (*g*), the float rises and allows the blood to flow to the artery When, at the end of the transfusion, air under pressure enters the apparatus, the float drops and closes hermetically, thereby preventing air from reaching the artery, and so avoiding the danger of air-embolism The float contains in its interior such a weight of small glass or metal beads (*k*) that its upper part, when floating, just reaches the surface of the blood Several small glass spikes (*l*) on the surface of the float prevent its adhering to the glass container while dropping To the lateral glass tube (*m*) is attached a short rubber tubing with clip (*n*) and a metal conus (*o*) made to fit an ordinary syringe

This arrangement serves four purposes

1 It allows air to escape while blood enters the apparatus
2 It allows injections into the artery
3 It allows the lowering of the blood level if it rises too high (*a*) by injection of air, or (*b*) by letting excess blood escape
4 In conjunction with a sphygmomanometer it allows the measurement of blood pressure in the artery At the same time, of course, the tubing between the blood reservoir and the apparatus must be clamped

All parts of the apparatus are easily and separately detachable for cleaning and sterilisation by boiling or autoclaving

The apparatus will shortly be obtainable from A. Boulliech, 9 rue des Canettes, Paris

Alexandria, Egypt HARRY SCHAEFFER

PATHOGENIC STAPHYLOCOCCI

Sir,—Our experience during the past sixteen months may be of interest From Dec 1, 1951, to the end of March, 1953, 1509 wound swabs, including pus, from various units of this hospital have been received by this laboratory From approximately 42% of these wound swabs pathogenic staphylococci were isolated, and approximately 81% of these staphylococcal infections were penicillin-resistant

Specimens found to contain coagulase-positive staphylococci were as follows

Specimen	*Penicillin resistant*	*Penicillin sensitive*
Wound swabs	519	118
Throat swabs	28	1
Nasal swabs	19	1
Sputa	34	21
Urines	22	6
Cerebrospinal fluid	1	0
Blood cultures	1	2

Bangour Hospital Laboratory
Broxburn, West Lothian
Scotland

ISABELLA A PURDIE

EXCRETION OF MUCOPOLYSACCHARIDES IN URINE

Sir,—We were greatly interested in your annotation[1] on Butt and Hauser's investigations which throw new light on the relation between protective colloids and the physiology and pathology of renal excretion Their results agree with our observations on mice which had been given parenteral injections of foreign protein,[2] and on vitamin-C-depleted guineapigs[3] In the kidneys of these animals the cells of the whole tubular section of the nephron and the tubules themselves contained a considerable amount of polysaccharide, which was not glycogen *These findings raised the question of how such mucopolysaccharides were excreted by the kidney*

After identifying hexosamine containing polysaccharides in normal rabbits' urine, we gave intravenous injections of 80–480 mg of hyaluronate and chondroitin sulphate to rabbits weighing between 1 5 and 2 kg *Part of these substances was excreted in the urine 24 hours after the injection*, the proportion excreted seemed to be inversely proportional to the injected dose, and ranged between 54% and 19% for hyaluronate and approximately between 90% and 31 5% for

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[1] Bingham, D L C *Lancet*, 1952, ii, 157

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[1] *Lancet* 1952, i 1198 , see also *Lancet*, Feb 14 1953 p 332
[2] Benassi, G *Boll Soc ital Biol sper* 1952 28 970
[3] Tinacci, F *Arch Sci biol* , Napoli, 1952, 36 127

New members: **Charles Grosch,** M.B.; **H. H. Langston,** F.R.C.S.; Miss D. Morris; H. T. Townsend; Surgeon Lieut.-Commander **Reginald Bennett,** B.M., M.P. (until March 31, 1955).

WELSH REGION

Reappointed: William Berriman; Alderman William Casey, J.P.; Alderman Thomas Davies, J.P.; Alderman Walter Davies; Councillor Eddie Jones, J.P.; Alderman James Panes, O.B.E.; **Dyfrig Pennant,** D.S.O., M.D., Sir Ivor Thomas, J.P., D.L.; Prof. **Owen Williams,** F.R.C.S.

New member: Alderman R. D. Briercliffe, O.B.E., J.P. (until March 31, 1954).

BIRMINGHAM REGION

Reappointed: J. E. Roberts; Mrs. V. Evershed; Alderman H. Barber; Prof. **C. F. V. Smout,** M.D.; Alderman P. Williams, J.P.; Alderman L. Whitehouse, J.P.; Mrs. S. A. Ward, O.B.E.; E. P. Major, F.C.A.

New member: David Rhydderch, J.P.; one appointment outstanding.

MANCHESTER REGION

Reappointed: Walter Barnes, J.P.; Alderman G. D. Hastwell, O.B.E., J.P.; Prof. **A. D. Macdonald,** M.D.; Alderman W. Onions, M.B.E., J.P.; Sir **John Stopford,** F.R.C.P., F.R.S.; J. T. Waite; Mrs. E. A. Watson, J.P.

New members: **H. Pigott,** M.B.; **A. Poole,** M.B.; one appointment outstanding.

LIVERPOOL REGION

Reappointed: Miss A. L. Bulley; Sir **Henry Cohen,** F.R.C.P., J.P.; G. N. Fullagar, F.C.A.; **A. A. Gemmell,** M.C.P.R.C.O.G.; T. W. Harley, M.B.E., M.C.; Alderman H. Platt, J.P.

New member: **S. Barton Hall,** M.D.

Parliament

Hospital Pay-beds

In the House of Commons on April 29, Mr. ARTHUR BLENKINSOP in moving the annulment of the recent regulations on pay-bed accommodation in hospitals,[1] charged the Government with a change of policy in relation to pay-beds. Private pay-beds had always been an anomaly in a health service which had tried to ensure a single standard of service for everyone, and there had always been complaints from those who were told that they must wait for treatment, while those who could afford a pay-bed had been able to get treatment straight away. The regulations, he held, were designed to ensure an increased use of pay-beds, and this would increase the sense of injustice among those who found themselves pushed further back in the queue for free treatment. Furthermore, the regulations undoubtedly added to the favoured position of the part-time as against the full-time specialist. Yet Mr. Blenkinsop thought that it was the position of the part-time specialist which should be re-examined, for there was a great deal of agreement that the full-time specialist gave on the whole the most economical service to the health service. No doubt he would be told that the regulations were designed to ensure that pay-beds were more fully used. But if there were at present unused pay-beds why were they not being used for patients receiving free treatment? Many of these beds, he maintained, were being sterilised for the use of specialists. The regulations were really an excuse for the Minister to avoid finding the extra funds to enable the hospitals to provide an adequate service. They encouraged the extension of a two-level service, one for those who could afford to pay and another at a lower standard for those who could not afford to pay so much.

Mr. FREDERICK MESSER recalled that when the original National Health Service Bill was introduced many felt that the pay-bed proposal was dangerous but that it was justified as an experiment. After five years it had been shown that as a consequence of this provision there were empty beds in hospitals and people waiting for treatment and not able to get into them. The regulations would improve the position of the specialists, who had already not done too badly out of the health service.

Mr. SOMERVILLE HASTINGS pointed out that an increased demand for these pay-beds would increase the cost of the N.H.S. At present almost half were kept vacant. He knew that the Minister wanted these beds used for ordinary patients, but the doctors thought otherwise, and they were on the spot. He had had some experience of these pay-beds and he maintained that there had been a great misuse of them. The doctors pressed to keep the pay-beds empty so that patients could be admitted to them more quickly than to the ordinary beds. Mr. Hastings also attacked the regulations on the grounds of their complexity and vagueness. Their many doubtful and undetermined points were disastrous and would increase the difficulties of those who administered the hospitals.

Mr. ANEURIN BEVAN said that discussions with the Royal Colleges had convinced him that if specialists were not allowed to have private patients in hospitals they would be encouraged to go to nursing-homes. But the colleges believed a specialist could only do his best work in a hospital where the tools of his craft were to be found. Mr. Bevan admitted that he had been reluctant to agree because he saw the provision of pay-beds as a grave breach of the general scheme. The fact that there were empty pay-beds was evidence of maladministration. There was no justification for a hospital to have a waiting-list and empty beds. He affirmed that these beds were kept empty so that specialists could offer a bed at once to patients who could afford to pay. He had always intended that a hospital should be a homogeneity, and that public patients should have access to all the beds of the hospital if there were any beds available. He never intended that pay-bed blocks should be a physical part of the hospital. Some members of the medical profession had proved themselves unworthy of the responsibility with which they had been entrusted. They had used their considerable influence to deny beds to patients, to make them available for their private patients. Furthermore, the extra facilities granted to these part-time specialists were causing a great deal of heart-burning among the full-time specialists upon whom the hospital service mainly depended. Yet these regulations, instead of narrowing the gulf between the status of the part-time specialist and the full-time specialist, widened it.

Mr. IAIN MACLEOD, the Minister of Health, began his reply by saying that with the new regulations he had sent to hospitals a circular stressing that patients should have the system of amenity and pay-beds explained to them. He admitted that the new regulations were complicated but this was because the original regulations in practice had proved inadequate in detail. Their object, he insisted, was not to reduce the charge to private patients, though they might have that result. The object was to carry out fairly the 1946 Act.

Turning to the question of fees, Mr. Macleod said these had been unaltered since 1948, and the profession suggested early in 1949 that alterations should be made. Since then consultations had taken place and the new figures represented fairly general agreement. Boards and committees might, exceptionally, allow an increase from 75 guineas to 125 guineas, for an operation in a field of surgery where complicated new techniques had lately been developed.

The number of section-5 beds at the latest count in February this year, Mr. Macleod said, was 6113, or 1·2% of all staffed beds. The proportion of section 4 beds was 1·3%. It followed, therefore, that 97·5% of all beds in the service were absolutely free, and indeed a high proportion of the beds that were nominally pay-beds were in fact occupied by people under the proviso to section 5. These figures, compared with those for the end of 1950, showed that there had been in 1951 and 1952 a decrease of 4·5% in the section-5 beds and an increase of 13% in the section-4 beds, while the section-3 beds—the free staffed beds—had increased by 18,156, or 4·1%. In view of these figures no-one could conceivably say that the present Government had taken advantage, or would take advantage, of section 5 of the Act to multiply chondroitin sulphate They were excreted largely, if not wholly, in the form of polymerised molecules which liberated hexosamine after acid hydrolysis On the second day no abnormal excretion of polysaccharides could be demonstrated Part of the dose injected was, however, retained, and was possibly metabolised in the tissues Perhaps cells of the histiocytic type are involved, for in organs (particularly the liver) of rats given hyaluronate and chondroitin sulphate intravenously it is possible to see, in the first hours following the injection, a histological picture which can be ascribed to transitory activation of the mesenchyme, with formation of small nodules by lymphohistiocytic cells

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[1] See *Lancet*, March 28, 1953, p. 637.

Istituto di Patologia Generale,
University of Bologna, Italy

G BENASSI
F TINACCI

GENITAL TUBERCULOSIS

SIR,—Dr Barns and his co-workers (April 25), in discussing reinfection in tuberculous endometritis, have clearly misinterpreted my views I wrote "Pelvic tuberculosis is a blood-borne disease and the focal point must often be outside the gynæcological field"[1] I do not dispute that the endometrium can be infected from the fallopian tubes Sharman[2] has shown that this is not always the method of reinfection Extirpation of the fallopian tubes in four of his patients did not lead to cure of the endometrial lesion

The authors' claim to have shown that genital tuberculosis is an early postprimary manifestation cannot be sustained on the evidence cited "I think there is evidence to suggest that genital tuberculosis, whether latent or active, should be regarded as one of the earliest post primary infections "[3]

Department of Pathology
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London, S W 3

MAGNUS HAINES

CAN CURRENT PRACTICE BE NEGLIGENT ?

SIR,—This grave issue is raised by the case reported by you last week in which £4000 damages was awarded The judge took the view that the anæsthetist had shown "regrettable slackness" in omitting to read Ewing's (1950) paper on Postoperative Paralysis of the Upper Extremity which had been published six months before the operation

Having attended the whole proceedings and heard the judgment, I feel these new dangers must be brought fully home to the profession British law is case law, and this judgment, unless reversed in the Court of Appeal, will carry much weight in future actions of which there are a number already in the list

In respect of the operation and transfusion nothing was done or left undone which in any way departed from widely accepted practice at that time—practice which, in the case of the defendant anæsthetist, had preserved his patients from a brachial palsy throughout his long professional life. Abduction of the arm had been only at an "angle of 80° or thereabouts" combined with the Trendelenburg position The anæsthetist, in conformity with a large section of opinion at that time, regarded 90° as the danger-point Mr Ewing had expressed the view that abduction at any angle was dangerous On the other hand, a consideration of elementary mechanics and my own dissections strongly suggest that added tension from abduction cannot possibly begin until about 45° abduction We still have a lot to learn about cause and prevention in this, as in many things

A judgment that current practice, if it ignores some warning given in a recent journal, can be negligent, is so serious a matter for every one of us that it must be taken to the Court of Appeal and even, if need be, to the House of Lords

Neurological Unit,
Whittington Hospital, London

MICHAEL ASHBY

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[1] *Lancet*, 1951 i, 436.
[2] Sharman A. *J Obstet Gynæc* 1952, 59, 740
[3] Snaith L M *Ibid* p 745

Public Health

Fall in Tuberculosis Mortality

FIGURES published by the World Health Organisation[1] demonstrate the remarkable fall in tuberculosis mortality that has taken place in many parts of the world since 1939 Combined statistics from 21 countries (including the United Kingdom), with a total population of 404 million in 1950, show that the death-rate has been roughly halved in the past fifteen years The chief causes are thought to be the energetic mass action directed towards the early detection of the disease by radiography and its prevention by B C G vaccination and the control of milk; improved medical facilities and progress in treatment have also contributed to the success The decline in mortality has been greatest in children and adolescents The male mortality-rate has always been higher than the female and the difference between the two is becoming greater because it is suggested, recent social progress and improvements in hygiene have had more effect on women's living conditions

England and Wales in 1952

The Registrar-General's provisional figures[2,3] for England and Wales in 1952 give a new low record for maternal mortality The figure was 0 59 per 1000 total births, compared with 0 66 per 1000 in 1951, the previous best year The birth-rate of 15 3 per 1000 population was the lowest since 1941, and was 0 2 less than in 1951 The death-rate was 11 3 per 1000 population, compared with 12 5 in 1951, this is the second lowest rate on record The neonatal-death rate was 18 9 per 1000 live births, compared with 18 8 per 1000 in 1951 In 1939 the figure was 28 3 per 1000 The provisional death-rates for all forms of cancer were 2149 per million population for men and 1850 per million for women; the corresponding figures for 1951 were 2120 and 1822 The rise in the male death-rate included an increase from 530 to 567 per million in deaths assigned to cancer of the lung and bronchus; deaths from this cause have now increased by 47% since 1947 The death-rate from respiratory tuberculosis was 212 per million population —a decrease of 23% from 1951 The rate for other forms of tuberculosis was 28 per million, compared with 41 per million in 1951

Estimate of Births

The Registrar-General's final estimate[2] of live births in England and Wales during the quarter ending June 30 is 178,000, and his provisional estimate for the quarter ending Sept 30 is 168 000 The live births registered in the June quarter of 1952 numbered 174,089 and in the September quarter 167,938

Infectious Diseases in England and Wales

Disease	Week ended April			
	4	11	18	25*
Diphtheria	11	19	18	25
Dysentery	423	325	284	419
Encephalitis				
Infective	4	3	1	4
Postinfectious	6	2	2	2
Food poisoning	63	65	56	88
[illegible]	21 191	23,410	18 996	13,731
	43	60	54	44
	36	40	48	30
Paratyphoid fever	7	9	7	8
Pneumonia primary or influenzal	938	925	810	681
Poliomyelitis				
Paralytic	31	28	26	34
Non paralytic	7	10	8	7
Puerperal pyrexia	221	265	208	220
Scarlet fever	1404	1267	1010	1047
Smallpox	6	1	3	1
Typhoid fever	6	2	2	2
Whooping-cough	2512	2618	2897	3206

*Not including late returns.

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[1] See *Times* May 4 1953
[2] Registrar-General s Return for the Week ended April 25 1953 H.M Stationery Office Pp 20 1*s*
[3] Registrar General s Quarterly Quarterly Return for England and Wales Quarter ended Dec 31 1952 H.M Stationery Office Pp 36 2*s* 6*d*

the number of pay-beds beyond what was conceived in the original Act.

Dealing with the contention that this was a new policy, which favoured the specialists, Mr. Macleod pointed out that in their comments in the *British Medical Journal* of March 28 the joint committee of consultants had not a word of approval for him. The specialists had in fact wanted to abandon the detailed schedule, but to this he could not agree. They said that they did not want a detailed price ceiling, but a few general ceilings and the specialists would adjust their amounts to the paying capacity of the patients. It was well known how generous the medical profession could be, but Mr. Macleod felt that whatever might happen in the future the time was not ripe for this change. The specialists had also asked for a reduction straight away in the case of pay-beds, but he had pointed out that this was impossible without new legislation, and he saw no prospect of that.

Mr. BLENKINSOP asked what proposals the Minister had in mind to ensure that the empty beds were used for ordinary patients in the hospitals, and Mr. MACLEOD replied he had called for a special report on the question of the occupancy of these beds. As soon as he had the details—and they were almost complete—he would be happy to discuss the matter. The motion was negatived by 261 votes to 233.

Home or Hospital ?

National insurance, Mr. OSBERT PEAKE explained in the House of Commons on April 28, provides for interruption of earning power due to unforeseen misfortunes, or to cessation of earning power in old age, which was inevitable. Motherhood, he admitted, did not readily fall into either category, for most parents did not regard it as a misfortune, it was not inevitable, and it was foreseeable though only for a limited time. But it sometimes meant a loss of earnings and it always brought extra expense to the family. It had therefore been accepted as a proper subject for national insurance. Mr. Peake was moving the second reading of the National Insurance Bill, whose provisions were lately briefly set out in our columns.[1]

Most of the discussion during the debate centred round the new "home confinement grant" of £3 which is offered to a mother who does not have her baby in a free National Health Service bed. There was a growing feeling, Mr. Peake said, that it was unfair that the mother who had saved quite a lot on food and household expenses by having her baby in free hospital accommodation should receive the same amount of benefit as the mother who had her baby at home and had these extra expenses to meet.

Dr. EDITH SUMMERSKILL believed that many harassed hospital authorities devoutly wished that the home confinement grant would induce mothers to stay at home, to leave hospital beds for medical and surgical cases. She was concerned lest the poor woman should be tempted to sacrifice herself for the sake of a few pounds. It was useless to argue that the interests of these women would be safeguarded by midwifery services, because the woman herself had the last word. The doctor, or the health service officials, might say that home conditions were unsatisfactory, and that the woman should go to hospital, but she was free to stay at home. If the extra £3 tended to make a woman sacrifice herself in this way, then the Bill marked the end of an era of enlightened midwifery. No-one would contend that there was no relationship between the record low maternal-mortality rate and the provision of maternity hospitals in the last 20 years. Dr. Summerskill looked forward to the day when every woman would be able to choose between hospital and home in precisely the same way as a wealthy woman could choose between a private ward in a hospital, or even a private nursing-home, and her home. Nor was the obstetrical service offered in hospitals the only consideration. A hospital afforded a mother rest after her confinement which she was often denied in her own home. A hospital confinement, she urged, must not be regarded by the prejudiced as a waste of a bed, but as offering a safe delivery and a period of rest to a woman who had emerged from a trying ordeal and was now to be called upon to tax her resources to feed her baby. Was it surprising, Dr. Summerskill asked, that a third of babies were bottle-fed when we knew the pressure brought upon women to remain outside hospital for their confinement ?

Mr. ARTHUR BLENKINSOP was also anxious lest the new proposals should encourage mothers, who on medical grounds should go to hospital, to have their confinements at home, and he wondered whether provision was being made for the increase in home confinements which he thought we might expect. He did not himself believe that ideally every confinement should take place in hospital. There was a danger that by extending the use of hospital facilities we might get the second best, for owing to pressure on accommodation shorter stays in hospital were being accepted as reasonable. In areas where housing was bad the problem was different and we must watch the effect of the new grant in these areas, where it should be our anxiety to encourage hospital rather than home confinements. He was also anxious that smaller provision was made in the estimates for midwifery services. If we were to encourage confinements at home we must ensure that still higher standards were set for our domiciliary services.

Mr. ENOCH POWELL thought that any measure which tended to take out of the hospital cases which could be dealt with as effectively in the home was a contribution to the efficiency of the health service itself. He suggested that the grant should be large enough to remove a financial obstacle to domiciliary confinement and yet not so large as to weigh the scales unduly in favour of home confinement. He did not think the sum of £3 was excessive.

Mrs. EVELINE HILL pointed out that the women who just could not get into hospital would be grateful for the help of this new grant. Mrs. E. M. BRADDOCK was inclined to believe that the Ministry of Health might use the new grant to urge that there was no need to provide additional maternity-hospital accommodation.

Mr. R. H. TURTON, parliamentary secretary to the Ministry of National Insurance, assured the House that the new grant was fixed at such a rate as to offer the mother compensation for the extra expense of having her baby at home without providing an incentive in determining her choice. The National Insurance Advisory Committee had estimated £2 10*s.* as the extra cost of having a baby at home. According to hospital costing returns the average cost of maintenance in a maternity hospital was £13 16*s.* a week, and the cost of the items the parents would have to pay for if the confinement were at home was £3 5*s.* 8*d.* He was satisfied that £3 was a fair sum. In his view whether the baby was born at home or in hospital was not a matter to be decided by politicians but by the mother on the advice of her doctor.

Food Hygiene

In the House of Commons on April 30, Mr. BARNETT JANNER called attention to the need for further action to encourage cleanliness in the handling of food. In 1951 5797 cases of food-poisoning were notified; in 1952, 6021; and in the first quarter of this year 1035. He understood that doctors agreed that the actual number of cases was much larger.

Dr. CHARLES HILL, parliamentary secretary to the Ministry of Food, said that nowadays this problem was primarily one of germ infection. The old fears of metallic contamination and the like had largely disappeared. It was also largely a problem of meat and milk products—mainly meat. The danger lay in dishes that were not eaten as soon as they were cooked, if indeed they were cooked, but were left exposed to flies. The public should realise that it was not necessarily the food that smelt that was dangerous; the greater danger lay in foods that were not obviously contaminated. It was wrong in the home or in a food establishment for a person suffering from diarrhœa, or from a superficial infection of the skin, however apparently trivial, to handle food.

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[1] *Lancet*, March 28, 1953, p. 634.

Smallpox

By noon on May 5 the total of confirmed cases of smallpox in the outbreak in Lancashire and the West Riding was 27, including 7 deaths The 16-year-old Colne Valley boy, mentioned in our report of April 25, died on May 4. He fell ill on April 9 and had been in hospital since April 15 A Leeds mortuary attendant was admitted to hospital on May 2 with what has now been confirmed as smallpox A soldier, who arrived home from Egypt on April 23, was admitted to a hospital near Sheffield on April 27 from his home at Warsop, in Nottinghamshire He may have modified smallpox, but laboratory investigations have so far been negative

Retirement of Dr Clark

Dr W G Clark has recently retired from the office of medical officer of health for the City of Edinburgh Nearly all his professional life has been spent in the public-health service—in Glasgow, where he understudied Sir Alexander Macgregor, and in Edinburgh, to which he was appointed to succeed the late Dr Guy Dr Clark was long a pillar of the Society of Medical Officers of Health, of which last year he served as president He has been an outstanding medical officer of health, with a forthrightness that perhaps owed something to his naval service in the first world war, and his many friends will wish him happiness in his new leisure

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Obituary

DAVID THOMAS ROCYN JONES

Kt., C B E, M B Edin., D P H, J P, D L

Sir David Rocyn Jones, medical officer of health for Monmouthshire for nearly forty years, died on April 30 at the age of 80

He was descended from the well-known family of Cardiganshire bonesetters, and his father, David Rocyn Jones, of Rhymney, was the friend of Hugh Owen Thomas From Lewis's School at Pengam, Sir David went to University College at Cardiff, and later he continued his medical studies at University College, London, and at the University of Edinburgh where he graduated M B in 1897 Soon afterwards he accepted the post of surgeon to the Cambrian Collieries in Clydach Vale and settled in general practice in Abertillery He also served as part-time M O H to the town and in 1904 he took the D P H Four years later he became the first whole-time M O H. for Monmouthshire

The rest of his life was thus spent on the Marches of Wales, but there was never any doubt as to which side of the border his sympathies lay He was a member of the court of governors of the University of Wales and of the council of the Welsh National School of Medicine, he was one of the five founders of the Welsh National Memorial Association. He was a Knight of Grace of the Order of St John of Jerusalem in the Priory of Wales, and during the second world war he was chairman of the joint war organisation of the British Red Cross and the Order At one time he was a member of the consultative council of the Ministry of Health for Wales, and later he sat on the Welsh Regional Hospital Board For twenty-five years he was chairman of the Bedwellty division of Monmouthshire magistrates An outstanding personality in Welsh rugby football circles, he was a member of the Welsh rugby union for forty-six years and president from 1947. This long record of public service had earned many public honours He was appointed O B E in 1920, and he was created knight bachelor in 1948 He was also a deputy-lieutenant of his county

Lady Rocyn Jones, who was the daughter of Alderman S N Jones, J P, of Abertillery, died in 1950 One of their four sons was killed in Italy late in the war Of the remaining three two are doctors Mr Nathan Rocyn Jones is orthopædic surgeon to the Welsh Regional Hospital Board, and Dr Gwyn Rocyn Jones has succeeded his father as M O H. for Monmouthshire

LEONARD MORTIMER ROSE

M.A., B M Oxfd, M R C P

Dr Rose, medical registrar to the professorial unit of The Children's Hospital, Birmingham, died on April 28 at the age of 32 He was the elder son of Dr Jack Rose of Baildon formerly of Bradford, and he was educated at Bradford Grammar School

He was a scholar of Queen's College, Oxford, and he graduated B M in 1944 After holding a resident post at the Radcliffe Infirmary he served in the R N V R for three years, partly in H M S *Vanguard* He returned to the Radcliffe in 1947, and the following year he obtained the M R C P After a year as clinical assistant at the Children's Hospital in Sheffield he was appointed R M O at the Children's Hospital, Birmingham, where he later became registrar

Two of his colleagues at Birmingham write "We remember Toby Rose as a somewhat rotund figure, with smiling eyes, he was a cheerful enthusiast, who loved ships and the sea, who had a taste for good cooking and a deep attachment for his pipe and a book by the fireside But doctoring meant more to him than all these things He was a careful observer, a kindly and understanding physician who, although exceptionally gifted, was without affectation, having the simple sincerity of the children among whom he worked Success seemed certain when he had secured an appointment in Vancouver But while he was still working with us illness began to cast a shadow over his usually cheerful disposition He never complained and he never gave in even when the full gravity of his illness became known It is indeed good to have known him "

THOMAS WYPER STEWART

L R C P E

Dr T W Stewart, a senior medical officer of the London Transport Executive, died at his home at Harrow-on-the-Hill on April 20 at the age of 61

He was born at Hamilton, Lanarkshire, and was educated at St Mungo's College, Glasgow, and at Glasgow University While holding a post in the bacteriology section of Glasgow City health department he became interested in medicine, and he began his medical studies while still engaged in this work He qualified in 1920, and after spending a short time as assistant to his brother in Nelson, Lancashire, he was appointed medical officer of health for the Isle of Tiree in the Western Hebrides For seven years he was the only doctor on the isle, a six-hour journey from the mainland by sea—when the sea was not too rough Here he had the valuable experience of handling every medical situation unaided and he came to be greatly respected and revered by the islanders

Anxious as he always was to keep in touch with modern medical developments, Dr Stewart returned to general practice on the mainland at Easdale, Oban In 1929 he settled in practice at Accrington, Lancashire In 1938 he came south to Whiteparish, Salisbury, before starting a new practice in Perivale, Middlesex Owing to war-time difficulties and the serious illness of his wife, he gave up practice and accepted an appointment with the Ministry of Pensions, becoming deputy commissioner of medical services in Leeds Ten years ago he joined the staff of London Transport

L G N writes "In all his medical career, although his roving instinct seldom let him settle for long, Dr Stewart took an exceptional interest in the welfare of his patients He was blessed with a lively sense of humour, which made him a most entertaining companion His stories of his experiences on Tiree were told with a racy Scottish wit, and he delighted to relate, for instance, how in his limited Gaelic he once informed a patient that she had given birth to a fine cockerel, the lad, needless to say, was known thereafter by this pseudonym

"He was more sensitive than appeared on the surface and he was essentially a shy man He was a loyal and generous friend In his later years he set an example to younger colleagues of the highest standards of personal and professional qualities, and he always made his points with a deftness which earned him their admiration and respect Dreading retirement, he vowed that he would die 'in harness'; and happily his wishes were met, It was essential for people to wash their hands before handling food and also after using a lavatory. Unsatisfactory conditions, he pointed out, were preventable, and admirable work in health education was being done by the Central Council for Health Education, the St. John Ambulance Association. the Red Cross. and some firms and trade associations. On the initiative of Dr. Belam, the M.O.H. for Guildford, food guilds had been formed in various parts of the country to make clean-food principles better known among the general public. Today eating in the mass was much more common than it used to be, and one careless food-handler could infect 200 or 300 people. We could not deal with this problem on the basis of the Factory Acts as an offence. It was, Dr. Hill held, a matter for health administration, and for persuasion rather than regulation. The solution must lie in the field of personal conduct, but he admitted that present legislation could be improved.

QUESTION TIME

National Health Service Expenses

Mr. JOHN MORRISON asked the Minister of Health the total cost of meeting loss of remunerative time and for travelling and subsistence expenses sustained by members of all boards and committees established under the National Health Service Act for the year ended March 31, 1952.—Mr. IAIN MACLEOD replied: About £105,000.

Mass Radiography

In answer to a question, Mr. MACLEOD stated that since the inception of the mass-radiography units 10,644,695 cases had been X-rayed up to Dec. 31, 1952.

Dentists' Fees

Mr. HENRY PRICE asked the Minister whether he was able to make a statement on increased National Health Service fees for dentists.—Mr. MACLEOD replied: The Secretary of State for Scotland and I have informed the British Dental Association that we are ready to embark at once on an inquiry to obtain all the facts about dental remuneration, but that the information at present available is not in our view sufficient to justify any immediate increase.

Mr. PRICE: Does this mean that the dentists' demand for the restoration of the 10% cut has been rejected? Does he realise the disappointment and anxiety that this will cause among what might be called the depressed section of this profession which is almost entirely dependent on the National Health Service?—Mr. MACLEOD: Yes. It means that the claim for the restoration of the 10% cut has been rejected, because I do not think I have sufficient evidence. I have a duty to the dental profession. but equally I have a duty to the taxpayer, and I must discharge both.

Ministry of Health Statistical Unit

Mr. A. BLENKINSOP asked the Minister whether he would set up a statistical unit in his department to assist both in publishing more information for the general public and in providing detailed figures for the use of the department.—Mr. MACLEOD replied: This method of collecting statistical material has not so far been adopted, but I always have this subject in mind and I shall have to consider, as experience grows, whether it is necessary to alter the present arrangements for the purposes mentioned. There is a flood of information coming in now about costing and other financial aspects of the health service. If I can set up a department without exceeding my present establishment, I think it will be more convenient to keep it centrally within my Ministry.

Prices of Proprietary Products

Mr. BLENKINSOP asked the Minister whether he was in a position to make a statement arising out of his discussions with manufacturers of pharmaceutical goods about the prices of proprietary brands.—Mr. MACLEOD replied: Not at present. Mr. BLENKINSOP: Can the Minister say when he hopes to be able to take some action on this matter, which, after all, was referred to by the Public Accounts Committee some considerable time ago?—Mr. MACLEOD: I have taken a good deal of action on the lines recommended by the Public Accounts Committee, and this is a matter which, without going into details, I can say is under very serious consideration by the Government.

In England Now

A Running Commentary by Peripatetic Correspondents

SURGEONS are strangely quiet in their official attire. Once introduced to the blaze of academicals in other branches of the profession, a Martian or other foreign visitor might well undervalue these douce blackbirds with nothing more ornamental about them than a couple of red stripes down the front. But when they received Her Majesty the Queen, their most distinguished Honorary Fellow, in Lincoln's Inn Fields last Tuesday, the vast blue and white marquee supplied plenty of colour—from the massed flowers, and fine needlework chairs on the dais to the modest but telling creations worn by the ladies. The memorial stone, with its simple inscription, dangled above its pillar, the band played popular airs, the arc lights shone, and the boards of the faculties processed to their places at exactly the moments appointed. And so with royal punctuality did Her Majesty. All went perfectly: the casket filled with historic documents was closed and laid in its place, the stone, after a momentary hesitation, sank majestically down on it, and the Queen declared it well and truly laid. All who were there will remember that engaging look of interest and pleasure by which our national life is now so often refreshed.

* * *

The versatility of the human mask is only equalled by the variety of techniques for transferring it to canvas. This year's Royal Academy exhibition fairly beams with portraits, and by far the greater part of them, in spite of being orthodox, are good. It is perplexing to know why a good, careful likeness by a competent artist should be so much better than a photograph. A colleague tells me it is because the camera can only crystallise a moment of time, while a painter can bring to his picture a whole background of knowledge—not only of his sitter's character and qualities, but of the nature of physical movement—the notion of carry-through to the completed act. I think this theory applies well to the portrait of *Ralph Vaughan Williams, O.M.*, by Sir Gerald Kelly. A camera might equally have caught him turning in a chair: it could hardly have conveyed this sense of a man of many friends, all of whom know this familiar movement, presently to be completed: that has been given us by the painter's apperception of many kinds of data. Harold Knight's beautifully painted likeness of *The Rt. Hon. Sir Travers Humphreys* has this same kind of insight, and so has Dr. Henry Lamb's portrait of *Prof. T. R. Elliott*. Once I was fairly launched on the portraits I sought familiar faces; but, apart from Professor Elliott and the benign bronze head (by David McFall) of *Hugh J. Taggart Esq., F.R.C.S.* doctors, were strangely rare this time. There was, of course, Sir Alexander Fleming (by Henry Carr), looking well in red velvet sleeves; and there were a fair sprinkling of D.SC.S, Mrs. Marie Stopes among them—the pale yellow taffeta and scarlet cloth of her gown so exquisite (thanks to Sir Gerald Kelly again) that no other academic dress could compare with it. Many faces might have belonged to doctors, and I hurried in turn from Sir Thomas Beecham (misleadingly wearing a white gown, and looking, even under the inspired hand of Simon Elwes, every inch a senior surgeon) to Arnold Mason's *Gilbert P. Norton, Esq., C.B.E., D.S.O., T.D., D.L., F.C.A.* (who could surely have squeezed in an M.B. somewhere among that lot) and Alfred R. Thomson's *Grahame B. Tubbs, Esq., F.R.I.B.A.*, who seemed built for the part of family physician. One face which I had confidently decided could *not* belong to a doctor, bore the disconcerting title, *Portrait of a Gentleman*. The only other pictures of medical interest were a pleasant landskip, *At Birdham, Sussex*, by Adrian Hill, the pioneer of art therapy in hospitals. John Wheatley's very good painting of the chairman of the Sheffield Regional Hospital Board, and a jaunty little view by John Cole of a chemist's shop in Wigmore Street.

I spent so much time looking for a doctor that I saw very little of the other pictures. Here and there, however, my eye rebelled, and lingered on something pleasant: on the subtle pink of the sky in Edward Bawden's *Hadrian's Villa*, on Stanley Spencer's mongoloid but entirely delightful pale-coloured children climbing through for he was actually working until the day of his death He leaves behind a memory of devoted service which his friends and colleagues will never forget "

Dr Stewart married in 1912 Janet Miller Dyer, of Hamilton, Lanarkshire She survives him with a daughter and a son who is also a doctor

Births, Marriages, and Deaths

BIRTHS

WRIGHT —On April 29, at Woodlands Road Hospital, Barry, to Sheila (née Smith), wife of Dr Martin Wright—a son

DEATHS

ROSE.—On April 28, after a long and painful illness, Leonard Mortimer (Toby) Rose, B.M. B CH. Oxfd, M R.C.P aged 32, elder son of Dr and Mrs J Rose Woodside Green Lane, Baildon, Yorkshire

Appointments

AITCHISON, WILLIAM M C M.A M B , B SC. Edin , D T.M & H , D P H. asst county M O and district M O H , N Walsham urban district, Blofield and Flegg rural district, and Smallburgh rural district

HOLLAND JEAN M.B Glasg M O regional blood transfusion unit, E Anglian Regional Hospital Board

MCARTHUR, J M , M B Lond , F R.C.S , D M.R.T part-time consultant radiotherapist United Newcastle upon Tyne Hospitals

MCINTOSH, G D , M.C , M.B Edin. M O H M Prison, Inverness

POWELL. B W , B.A M.B Camb , M R.C P D C.H consultant pædiatrician, Peterborough area

Appointed Factory Doctors

ROBINSON INNES M.B Birm Audley, Staffordshire

SAPHIER, EMANUEL, M.R.C S Sutton, Surrey

SEEAR, P G , M.R.C S Colchester, Essex.

Colonial Service

ATTARD J A. M.D Malta M.O Gold Coast

BARCLAY H J , M B St And resident M.O , Northern Rhodesia

BRADFIELD J A. D M B Dubl M O , Nyasaland

BRICK, T D M.B Dubl D.M R.D radiologist, Federation of Malaya

DAVIES, H N O.B E , M.B Edin , D T.M senior specialist, Tanganyika

EVISON, D E , M B Witwatersrand M O.H , Northern Rhodesia

GRATTAN E O D C , M.B Camb , F.R C.S D T.M & H surgeon specialist, Kenya

HOBSON A. C S M.B Lond , M.R C P . M O , Federation of Malaya

JARVIS J F , M B Lond , F R C.S D L O , D T.M & H ear, nose, and throat specialist, Kenya

JEFFERY, G A. M.B Birm M O Nyasaland.

KIRKCALDY-WILLIS W H , M B Camb F.R C S E orthopædic specialist Kenya

KISSAUN, A M G M D Malta M O , Nigeria

MERRETT W E S O B.E , B M Oxfd principal Medical School Nigeria

STREET, S P W F.R.C.S surgeon specialist, Jamaica

THOMPSON M R. F.R.C S surgeon specialist, Jamaica

Manchester Regional Hospital Board

BENTON F M M B Manc. D.M.R.T asst radiotherapist, Christie Hospital and Holt Radium Institute Manchester

CUNNINGHAM R C M B Glasg D.P.H , D P.M. consultant psychiatrist and medical superintendent, Royal Albert Hospital Lancaster

DONOVAN J F M.R.C.S D P M. consultant psychiatrist and deputy medical superintendent, Prestwich Hospital, Manchester

TEASDALE, D H. M.B Lond , F R C S consultant general surgeon, Rochdale hospital centre

THORBURN A L M.D Belf D P.H. tuberculosis physician, Walford and W Manchester hospital areas

South East Metropolitan Regional Hospital Board

AINSLIE J A. B.SC. Lond , M.R.C S D P.M. consultant psychiatrist St Augustine s group of hospitals

BENTLEY, A. P M B Lond asst chest physician, Preston Hall group of hospitals

HAMBLING JOHN M B Birm M R C.P consultant psychiatrist, St. Augustine s group of hospitals

JASMANICKI B Z , M D Lwow consultant radiologist Dartford, Medway, and Gravesend group of hospitals

NIXON H H M.A. M B Camb F R.C S consultant children s surgeon Bromley group of hospitals

RUNES, J N , M.D Vienna asst psychiatrist Leybourne Grange group of hospitals

West Riding of Yorkshire County Council

PULLAN MARY M.B Leeds asst M.O Harrogate borough Knaresborough urban district and Nidderdale rural district

SHAW, ETHEL M B N U I asst. M.O , Colne Valley division.

SMITH JEAN, M.B St And , D.P H senior asst M O , Hoyland Nether, Penistone and Stocksbridge urban district councils, Penistone and Worthey rural district councils, and W Riding County Council

TAYLOR CECILIA M.B Leeds D C.H. asst M O , Pudsey borough, Aireborough and Horsforth urban districts

WALL DOROTHY B.A. Oxfd M.R.C.S asst M.O Baildon, Bingley Denholme and Shipley urban districts

Notes and News

N.H S ACCOUNTS

EXPENDITURE on the National Health Service in England and Wales during the year ended March 31, 1952, is set out in the Summarised Accounts now published [1] with the report of the Comptroller and Auditor General thereon The corresponding report for Scotland has already appeared [2]

Among the subjects discussed by the Auditor General are the joint purchase of supplies by hospitals in the same area , the financial deficit on hospital farms and gardens, which amounted to £614,033 , and the inadequacy of store accounts and inventories at many hospitals

A foreword to the Accounts shows the average weekly cost of maintaining a bed in 717 ' wholly general " hospitals in 1951–52 as £18 5*s* , which may be reduced to £14 5*s* 11*d* by adjustment to exclude notional outpatient expenditure, and to £12 5*s* 9*d* by further adjustment for vacant beds A table shows how this £18 5*s* is composed The running charges of £4 13*s* include £1 17*s* 10*d* for provisions and £2 0*s* 2*d* for drugs, dressings, &c The total standing charges of £14 11*s* 6*d* include £2 15*s* 4*d* for doctors' salaries, £4 3*s* 1*d* for nurses' salaries, £5 7*s* 7*d* for the salaries and wages of other staff, and 19*s* 5*d* for fuel light power, and water, but they are reduced to £13 5*s* 11*d* by certain direct credits, including receipts from staff for board and lodging

The Auditor-General recalls that since March, 1950, the Ministry of Health has had a central investigation unit charged with reporting instances of extravagant prescribing and says that in the thirteen months ended Dec 31, 1952, reports were made on 282 doctors who appeared to have been prescribing excessively Most of these were visited by the Ministry's regional medical officers, and in addition warning letters were sent to over half of them As a rule (the Ministry stated) the doctor's coöperation was obtained and substantial economy in the cost of prescribing was secured without detriment to the treatment of patients , but reports on 11 doctors who apparently continued to prescribe excessively were referred to the local medical committees Fines of £50 and £250 were imposed on one doctor, the cost of whose prescriptions in one month was £972 compared with an average of £172 for patients' lists of similar size in the same area , and smaller fines were imposed on two other doctors

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

IN the school's department of public health, under the direction of Prof J M. Mackintosh, students continue to work in groups on chosen subjects Evidently they value this experience , for, according to the school's report for 1951–52,[3] an overwhelming majority have declared that they find it more interesting than classroom work, and 55% have thought it more effective Among the surveys by different groups was one of family welfare, which revealed, among other things, the importance of the pilot survey, the lack of universally accepted technical terms for sociological studies and the need for careful classification of headings to avoid differences of interpretation and for the use of accepted statistical methods of handling data. Another group investigated the maternity services of a London administrative division, and discovered important deficiencies—lack of integration, discontinuity of supervision, and little attention to the educational aspects of antenatal care A third group set out to discover, by means of a questionary, the effect of hardness of water on the domestic consumer In a hard-water district in London housewives were spending more on soap then housewives in a soft water district in Birmingham The group found that to soften all of London's water would be impracticable , but in smaller units—for example, blocks of flats—the cost of a softening plant would probably be met by the saving in soap One of the other groups studied adoption and came to the conclusion that there should be research into the efficiency of the present system of placing children , at present, after the adoption order has been made all official contact with the child ceases

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[1] National Health Service Acts 1946 to 1951 Accounts 1951–52 H.M Stationery Office Pp 41 2*s*

[2] See *Lancet*, April 18 1953, p 802

[3] Report on the Work of the School for the Year 1951–52 London School of Hygiene and Tropical Medicine (University of London) incorporating the Ross Institute Keppel Street Gower Street London W C 1

The Barbed Wire Fence, on the stout reliable characters in Alfred Daniels's *Village Wedding*, on the delicate minute brilliance of S. R. Badmin's *A Bright Winter Day*, on Erich Wolfsfeld's yawning studies of a baby, and on the superb wintry weather of Leslie C. Worth's *The Market Cart*, which I should like to own. Sir Winston Churchill, in his un-Gartered days last year, painted a bold and cheerful view of *Cap d'Ail*, and Sir Alfred Munnings has painted, several times, that friend of man, and of Sir Alfred Munnings, the horse. Among the sculptors, Willi Soukop has achieved the impossible by combining Rossetti with Henry Moore in his *Woman Waiting*.

* * *

I used to wonder why my late chief, an excellent diagnostician, would occasionally send a patient into hospital with a diagnosis wide of the mark. But now I understand. The difficulties of consulting in the home, compared with the serene and objective atmosphere of a hospital, are striking. There is the air of apprehension, most obvious if one makes the mistake of allowing relatives to remain in the room during the examination. Then there are physical hazards—poor lighting, bizarre garments that cling like limpets and defy efforts at removal. In poor homes, a mixture of filth, sweat, and pallor often gives a frightening but false impression of moribundity which disappears magically in the ward. Worst of all, it is often necessary to examine the patient from the " wrong " or unaccustomed side. Why, in the name of Heaven, are teachers and examiners so obsessed that students should always learn to approach the patient from one side only ? Outside a hospital, this is quite impracticable, unless one is accompanied by a carpenter. For the bed is often fixed against a wall and an ill patient cannot always be moved around to the other end, apart from the absurdity of doing so. Students should surely be taught to be equally familiar with the examination of a patient from either side of the bed.

* * *

Most doctors spend a great deal of time in work outside their usual routine for which they get no credit. Getting credit is perhaps putting it badly. There is no credit in doing what you like of your own free will. For several years my own particular sideline has been psychotherapy —of the superficial kind, I hasten to add. (I never refer to those two well-known characters Uncle Œdipus and Auntie Electra.)

Out of curiosity I counted up the time I had spent on N.H.S. patients during the past quarter. The interviews took place by appointment usually on Saturday and Sunday, and in the evenings after surgery hours. Each lasted an hour. It was a light quarter, for the influenza curtailed my free time. Even so the total came to 102 hours. Of this time three patients shared 72 hours between them. If I added 12 hours for instruction courses and another 12 at least for writing up case-reports, the total came to 126, and yet I could have usefully put in three times as long. The present epidemic-free quarter will, I hope, be more leisured, and I expect to top the 200.

I know plenty of colleagues who do the same. We do not complain, and we are not even asking for more pay, for the very simple reason that we like doing it. But isn't it a good thing for our patients that we do ?

* * *

Thanks largely to the duty on the stuff that cheers and inebriates we are a tight little island no longer. On the other hand, more of us smoke and many of us who smoke smoke more than we used to and more than we can afford. It is also true that more and more of us lead what Dr. Ffrangcon Roberts describes as " a medicated existence." Is there not perhaps some connection between these facts ? It looks as though most people must have something to help them to cope with modern conditions of living : beer or barbitone, sherry or sedatives, vodka or valerian. If the price of honest liquor were drastically reduced might there not be a more than corresponding reduction in the national drug bill ?

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News from the Nuffield Foundation.—" Other grants include help for the development of promising administrators and of ' backward ' working girls."

Letters to the Editor

THE PROBLEM OF PEPTIC ULCERATION

SIR,—Sir Heneage Ogilvie writes so well and so convincingly that one almost begins to feel one's surgical beliefs slipping. I see, however, from his letter (April 11) that he is not averse to criticism, and so I venture to question some of the conclusions in his lecture published in your issue of March 21.

In the first place, there seems to be some confusion about the Finsterer partial gastrectomy. In company with some colleagues I paid a visit to Professor Finsterer's Clinic in Vienna, between the wars ; and the operation which we saw him regularly perform, and at which we assisted on several occasions, was not one of his own devising but the Hofmeister partial gastrectomy. This Finsterer acknowledged.[1]

In this operation the upper half of the cut surface of the stomach is closed and embedded, and the jejunum is anastomosed to the lower half behind the transverse colon. The proximal loop of the jejunum is sutured to the stomach for a little way to cover the junction of the embedded and anastomosed portion, and the transverse mesocolon is sutured to the stomach proximal to the anastomosis. Even with this lower attachment the transverse mesocolon is dragged upwards and away from its natural position when the clamps are released, and the stomach remnant rides high beneath the dome of the diaphragm.

It must be granted that in this operation there is little regurgitation or vomiting of bile, and the stomach empties rapidly—too rapidly, in fact—giving rise to the dumping syndrome.

Partial gastrectomy does not necessarily ensure that the patient will not develop an ulcer of the anastomosis or in the jejunum. If this happens the surgeon must undertake an operation which in the first place he sought to avoid, and which in the second place is made infinitely more difficult by the anastomosis being retrocolic. If the operation has been done anteriorly the structures are, so to speak, to hand without a difficult dissection. For these reasons I some years ago abandoned the retrocolic anastomosis.

As Sir Heneage says, every surgeon has his own pet way of doing partial gastrectomy, and I apologise for boring the reader with one which I have found most satisfactory.

The great omentum is removed with the amount of stomach adequate for the particular case. The cut surface of the stomach is closed for a short distance at the lesser and greater curvature, thus leaving a central opening to which the jejunum is anastomosed in front of the transverse colon giving a stoma of about two to two and a half inche [illegible] jejunum is applied by seromuscular suture to the s[illegible] above and below, as well as around, the stoma. Thus is formed an upper and lower valve in the stomach to ensure slow emptying. The operation is completed by the anastomosis of the proximal to the distal loop of the jejunum. This adds about another ten minutes to the operation, but it is worth while for it prevents immediate and remote regurgitation or vomiting of bile. With this operation there is no ' dumping,' and it does not seem that the transverse colon lies heavy upon the loops of the jejunum, nor have I experienced difficulty in bringing the loop of the jejunum to the lesser curve in front of the colon. If such a difficulty did occur I see no reason why the mesentery should not be lengthened after the practice of Yudin. The bowel here is very well supplied with blood-vessels, and division of a few evidently runs no danger of damage to gut.

Sir Heneage has a poor opinion of gastrojejunostomy as surgical treatment for duodenal ulcer. Some time ago Sir Robert Hutchison invited him to have a look at the statistics of James Sherren[2] and Sir James Walton[3]

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1. Finsterer, H. Local Anæsthesia in Abdominal Surgery. New York, 1923.
2. Sherren, J. *Lancet*, 1925, ii, 1007.
3. Walton, J. Surgical Dyspepsias. London, 1923.

HALLUX VALGUS

In a recent letter[1] Mr Charles A Pratt, M C S P, mentioned the difficulty of buying shoes—correctly designed with a straight inner border—which would not favour the development of hallux valgus Messrs Hardy & Son, of 6, Baker Street, London, W 1, inform us that they have been making shoes for customers with difficult feet since 1903, and are now in the act of developing a wide range of shoes with straight inner borders Unfortunately they have given these the name of "corrective footwear," where "normal footwear" would have been more appropriate But it is useful to know that shoes of this kind are, in fact, on the market for all to buy

COURSE FOR MATRONS

King Edward's Hospital Fund is arranging to hold in London residential management training courses for prospective matrons and assistant matrons The first course will consist of three terms of about six weeks and will begin on Sept 28 Hospital management committees and boards of governors in the four Metropolitan regions are asked to nominate candidates from among their sisters by May 28 The course is free and employing authorities will be able to grant study leave with pay Further particulars may be had from the director, Division of Nursing, King Edward's Hospital Fund for London, 21, Cavendish Square, W 1

FOOD-SUPPLIES, POPULATION, AND WAR

On May 2 the Medical Association for the Prevention of War held a conference in London at which Dr Duncan Leys recalled questions raised by Prof A V Hill in his presidential address last year to the British Association Professor Hill had suggested that scientists in the "free countries" faced a moral dilemma in the question Are we justified in doing good when the foreseeable consequence is evil? "Doing good" in this context meant the application of modern methods for the prevention and cure of disease in areas where it was thought that the population threatened to outrun the food supply But, said Dr Leys, the destiny of the peoples of Asia lay in their hands, not in ours It would be presumptuous for the peoples and scientists of Europe and the U S A to suppose that they had it in their power to influence—except perhaps in minor ways and very temporarily—the course of events in Asia As to birth control Dr Leys thought it a savage irony that this could be held up as a sort of threat to the people of Asia—"Limit your families or else " What was needed was the *right* of easy access to methods of birth control, and this was denied even to women in Britain at the instance of people with the highest moral principles This right would no doubt be established all over the world, but Dr Leys believed that the building up of higher standards of life would be the most important factor in reducing birth rates With the immense new possibility of manipulating the environment, it was morally wrong to have peoples in different parts of the world with greatly differing standards of life the world was one

Prof J B S Haldane, F R S, dealt with the malthusian view held, it seemed, by Professor Hill—that the growth of a population is restricted by food-supplies, that famine sets a limit to the increase of a species In Professor Haldane's opinion this view could not be sustained Populations had fluctuated among birds and mammals which had been long and carefully observed, but no disastrous fall of a population due to competition for food supplies ever occurred In general the same was true of the human species Industrialisation in a country was constantly observed to affect the growth of its population After a generation or two the birth rate tended to fall, and this would probably happen in India and other Asian countries as had happened in the West

Mr N W Pirie, F R S, said that over population of the world was not imminent since the possibilities of increasing the production of food on a world scale were enormous even with present agricultural methods supplies could probably be trebled or quadrupled Nevertheless there was a need to develop more satisfactory methods of birth control so that the birth rate would reflect a demand for children and nothing else

Prof L S Penrose, F.R S, questioned the assumption made by several speakers that over population led to famine, which in turn led to war The Nazi demand for *Lebensraum* had been useful as propaganda for an expansionist policy but was not supported by facts In fact, there was no evidence that any European wars had been due to such a sequence of events

THE EYE OF THE BEHOLDER

Prof János Plesch, who has made a long study of Rembrandt, approaches his subject somewhat individualistically in a new book[1] He has given much thought to the special character and setting of the master's work, and moreover of their impact upon the beholder In particular, he has investigated the "subsidiary" and "spatial" *figures*, which he claims exist in a considerable number of the paintings, etchings, and drawings In illustration of this thesis, the volume contains a series of plates, the figures in question being indicated by arrows Dr Plesch implies the subjective nature of much of his material by suggesting that success or failure to perceive these figures is a test of artistic sensibility On somewhat firmer ground is some evidence for Rembrandt's high degree of hypermetropia, and its effect upon his rendering of contours Finally, the position of Rembrandt in relation to the historical significance of syphilis is discussed in an appendix

University of Oxford

At a convocation to be held on July 1 in celebration of the centenary of Cecil Rhodes and jubilee of the Rhodes scholarships, the honorary degree of D C L will be conferred on a number of former Rhodes scholars, including Prof W G Penfield, O M, F R S

Royal College of Physicians of London

At a comitia held on April 30, with Sir Russell Brain, the president, in the chair, the following members were elected to the fellowship

F B Byron Sydney, Richmond Jeremy, Sydney, Alan Trevor Jones Cardiff M McC Baird Vancouver, B C, E B Brooke, Carshalton, Bir Bhan Bhatia Lucknow, T F McN Scott, Philadelphia, J S Harris, Woodford Green, J N Cumings, London, O F Thomas, Liverpool, Robert Knox London, J MacD Holmes, Stafford, Mary J Wilmers, London H E Holling, London, Beryl D Corner Bristol, George Davison, Cramlington J R Forbes Flintshire, R M Kark, Oak Park, Ill, F H Kemp Oxford, Samuel Lazarus, Glasgow, Joseph Smart, London, J F Bromley, Birmingham, Muriel J L Frazer, Belfast Sir Paul Mallinson London H G Miller Newcastle upon Tyne, A W Woodruff, London W W Goody London, A G W Whitfield, Sutton Coldfield, D I Williams, London, R A Henson, London

The following were elected to the fellowship under by law 39b, which provides for the election of non members "who have distinguished themselves in any branch of the service or practice of medicine"

Sir Macfarlane Burnet, F R S Melbourne John Farquhar Fulton, New Haven, Conn, Geoffrey Keynes, London Charles Laubry, Paris

The following, having satisfied the censors' board, were elected to the membership

J M Bishop, M B Birm, Brian Bronte-Stewart, M.D Cape Town, L J Clein M B Dubl, T B Counihan M B N U I Aubrey Cumin, M B Witw'rsrand R B Goudie, M B Glasg R E Gruchy M B Camb, P F Hall, M B Sydney R E D Harvey Samuel M B Camb, P M Higgins M B Lond, Raymond Hoffenberg M B Cape Town, R A Hunter M D Lond, C S Livingstone M B Lond, Suzette M Mettrick, M B Leeds I H Mills, M B Camb, M A Pears M D Lond, Adolf Polak, M B Camb A. T Richardson, M B Lond, Jean K Ritchie, B M. Oxfd, J H Ross, M B Camb Irene P Rowlands, L.R.C P, J R Seale M.B Camb Boris Senior, M B Witw'rsrand J D Sheward, M B Bristol, P B Stewart, M B Lond W K Stewart, M B St And Basil Strickland, M B Lond, Rajadurai Selliah Thanabalasundrum M B Ceylon, J P D Thomas, M B Camb J I Wand Totley M B Lond, E K Westlake M B Camb W D Wilkey, M D Univ of Western Ontario, D P Winstanley B M Oxfd A R H Worssam, M B Camb

Licences to practise were conferred upon the following 136 candidates who have passed the final examination of the conjoint board

R G Attenborough, Bridget K Attlee, N J Badham, Patricia M Banks, A F Barrott, B A J Barrow, A R Bearn, J S Bennett E P C Benson P W S Blake J S Bland, Evelyn A. M Boesen, P D Bowen J J Bradley, Cynthia L Breillat R C Brookes, Jennifer T Bryant, E A C Buckell, Katharine M Cadbury, Ailleen M Caldwell Elizabeth O Castell, P S N Chappell Ah Kwan Chia, Gillian M Churcher Richard Clark, D B Clarke Mary Clothier, James Cocker, A D Cole, Barbara P Coppen D C Cornish, I J Cunningham, J C B Daman Robert Danbury Shirley F Dauncey, Diana M Dean, R A S Dunn J V Dyer, K B Edwards W K Fitringham R W Emmerson Gwilym Evans, Alan Fletcher, William Foster, D B Fox, R C Francis P W Franks A C Fraser Gilliam M Gandy D C Gardner R E M Geldart, M W Gott B G Gradwell J L G Griffiths Hanna Grodzicka J A Gumbrell J L Harrington, G G Hill P O Hirsch E M James Richard James R A James F C Johnson, Vivian K Jones, Terence Kavanagh, Kevin Kelly, S M

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[1] *Lancet* April 11 1953 p 746

[1] Rembrandt im Rembrandt Basle Holbein 19 , Pp 115 Sw fr 22 50

for this operation—very indigestible stuff, it must be granted, for a confirmed gastrectomist. I had the good fortune to work for these two surgeons, and so was in a position to appreciate not only their skill but their results, which are sometimes different from statistics. Their results were outstanding, for, as Sir Robert Hutchison [4] and Dr. Christopher Howard [5] have emphasised, they knew how to do the operation, and, what was more, they knew when not to do it. Their experience taught them that there were cases not at all suitable for the operation, not only on pathological but also on anatomical grounds. Here is an example—the last case on which Sherren operated before resigning from the London Hospital:

> At operation the patient, a man in the early fifties, was found to have a large mass at the pylorus. Sherren, with all his experience, could not decide on the nature of the tumour. Removal was out of the question, and he decided to do a short-circuit. The transverse mesocolon was fat-laden, and the lesser sac practically obliterated by adhesions. He brought the jejunum through the omentum in front of the colon and anastomosed it to the greater curvature of the stomach, from which the gastrocolic omentum was cleared for the required distance. The patient did well until the 16th day, when he died suddenly from coronary disease. Necropsy showed that the tumour was caused by inflammatory reaction due to duodenal ulcer on the posterior surface. The ulcer had practically healed except for a tiny portion in the centre. Sherren did not use a clamp on the jejunum for fear of causing a clamp ulcer, nor in his anastomosis did he remove any mucous membrane from the stomach or jejunum. It was almost impossible to identify the line of anastomosis, but there was a well-marked clamp ulcer of the stomach which was also in the process of healing.

Sherren and Sir James Walton believed that if it were possible to cure a patient's duodenal ulcer, and still leave him with the whole stomach, this should be done: better a whole stomach than an austerity remnant with its dumping syndrome and all that. It was not that they shied away from the operation of gastrectomy, for I have yet to see a surgeon who could surpass them in the art of gastrectomy. Nor was it that they failed to recognise the complication of anastomostic or jejunal ulcer; for they were among the first to recognise it, and none was more competent to deal with this complication. Their mortality for gastrojejunostomy, plus that of gastrectomy for the complication of anastomostic ulcer, was infinitely less than that of those who did gastrectomy only for duodenal ulcer.

It is remarkable that at the time when Sherren and Walton were getting such good results with gastrojejunostomy, the Mayo Clinic claimed 94% success for the operation, and Moynihan said of the operation: "I am an ardent and sanguine advocate of this operation than which I think there is none in all surgery more completely satisfactory."

Perhaps stomachs have altered much in the last quarter of a century. The British stomach may have lost its phlegm and turned sour under the weight of taxation and restrictions, but I think some discretion ought to be exercised in selecting cases for gastrectomy, particularly with regard to age. Unless there is real need stomachs should not be sacrificed, and lives hazarded, on the altar of gastrectomy. Doctors themselves when afflicted with duodenal ulcer do not rush to operation, and they have gastrectomy done on themselves only when this is a dire necessity. Charles Mayo, who was no fool in surgery, was reputed to have said: "A man who would take away a large part of my stomach for a small ulcer in my duodenum would have to run faster than I!"

London, W.1. MICHAEL SMYTH.

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[4] Hutchison, R. *Brit. med. J.* 1952, ii, 513.
[5] Howard, C. *Ibid*, p. 613.

NOTIFICATION OF TUBERCULOSIS

SIR,—I quote from the latest instructions on the notification of tuberculosis issued by the Ministry of Health:

> "A person who should be notified as 'suffering from tuberculosis,' therefore, is a person who, because of tuberculous infection, may infect others: or a person who is suffering from an active tuberculous lesion which calls for medical treatment or for some modification of the patient's normal course of living."

A child suffering from the (usually mild) disease caused by primary tuberculous infection does not fall into either of these classes, and so is not to be notified. Yet a search among the contacts of such a patient may be most fruitful in revealing hitherto unknown sufferers from phthisis. Why does the Ministry deliberately discard this most valuable weapon?

Whipps Cross Hospital, London, E.11. E. HINDEN.

PROFESSIONALISM IN THE HEALTH SERVICE

SIR,—May I comment on the letters you have received on this subject.

I have been accused of uttering "severe strictures" on the medical profession but no-one has said which of the alleged strictures is untrue or stated unfairly.

Dr. Lindsey Batten (May 2) has, I think, overlooked the fact that besides industries productive of material goods there are industries that exist to produce services. But however the N.H.S. is regarded, the efficiency of its organisation and operation is important if what is done to give "medical aid, comfort, and advice to those citizens who need or ask for it" is not to fall short of what could be done with the knowledge, people, and resources available. That is how I view efficiency, and I believe that for its attainment we are largely dependent upon the actions of the free self-governing professions.

Against Dr. Walshe's pronouncement on the distinctive features of a profession (April 25) may be set the conclusions of several authorities (e.g., T. H. Marshall, and Lewis and Maude) who have published dispassionate studies on the subject.

London, N.W.11. L. FARRER-BROWN.

TREATMENT OF ADVANCED MALIGNANT DISEASE WITH RADIOTHERAPY AND A.C.T.H.

SIR,—The letter from Dr. Houghton and Dr. Walter (April 18) calls attention to the possible applications of adrenal cortical hormones in conjunction with radiotherapy.

A case of advanced malignant disease, treated by us with X-radiation and cortisone, has given results similar to those reported in their series.

> The patient, a man of 65, had a primary squamous-cell carcinoma of the pyriform fossa with secondary deposits in both groups of cervical nodes. These formed large masses, measuring 13·5 × 8·8 cm. on the right side, and 8·8 × 7·8 cm. on the left. The larger group of glands had ulcerated a small area of the overlying skin. A course of radiotherapy with 220 kv. X rays was given to both sides of the neck on two fields of 15 × 15 cm.; a total dose of 4020r was given to each field in 28 days, with a maximum skin dose of 4500r.
>
> On the 10th day of treatment cortisone acetate (Merck) was administered in a dose of 120 mg. This dose was repeated each day for 21 days, and was then gradually reduced to zero in a further 8 days. Symptoms of radiation sickness (general fatigue and anorexia), which had appeared before cortisone therapy was commenced, disappeared within 24 hours and did not recur throughout treatment. Erythema of the skin of the neck appeared on the 20th day of treatment; the skin reaction was slight and did not progress beyond the stage of dry peeling. A moderate membranous reaction was produced on the pharynx, but the patient was free of dysphagia throughout treatment. On the 20th day of treatment the patient developed signs of bronchopneumonia at the base of the left lung, associated with a raised temperature and

Lacey, C E Lay Agnes D F Lodhi Hyder Peter Los Ann H Low, Margaret R. McDonald, H R. Marker L T Martin, J D Meehan R S Miller Patricia E Mortimer Lilias M A Munro A I C Napier C G H Newman Jack Nickson Norma H W Noakes, Jean M North J S Ogilvie Elizabeth S Ordish Pamela M Ordish C G Owen Mohan Kumar Panikkar, Elizabeth M Phillips Kathleen M Pick D A. Potts Rosemary D Prior R D H Reddy, P I Reed, D B Reynolds, S B Rosalki, Annette B Rosenkranz, A. T Rowe, N R Sales, Dorothy Sanderson, J R B Saxby, J R Scarr, Jane M Scott Brown Muriel J Seaman, Elkan Silverstone S E J Smith, J T Smyth, J D Spouge T B Stephen J W Stephenson [illegible] Swallow Gweneth I Taylor Patricia I [illegible] H Tooley, S H Triay, A H Yaug [illegible] Walker, P J C Walker, T H M W [illegible] D Wardle R K Waterhouse, G C [illegible] Margaret P Watson Joy E West, V B Whittaker Margaret S I Williams R S Williams T C G Williams, Shelagh R Wimhurst, Cynthia Wright D E Wright

The following diplomas and those mentioned in our issue of April 18 (p 803) were conferred jointly with the Royal College of Surgeons

D C H—June P [illegible] Ball, D M G Beasley, Bryan B [illegible] ower, Mary C Buchanan, Vasavi [illegible] Barney Cohen, Subrahmanyam D [illegible] mabhai Chhakaddas Desai, Stella [illegible] beth P Duncan, W E B Edge Ja [illegible] W A Forbes Valerie M Fox, M [illegible] Game Sabitri Ghose, J W G G [illegible] ordon Seymour Hoffman, Abdul [illegible] Zilla M Kaye, B F Laidler, Margaret A Lees, Annie D Lindsay, Marjorie J Lyon, Violet D MacDermot F A McDonnell, F A Mackenzie, D A MacLeod, Angela B Manning, E J Masters, Althea G Matthews, Elizabeth L Millar, Ruth E Mitchell Latima Kamya Musoke, Jean M Naylor, Marianna Newman Chandar Parkash, Dorothy A Percy, H P M Perera O A Prosser, N G Rees, Joan C C Reeves, Ruth V Robson, A. L Roith, Thea G T Rose, N J Rothfield, Barbara J Salisbury A J Salmon C E P Samarasinghe, Nirmal Kumar Sarkar Kathleen J C Shaw, Jean McI Smellie, June M Smith, Elizabeth J Sutton, Elizabeth M Sweet, H M Thomas, Shirley L Tonkin, P A Vardy, Barbara J Walker, Joan Walker Josephine P Worren, Patricia L Wheatley, Phoebe M White, I H Wood Bernard Zilberg

D T M & H—I H T Wilson

Royal College of Obstetricians and Gynæcologists

At a recent examination for the diploma in obstetrics the following were successful

J F Adams D B Allsop, Avice M A [illegible] A L Baccarini C L Baker, Dinabandh [illegible] Basu G B Batchelor, C H Bearblock E R Blay, J F Boyle Christine A Bratt B I Brest A R Brighten, B St J Brown Sheena M Buchanan, J A B Burn, Evelyn M Camrass, G W Cardno, C R K. Carroll, R L Carson, Prafulla Chandra Chaudhury, N V Chivers, Mary J Clifford Jean K M Clift Pauline V Coetsee Eithne M Conlon Gladys Connor, M R Coster, P W Dagger I M L Davies, R McN Dean, Cyril Dexter, Alak Nath Dhole Jeanette Diamond P L C Diggory Jean A Drinkwater F G Elvins Yusuf Ali Eraj, D V I Fairweather, Patricia D Fletcher, T A Forster Margaret Fyfe Sadhona Ghosh E O Gibson, M C Gill Carey I R Gilmore, Agnes M Glen Bott Elsie M Glennie Winifred J A Graham A J Gray, Mary E S Gray David Greenbaum J F Grehan J V Groundes Peace, M H Hambling, A S Harris Margaret T Harvey J B Hickling N L Higgins C H Hodge Thomas Horner R J Howat Beryl O Howie Penelope C Humphries Elsie S Jaikaran, Shanta Jaya Jayawant Margaret F Johnson E E Jones Jayashree Kirloskar, Tehmi Kapadia Brendan Keane Mea Wallace Kelso P McC Kinloch A G Laing Irene Leeser, R S Lindsay P W Lumley T F Lynch, W J Lyness B O Lyons, J D Campbell Lyons K M McFad [illegible] J R McGregor, Anne E C MacKinnon, [illegible] MacPherson, F M McQuitty, R I Maitla [illegible] W W Marshall V T Mason, Jayatiss [illegible] Robert Moncrieff, Ann G Morgan W H [illegible] Morton E I Mulholland H H Neifeld, [illegible] O Brien, Okoronkwo Kesandu Ogan M S O'Grady Gweneth L O'Reilly D R M P B O Sullivan W J O Sullivan, Sheila J Parker N L Paros J E Phillips, H O Phillipson D G Price I M Quest, Dorothy H E R [illegible]

S

G F Smith, J G Smith Margaret C Smith Margaret [illegible] A Smith D J Stephens R E Stewart Elizabeth L T Stoddart Vera Taylor E T Tewson A C Trevan, W M E Tweed Mary Uprichard, R J Venn A F Verney Anna M Walsh, Jean M Webb, C P Wendell Smith Dorothy M A White C R Whitfield D K Williams Gwilym Williams A R Wilson C G Wilson, J T Woodall E H Wyatt

Institute of Dermatology

No charge is being made for attendance at the lectures of the summer course, to be held at the institute, Lisle Street, London, W C 2, during May and June

Nuffield Provincial Hospitals Trust

The Investigation into the Functions and Design of Hospitals has moved from 33, Doughty Street London, W C 1, to the Trust's headquarters at Nuffield Lodge, Regent's Park, N W.1 (PRI 8871)

Empire Rheumatism Council

Lord Horder has resigned from the chairmanship of the council Dr W S C Copeman, who has been medical secretary of the council for nearly 18 years, succeeds him

Newsholme Lectures

Prof Alan Moncrieff will deliver the Newsholme lectures at the London School of Hygiene and Tropical Medicine, Keppel Street, W C 1 on Tuesday Wednesday, and Thursday, May 19, 20 and 21, at 5 15 P M He will speak on Child Health and the State

St. Bartholomew's Hospital, London

The hospital is holding an exhibition of its historical documents and other treasures on Thursday, Friday, and Saturday, May 14, 15, and 16 The exhibition will be open to the public each day from 10 30 A M to 6 30 P M (Note change of times of admission)

Ross Institute Industrial Advisory Committee

At a meeting to be held by the committee at the Rubber Growers' Association, 19, Fenchurch Street, London, E C 3, at 2 15 P M, on Thursday, May 21, Mr C R Harrison, chairman of the committee, will open a discussion on Tropical Health Problems and their Connection with Industrial Relations, and Prof George Macdonald, director of the Ross Institute, will speak on International Health Work

Society for Endocrinology

The following office bearers have been elected chairman, S J Folley, hon secretaries, C H Gray and N F Maclagan, hon treasurer, G W Harris, editor of society's proceedings, S Zuckerman, members of committee, T Mann, C J O R Morris, I W Rowlands, and S L Simpson Communications should be sent to the hon secretary, Department of Chemical Pathology, King's College Hospital, Denmark Hill, London, S.E 5

Laboratory Animals

The Laboratory Animals Bureau is holding a symposium at 1 Wimpole Street, London,-W 1, on Thursday, May 14, at 2 30 p.m Dr H J Parish will be in the chair Mr A N Worden, M.R C V S, will speak on the Feeding and Husbandry of Laboratory Animals, Mr A. E Mundy on the Function of the Animal Technician, Mr J Scarnell, M R.C V S, on the Control of Infection in Small Animal Breeding Units, and Mr J S Paterson, PH.D M R C V S, on the Provision of Animals for Research Further particulars may be had from the bureau, M R C Laboratories, Holly Hill, London, N W 3

British Occupational Hygiene Society

A meeting to inaugurate this society was held at the London School of Hygiene and Tropical Medicine on April 27 The founder members include—as well as doctors—engineers, chemists, and physicists, who are concerned with the maintenance of healthful conditions of work Mr T Bedford, D SC, director of the Medical Research Council's environmental hygiene research unit has been elected president, Mr E J King, D SC, professor of chemical pathology in the University of London, president elect, Mr P C G Isaac, lecturer in public health engineering, King's College, Newcastle upon Tyne, hon secretary, and Mr D E Hickish, of the department of applied physiology, London School of Hygiene and Tropical Medicine, hon treasurer

The Lister Institute of Preventive Medicine

Prof W T J Morgan, F R S, has been appointed deputy director of the institute

The institute has recently accepted a charitable endowment from Messrs Arthur Guinness & Sons, for the establishment of a Guinness Lister research unit in general microbiology Dr B A. D Stocker has been appointed as head of the unit, and he will take over his duties in October

Dr Stocker is 35 years old After a war career in the medical branch of the R.A.F V R, with which he served mostly in India and Burma he was successively demonstrator lecturer, and senior lecturer in the department of bacteriology and immunology at the London School of Hygiene and Tropical Medicine His research work has been directed mainly to bacterial genetics, particularly mutation rates of flagellar antigens in *Salmonella typhimurium*; and during the ten [illegible] United States, with [illegible] Fund fellowship in the [illegible] the transduction of [illegible] pneumococcus and with [illegible] bacteriophages in which he applied the discoveries of Zinder and Lederberg to the transduction of flagellar characters in salmonella leucocyte-count. This infection responded to penicillin, without cessation of cortisone therapy. 10 days after completion of radiotherapy the mass on the left side of the neck had regressed to scattered small nodules which were not measurable; on the right side regression had occurred to approximately one-third of the original size.

It is clear that considerable clinical investigation will be required to evaluate this method of treatment. While there is evidence, which formed the basis of this clinical trial, that cortisone modifies or suppresses the skin lesions produced by ultraviolet light in man [1] and by soft X rays in animals,[2] there is no existing evidence on the possible effect of such therapy on the radiosensitivity of tumours. Owing to the action of cortisone or A.C.T.H. on inflammation and œdema in the neighbourhood of the tumour, and on the stromal reaction during radiotherapy, it is probable that the effects may be considerable, and the value of the method depends on their favourable direction.

The danger of severe sepsis during hormone therapy, pointed out by Dr. Houghton and Dr. Walter, is probably greatest in cases of carcinoma of the lung, and may not present such a serious problem in other types of tumour.

The cortisone employed in this investigation was supplied by the Medical Research Council.

Radiotherapy Department and
Bernhard Baron Institute of
Pathology, London Hospital, E.1.

G. W. BODEN
A. H. E. MARSHALL
J. A. ORR.

EFFECT OF OÖPHORECTOMY AND SPLENECTOMY ON MALIGNANT DISEASE

SIR,—In 1936 I published [3] a report of two cases of carcinoma in each of which both ovaries and the spleen had been removed; and I now take this opportunity to complete their clinical history.

The first patient, a woman aged 41, had had her uterus and ovaries removed 2 years previously for carcinoma of the uterus. When I saw her 2 years later, the disease had recurred in Douglas's pouch, and had extended to the bladder on the one side and the rectum on the other, with a considerable quantity of blood in both bladder and rectum. There was also extensive abdominal glandular infection.

I removed the spleen and gave her daily subcutaneous injections of splenic extract, beginning with a daily dose of 4 ml. and gradually reducing it to 1 ml. daily. During the time 4 ml. was given, the disease steadily got worse, and only after the dose had been reduced to 1 ml. and continued for 2 months was slight improvement noted. These injections were continued altogether for 3½ months with slight improvement. After they were stopped, the patient's condition steadily improved, and at the end of a year there was no sign of malignant disease. 16 years from the time her spleen was removed she died of coronary thrombosis with no sign of recurrence.

In the second case the result was not so satisfactory, for the patient died 5½ years after removal of both ovaries and spleen. For the first 4 months after the operation, the disease appeared to remain stationary; it then began to improve and continued to do so, till 10 months after her operation all traces had disappeared. She remained apparently well for 5 years, when symptoms developed pointing to involvement of the liver with some ascites. These symptoms gradually increased till she died 6 months later.

I did quite a number of operations similar to the second, but the result was always the same—death at varying intervals after removal of the spleen and ovaries.

Is there any possible explanation of why the result should have been so different in these two patients? The only one I can offer is the length of time between removal of the ovaries and of the spleen; in the first case the interval was 2 years, whereas both were removed at the same time in the other cases. I can offer no explanation why a late removal of the spleen, as against both ovaries and spleen at the same time, should have this effect, but it seems to me that in the first case some change takes place in the fluids of the body which is deleterious to the growth of malignant cells.

Cove, by Helensburgh. PETER PATERSON.

THE SENIOR REGISTRAR

SIR,—We agree with Mr. Leacock that the number of doctors of registrar or equivalent status, who are likely to compete for consultant vacancies, is greater than the figure we cited (April 18). We now know that senior registrars in their final year in the United Kingdom total more than 327. We could not include research assistants in our figures because of difficulty in obtaining accurate information, and we excluded university posts since each appointment of this type, if vacated by a man who has obtained a consultant post, leaves a gap which can conveniently be filled by an ex-registrar.

We also agree with Mr. Leacock's suggestion, in his letter last week, that in general medicine and surgery even the agreed senior-registrar establishment is not truly related to future prospects and should be reviewed. So far as the present generation of senior registrars is concerned, it is open to Mr. Leacock to suggest a *coup de grâce*; but we do not feel that under present circumstances there would be much grace about the coup, and certainly we are not in a position to recommend such a step as long as there are other methods of dealing with the problem.

We would point out, however, that while we are asking that the best of the present generation be given the opportunity of an extended tenure, we do so with the full knowledge that the improvement in each individual's chances will be only slight without parallel expansion of the consultant service. If our proposal is accepted, any senior registrar who seeks to continue must do so with his eyes open. All we can hope to do is to suggest means to this end for those who can see a real prospect of a consultant post in the future. We shall continue with our endeavours to make this a reality and not a mirage.

R. M. FORRESTER
Late chairman.
JOHN N. WALTON
Chairman, Registrars' Group, B.M.A.

DISORDERS OF MOTILITY OF THE SMALL BOWEL

SIR,—The valuable work of Professor Frazer and his associates to which Dr. Hawkins draws attention in his letter (April 18) was known to us. I do not believe, however, that the cases described by me (April 4) corresponded exactly to those discussed by Dr. Hawkins. The fault is perhaps mine for failing to clarify the distinction.

In a follow-up of any large series of patients who have undergone gastrectomy, cases of deficient fat absorption associated with anæmia and riboflavine deficiency are not infrequently encountered. Such patients do not suffer severe abdominal pain, and kymographic studies show a distinct lack of tone and a diminished small-bowel motility pattern. In addition, radiographic examination usually demonstrates dilatation of the jejunum. In the four cases I have described, however, severe griping abdominal pain is the patient's chief complaint, a pain which persists for upwards of one hour without relief. Kymography in three of these cases demonstrated increased intestinal tonus and irregular spasmodic contractions without any increased rate of passage of food in the gut. I would hesitate to suggest that the condition described is any more than a variant of the more typical deficiency pattern encountered either after gastrectomy or in the sprue syndrome. The clinical features are, however, sufficiently distinctive to allow separation of the two conditions.

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1. Järvinen, K. A. J. *Brit. med. J.* 1951, ii, 1377.
2. Marshall, A. H. E. *Acta radiol., Stockh.* 1953, 39, 73.
3. Paterson, P. *Lancet*, 1936, i, 1402.

Royal Appointment

Brigadier F C Hilton Sergeant, late R A M C, has been appointed honorary physician to the Queen in succession to Major General A J Beveridge, late R A M C

Scientific Film Association

A film appraisal meeting is to be held at St Bartholomew's Hospital Medical College, West Smithfield, London, E C 1, at 5 30 P M on Tuesday, May 12 The following films will be shown *Effect of Metallic Ions and Osmotic Disturbances of the Heart*, *Gastric Secretion*, and *The Mitral Valve* Medical students and doctors are invited

London Health Exhibition

On Monday, May 11, at 2 30 P M, at Woodberry Down Health Centre, Green Lanes, Stoke Newington Prof James Mackintosh will open an exhibition illustrating the health services available to the people of London The exhibition will be open daily from 10 A M to 8 P M till May 16 and the programme includes film shows talks, physical training displays, and cookery demonstrations

The Ministry of Food has published a new edition of the memorandum for doctors which sets out the arrangements for granting special rations and priority allowances of food to invalids and others needing special diets The revised memorandum, which is known as Med 2 (1953), replaces Med 2 (Revised 1950) Copies are being sent to all doctors in the United Kingdom, but additional copies can be obtained from the local food offices

CORRIGENDUM *Surgery of Varicose Veins*—Mr Rowden Foote's film (*Lancet*, April 25, 1953, p 858) runs for 28 (not 18) minutes

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On April 18 the Harveian Librarian of the Royal College of Physicians appealed through our columns for a copy of the Harveian oration for 1849 which was needed to complete the college's collection of these orations We understand that the missing copy has been supplied by the president of the Royal College of Surgeons The Harveian Librarian is still seeking a portrait or photograph of Dr George Oliver of Harrogate and London, founder of the Oliver Sharpey lectures (see *Lancet* March 21, 1953, p 605)

Information about appointments in the Colonial Service is given in a new edition of a Government publication (*Appointments in Her Majesty's Colonial Service* H M Stationery Office Pp 130 3*s* 6*d*)

Diary of the Week

MAY 10 TO 16

Monday, 11th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W C 2
5 P M Prof H R Dew Postoperative Intravascular Thrombosis (Hunterian lecture)
UNIVERSITY COLLEGE, Gower Street, W C 1
4 45 P M Sir Rudolph Peters, F R S Inhibitors and Intracellular Chemical Dissection (Third of four lectures)
POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 12
4 P M Dr H S Banks Coliform Infection in Gastro-enteritis
INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S E 5
5 30 P M Dr E Stengel lecture demonstration
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W 1
8 30 P M Sir Russell Brain, P R C P The Need for a Philosophy of Medicine (Annual oration)
WEST LONDON MEDICO CHIRURGICAL SOCIETY
8 30 P.M (1, Wimpole Street, W 1) Viscount Simon The Doctor in the Witness Box (Cavendish lecture)
UNIVERSITY OF ST ANDREWS
5 P M. (Medical School Small's Wynd Dundee) Sir Heneage Ogilvie Problems of Gastro œsophageal Junction

Tuesday, 12th

ROYAL COLLEGE OF SURGEONS
5 P M Dr R B Cattell (Boston) Extra Hepatic Obstruction of Bile ducts (Moynihan lecture)
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St Mary's Hospital Medical School, W 2
5 P M Mr J G Davis, D SC Public health Aspects of Milk (Almroth Wright lecture)
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
5 30 P.M *Section of Experimental Medicine and Therapeutics* Members of Chemical Defence Experimental Establishment, Porton Poisoning with Anti cholinesterase
8 P M *Section of Psychiatry* Dr Linford Rees Emotional Factors in Causation of Asthma, Urticaria, and Nasal Disorders
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street, W C 2
5 30 P M Dr J A Dudgeon Virus Diseases
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P M (Hammersmith Hospital, Ducane Road W 12) Prof Chassar Moir Use of Radiology in Labour
UNIVERSITY OF ST ANDREWS
5 P M Sir Heneage Ogilvie Pitfalls in Surgical Diagnosis

Wednesday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M Prof A C Frazer Disordered Function of Small Intestine (First of two lectures)
2 P M Mr R J Ludford, D SC Malignant Growth (Second of two lectures)
ROYAL SOCIETY OF MEDICINE
5 P.M *Section of Proctology* Dr Cattell, Mr J C Goligher, Mr R S Corbett, Mr Stanley Aylett Surgery of Ulcerative Colitis
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Dudgeon Virus Diseases
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION
8 30 P M. (Royal Free Hospital School of Medicine, 8, Hunter Street W C 1) Miss Sybil Campbell Day in the Life of a Metropolitan Magistrate—with particular reference to Problems of Punishment
MANCHESTER MEDICAL SOCIETY
4 30 P M (University of Manchester) *Sections of Pathology and General Practice* Dr Miles Parkes, Dr F B Smith Prof Fraser Brockington Laboratory Facilities for the General Practitioner

Thursday, 14th

UNIVERSITY OF LONDON
5 P M (Guy's Hospital Medical School London Bridge, S E 1) Dr N G Emmelin (Lund) Secretion of Saliva
ROYAL COLLEGE OF SURGEONS
5 P M Surgeon Commander Frank Ellis Desirable and Tolerable Levels of Warmth in Warm Climates—with special reference to Requirements of Men in Royal Navy (Hunterian lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr G E Burch (Tulane University, Louisiana) Vector cardiography
BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W 1
8 30 P M Mr L H Gray, PH D Initiation and Development of Cellular Damage by Ionising Radiation. (Silvanus Thompson lecture)
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Structure of Pathogenic Fungi and their Identification
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P M (Chelsea Hospital for Women Dovehouse Street, S W 3) Mr A W Bourne Hypertension in Pregnancy and its Prognosis
ALFRED ADLER MEDICAL SOCIETY
8 P M (11 Chandos Street, W 1) Dr D S Macphail Psychotherapy for Criminals
UNIVERSITY OF CAMBRIDGE
5 P M (Senate House) Prof A D Gardner Proper Study of Mankind (Rede lecture)
NUFFIELD ORTHOPÆDIC CENTRE, Wingfield Morris Orthopædic Hospital, Oxford
8 30 P M Mr Philip Wiles Posture
HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings, Teviot Place, Edinburgh) Dr C F Rolland Diabetes in Pregnancy
UNIVERSITY OF ST ANDREWS
5 P.M Prof G Gustafson (Malmö) Modern Methods in Dental Histology

Friday, 15th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS, 58, Queen Anne Street, W 1
5 P M. Mr Henry Roberts Micturition in Female (Blair Bell lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Mr John Bruce Hazards of Major Surgery
4 P M Professor Frazer Disordered Function of Small Intestine (Second of two lectures)
GUY'S HOSPITAL MEDICAL SCHOOL
5 P M Sir Lawrence Bragg, F R S X ray Analysis of Protein Molecules (Fison lecture)
ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington, W 2
5 P M Mr Howard C Hanley Urological Problems during Pregnancy
ROYAL SOCIETY OF MEDICINE
4 30 P M *Section of Epidemiology and Preventive Medicine* Dr J Stevenson Logan, Dr A P Goffe, Dr W Ritchie Russell Poliomyelitis
FACULTY OF RADIOLOGISTS, 45, Lincoln's Inn Fields W C 2
2 15 P M *Diagnosis section* Dr R Astley Tricuspid Atresia Dr D E Truscott Radiological Control of Kidney Injuries Dr P G Keates Physiological Observations made during Excretion Urography Dr W Homer Smith Reliability of Excretion Urography in Diagnosis of Bladder Tumours
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R T Brain Common Skin Diseases in Children
OSLER CLUB OF LONDON
7 45 P.M (11, Chandos Street, W 1) Dr J N Morris History of Social Medicine
UNIVERSITY OF OXFORD
5 P M (Radcliffe Infirmary) Dr Cattell Pancreatic Surgery
UNIVERSITY OF ST ANDREWS
5 P.M Sir Heneage Ogilvie Independence and Authority in Medical Practice

Saturday, 16th

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
11 A M (Queen Charlotte's Hospital, Goldhawk Road, W 6) Prof W C W. Nixon Disordered Uterine Action
BIOCHEMICAL SOCIETY
1 45 P.M (Medical School, Hospitals Centre, Birmingham, 15) Scientific papers

EXPERIMENTAL DATA

Dextran of various types has been infused into patients undergoing surgical operation. The observations reported have been made on five types of dextran whose molecular-weight distribution makes them of special interest. The first two types described were each given to 5 patients, the third type to 58 patients, the fourth to 22 patients and the fifth to 36 patients.

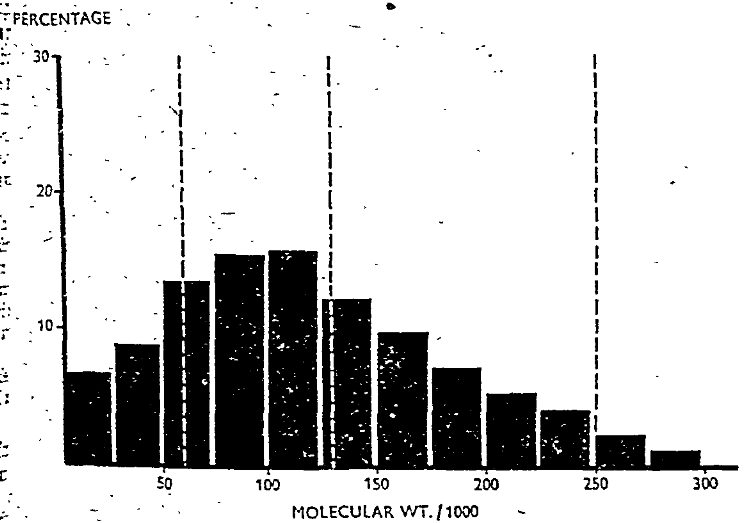

Fig. 2—Distribution of molecular weight of dextran as used by Bull et al. (1949).

To estimate the excretion-rate the patients' urine was collected in two batches: (1) for the first twenty-four hours after the start of the infusion; and (2) for from twenty-four to forty-eight hours after. Blood samples were taken before infusion and at five minutes, and six, twenty-four, forty-eight, seventy-two, ninety-six, and one hundred and twenty hours after the end of infusion.

Discussion of the techniques and problems of accurate estimation of the amount of dextran remaining in the circulation is beyond the scope of this paper.

To obtain a true value it is necessary to measure the blood volume at the time of taking each sample, and this is not always feasible in the postoperative patient. It has been found, however, that reliable results may be obtained by taking the five-minute sample as a reference level and applying a correction factor—0·9 in the case of the low-excretion types of dextran—to the later readings.

Patients who experienced severe hæmorrhage or with postoperative oliguria or other factors which might have influenced the results were excluded from the series. Patients who received blood or any other supportive therapy in addition to the dextran were likewise excluded.

In the cases reported the amount infused was two bottles—about a litre—of a 6% solution of the dextran under test in physiological saline solution.

The first type to be investigated was a standard material prepared by long hydrolysis and fractionation to remove any large molecules which might still be present. The molecular-weight distribution of this type is shown in fig. 1 as an equal-area diagram. Each block in the diagram has a molecular-weight range of 25,000, and the height of any block represents the amount of dextran in that particular range expressed as a percentage of the whole. As would be expected of material having a preponderance of small molecules, the excretion-rate was high—35% in twenty-four hours—and the blood level at the end of twenty-four hours was low, being 20% of the amount infused.

The distribution of the next type of dextran is shown in fig. 2. This standard material was similar in character to that reported by Bull et al. (1949), being prepared by short hydrolysis followed by fractionation to remove the large molecules. However, it still contained a small quantity of the molecular range we consider undesirably high. Because of the fewer small molecules the excretion-rate was reduced to 20%, but the twenty-four-hour blood level was only raised to 35%. This meant that during the first twenty-four hours after infusion more of the dextran was lost from the circulation than remained in it.

The observations made at this stage suggested that, to obtain a satisfactory twenty-four-hour blood level, a type of dextran must be made containing a much greater proportion of molecules in the middle range immediately above the diffusion threshold. It was also felt that the larger molecules should be completely removed. These requirements necessitated a re-design of the process of manufacture and the development of a large-scale method of intensive fractionation.

We have called material prepared by this method "narrow-fraction dextran" to distinguish it from that prepared by methods not involving intensive fractionation. We are aware that the purist physical-chemist may object to the designation on the grounds that the material contains molecules outside the desired range, but we are unrepentant.

The molecular-weight distribution of the third type of dextran (narrow-fraction A) to be investigated is shown in fig. 3. It will be seen that most of the material is in the molecular ranges close to the diffusion threshold. The excretion-rate was 11%, and the twenty-four-hour blood level was 47%, which was felt to be encouragingly close to the 50% considered to be the desirable minimum. This was achieved with narrow-fraction B (fig. 4) with an average twenty-four-hour blood level of 55%. This material had a slightly higher proportion of small molecules than the previous type, and the excretion-rate was in consequence raised to 14%. The final type investigated in this series, narrow-fraction C (fig. 5), had the highest blood level so far obtained, 68%, at twenty-four hours and also, at 8%, the lowest excretion-rate.

As would be expected, the material with the highest twenty-four-hour blood level is also the best maintained over longer periods. At the end of the five-day period about 20% of narrow-fraction C dextran remained in the circulation as opposed to less than 15% of narrow-fraction A and B.

CLINICAL DATA

Complete clinical assessment of the rôle of narrow-fraction dextran must depend on observations on a large

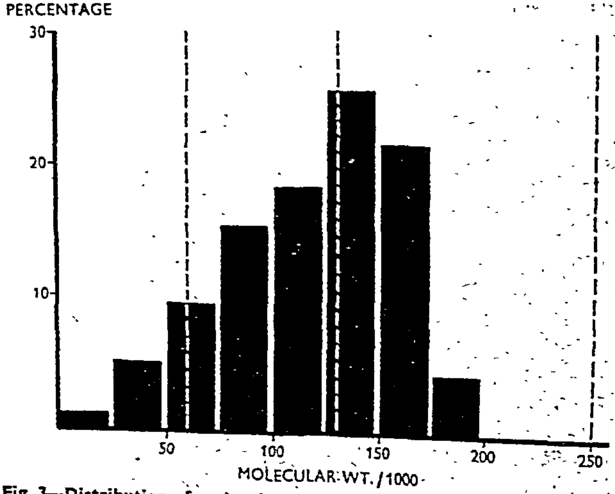

Fig. 3—Distribution of molecular weight of narrow-fraction A dextran.

number of cases of various types From study of about 120 cases in which narrow-fraction dextran has been used it is possible to make some general observations

Prophylaxis

The use of narrow fraction C dextran as an infusion for patients undergoing major surgical operations enables supportive therapy to be given in the simplest possible manner The infusion is started soon after the patient is anæsthetised and while he is still in the anæsthetic room The dextran is run in slowly—ten to twenty drops a minute—at first At the first sign of any fall in blood-pressure during the course of the operation the infusion-rate is increased By occasional adjustment of the drip it is possible to maintain the blood-pressure at a steady level through even the most severe operations

Since narrow-fraction dextran is retained in the circulation at an adequate level over the critical post-operative forty-eight hours, it is rarely necessary to continue the infusion after the operation has been completed This presents a considerable advantage, since it enables the drip to be taken down while the patient is still in the theatre Apart from the psychological effect—the patient recovering from anæsthesia to find an infusion in progress immediately fears the worst—he is not cluttered up with the paraphernalia of the infusion equipment, and the nurses are consequently spared complicated manœuvres in attending to him

Unless there is excessive loss of blood during the operation, narrow-fraction dextran is all that is needed The requirements for the prevention of shock are the maintenance of circulation volume and blood-pressure, reduction of the oxygen-carrying capacity of the blood by dilution with dextran is now of minor importance, because with the narrow-fraction material the total volume of the infusion required is far less than with the earlier standard material, which was rapidly lost from the circulation If there is severe hæmorrhage, blood may be given at the same time as the dextran It is an advantage to give blood and dextran simultaneously, rather than to replace the dextran by blood In some cases dextran has been more effective than blood in restoring a falling blood-pressure

Shock

If the patient arrives at the hospital with the shock syndrome already established, a sample of blood is taken for typing (see below), and a bottle of dextran is next infused as rapidly as possible A second bottle is given at a rate depending on the blood-pressure

Most of the patients in this series have responded adequately to the infusion of two bottles of narrow-fraction dextran, but occasionally a third bottle has been found desirable After the infusion of three bottles of dextran a bottle of blood should be given to prevent undue hæmodilution If further infusion is then necessary, dextran and blood may be given alternately

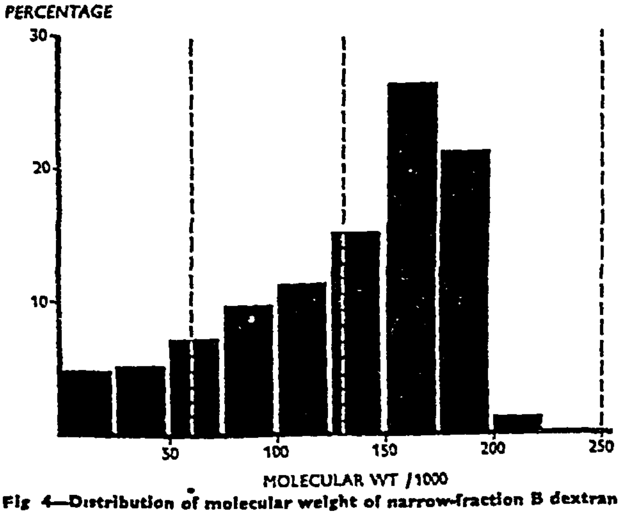

Fig 4—Distribution of molecular weight of narrow-fraction B dextran

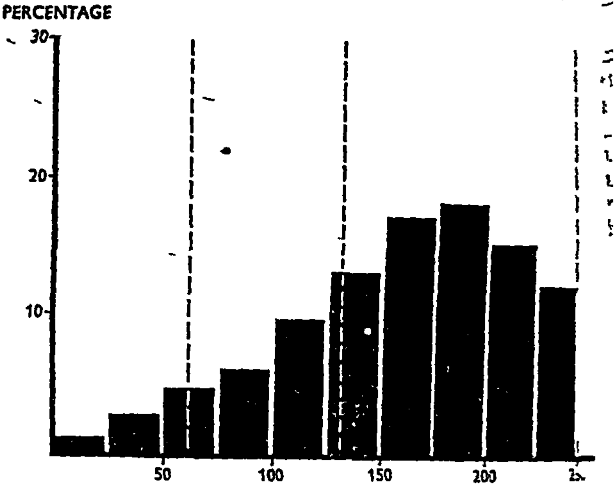

Fig 5—Distribution of molecular weight of narrow fraction C dextr

An inadequate number of cases of burns have been observed for any definite pronouncement to be made now Since the primary cause of loss of fluid from the circulation is effusion from the damaged capillaries of the burnt areas, it seems logical that the less easily diffusible material would be the better This, however, must be the subject of further investigation

Reactions

No reactions have been observed with any of the cases infused with narrow-fraction dextran in the surgical professorial unit at Manchester Royal Infirmary A mild rigor after the infusion of this material has been reported from one of the associated hospitals Since the incidence of reactions with a standard type of dextran containing molecules of a higher molecular weight than any of the narrow-fraction dextran used has been shown to be very low (Maycock 1952), any attempt to estimate the reaction rate must be left until several thousand patients have been infused

Other Observations

Many macromolecular substances, when present in the serum, have been shown to produce a pseudo agglutination which may make cross matching difficult for the inexperienced, and narrow-fraction dextran is no exception to this rule A routine blood sample to enable grouping to be done should therefore be taken before the administration of dextran In common with other types this dextran also has a pronounced effect on the erythrocyte sedimentation rate (E S R), which is increased for from three to five days after infusion Gronwall and Ingelman (1945) have shown that the E S R increased with the concentration of dextran, and Thorsen and Hint (1950) have shown that with a given concentration the increase depends on the molecular size Hardwicke et al (1950) have demonstrated a relationship between these parameters

Experiments are at present being made as a result of which it is hoped that it will be possible to obviate both the effect on the E S R and on the blood grouping

At one period during the investigation alarm was caused by the incidence of hæmatomata in patients in this series It was at first thought that this might be due to some hitherto unobserved effect on the bleeding time by dextran molecules of the range used when present in sufficient concentration It was then found that a common factor in all these cases had been the use of gallamine as a muscle relaxant Similar cases were then

THE NEED FOR A PHILOSOPHY OF MEDICINE *

Sir Russell Brain
D.M. Oxfd, P.R.C.P.

PHYSICIAN TO THE LONDON HOSPITAL AND THE MAIDA VALE HOSPITAL

The *Shorter Oxford Dictionary* gives a number of definitions of philosophy. The first is "the love, study, or pursuit of wisdom, or of knowledge of things and their causes, whether theoretical or practical." Later, philosophy is defined as "the study of the general principles of some particular branch of knowledge, experience or activity."

Philosophy in fact has slowly changed its meaning over the centuries: long ago its purpose was the pursuit of wisdom, but it has become increasingly preoccupied with technical problems of thought, until today philosophers are almost exclusively concerned with the process of knowing, and so little with knowledge that they would hastily disclaim any pretensions to be wiser than anyone else. With occasional partial exceptions, philosophy has lost its comprehensive outlook, and wisdom is above all comprehensive; indeed it now seems almost a paradox to say that only the comprehensive can comprehend. We do not ask with Job: "Where shall wisdom be found?" nor do we even lament with Omar that it yields such a disappointing harvest. The present generation would possibly be more inclined to agree with Blake that "the road of excess leads to the palace of wisdom." But perhaps, after all, wisdom is somewhat of an obituary virtue, more obvious in the dead than in the living, and more tolerable when sententiousness is safely silent and can no longer be embodied in a lecture. Is there indeed any substantial difference between the two definitions of philosophy which I quoted from the dictionary, for does wisdom really imply any more than a grasp of general principles, the ability to see the wood as well as the trees?

A philosophy of medicine, then, means the enunciation of general principles within medicine; but it also means something more, for it should include the criticism of medicine and its own general principles by means of the wider principles embodied in philosophy. This is a process which is going on in many fields of knowledge, notably in physics. One of the striking developments of thought in the present century has been the growth of scientific philosophy—i.e., the application of philosophical principles to science. This important task is one which can be carried out only by the scientists themselves, because the philosophers lack the necessary scientific training. At first sight it is rather surprising that this need has been so little recognised in medicine, where the opportunities are so rich; for we have no physician-philosophers to compare with the physicist-philosophers such as Eddington, Jeans, Planck, Dirac, and Schrodinger, nor with Russell and Whitehead who came to philosophy by way of mathematics. No doubt doctors are too fully occupied with their day-to-day work in applying the new discoveries of science to find time to discuss their more remote theoretical implications. Nevertheless I shall maintain that this need is real and urgent, and that, abstract though it may sound, a philosophy of medicine greatly concerns the welfare of our patients in many ways.

For this reason, though it is possible to discuss the question primarily in terms of abstract thought, I prefer to begin with practice; and I shall try first to show how a philosophy of medicine is necessitated by our practical needs. Since I am aiming at a comprehensive view, I must necessarily deal far too briefly with a number of aspects of the question, any one of which alone is important enough to justify far more discussion.

The Differentiation of Medicine

In order to understand how our present problems have arisen I must review certain of the recent developments of medicine; and, though in doing this I shall tell you nothing which you do not already know, I shall try to present the familiar facts as illustrating a single underlying principle. This is that the evolution of medicine during the last century has involved a process of differentiation, which has gone parallel with, and been intimately related to, the increase of knowledge. Two points need to be noted about this process: the first is that it has never been based entirely upon scientific considerations. Social and other factors, which from a scientific point of view were accidental, cut into it and profoundly influenced it. Secondly, the differentiation of medicine is reflected not only in the specialisation of the various groups of doctors, but in bricks and mortar, in the structure and the geographical arrangement of hospitals.

The time-honoured division between medicine and surgery was based, of course, upon a difference of therapeutic technique. Necessarily they overlapped—in diagnosis for example, and when a medical disorder developed into a surgical one, or conversely. Nevertheless the distinction remained a rigid one for centuries. The third great division of medicine—obstetrics and gynæcology—arose on an entirely different basis, for midwifery had its roots in a physiological function and its domain was demarcated by the appropriate anatomy. Gynæcology was an offshoot of the main stem. But because the basis of both was anatomophysiological—and, may one not add, also psychological?—obstetricians and gynæcologists became and remained both physicians and surgeons, and many will have known obstetricians who liked to be called "Doctor."

Increasing knowledge during the 19th century brought a new mode of differentiation into both medicine and surgery—the anatomical. Ophthalmic surgery was one of the first instances of this, its sphere combining disease of the eye as an anatomical structure with disorders of vision, which extended its scope into related anatomical structures such as the visual pathways in the nervous system. The contemporary development of neurology, dermatology, and otorhinolaryngology illustrates the same principle—that of differentiation on an anatomical basis; and, of course, many similar special branches of medicine and surgery have developed since. It must not be supposed that because I call the basis of these specialties anatomical they are not concerned with physiology. Of course they are: but the demarcation of their spheres of activity is anatomical, and they study physiology as the science of the functions of particular organs—an important point to which I shall return. The delimitation of all these branches of medicine and surgery was complete in hospital structure at an earlier stage than in medical practice; for special hospitals isolated patients suffering from diseases of the eye, ear, nose and throat, skin, and nervous system at a time when doctors interested in these subjects were usually still practising general medicine or surgery as well.

Meanwhile advances in science were creating new specialties based upon special techniques. The discovery of X rays established radiology as a diagnostic technique covering the whole field of medicine. This in turn gave birth to radiotherapy—also widely applicable; and the utilisation of other physical agencies, including the hands of the masseuse, for purposes of treatment, produced

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* The Annual Oration delivered at the Medical Society of London on May 11, 1953.

CASE 2.—A woman, aged 48, whose diabetes had been diagnosed for six years but poorly controlled by diet and insulin, complained of pain and swelling in the thighs

Examination showed the reported swellings to be prominences of normal tissue lying between areas of atrophic muscle These were circular about 3 in in diameter, overlying each iliac crest and lying behind the tensor fasciæ latæ muscles Less well defined areas lay in the upper thirds of each thigh A further lesion 1 in in diamter was present in the right triceps brachialis muscle Physical examination was otherwise normal

Insulin had usually been injected into the thighs, seldom in the arms, but not into the buttocks

CASE 3.—A woman, aged 46, who had been in satisfactory diabetic control on diet and insulin for ten years, noticed weakness and wasting of the thumbs for eight years, loss of flesh in the arms for five years, and in the right buttock for a year

She was found to have circumscribed areas of atrophy of the muscle and fat in the following sites the right masseter muscle, the biceps muscle of one arm and the triceps muscle of the opposite arm, the right buttock, on the natal fold These were such that the examining finger sank into them to the depth of bone The short adductors of the thumbs were also wasted. She also showed a tabes like neuropathy the Wassermann reactions of the blood and of the cerebrospinal fluid being normal

CASE 4.—An obese female, aged 66, with poor control of her diabetes by diet and insulin, had a deep area of atrophy of fat and muscle, about 1 in in diameter, in the right deltoid muscle The deltoid and triceps muscles were weak in this arm and the triceps jerk absent Neurological examination was otherwise normal

The right hand was always used for insulin injection, which was normally into the left arm

CASE 5.—A woman, aged 69, who was admitted to hospital after cerebral thrombosis, had had diabetes for eleven years, adequately controlled with diet and insulin

Examination showed a right spastic hemiparesis with moderate dysphasia and comprehension defect Sensory examination gave uncertain results. There were three discrete areas of muscular atrophy in the left thigh, immediately overlying the femoral artery in Scarpa's triangle (fig 2), was a roughly circular area 3 in. in diameter; a linear lesion, 2 × 1 in., ran below the left deltoid, and a circular area, 1 in. in diameter lay in the right triceps brachialis muscle

The patient and her daughter normally coöperated in injecting insulin and invariably used the arms

CASE 6.—A woman, aged 68, who had controlled her diabetes moderately well for eight years with diet and insulin, complained of aching pains in the legs for years and of weakness in the legs since a bowel disturbance with mild ketosis a month before

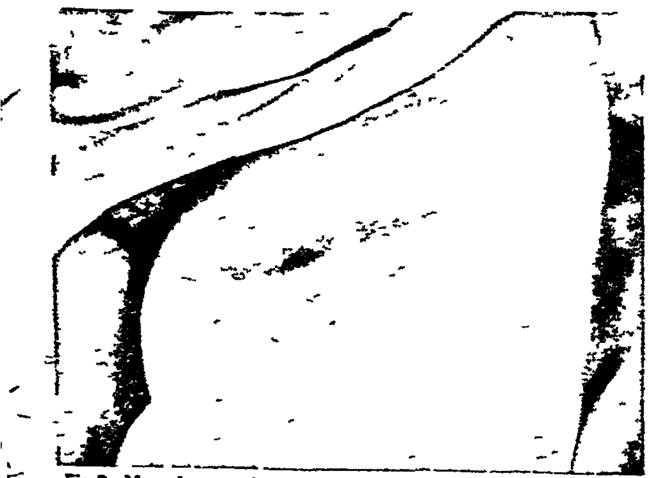
Fig 2—Muscular atrophy over Scarpa's triangle in left thigh (case 5)

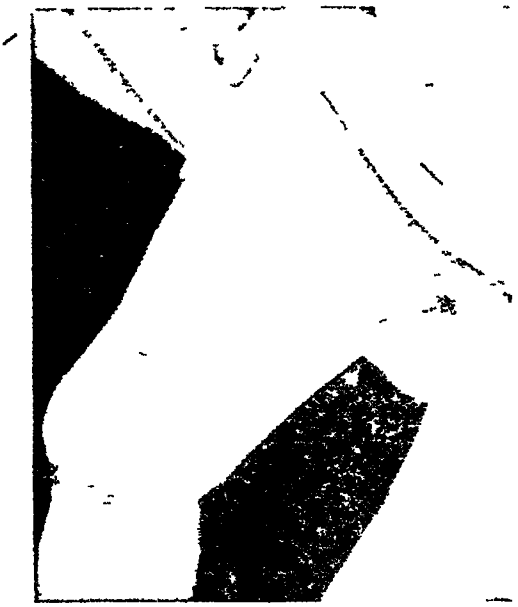
Fig 3—Muscular atrophy on inner aspect of right thigh (case 6)

Examination showed areas of muscular atrophy $^1/_2$ to 1 in in diameter, on the inner aspects of each thigh and the outer aspect of the left thigh (fig 3)

The patient normally injected insulin into her arms and insisted that only on three or four occasions had she had injections in her legs

DISCUSSION

These localised areas of muscular atrophy in diabetics are distinct from insulin atrophy. In the present cases the usual sites of injection have been spared, and the characteristic induration found with insulin lesions has been absent The atrophy has been found in unusual places for injection, in case 3 injection in the situation of the lesions may be regarded as impossible I have not seen any similar lesion in a patient not taking insulin, but in the pre-insulin era apparently similar lesions were reported by Bernard and Fere (1882), Auche (1890), and Pitres and Marchand (1917)

Joslin (1946) described ectopic lipodystrophy in the face, breast, and submental regions A photograph published by Rudy and Epstein (1945) appears to be of a lesion of the kind described here, and Rudy (1945) expressed the view that "occasionally isolated muscle atrophy may be mistaken for insulin atrophy" Yohalem and Pollack (1949) found no evidence of insulin atrophy remote from the site of injection

Panatrophy (Kinnier Wilson 1940) has not been described in diabetes, and in panatrophy the skin is abnormal, a feature absent in the present cases

Half the cases described showed neurological abnormalities, but the muscle lesions did not correspond to any nerve distribution The existence of separate diabetic lesions in one patient is a common chance occurrence

SUMMARY

Six cases of localised areas of atrophy of muscle and subcutaneous tissues in diabetes are described

The condition probably represents a specific diabetic lesion and is independent of insulin lipodystrophy.

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Yohalem M, Pollack, H. (1949) *J Mt Sinai Hosp* 15, 320

the specialty of physical medicine. But during the last hundred years medicine has been cross-cut by a quite different differentiating factor—namely, the social implications of certain kinds of disease. Those of the mentally sick who were dangerous or offensive to others had long been segregated: with the growth of law and humanitarianism such confinement had to fulfil legal requirements, and the mental hospital system brought into existence a peculiarly limited specialty, presided over by a Government department, the Board of Control. Somewhat similar social considerations led to the segregation of patients suffering from infectious diseases. From this sprang the fever hospitals, the hospitals and clinics for venereal diseases, and the tuberculosis sanatoria. Other specialists who were differentiated by social need were the experts in industrial medicine and hygiene, the school medical officer, the medical officer of health, and the medical Civil Servant in Whitehall.

All these are instances of the differentiation of medicine. Before I consider the advantages and disadvantages of this process let me draw attention to the evidence that for some time now a reverse process of re-integration has been going on. Since the fundamental division was that between medicine and surgery, the most significant reversal of this process is to be found where medicine and surgery have drawn together again. This is the result of a number of factors, especially increasing knowledge of physiology, pathology, bacteriology, and pharmacology, and also increasing specialisation. In many fields the surgeon has drawn nearer to the physician and, reciprocally, the physician has become more of a surgeon. For the surgeon, concentrating his attention increasingly upon disorders of function, is tending to become an operating physician. At the same time the physician, working in much closer collaboration with the surgeon, has had to acquire a greater knowledge of the technique of surgery, even though he never practises it himself. Hence, for example, in gastro-enterology, chest diseases, cardiology, neurology, and to some extent psychiatry there is a considerable ground which is common to both the physician and the surgeon.

A similar fusion of previously separated interests has occurred in the diagnostic field. As the knowledge within a specialty has increased, its demand upon diagnostic radiology has similarly became greater, and it has been found advantageous for cardiologists, chest physicians, and orthopædic surgeons, amongst others, to do some at least of their own diagnostic radiology. This has led to further increases in knowledge, and it has not meant the withdrawal of this specialised work from the radiologist; but, on the other hand, the new knowledge gained has often led to the development of fresh diagnostic techniques which can only be carried out by the physician or surgeon and the radiologist in collaboration. A variant of this process is to be found when the radiologist has himself specialised in a particular branch of medicine or surgery and has brought the knowledge he has thus gained to the enrichment of his radiological technique, as has happened, for example, in neuroradiology.

A quite different method of re-integration of medicine has taken place when a general physician, instead of endeavouring to comprehend as his province all the specialties at all ages, has limited the demands of such generalisation by specialising in patients of a certain age-group. Thus, the pædiatrician at one extreme of life, and the geriatrician at the other, reassert the claims of generalisation and its comprehensiveness in respect of many specialties. Finally, the increasing collaboration between physician and surgeon in various spheres is only an example of a more general tendency towards team-work between different kinds of specialists, which is now a commonplace in diagnosis and treatment.

The Effects of Differentiation

The evolutionary process which I have called differentiation in medicine has produced such a great increase in our knowledge and therapeutic powers that its benefits are too obvious to need elaboration now. Indeed their very magnitude has tended to obscure the price which we have had to pay, and are still paying, for them. The separate development of psychiatry and neurology in this country is an example of this. As I have already pointed out, psychiatry here developed in the remote isolation of the mental hospital, while neurology flourished in two special hospitals and later in the neurological departments of general hospitals. An early opportunity to bridge this gap was missed when the pioneer work of Ferrier, carried out in a mental hospital, failed to develop into any permanent relationship between neurology and psychiatry. The progress of English psychiatry might have been advanced by at least half a century if the genius of Hughlings Jackson could have found disciples in the mental hospital world. As it was, alienists, as they were called, remained caretakers of the incurably insane, while minor mental disorders, and minor degrees of graver ones, were treated chiefly by neurologists. There remained a few consultant psychiatrists outside the mental hospitals, in which they had chiefly gained their experience, who were called in to certify patients. As a consequence the psychological and neurological aspects of mental disorder, biologically indissoluble, were forcibly kept apart; and the new ideas of analytical psychopathology and therapy, when they reached this country after the first world war, were taken up and developed independently of both psychiatry and neurology.

A drawback of a similar kind arises from the isolation in special hospitals of patients suffering from infectious diseases, and the development within this field of a specialty solely concerned with a single disease of a single organ—pulmonary tuberculosis. However important the fact of infectivity may be for a community, it has led to what is otherwise a quite artificial separation of certain diseases from the main body of medicine—diseases which in general, and even in spite of their being infectious, may have less in common amongst themselves than they have individually with other diseases treated in general hospitals. Both general medicine and the artificial specialties of fevers and tuberculosis have been impoverished by this separation, and the disadvantages have extended also to nursing.

The division of medicine and surgery into specialties based upon anatomical systems, though it has produced a rich and ever-growing harvest of fresh knowledge, has led also to the existence of gaps between such specialties and the general body of medicine and between one specialty and another, the effect of which upon medical science I shall consider in more detail later. It has also created two major problems which confront us today, in medical education and general practice.

For many years the student has had to obtain a limited amount of his medical teaching and experience in institutions outside his teaching hospital—for example, courses of lectures and demonstrations at mental hospitals and fever hospitals. This was not only geographically inconvenient but inevitably caused the student to feel that mental disorders and infectious diseases were events outside the run of ordinary practice, and in which he seemed likely to be concerned only with diagnosis and disposal. These, however, had been regarded as separate branches of medicine so long that their relative isolation was taken for granted. Until after the first world war, however, there were very few special departments in the teaching hospitals. Since then so many have come into existence that the student now has to obtain much of his experience and teaching in depart-

ASCORBIC ACID, GLUCOSE-1-PHOSPHATE, AND LYSERGIC-ACID DIETHYLAMIDE IN RHEUMATOID ARTHRITIS

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Long and Miles (1950) found that cortisone and adrenocorticotrophic hormone (A C T H) diminished experimental tuberculin hypersensitivity in the guineapig Postulating a possible analogy between this form of allergy and the tissue reaction in rheumatoid arthritis, Long et al (1951b) suggested that other factors influencing experimental tuberculin hypersensitivity might also influence arthritis in man They described several such factors (Long et al 1951a and b, Fisher et al 1951, Cornforth and Long 1952) In man we found that cortisone and A C T H diminished the tuberculin reaction more conspicuously than other inflammations studied, and we considered the possibility that this reaction might reflect the nature of the disease process in rheumatoid arthritis (Lovell et al. 1953) We therefore tried to discover if some of the factors shown by Long and his colleagues to effect experimental tuberculin hypersensitivity influenced rheumatoid arthritis, we also studied their effect on the tuberculin reaction in man We report these studies here

Long et al (1951a) suggested that, in guineapigs, the desensitising action of cortisone and A C T H was mediated by an indirect effect on the metabolism of ascorbic acid In laboratory animals deficient in ascorbic acid but not clinically scorbutic, fed on a synthetic pelleted diet, sensitivity to tuberculin was high and could be diminished by giving ascorbic acid but not by giving the hormones The hormones did not enhance the desensitising action of ascorbic acid If tuberculin sensitivity in the guineapig and rheumatoid arthritis in man were analogous, and the mode of action of cortisone and A C T H was comparable in the two conditions, a deficiency of ascorbic acid might be expected to enhance the inflammation in rheumatoid arthritis and at the same time to diminish the responsiveness of the disease to the hormones In a state of depletion of ascorbic acid, treatment with ascorbic acid might diminish the activity of the arthritis In our first study we examined these possibilities

Our second study was of the effects on rheumatoid arthritis and tuberculin reactions of two substances which modified experimental tuberculin hypersensitivity in the guineapig—namely, glucose-1-phosphate and lysergic acid diethylamide (L S D) Cornforth and Long (1952) found that tuberculin sensitivity in guineapigs was reduced by a subcutaneous injection of glucose 1 phosphate 0 01 mg per kg body-weight and by L S D 0 00018 mg per kg body-weight We are not aware of any reports of the effects of glucose 1-phosphate in man The effects of L S D both in normal and in psychopathic patients have been reported by several workers—e g, Rinkel et al (1952) It causes transient mental changes and disturbances in the autonomic nervous system The effects have sometimes been observed with doses as small as 0 02 mg , and 0 04–0 1 mg is reported to be active in most cases, though individual variation in responsiveness seems to be great

Methods

Ten patients studied had active rheumatoid arthritis, and one had polyarteritis nodosa with predominant involvement of the joints All were treated by rest in bed, controlled exercises, and, when necessary, splinting of acutely inflamed joints

All the patients received acetylsalicylic acid ('Disprin'), gr 30–60 daily, and sometimes tab codeine co *B P* We have found in man that tuberculin reactivity is unaltered by salicylates, and Long (1952) has found salicylates to be without effect on tuberculin sensitivity in guineapigs Salicylates do not modify the beneficial therapeutic effects of cortisone and A C T H We did not therefore feel justified in withholding these analgesics Their use, however, implies a more severe test of factors possibly giving mild relief of symptoms in arthritis than would have been imposed if they had been withheld,

TABLE I—SUMMARY OF RESULTS OF ASCORBIC-ACID STUDIES

Patient	Study	Régime	Duration in weeks	Blood ascorbic acid (mg per 100 ml)	Course of arthritis
1	A	(*a*) Ordinary diet		0 3	
		(*b*) Scorbutic diet	11	0 3→<0 1	
		(*c*) Scorbutic diet + 1 g ascorbic acid daily	5	2 1–2 5*	
		(*d*) Scorbutic diet + 1 g ascorbic acid daily + cortisone	1½	1 9	
		(*e*) Ordinary diet + ascorbic acid 1 g daily	2	2 1	Relapse lasting 2 weeks
	B	(*a*) Scorbutic diet	10	2 1→<0 1	Fluctuating
		(*b*) Scorbutic diet + cortisone	3 }	<0 1	Conspicuous improvement
		Scorbutic diet + A C T H	3½ }		
		(*c*) Scorbutic diet	4	<0 1	Relapse after 3 weeks
		(*d*) Scorbutic diet + 0 5 g ascorbic acid daily	1	1 9*	Relapse continued
		(*e*) Ordinary diet	8		Relapse continued 3 weeks, *then* improvement
2	A	(*a*) Ordinary diet		0 4	
		(*b*) Ordinary diet + 100 mg ascorbic acid daily	3	1 0–1 3	Slight improvement
		(*c*) Ordinary diet + 100 mg ascorbic acid daily + cortisone	2	0 9–1 2	Conspicuous improvement
		(*d*) Ordinary diet	6		Relapse after 4 weeks
	B	(*a*) Scorbutic diet	9	0 13→<0 1	Fluctuating
		(*b*) Scorbutic diet + cortisone	3 }	<0 1	Conspicuous improvement
		Scorbutic diet + A C T H	3 }		
		(*c*) Scorbutic diet	1	<0 1	Moderate relapse
		(*d*) Scorbutic diet + 0 5 g ascorbic acid daily	1	1 4†	Unchanged
		(*e*) Ordinary diet	8		Unchanged
3		(*a*) Ordinary diet		0 3	
		(*b*) Scorbutic diet	9	0 3→<0 1	Unchanged
		(*c*) Scorbutic diet + 1 g ascorbic acid daily	2	1 9	Unchanged
		(*d*) Scorbutic diet + 1 g ascorbic acid daily + A C T H	3½	1 6	Conspicuous improvement
		(*e*) Ordinary diet			Relapse after 3 weeks

* Attained with 3 g ascorbic acid † Attained with 2 5 g ascorbic acid

ments which, except that they are under the same roof, are sometimes almost as much differentiated from the general body of medicine as the mental hospital and the fever hospital of the old days. The problems which this creates for medical education are becoming well recognised. Moreover, the more complex and difficult medicine becomes, the greater the tendency to send patients who constitute obscure diagnostic problems to centres where the necessary investigations can be carried out, and except for the special hospitals these are almost invariably at teaching hospitals, which in consequence receive a disproportionately large number of rare and difficult cases. Then, as the number of special departments increases, the time which the student can spend in each of them necessarily grows less, so that the question arises whether periods of a month or six weeks spent successively in a number of special departments possess the same educational value as three months, or longer, spent on individual medical and surgical firms. Another teaching drawback arises from the fact that a student attending a special department deals with patients who have already been to some extent diagnostically sifted, so that the curriculum contains less opportunity for him to meet the situations which will confront him in practice, when he has to examine a patient for the first time without any clue as to the system affected and not even knowing whether the condition will turn out to be medical or surgical. Finally, it is widely felt that the increase in our detailed knowledge of individual anatomical systems makes it increasingly difficult to present the student with a concept of the patient as a whole, a point to which I shall return.

But, after all, most students are being educated for general practice, and the differentiation of medicine, which I have been tracing, has created problems for general practice which need to be solved not only for their own sakes, but also because unless we know what should be the future work of the general practitioner we are in no position to educate students for general practice. The effect of the increasing complexity of medicine, particularly of its diagnostic and therapeutic techniques, upon general practice is now so widely recognised that I need not elaborate it: it has led to an overemphasis on the hospital at the expense of the general practitioner, since at present it is only at the hospital that many investigations and the more elaborate treatments can be carried out. It is no part of my present purpose to say what could, or should, be done about this. I merely mention it as one of the by-products of the process of differentiation.

Finally, just at a time when we need all our energies to cope with these fundamental questions, so important for the welfare of medicine as an art and a science, political action has confronted us with an equally difficult set of problems arising out of the transformation of the organisation of medicine in this country. Although the two may at first sight appear independent, I believe that they are closely interlinked. Some reorganisation of medicine, whatever one may think about the precise form it took or the rate at which it was carried out, was necessitated by the very changes in medical science which we have been considering. But we cannot hope to solve the problem of medical organisation until we have discovered the principles upon which medicine should be organised—in other words, until we possess a philosophy of medicine. This cannot be supplied by politicians nor by Civil Servants, but only by ourselves; and until we have it we shall have no adequate defence against political empiricism and administrative bureaucracy.

A Philosophy of the Organism

What, then, should be the basis of a philosophy of medicine? Medicine is a branch of biology, and I believe that its philosophy should be based upon a re-examination of the conception of the living organism as a whole. I have pointed out how large a part differentiation has played in the evolution of medicine during the last hundred years. Sherrington (1947) quotes with approval Herbert Spencer's dictum that integration must keep pace with differentiation, but the same thing was said 80 years ago by that other great neurologist, Hughlings Jackson (1932), himself a disciple of Herbert Spencer. On this very occasion, Hughlings Jackson, delivering the Society's annual oration in 1877, said:

> "As scientific medical research goes on, there is greater specialisation of investigation, just as, in the development of society, there is that continually increasing specialisation, called division of labour. This being so, all the more need is there that there should be greater integration, just as along with division of labour there is need for coöperation of labourers. . . . There is no harm in studying a special subject; the harm is in doing any kind of work with a narrow aim and a narrow mind. Differentiation of medical investigation has led to results of inestimable value. If, in the smallest degree, I succeed in furthering the integration which should quickly follow this necessary differentiation, I shall feel that my address will be of some little value."

If Hughlings Jackson, with foresight in this as in so much else, recognised that need then, how much more necessary is it today that we should achieve an integrative view of the human organism; and this, I believe, must find its applications at the physiological, psychological, and social levels of thought.

Let us first consider the physiological. Visual form exercises a highly determining effect upon our thinking, and no doubt that explains why medicine has tended to divide the body into anatomical organs upon which special branches have been based. Thus, the cardiovascular system, the nervous system, the urinary system are all clear-cut anatomical structures which can be neatly dissected from the rest of the body. We recognise, of course, their physiological aspects, or functions; but we tend to regard functions as secondary or subordinate to form, and this is reflected in our way of speaking, for we speak of the functions *of* a particular organ. What, we ask, does it do? This use of words suggests that there is something, an organ, which exists in some way independently of what it does. This is a perfectly permissible way in which to describe a motor-car. The function of a motor-car is to move from one place to another, but the car continues to exist in the same form when it is at rest and not performing its function. This is not true, however, of the organs of the body; for during life an organ can be separated from its functions only by an artificial abstraction. In the living organism form and function are two aspects of the same thing.

Our tendency to look upon function as subordinate to form has had far-reaching consequences, for this makes it difficult both to think of functions which cannot be fully described as the functions *of* particular organs, and also to conceive of the organism's functioning as a whole.

The American philosopher John Dewey has described the evolution of scientific thought in a way which has, I believe, fertile applications to medicine. Dewey and Bentley (1949) distinguish three historical stages in the development of our ways of explaining the phenomena which we observe. The first is the stage of *self-action.* The behaviour of a body is held at this stage to be self-explanatory: it behaves as it does because that is its nature. The next stage is the stage of *interaction* in which the behaviour of bodies is explained by their mutual relationship, which nevertheless is regarded as leaving each of them essentially unchanged. The third stage is the stage of *transaction.* In this stage we are dealing with an event which involves several constituents for salicylates afford some such relief However, it was against the more conspicuous effects of cortisone and A.C.T.H. treatment that we wished to measure an effect, if any

The arthritis was assessed at least twice a week in the long studies, and daily in the shorter ones, by measurements of heat, swelling, tenderness, and functional capacity of the joints To the patients treated with glucose-1-phosphate and L.S.D., dummy preparations were usually administered for up to 14 days before treatment

Cortisone (Merck) 200 mg daily was given orally in case 1 and by intramuscular injection in case 2 A.C.T.H. (Armour) 100 mg daily was given by intramuscular injection Ascorbic acid (Roche) was given orally

When a scorbutic diet was given, all the cooking was done in copper vessels Fruit, fruit juices, and vegetables were not allowed All the milk was boiled. Potatoes were boiled, mashed, and kept hot for at least an hour before being served Ascorbic acid in whole blood was measured at least once a week by the method of Roe and Kuether (1943)

The α-D-glucose-1-phosphate was prepared by Roche Products Ltd as a solution containing 50 mg of the dipotassium salt per ml The preparation was confirmed by Dr D A Long to be active in reducing tuberculin hypersensitivity in guineapigs Intramuscular and subcutaneous injections caused intense pain this could be mitigated by mixing the solution with procaine hydrochloride, but such a mixture was found by Dr Long to be inactive in the guineapig The glucose-1-phosphate was therefore given intravenously, by intermittent injections, or by continuous intraveonous drip in physiological saline solution The doses ranged from 4 to 800 mg. daily

Lysergic-acid diethylamide was supplied by Sandoz Products Ltd both as a powder and as a liquid Because of its instability, solutions made from the powder were freshly prepared every 5 days, fresh ampoules of liquid were opened for each dose The drug was given by mouth in about 30 ml of water before breakfast Doses ranged from 0·005 to 0·1 mg daily.

Tuberculin reactivity was tested by intradermal injections of serial dilutions of purified protein derivative (P.P.D.); as described by Lovell et al (1953) In patient no 3, the tests were made at intervals of 1–2 weeks In the other cases comparisons were based on between one and four tests done before and during treatment

Eosinophils in capillary blood were usually counted twice weekly and erythrocyte sedimentation rates (E.S.R.) were measured once a week

Results

ASCORBIC ACID

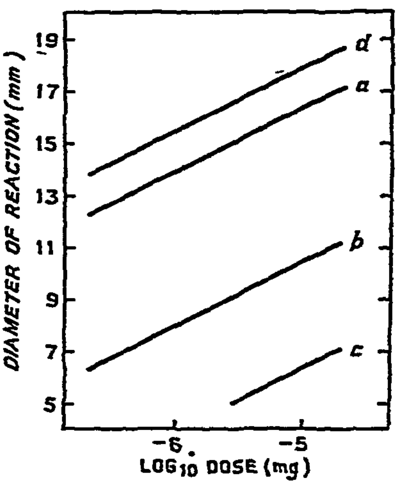
The results are summarised in table I

Patient 1 —Female, aged 34 Active rheumatoid arthritis for 8 months had involved almost all joints. During 11 weeks on scorbutic diet the arthritis improved. When the patient was saturated with ascorbic acid, the trend of improvement (already established) continued, and later there was a conspicuous clinical response to cortisone During a subsequent 10 weeks on scorbutic diet the arthritis fluctuated in severity, but there was no definite trend in its course While the patient was still on scorbutic diet the response to cortisone was again conspicuous and the improvement was sustained during a course of A.C.T.H.

Patient 2 —Female, aged 17 Active rheumatoid arthritis for 2 years affecting fingers, hands wrists elbows, and knees During 9 weeks on scorbutic diet the rheumatoid arthritis fluctuated in severity, but no definite trend was discernible The therapeutic response to cortisone when the patient was depleted of ascorbic acid appeared as full as an earlier response induced when there was no depletion. The disease responded to A.C.T.H. during the 13th to 15th weeks of scorbutic diet Saturation with ascorbic acid after 19 weeks on scorbutic diet, and subsequent return to full diet caused no appreciable change in the course of the disease

Patient 3 —Female, aged 50 Rheumatoid arthritis for 20 years Active inflammation in hands, wrists, right hip, and both knees During 9 weeks on scorbutic diet there was no change in the arthritis which could be attributed to this régime, nor was there one when the patient was saturated with ascorbic acid When the patient was saturated with ascorbic acid the symptoms were improved while A.C.T.H. was given

Tuberculin reactions were studied in patient no 3 At the beginning of the scorbutic diet, P.P.D. solutions weaker than 0·2 mg per ml did not evoke a response and this solution caused a lesion of only 10 mm diameter After a month's scorbutic diet, when the blood-ascorbic-acid level had fallen to about 0·1 mg per 100 ml, the reactivity was increased, a solution of 0·002 mg per ml giving a response just short of necrosis Tests with serial dilutions were made thereafter with 0·0002, 0·00002, and 0·000002 mg per ml (see figure) The reactivity was high when the blood-ascorbic-acid level was less than 0·1 mg per 100 ml, it fell when the patient was saturated with ascorbic acid and it fell further when A.C.T.H. 100 mg daily was given After A.C.T.H. was stopped reactivity rose to approximately the same level that was attained in the scorbutic state, though now the patient was still saturated with ascorbic acid



Patient 3.—Calculated mean parallel regressions of diameters of reactions on log dose of P P D injected during (a) ascorbic acid depletion, (b) ascorbic-acid saturation (c) A.C.T.H treatment, (d) after A.C.T.H For differences between (a) and (b), $0{\cdot}02 < P < 0{\cdot}05$ (b) and (c) $0{\cdot}05 < P < 0{\cdot}1$ and (c) and (d) $0{\cdot}01 < P < 0{\cdot}02$

Conclusion —Rheumatoid arthritis was uninfluenced by ascorbic-acid depletion or saturation, nor did these factors appear to influence the therapeutic effects of cortisone and A.C.T.H. In one patient reactivity to tuberculin increased during depletion of ascorbic acid, decreased after saturation, and decreased still further when A.C.T.H. was given When A.C.T.H. was withheld the reactivity to tuberculin rose to a level comparable to that attained during the period of ascorbic-acid depletion

GLUCOSE-1-PHOSPHATE

Patient 4 —Male, aged 47 Active rheumatoid arthritis for 3 years Main disability now due to inflammation in the knee-joints Glucose 1 phosphate 500 mg in 1 litre of physiological saline solution was given daily for 8 days by intravenous drip Each infusion lasted 12–16 hours There was no modification of the arthritis, which had improved conspicuously in the first 8 days of cortisone administration a year earlier Tuberculin reactivity was not changed significantly (table II), though it had been reduced about 100 fold during previous cortisone treatment (case 6 in paper by Lovell et al 1953)

Patient 5 —Male, aged 56 Active rheumatoid arthritis for 6 months involving mainly fingers, hands, wrists, and knees Received six intravenous injections of glucose-1-phosphate in doses of 10, 20, 50, 100, 200, and 200 mg There was no subjective or objective change in the arthritis Injections of 100 and 200 mg caused rigors owing to a pyrogen in the solution injected which cannot be treated in isolation from the event or from each other.

The characteristic feature of our present epoch in medicine is the growing significance of the idea of transaction. Many of the most important things that happen in the body can no longer be explained simply as the result of the interaction of two or more organs, but require the conception of a dynamic transaction which itself integrates the activities of the organs. Let me illustrate this. The electrolyte balance is equally vital to the life of the organism, and to the activity of all the tissues. The behaviour of the electrolytes in the body is the result of a complicated set of transactions involving the intake of fluid and salts, exchanges between the blood and tissues, the secretions of the suprarenal cortex, the excretory function of the kidneys, and many other factors. In these processes the constituents which I have mentioned are themselves affected by what goes on. We are here dealing, therefore, not with the interaction of unchanging objects like billiard balls, but with events which can only be expressed in transactional terms. In other words, though physiology and pathology have to take account of what is happening in individual organs, the transaction as a whole is the more important and unifying factor.

It is easy to find examples of the importance of the transactional view in every department of medicine. Hypertension due to unilateral renal damage, as Wilson showed in his recent Oliver-Sharpey lectures, is the outcome of the interplay of the two kidneys (each of which behaves differently), the suprarenal cortex, the electrolyte balance, and, of course, the cardiovascular system; and there are probably other unknown factors concerned. The bones, so hard and firm that they positively symbolise rigidity, are maintained by a continuous metabolic give-and-take which involves the dietary consumption of calcium and vitamin D, their absorption from the intestines, the power of the kidneys to eliminate calcium or to withhold it, and the influence of the parathyroids upon the whole. Hence it is equally artificial to describe renal rickets as a disease of the bones or as a disease of the kidneys, and the simplest fracture needs to be considered not merely as a response of a rigid structure to stress, but as possibly reflecting dietary insufficiency or defective metabolic function. Ogilvie (1953) has recently pointed out that there are at least four varieties of duodenal ulcer which differ in their ætiology: in other words, they are the outcome of the disorder of different kinds of bodily transaction; and it is possible, indeed that even pathologically identical peptic ulcers in different individuals are the result of different kinds of transactional disorders depending upon the different constitutions of the sufferers. If so, we are not entitled to infer, even from a common pathology, a common ætiology. The discovery of the first vitamin, an "accessory food factor" essential to health, was deceptive in its simplicity, but it introduced us to a biochemical world of astonishing complexity. Not only have we to take into account dietary intake, absorption, storage, and delivery of vitamins to the tissues, but in the tissue cells themselves the vitamins are integrated into most complicated chemical processes. Lack of vitamins may generate toxins: toxins may impair the utilisation of vitamins; and we are still far from understanding the full range of the interrelationships of vitamins with the endocrine glands. The importance of hereditary factors in the ætiology of disease is increasingly recognised, and transactional approach seems essential if we are to interpret the interplay of genetic endowment with the environment of the individual and his own initiative in dealing with both.

Returning, now, to the relation between form and function, we see that the units with which the doctor has to deal are not individual organs, carrying out particular functions, but highly complex functional transactions which can only be properly understood as functions of the organism as a whole. The visual form of an organ is a deceptive unity, and to ask what are the functions of the suprarenal is an examination question at a level of scientific thought which is in reality outmoded. The suprarenal produces a variety of chemical substances which influence the circulation, the electrolyte balance, sexual activity, and many other functions of the body; but it has only a geographical unity, like that of a factory which turns out parts for aeroplanes, vacuum cleaners, and mowing-machines. Our emphasis upon the individual organ arises partly from the dominant influence of visual form upon our thinking, but even more perhaps from the fact that so much of our time, whether as physicians or surgeons, is spent in dealing with what we call disease of an organ; but by the time an organ is diseased we are looking at the end-results of the breakdown of a complex set of transactional functions in which that organ is normally involved.

The transactional view shifts the emphasis in space from the diseased organ to the functional disorders of which it is a manifestation, and in time from the stage at which the organ is already diseased to the earlier stage at which the functional disorder has not yet led to permanent structural change. For example, it transfers attention from myocardial infarction to those unknown transactional disorders which produce atheroma, and which, in particular cases, determine its predominantly selective incidence upon the coronary arteries. Research has thus to turn from the simple and tangible—the organ which is literally tangible at operation or autopsy—to the complex intangible and ever fluctuating interplay of functions.

Medicine and the Mind

There is one sphere of thought in which the relationship between form and function raises quite peculiar difficulties, but is of unique importance—I mean the body-mind relationship. It is a curious paradox that at a time when the influence of the mind upon the body is more generally and profoundly recognised than it has ever been before, the predominant philosophies of the age regard mind as an outmoded concept. Today there are philosophers who make their living by expounding the non-existence of their own minds, and there are others who seem to regard mind as a slight logical indecency—a word which, though it may slip out now and again, must be hastily apologised for. I do not propose now to discuss in detail the age-long controversies which have raged, and still rage, around this topic.

There are two reasons why the body-mind relationship assumes great importance for a philosophy of medicine. The doctor has unique opportunities of observing the correlations which exist between states of mind and states of body, and which range from the broad experiences of everyday practice to the more precise studies of the neurologist and psychiatrist. These observations provide data which any philosophical theory of the relationship between body and mind must take into account. But, in addition, such a philosophical theory is of great practical importance for us as doctors; for until we understand better than we do the logical relationship which exists between our description of states of mind and our account of their corresponding neurophysiological states we shall not be able to think clearly about the way in which we ought to speak of states of the brain causing states of mind and conversely.

Pragmatically, as practising doctors, we do believe in the mind and we do assume a two-way relationship between mind and body. We accept the fact that when spirochætes attack the ganglion cells of the cerebral

Patient 6.—Male, aged 46. Rheumatoid arthritis for 7 years, and a severe relapse for past 3 months with active inflammation in fingers, hands, shoulders, hips, and knees. Glucose-1 phosphate 100 mg. was given intravenously twice daily for 4 days and 200 mg. twice daily for 3 days. There was no subjective or objective change in the arthritis and no significant change in tuberculin reactions (table II).

Patient 7.—Male, aged 52. Polyarteritis nodosa for 5 years, involving mainly the joints and skin. A maintenance dose of cortisone 50 mg. daily was incompletely suppressing the arthritis, which was most conspicuously active in wrists and knees. Intravenous glucose 1 phosphate 1 mg. was given four times daily for 1 day, 100 mg. for 3 days, and 200 mg. for 3 days. There was no subjective or objective change in the arthritis, though, when the treatment was stopped, there was relief of pain with objective improvement 4 days after the dose of cortisone had been increased to 100 mg. daily.

Conclusion.—In the doses used glucose-1-phosphate did not influence the course of the arthritis in four patients or the size of the tuberculin response in the two patients tested. No effects were discerned on eosinophil-counts or E.S.R.

LYSERGIC ACID DIETHYLAMIDE

Patient 8.—Female, aged 39. Active rheumatoid arthritis for 18 months, with inflammation mainly in hands, wrists, shoulders, and right knee. Subjective improvement in the arthritis took place during a fortnight's observation on dummy medicine. L.S.D. was given for 9 days, starting with 0.005 mg. and increasing to 0.025 mg. daily. The patient was troubled by flushing of the face during treatment. Subjective improvement continued, but there was no objective change in the joints.

Patient 9.—Male, aged 33. Rheumatoid arthritis for 4 years, and a relapse of 2 months' duration. Wrists, finger, elbow, shoulder, and knee joints were inflamed. L.S.D. was given for 11 days, starting with 0.025 mg. and increasing to 0.1 mg. daily. There were no side effects, no objective change in the arthritis, and no significant change in tuberculin reactions (table II). This patient had shown a conspicuous therapeutic response to A.C.T.H. during an episode of active arthritis a year previously.

Patient 10.—Female, aged 52, had 10 years' history of active rheumatoid arthritis with advanced structural changes in many joints. Active inflammation in the wrists and knees. L.S.D. was given for ten days, starting with 0.025 mg. and increasing to 0.1 mg. daily. No side effects and no subjective or objective changes in the arthritis were observed.

Patient 11.—Male, aged 23. Acute polyarthritis for 10 months and bronchiectasis. Acute inflammation in hands, wrists, elbows, shoulders, hips, knees, and feet. L.S.D. was given for 11 days, starting with 0.025 mg. and increasing to 0.1 mg. daily. Conspicuous dilatation of the pupils developed during treatment. There were no subjective or objective changes in the arthritis. The size of the tuberculin reaction was not significantly changed (table II).

TABLE II—CHANGES IN DIAMETERS OF TUBERCULIN REACTIONS DURING TREATMENT

Patient	Treatment	Mean lesion diameter before treatment (mm.)	Change in diameter during treatment ± standard error	*Significance*
4	Glucose 1 phosphate	11.5	+1.5 ± 0.9	0.3 < P < 0.4
6	Glucose 1 phosphate	16.7	+1.7 ± 2.5	0.5 < P < 0.6
9	Lysergic acid	9.4	+1.3 ± 1.3	0.3 < P < 0.4
11	Lysergic acid	12.7	−1.0 ± 2.3	0.6 < P < 0.7

Conclusion.—In the doses used L.S.D. did not influence the course of rheumatoid arthritis in four patients or the size of the tuberculin reaction in the two patients tested. No effect was evident on eosinophil counts or the E.S.R.

Discussion

Although cortisone and A.C.T.H. diminish both experimental tuberculin hypersensitivity and the inflammation in rheumatoid arthritis, the disease has proved to be unaltered by other factors affecting experimental hypersensitivity. The degree of ascorbic acid saturation appears to be without influence on the disease, or on its responsiveness to cortisone and A.C.T.H., and glucose-1-phosphate and L.S.D. have no discernible cortisone-like effect, even in doses proportionally greater than those which diminish experimental hypersensitivity. These studies therefore provide no evidence to support an analogy between experimental tuberculin hypersensitivity and the tissue reaction in rheumatoid arthritis. On the other hand, because of the difficulties inherent in duplicating experimental conditions in man and the guineapig, such an analogy is not refuted. In the ascorbic acid studies especially, there were the inevitable differences in the basal diets.

In patient no. 3 the trends of change in the tuberculin reactions during ascorbic acid depletion and saturation were comparable to those described in guineapigs (Long et al. 1951a). We should hesitate, however, to conclude, from this single observation, that the changes observed were not fortuitous, for we have not previously studied tuberculin reactivity so long in untreated persons. The possibility of an association between ascorbic acid saturation and tuberculin reactivity in man merits further study.

Though cortisone and A.C.T.H. diminish the tuberculin reaction in both the guineapig and man, the reaction in man appears to be uninfluenced by glucose 1-phosphate and L.S.D., which have cortisone-like effects in the guineapig. We have therefore been unable to test the possibility that substances other than cortisone and A.C.T.H., which diminish the tuberculin reaction in man, may also affect the tissue reaction in rheumatoid arthritis. The study in patient no. 3 has confirmed our earlier impression that there is ordinarily no correlation between the level of tuberculin reactivity in a given person and the activity of the arthritis.

It is possible that the means by which cortisone diminishes the tuberculin reaction are different in the guineapig and in man. Though the dose used by Long and Miles (1950) in guineapigs was, on the basis of weight, comparable to that which we found necessary to reduce the tuberculin reaction in man (Lovell et al. 1953), the resulting reduction in reactivity in the guineapig was about 4-fold, whereas in man the reduction ranged between 15-fold and 170 fold. However, the variability in species responses to the hormones, and the fact that Long and his colleagues usually confined their observations to effects attained within a few hours of single injections of hormones, make comparison in the two species difficult.

Long and his colleagues have interpreted the cortisone effect in the guineapig as reflecting a reduction in its hypersensitivity. Some support for this thesis has been provided by Leahy and Morgan (1952), who found that cortisone inhibited the cytotoxic action of tuberculin on sensitised guineapig cells in vitro. The means whereby cortisone diminishes the tuberculin reaction in man has not been identified. In the doses we used we found that the inflammation evoked by a direct irritant, manganese butyrate, was also reduced by cortisone, and a similar effect has been described on the inflammation evoked in human skin by ultraviolet light (Järvinen 1951). Possibly therefore, the action of cortisone on the tuberculin reaction in man reflects, at least in part, a non-specific diminution of an inflammatory response, rather than an interruption of the immunological mechanism which initiates a hypersensitivity reaction.

Summary

The effects of some factors which modify experimental tuberculin hypersensitivity have been studied in patients with rheumatoid arthritis.

Ascorbic acid depletion and saturation did not influence the course of rheumatoid arthritis or the therapeutic effects of cortisone and A.C.T.H.

cortex the mind is damaged, and we know that mental stress and anxiety influence the functions of the body and may in time lead to disorder of its structure. Nevertheless, in the past, and at present, a lack of clear thinking about the body-mind relationship has tended to lead to overemphasis upon one or other. On the one hand there have been many dynamic psychologists who have overstressed the psychological and disregarded the physical factors in the causation of mental disease: on the other hand an exaggerated emphasis upon the importance of the physical state of the nervous system has sometimes encouraged a nihilistic attitude to psychotherapy. At present a much more balanced attitude is in general tending to prevail. It is recognised that a depression can usually be most readily abolished by attacking its physical basis, empirically, by electrical convulsant therapy: on the other hand, even though it be conceded that ideas and feelings have their counterpart in the organisation of the nervous system, it is often impossible to change a patient's ideas and feelings, including their neurological basis, except by presenting other ideas and feelings to his conscious mind. Whatever our philosophical view, then, most of us can agree that mind has a pragmatic importance as a function of the organism.

Some people will say that this is enough: why bother with the philosophical niceties? In the long run I believe it does make a profound difference, not only to individuals, but also to the whole of a culture whether the mind is regarded as being explainable in terms of neurophysiology or not. The man who regards the mind as a function of the nervous system is necessarily analytical in his approach. He seeks to explain the whole in terms of the parts, the parts being the last resort the electrical impulses in the individual neurones, and it makes little difference whether he seeks to explain human behaviour in physiological terms or, like the psycho-analyst, in terms of conflicting psychological drives or other partial mental organisations. Over against these ideas stands the holistic view, which, whether through philosophical reasoning, act of faith, or mere empiricism, still believes that man is more than can be explained as the summation of his nervous impulses or the resultant of his conflicting complexes. This view is unfashionable in some quarters at the moment, but even by a mere pragmatic test it may yet prove a better basis for our understanding of our patients and, indeed, a better foundation for civilisation than the alternative.

Philosophy in Practice

What are the implications for medical thought and practice of a philosophy of medicine based upon the idea of the organism as a whole? Its intellectual climate would permeate the whole of medicine, for it is not a form of thought peculiar to some kind of generalist as opposed to the specialist: on the contrary, it is the essential background of specialism. The specialist needs to look at the whole man from his own particular angle, while the generalist looks at all the angles from the standpoint of the whole man. Dermatology, for example, however superficial its subject matter, has long ceased to be merely skin-deep, for it includes in its scope the whole range of life from the human mind to the filterable virus, a vast external environment, and complex metabolic transactions within the body. But the differentiation of medicine, and the development of specialties on an anatomical basis, has necessarily led first to those discoveries which could most easily be made by observation of the system concerned, while those disorders which involve complex transactions of the whole body often still elude our understanding. Hence, in the field of research a team of varied experts and close liaison between specialties is becoming increasingly necessary.

If we are not to become lost in the increasing complexity of medical science and endless multiplication of facts, we must always keep in mind the need for clarification and simplification by means of general principles. These are essential not only for the instruction of students but also for the continued education of doctors themselves. Nowadays none of us can hope to grasp in detail more than a fragment of the available knowledge: for the rest, when it comes to practice, we have to do what the experts tell us. In this situation the danger is that the inevitable modern emphasis upon techniques will end by making us all for much of the time mere technologists. We can be saved from this only if we understand the basic principles underlying the techniques, and if we can relate them to a philosophy of medicine.

In this context the general physician has, in my view, two contributions, to make which are of peculiar value and which, though distinct, are in no way mutually exclusive. In practice he has to survey the patient as a whole from the diagnostic and therapeutic points of view, while in thought it is he who is at present best equipped to develop and expound the transactional view of medicine. This, however, is a task in which joint discussions can play a most important part, whether by a diagnostic team or a joint round, a clinicopathological conference, a research group, or a medical society meeting.

The education of the medical student must be related to the functions which the general practitioner has to perform in modern medicine. This is a subject which has been, and is still being, much discussed. I wish to deal with only one aspect of it now—namely, how general practice might be animated by the philosophy of medicine which I have been discussing. It is almost a commonplace that the general practitioner is above all the doctor who sees the patient as a whole. He must be an expert in diagnosis over a far wider range than is either necessary, or possible, for any other kind of doctor. In treatment I hope it may be made practicable for him to treat not only minor ailments but a good many of the more serious conditions which do not require to be treated by highly specialised techniques. But the general practitioner above all deals with the patient as a whole man in relation to the environment in which his life is lived, his upbringing, his family life, his work, and his pastimes. He should know him through and through in mind, body, and estate, and no team of experts can ever take his place in the life of the patient.

It follows that undergraduate medical education needs to be the subject of more conscious planning than it has received, or, at any rate, acted upon: it should be designed first to educate the student in the general principles of medicine, and then to teach him their practical applications in the work which he will have to do as a general practitioner. Less than this is inadequate: more, during the undergraduate years, is a work of supererogation.

Finally, we are all, I believe, conscious of the existence of subtle threats to the status of the doctor in the modern community. The causes of these are varied and complex and I shall make no attempt to analyse them now; nor am I at the moment concerned with status as such. Status, however, is related to influence, and if the unique influence of medicine upon the community were to be diminished I believe that something of the greatest value would be lost. But is medicine really unique? That question is being asked in a spirit of scepticism in some quarters today and not only our place in the National Health Service, but the whole development of the service, depends upon how it is answered.

In what sense, then, is medicine unique? By what right do we doctors claim either special authority or the special privileges that go with it? The answer, I think, is simple. Medicine alone takes as its province the whole man. It is not concerned only with his needs α-D glucose-1-phosphate and lysergic-acid diethylamide had no effect on rheumatoid arthritis or on the tuberculin reaction in man

The possibility is discussed that the means by which cortisone diminishes the tuberculin reaction in the guineapig and in man may differ

We gratefully acknowledge the coöperation of the patients taking part in this study We are indebted to the Nuffield Foundation for their generosity in making the grant which enabled these studies to be undertaken, to Merck & Co for their gift of cortisone to the joint committee of the Nuffield Foundation and the Medical Research Council, part of which was used in these studies, and to this same committee for A C T.H , to Dr H. H Green, of the Ministry of Agriculture veterinary research laboratories, for the gift of P P D , and to Dr H M Sinclair for his advice on ascorbic acid estimations We also thank Roche Products Ltd for giving us glucose 1-phosphate, and Sandoz Products Ltd for giving us lysergic acid Finally we are indebted to Prof G W Pickering for his encouragement and to Dr D A. Long for much helpful discussion and for suggesting the trial of glucose-1-phosphate and lysergic acid

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CONTROL OF BLOOD-PRESSURE IN OPERATION FOR PHÆOCHROMOCYTOMA

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THOUGH phæochromocytoma is rare it is being diagnosed more often, and will become increasingly important if it can be shown to be amenable to safe surgical removal Complete and lasting cure of an otherwise fatal disease is thus possible

The subject has been reviewed by Mac Keith (1944) and Walton (1950) in this country, Burrage and Halsted (1948) and Cahill and Aranow (1949) in America, and others

Our purpose in reporting this case is to record the successful control by benzodioxane ('Piperoxane') of the rise in blood-pressure on handling the tumour, and by *l*-noradrenaline (*l*-arterenol) of the fall of pressure after its removal

CASE-RECORD

A married woman, aged 30, was first seen at the medical outpatient clinic in April, 1951 She complained that for the previous six months she had had headaches, usually vertical and coming on towards evening She also had attacks of faintness with loss of power in the limbs and with tingling in the hands After three or four minutes the power would return to the limbs, with simultaneous flushing of the face and pulsation in the head These attacks had become increasingly frequent, occurring almost every other day The headaches had, however improved a little As the attacks became stereotyped, she noticed in addition pallor of the face, arms, and hands, palpitation, aching in the shoulders, cramping abdominal pain nausea, salivation; and sweating Between the attacks she felt perfectly well, though she had recently tended to constipation and increased nocturnal frequency of micturition. Her past history was irrelevant, but she had had infective hepatitis within the previous year and had made a good recovery. She had two children, aged $7^1/_2$ years and 18 months, pregnancy and parturition were normal on both occasions

On examination the patient appeared healthy No abnormality was found on physical examination except a palpable right kidney, the significance of which at the time was doubtful The patient had, however, hypertension (170/120 mm Hg when sitting) Subsequent examination proved that this was persistent, but the blood-pressure was labile and showed changes according to posture—e g, lying 225/125 mm Hg, standing 160/100 mm Hg The patient was admitted to hospital twice for investigation, but the described attacks were not observed. Nothing abnormal was found in the urine Intravenous and retrograde pyelography suggested a deformity of the right renal pelvis, but the changes were minimal The basal metabolic rate was + 15%

The benzodioxane test was made on two occasions by two different observers, the method used was that described by Goldenberg et al (1947) On the first occasion the test was considered positive, but on the second inconclusive

In the absence of a more clear cut diagnosis it was decided to explore the right suprarenal area, and, if no tumour were found, to do the right side of a bilateral thoracolumbar sympathectomy

Operation (Dec 3, 1951)—Premedication with 'Omnopon' gr $^1/_3$ and scopolamine gr $^1/_{150}$ was given. Anæsthesia was induced one and a half hours later with 20 ml of 5% thiopentone and 15 mg of *d* tubocurarine chloride intravenously, and an orotracheal tube was passed Anæsthesia was maintained with nitrous oxide and oxygen, respiration was assisted by manual compression of the rebreathing bag for the first seven minutes To facilitate the rapid administration of benzodioxane and noradrenaline an intravenous-drip infusion was set up

The right suprarenal area was exposed extraperitoneally through the bed of the resected eleventh rib (Fey s incision), and a tumour was found largely taking the place of the suprarenal gland The blood pressure, which had been 160/90 mm Hg before induction, rose immediately the tumour was palpated very gently, but was reduced at once by an injection of benzodioxane (piperoxane) 15 mg into the intravenous tubing close to the vein (fig 1)

Removal was started by ligaturing all vessels at a distance from the gland without manipulating it When it became necessary to lift one pole from its bed to reach the vessels on the posterior aspect, there was a second rise in blood-pressure, which was only halted by a further injection of benzodioxane 15 mg, and a third injection of 13 mg was necessary to reduce it.

The tumour was removed, leaving two small pieces of apparently normal suprarenal tissue, which had been freed from it The blood pressure began to fall at once and was allowed to do so until it reached 110/80 mm. Hg, when the intravenous bottle was exchanged for one to which had previously been added noradrenaline ('Levophed') 8 mg per litre The rate of the drip was adjusted to deliver 8 µg a minute, and this raised the systolic pressure to about 130 mm Hg without materially altering the diastolic pressure

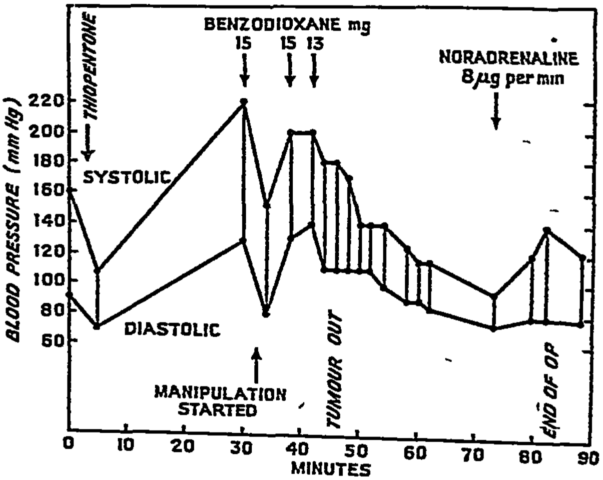

Fig 1—Blood-pressure during operation Premedication was given before administration of thiopentone.

for nursing, or with inquiries into his home circumstances or his difficulties in getting a job when he is disabled, or with this or that form of therapy, or even with him as a "through-put" item in a hospital bed in the health service. It is concerned with all these, but with how much more! With man in all the complexity of his body and mind from his conception to his last breath; and its concern extends increasingly beyond his sicknesses, to the conditions which make it possible for him to lead a healthy and a happy life.

We speak of medicine as both a science and an art, and surely these two aspects are complementary. Science is analytic, explaining, or seeking to explain, the whole in terms of the part: art is intuitive, and sees in the whole something more than can be explained as the sum of its parts. Alike in its comprehensiveness, its balance and, its insight, the medicine which we have inherited from the great masters of the past is unique; and if we remain true to its philosophy we need have no fears for its future.

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TREATMENT OF LUPUS VULGARIS WITH ISONIAZID

REVIEW OF FIFTEEN CASES

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IN May, 1952, encouraging reports appeared of the value of isonicotinic acid hydrazide (isoniazid) in the treatment of pulmonary tuberculosis. It was therefore decided to observe the effects of this drug on lupus vulgaris. Oral administration was considered likely to give the best results with extensive lesions, but local injections also seemed worth a trial for selected patients with single or small lesions. Local injections into the lesions had previously been found to be most effective by one of us (Russell 1951) when using calciferol; and it is useful in a chronic disease such as lupus vulgaris to have alternative remedies and even alternative routes of giving the same remedy, thus overcoming difficulties from gastric intolerance or from the contra-indication of the oral route for some other reason. It may also be possible by local injections to reduce considerably the total dosage given. Thus, thirteen fortnightly injections of 300,000 units of calciferol amount to less than 4,000,000 units for six months' treatment, whereas oral treatment for the same length of time needs over 22,000,000 units.

TREATMENT

There were 15 patients in the survey, of whom 3 had not previously received any treatment for the lupus. 5 patients were given tablets of 'Nydrazid' orally. 6 patients were treated by local injections of 'Rimifon,' and the remaining 4 patients had both oral and local treatment.

At first the oral dosage was 150 mg. daily, but later it was found that greater improvement could be achieved by using a dosage of 300 mg. daily. Because of the rarity of side-effects we have since sometimes used doses of 400 mg. daily for adults.

For local injection a preparation containing 50 mg. of isoniazid dissolved in 2 ml. of distilled water was used. Later, owing to the difficulty of injecting even 2 ml. into small lesions at sites such as the tip of the nose, the strength was increased to 100 mg. per 2 ml. Intradermal injections were made into the whole of a lesion if it were small, or into the same portion of it if it were larger. There was also, to a varying extent, infiltration of the adjoining dermis and subjacent hypoderm. Owing to the pressure needed to give these injections, especially into the increasingly fibrotic tissues as healing progresses, an all-glass syringe was used with a medium-length intradermal needle, special care being taken to prevent separation of the needle from the syringe while giving the injection.

Injections were usually given once a week, the amount injected varying between 50 and 250 mg. in 2–5 ml. of fluid. It is appreciated that, for fair clinical trial of this method, daily injections would be preferable, but this is rarely a practicable proposition, for economic reasons, with ambulant and working patients.

Results

Fully conscious of the fact that, even after prolonged treatment by all remedies used up to the present, the most healthy-looking scar may still harbour live tubercle bacilli, and that it is only permissible to contemplate a "cure" after all signs of active disease have been absent for at least five years, we decided to make a preliminary report of the effects of treatment in 15 patients after nine months' experience of using the drug, the results being classified as follows:

(1) Clinical clearance (4+).—Freedom from all signs of activity: no redness, scaling, infiltration, or "apple-jelly" nodulation.

(2) Marked improvement (3+).—Opacity of lesions, with faint residual scaling or discoloration.

(3) Moderate improvement (2+).—Lesions more opaque and with diminished scaling and discoloration, but with slight residual infiltration.

(4) Slight improvement (1+).—Slight but perceptible diminution of redness, infiltration, scaling, and translucency.

(5) No change (0).

All observations of progress have been controlled by photography, using standardised lighting, exposure, &c., throughout.

Case-records

ORAL ONLY

Case 1.—A woman, aged 44, had suffered from phlyctenular conjunctivitis at the age of 17. At 19 she developed lupus vulgaris on the tip of the nose and on the soft palate. It was treated until she was 32, after which the scar remained sound until a year ago, when further nodules appeared on the left side of her nose. These, in spite of treatment with the Finsen-Lomholt lamp, had slowly increased in number.

Examination showed deformity of the tip of the nose and of the front of the nasal septum due to scarring from former lupus vulgaris. Several "apple-jelly" nodules were present on the mucocutaneous junction of the left naris. Radiography of the chest showed a calcified focus at the left apex, and the erythrocyte-sedimentation rate (E.S.R.) was 8 mm. in 1 hour (Westergren).

Treatment.—Oral isoniazid was given, at first 150 mg. daily for twenty weeks, then increasing to 300 mg. daily for the next twelve weeks.

Result.—After four weeks' treatment all the nodules were less prominent, and after twenty weeks minimal scaling remained. At the end of thirty-two weeks there was no clinical sign of activity, but treatment was continued. (4+.)

Case 2.—A woman, aged 52, had suffered during late childhood from spinal caries with a psoas abscess, and from a tuberculous elbow-joint; both conditions had remained inactive for many years. When she was 15 she developed "abscesses" on each side of the face, followed at 21 by red patches on both cheeks; these had gradually spread, especially during the past five years.

On examination the face was covered with confluent lupus nodulation from the level of a line drawn from the bridge of

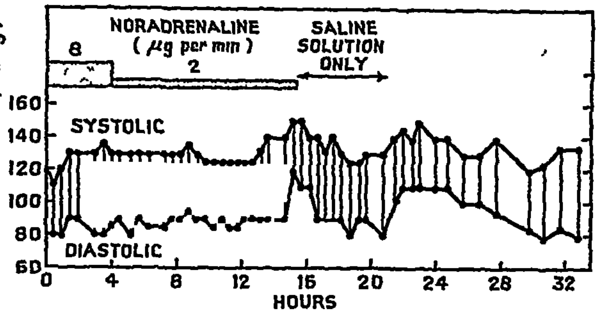

Fig 2—Postoperative blood pressure

The blood-pressure, which had been estimated as far as possible every two minutes during the operation, was recorded at five minute intervals thereafter for three hours, and subsequently at longer intervals For the first four and a half hours the same dosage of noradrenaline was continued, but, as the pressure gradually rose, the dose was reduced to 2 µg a minute, and this substance was discontinued altogether after a further eleven hours (fig 2)

Postoperatively the patient had a mild atelectasis, which rapidly resolved, and she left hospital on the twelfth post-operative day She was seen regularly until she left the district after six months At that time her blood-pressure had stayed steady at about 130/90 mm Hg since the operation and ten months after operation she reported that she remained entirely free from symptoms

Pathology—The excised tissue consisted of a rounded tumour measuring 6 × 4 × 3 cm, across which was stretched a thin layer of suprarenal tissue The microscopical appearances were typical of a chromaffin suprarenal tumour Unfortunately a biological assay was impossible

DISCUSSION

The original diagnosis was made tentatively from the history of the characteristic attacks Little support was gained from physical examination or from the doubtful results of the pharmacological test Despite admission to hospital no opportunity presented itself for a reliable observer to witness a paroxysm and therefore to detect any change in the blood-pressure Tests which depend on provoking an attack of hypertension were considered unsafe These included the histamine test of Roth and Kvale (1945), starvation, injection of adrenaline, and pressure on the supposed site of the tumour, although the latter procedure might have given valuable evidence of its presence and situation The insufflation of air round the kidneys was deemed unsafe

Both false-positive and false negative results of the benzodioxane test have been published (Dana and Calkins 1949, Goldenberg and Aranow 1950, Wilson 1950, Conley and Junkerman 1951, Soffer 1952, Tulloh 1952) Goldenberg and Aranow (1950) mention the possibility, in the case of false-negative results, that the dose of benzodioxane might be too small, and this may explain the different findings in the two tests in our case

The same considerations apply to the use of benzodioxane during operation, and the dosage (15 mg), which was calculated for our patient from the makers' table, need not necessarily be suitable for another person This dose produced an immediate fall in the initial rise of pressure, but did not protect for more than five minutes against a further rise when the tumour was handled Repetition of the same dose became necessary during the subsequent fifteen minutes before the tumour was removed, and there did not appear to be any cumulative action We were impressed by the prompt rise of pressure on minimal handling of the tumour, indicating its high degree of activity

Swan (1951) and Pantridge and Burrows (1951) used 'Dibenamine' to control excessive rise of blood-pressure, but the long action of this agent seems to render it less suitable than benzodioxane for use during operation

Bartels and Cattell (1950) attribute hypotension and collapse after removal of the tumour to left ventricular failure from excess of circulating adrenergic substances, but the satisfactory results obtained where noradrenaline has been used in the hypotensive phase strongly support the generally accepted view that hypotension results from sudden deprivation of these substances (Swan 1951, Pantridge and Burrows 1951)

Cases have been recorded (Crowther 1951) in which the hypotensive phase was treated with adrenaline infusion It seems to us that the side actions of adrenaline, which are known to vary from patient to patient, may be undesirable In particular, the rise of blood pressure from adrenaline is obtained partly at least by increase of cardiac output, and not necessarily by pure increase in the peripheral resistance Though some patients may respond satisfactorily to adrenaline, noradrenaline is theoretically the preferable agent because it probably constitutes the major part of the active material of which the patient has been deprived (Goldenberg and Aranow 1950, Crowther 1951, Pantridge and Burrows 1951, Swan 1951)

SUMMARY

Phæochromocytoma was successfully treated by surgical removal

The blood-pressure was satisfactorily controlled both during and after operation by benzodioxane and noradrenaline

These agents may reduce the risks in treating this disorder

The levophed (*l* noradrenaline) used in this case was provided by Bayer Products Ltd shortly before this drug became ordinarily available

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THE ADRENERGIC AMINES OF HUMAN BLOOD

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A FLUORIMETRIC method for the estimation of adrenergic amines in plasma has recently been described (Weil Malherbe and Bone 1952a), in which the amines are first isolated by adsorption on a column of alumina (Lund 1949) and then, after elution, treated with ethylene diamine (Natelson et al 1949) to form relatively stable fluorescent condensation products The method estimates the sum total of adrenaline and noradrenaline It was, however, noticed at an early stage that the condensation product formed from adrenaline differed in fluorescence from the noradrenaline derivative, the fluorescence of adrenaline being from yellow to orange and that of noradrenaline green We realised that this difference could be used as the basis of a differential the nose to the upper border of both ears, and extending downwards to the mid-neck and on to the shoulders posteriorly. Both pinnæ were involved, but the distal third of the nose, the circumoral region, and the nape of the neck were unaffected. There was no evidence of active tuberculosis elsewhere, and the E.S.R. was 44 mm. in 1 hour.

Treatment.—She was given isoniazid by mouth 150 mg. daily for six weeks, after which she was given 300 mg. daily for twenty-four weeks. She was also given general carbon-arc baths five times a week over the whole period, the face being shielded from the rays.

Result.—After two weeks' treatment the nodules were noticeably flatter, and after four weeks all the affected areas were paler and the nodules were becoming more discrete. Pigmentation had appeared, especially on the neck. By six weeks the affected area was considerably paler, the colour altering from deep reddish purple towards brown. The lesions have continued to involute slowly, in places leaving discrete brown pigmentation with atrophy, while elsewhere a reticulated pattern of erythema and pigmentation remained. At the end of thirty weeks' treatment, although there were still active nodules on the lobes of both ears and over the angles of the jaw, there was great diminution of infiltration and many areas no longer showed any activity. The E.S.R. had fallen to 18 mm. in 1 hour. (3+.)

Case 3.—A man, aged 54, gave no past history of other forms of tuberculosis. At 24 he noticed a tender spot on the upper edge of the right pinna with silvery scales, which he attributed to frostbite. The condition spread to involve the whole pinna about three years ago. While he was in hospital eighteen months ago for treatment of pneumonia, penicillin ointment was applied to his ear, causing a dermatitis medicamentosa.

Examination showed that the lupus was confined to the right pinna, there being a dusky erythema of the free border and lobe, with œdema, "apple-jelly" nodules, and scaling. There was a small fissure in the postauricular fold. Radiography of the chest showed scattered calcified healed foci: the E.S.R. was 32 mm. in 1 hour.

Treatment.—The patient was given oral isoniazid 100 mg. daily for a week, after which he noticed that the lobe was less swollen and no longer painful to touch. The dosage was increased to 300 mg. daily and this has been continued for thirteen weeks.

Result.—Six weeks after the start of treatment the œdema had subsided, the cracks had healed, and all the nodules were flatter and more discrete. After ten weeks' treatment minimal scaling remained and the ear was returning to its normal colour. (3+.)

Case 4.—A man, aged 48, had suffered from a tuberculous left knee-joint which had been ankylosed surgically. At 14 he developed lupus vulgaris, which spread and involved the right side of the nose and the chin-strap area as well as the palate and uvula. He had been treated for considerable periods with the Finsen lamp and had lived two years in a sanatorium. His recent relapse followed a period of twelve years without supervision or treatment.

On examination there was active lupus vulgaris involving the right side and tip of his nose, with nodules and scaling—the chin-strap area showed much scarring from previously treated lupus, among which were active nodules and scaling. The hard palate, soft palate, and uvula showed active tuberculosis, and there was a small cluster of "apple-jelly" nodules within the hair-line over the occiput. The E.S.R. was 6 mm. in 1 hour.

Treatment and Result.—He was given isoniazid 300 mg. daily by mouth, and after four weeks' treatment the most recent lesions, on the nose and over the occiput, were paler. After eight weeks the throat was no longer painful, but brownish nodules could be seen on the palate. Eighteen weeks after the start of treatment the nodules were much flatter and scaling was diminishing. (2+.)

Case 5.—A woman, aged 68, had tuberculous abdominal glands excised when she was 32. She has had extensive lupus vulgaris, since the age of 36, involving the greater part of her face. This has been treated with long courses of Finsen light and improved, but never with complete clearance of active lesions. She had proved intolerant of calciferol on three occasions. Radiography of the chest showed an old calcified focus at the left apex. The E.S.R. was 9 mm. in 1 hour. At the time of starting isoniazid orally she had had six weeks' rest from Finsen-Lomholt treatment. Over the face there were scattered nodules of lupus amidst extensive scar tissue resulting from past treatment. The most active lesions were on the nose, upper lip, and left supra-orbital ridge.

Treatment consisted of isoniazid 150 mg. daily for eight weeks, followed by 300 mg. daily for twenty weeks. At first she complained of indigestion, but this soon passed off. There was a history of duodenal ulceration.

Result.—After six weeks all the active areas were paler and the nodules flatter; there was general well-being, and the patient had less dread of mixing in public. When treatment had continued for twenty-eight weeks, almost all the scaling had cleared, the erythema had given place to pigmentation, and those nodules which persisted were much flatter. (1+.)

INJECTION ONLY

Case 6.—A man, aged 41, had from an early age a rash on his left elbow, which increased in size when he was 9. Owing to absence of pain or irritation no treatment was undertaken until he was 34, when lupus vulgaris was diagnosed and treated with the Kromayer lamp, with improvement until he defaulted. Three years ago he attended another hospital, where he was treated with calciferol, and some improvement followed a two-year course of treatment. Five months ago he first attended the London Hospital and was treated for a short time with the Finsen-Lomholt lamp, with some improvement.

Examination.—The active lesions covered an area 10 × 7·5 cm. just proximal to the tip of the elbow; scaling and "apply-jelly" nodulation were present amidst scar tissue. Radiography of the chest was normal, and the E.S.R. was 5 mm. in 1 hour.

Treatment consisted of weekly injections of isoniazid 50 mg. in 2 ml. of water into part of the lesion for eighteen weeks, followed by 200 mg. in 4 ml. for nine weeks.

Result.—Pallor and diminution in scaling were noted after the first three injections, and steady resolution has occurred since then, lesions near the site of injection clearing more rapidly than those at a distance. After twenty-seven weeks' treatment the skin was pale, supple, and free from scaling, with only a few remaining discrete flat nodules. (3+.)

Case 7.—A woman, aged 47, developed a localised area of lupus vulgaris below the left ear at the age of 39 and was treated elsewhere with calciferol. The condition extended locally, and she attended the London Hospital five years ago, but after only six treatments with the Finsen-Lomholt lamp she did not attend again until nine months ago, when a further attempt to give ultraviolet therapy had to be abandoned owing to a severe reaction.

Examination showed active lupus with prominent nodules, but minimal scaling over the lobe of the left ear with slight extension to the face nearby and to the scar of a former mastoidectomy operation. A radiograph of the chest was normal, and the E.S.R. was 12 mm. in 1 hour.

Treatment consisted of weekly local injections of isoniazid 50 mg. in 2 ml. of distilled water for twenty weeks, followed by 100 mg. in 2 ml. for seven weeks, the course of treatment being temporarily interrupted on three occasions owing to failure to attend.

Result.—Erythema and local swelling of the lobe of the ear diminished after two injections, and the nodules slowly decreased in size although they have not entirely disappeared. (2+.)

Case 8.—A man, aged 48, first developed lupus vulgaris on the tip of the nose when he was only 1 year old. It spread slowly, being treated with ointments and plasters. When he was 17 he first attended the London Hospital and was found to have another active lesion on the right arm; both were successfully treated with the Finsen lamp. He remained free from active lupus until he was 38, when a new lesion developed on the upper free border of the left pinna. This was successfully treated with the Finsen-Lomholt lamp. Four years ago there was a further relapse, for which he was given calciferol 100,000 units daily for nine months and intermittently ever since.

Examination showed sound scars on the left side of the nose and on the free border of the left pinna. In a wide area of scarring below the right elbow were discrete nodules and scaling. A radiograph of the chest was normal, and the E.S.R. was 9 mm. in 1 hour.

Treatment and Result.—Local injections of isoniazid 50 mg. in 2 ml. of distilled water were given weekly for twelve weeks. Treatment was then discontinued, because all the nodules had disappeared and only minimal fine scaling remained. (2+.)

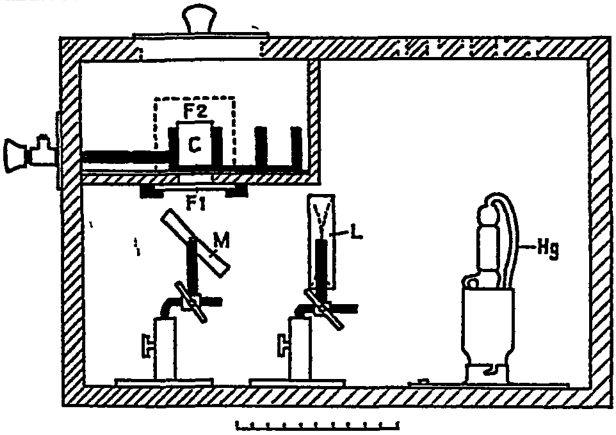

Fig 1—Fluorimeter C, silica cuvette, F_1, primary filter F_2 secondary filter, Hg 125W high pressure mercury-vapour lamp (type MBL/D, British Thomson Houston Co Ltd), L quartz lenses M, mirror

method of estimation, but the fluorimetric apparatus available at the time proved insufficiently sensitive to allow the use of the more specific, and therefore less transparent, colour filters required

It has now been possible to raise the efficiency of the fluorimeter sufficiently to overcome this difficulty Instead of the test-tubes previously used rectangular silica cuvettes (internal dimensions 23 × 23 × 10 mm) are placed closely opposite the window of the photocell box The primary radiation enters through the clear bottom of the cuvette after passing through an efficient condensing system consisting of 2 planoconvex quartz lenses (diameter 2 in, focus 5 4 in) and a first-surfaced microscope mirror (diameter 2 in) with the concave side towards the light The primary filter used (Chance OB 10) virtually isolates the 435 mµ mercury line The apparatus is illustrated in fig 1

PRINCIPLE

At our request the fluorescence spectra of the adrenaline and noradrenaline derivatives were determined by Dr W Jacobson, of Cambridge The strongest peak of fluorescence of the adrenaline derivative was found to be at about 580 mµ, whereas that of the noradrenaline derivative was at about 450 mµ. Measured with a blue green filter (Ilford Bright Spectrum Filter 623) the fluorescence intensities obtained from adrenaline and noradrenaline are almost identical, but measured with a yellow filter (Chance OY4) the adrenaline derivative has a fluorescence about four and a half times as strong as that of the noradrenaline derivative Although the results reported here were obtained with the filter combination mentioned, it may not yet be the best possible one, in fact we are still experimenting with others

Let

m = ratio of adrenaline/noradrenaline fluorescence with yellow filter
n = ratio of adrenaline/noradrenaline fluorescence with blue green filter
A = amount of adrenaline present in mixture
N = amount of noradrenaline present in mixture
y = amount of adrenaline corresponding to fluorescence measured with yellow filter
b = amount of adrenaline corresponding to fluorescence measured with blue green filter

Then the following 2 equations may be set up

$$A + N/m = y \qquad (1)$$
$$A + N/n = b \qquad (2)$$
$$\text{Hence } N = mn\,(b - y)/(m - n) \qquad (3)$$
$$\text{and } A = (y - N)/m = (b - N)/n \qquad (4)$$

EXPERIMENTAL

Procedure

The adrenergic amines are isolated from plasma and the fluorescent derivatives are prepared by the method previously described (Weil-Malherbe and Bone 1952a) Photocell currents are measured with the modified Unicam spectrophotometer Readings are taken first with the yellow filter and next with the blue-green filter Before each reading the instrument setting is adjusted by introducing into the light path in turn the reagent blank and the adrenaline standard and by setting the "transmission" dial at 0 and 100 respectively A second standard, containing 0 2 µg of noradrenaline in 10 ml, is prepared together with the adrenaline standard, and its fluorescence is determined with both secondary filters The values of m and n are determined by dividing 100 by the readings of the noradrenaline standard Under our conditions the following values were obtained (means of 17 observations with standard errors)

$$m = 4\ 44 \pm 0\ 045$$
$$n = 0\ 98 \pm 0\ 003$$
$$mn/(m - n) = 1\ 257 \pm 0\ 006$$

Analysis of Erythrocyte Extracts

After one washing in isotonic saline solution the centrifuged layer of red cells is suspended in distilled water up to the original blood volume (usually about 15 ml) The following solutions are then added (1) 5 ml of a solution containing 2% (*w/v*) sodium fluoride and 3% (*w/v*) sodium thiosulphate, and (2) 0 8 ml of 5% (*w/v*) cetrimide After standing for 30 minutes at room-temperature the stromata are spun off, and the supernatant fluid is prepared for adsorption on a column of alumina by mixing it with an equal volume of acetate buffer and adjusting the mixture to pH 8 4 (cf Weil-Malherbe and Bone 1952a)

Difficulties previously encountered with erythrocyte lysates were mainly due to incomplete hæmolysis This is avoided by the addition of cetrimide Even so, red cells must be worked up while fresh to prevent precipitation of the proteins and the clogging of the alumina columns The addition of the fluoride thiosulphate solution is designed to safeguard the adrenergic amines against oxidation during hæmolysis

Expression of Results

Whereas the results were given in terms of µg per litre of plasma in previous publications (Weil Malherbe and Bone 1952a and b, Liddell and Weil-Malherbe 1953), they are expressed here as µg per litre of whole blood The packed cell volume was determined in hæmatocrit tubes

Recoveries

Recovery experiments were made after adding adrenaline and noradrenaline in various proportions to a mixture of 10 ml of horse serum ('Wellcome Normal

TABLE I—RECOVERY OF ADDED ADRENALINE AND NORADRENALINE FROM HORSE SERUM

Exp no	Addition (µg)		Found (µg)		Error (%)	
	Adrenaline	Noradrenaline	Adrenaline	Noradrenaline	Adrenaline	Noradrenaline
1	0 02	0 10	0 0178	0 1030	− 11 0	+ 3 0
2	0 02	0 10	0 0196	0 0995	− 2 0	− 0 5
3	0 03	0 05	0 0307	0 0518	+ 2 3	+ 3 6
4	0 03	0 05	0 0283	0 0498	− 5 7	− 0 4
5	0 04	0 15	0 0418	0 1320	+ 4 5	− 12 0
6	0 05	0 15	0 0506	0 1435	+ 1 2	− 4 3
7	0 05	0 20	0 0490	0 1910	− 2 0	− 4 5
8	0 10	0 10	0 0962	0 1020	− 4 8	+ 2 0
9	0 10	0 10	0 0884	0 1082	− 11 6	+ 8 2
10	0 15	0 05	0 1392	0 0560	− 7 2	+ 12 0

—	Mean recovery (%)	Standard deviation of recovery (%)
Adrenaline	96 4	5 44
Noradrenaline	100 7	6 79

Case 9.—A woman, aged 67, had not had any other form of tuberculosis. Lupus vulgaris of the tip of her nose first developed when she was 51 and cleared after general carbon-arc baths and local treatment with the Finsen-Lomholt lamp. The scar remained sound until she was 62. In the last five years both calciferol and light treatment have been used.

Examination showed nodules and scaling still present on the tip of the nose. A radiograph of the chest was normal, and the E.S.R. was 10 mm. in 1 hour.

Treatment and Result.—Local injections of isoniazid 50 mg. in 2 ml. of distilled water were given for seven weeks, followed by 100 mg. in 2 ml. for ten weeks, with rapid diminution of local swelling but with slight residual scaling and nodularity. (2+.)

Case 10.—A man, aged 31, had a nephrectomy at the age of 27 for unilateral renal tuberculosis, and he also received a three-day course of streptomycin. His bladder has since been treated by diathermy on several occasions. At the age of 4 years an indolent ulcer developed at the site of an injury to the back of the left knee. When this healed, a bright red mark remained. At the age of 25 he fell from a bicycle and injured the same knee. Lupus was diagnosed and treatment with the Kromayer lamp and calciferol caused this lesion to heal. A year ago, after the occurrence of further lupus above the right knee, he was treated with the Finsen-Lomholt lamp. This caused considerable improvement, but active nodules remained amidst scar tissue.

Treatment and Result.—After 26 weekly injections of isoniazid 100 mg. locally the nodules became considerably flatter, with disappearance of scaling and freedom from local pain on movement. After four weeks' treatment urticaria developed but was not sufficiently severe to necessitate the abandonment of injections. This was the only patient in our series to develop any undesirable side-effects. (2+.)

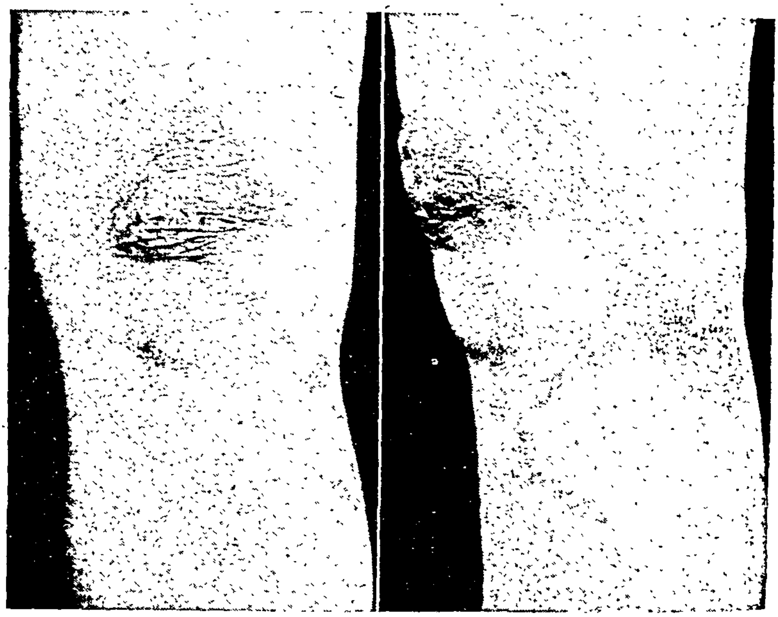

Fig. 2—Case 12 after treatment.

Case 11.—A woman, aged 51, had suffered from lupus since she was 41 and had been treated with general light-baths and the Kromayer lamp. Six years ago oral calciferol was given followed a year later by loss of weight and hæmoptysis. Radiography of the chest revealed active pulmonary tuberculosis. The chest condition has been treated with prolonged courses of *p*-aminosalicylic acid and streptomycin, both at home and in a sanatorium. The chest condition is at present quiescent. During this period the lupus received only intermittent treatment, principally with the Finsen-Lomholt lamp, with little success.

Examination showed a healed lesion over the anteromedial aspect of the right forearm, and an active lesion 6 × 4 cm. over the right elbow; hæmoglobin 88%; E.S.R. 20 mm. in 1 hour. Radiography of the chest showed mottled areas in both apices and extensive fibrosis of both upper lobes. No cavities were visible on tomography.

Treatment and Result.—Weekly injections of isoniazid were given into one portion of the lesion. For the first six weeks the dose was 50 mg. on each occasion, increased to 100 mg. for the next six injections, followed by eight injections of 250 mg. Further treatment could not be given, because she has been confined to her home with bronchitis. Although at first there was diminution of erythema and slight flattening of nodules no obvious change took place after the first six weeks. This was our only complete failure by either method of administration. (0.)

ORAL AND INJECTION

Case 12.—A woman, aged 46, gave a history of a dry scaly lesion behind the left knee since the age of 9 years. This was treated with ointments and was scraped on one occasion under general anæsthesia. The lesion remained static, but at the age of 17 an eruption appeared on the front of the left knee; this was diagnosed as lupus vulgaris and treated with ointments, without success. Two months before her first attendance at this hospital an ointment containing a sulphonamide had been applied to both active areas of lupus, producing a local dermatitis medicamentosa, which cleared when the use of the ointment was stopped.

On examination there were two erythematous lesions each about 8 cm. in diameter in the region of the right knee, with many "apply-jelly" nodules and much scaling (fig. 1). There was no active tuberculosis in other organs, and the E.S.R. was 9 mm. in 1 hour.

Treatment was begun with oral isoniazid 150 mg. daily for six weeks, increasing to 300 mg. daily for eleven weeks and then decreasing to 150 mg. for the subsequent eighteen weeks. In addition, one of the two lesions was treated with weekly injections of isoniazid 100 mg.

Result.—Both lesions have shown steady improvement, the one receiving local injections improving more rapidly. All scaling has disappeared, nodules are absent or almost flat, and pigmentation has taken the place of the former erythema (fig. 2). This case was considered to have undergone marked improvement. (3+.)

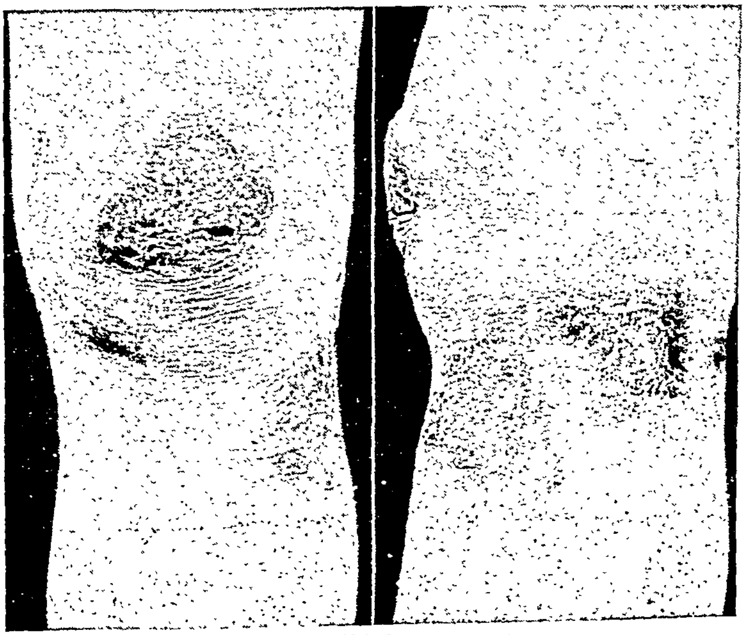

Fig. 1—Case 12 before treatment.

Horse Serum no 2 ') and 3 ml of fluoride-thiosulphate solution The amounts of adrenaline added were varied by a factor of 7 5, those of noradrenaline by a factor of 4, and their ratio by a factor of 15 In spite of this the results were accurate within ± 12%, with a standard deviation of about 6% (table I) Considering that we are dealing with unstable substances in dilutions of about 10^{-9} the result is satisfactory.

CONCENTRATION OF ADRENALINE AND NORADRENALINE IN BLOOD OF HEALTHY PEOPLE

The method has been applied to study the concentration of adrenaline and noradrenaline in the plasma and red cells of 22 male and 21 female healthy people aged 18–50 The blood was collected at about 10 A M while these people were engaged in their normal hospital duties They had not been fasting None of the females was known to be pregnant, but no inquiries were made about the phase of their menstrual cycle

The results are presented in fig 2 by plotting for each sample the concentration of adrenaline against that of noradrenaline The regression coefficient for *plasma is —1 39 ± 0 380, and that for red cells —1 32* ± 0 254 In both cases the regression is significant (P < 0 01), which means that there is an inverse correlation between the concentrations of the two amines the higher the adrenaline concentration, the lower the noradrenaline concentration is likely to be, and vice versa The regression coefficients for plasma and red cells, on the other hand, are identical within the limits of error

A striking sex difference was found in the distribution of adrenergic amines in red cells By drawing the dotted line in fig 2 the results could be separated into two groups, one of which comprises all the female samples except one, and the other all the male samples except one

Table II contains the mean values of the concentrations of adrenaline and noradrenaline and their ratio in the plasma and red cells of males and females, the statistical evaluation of the data is shown in the lower half of the table The differences between the intracellular and extracellular concentrations are highly significant for both adrenaline and noradrenaline in either sex Adrenaline concentration is highest in the red cell and noradrenaline concentration highest in plasma in men as well as in women, but the difference is less pronounced in women than in men Male plasma contains about five times as much noradrenaline as adrenaline, whereas male red cells, in contrast to female red cells, contain more adrenaline than noradrenaline Female plasmas contain significantly more adrenaline, and female red cells significantly more noradrenaline and less adrenaline, than the corresponding male blood fractions Astarabadi et al (1952) have shown that female rats are less susceptible to the lethal effect of intravenous adrenaline injections than are either male or castrated female rats

TABLE II—ADRENERGIC AMINES IN HUMAN BLOOD
(Mean values ± standard error of mean)

Subjects	Blood fraction	No of observations	Adrenaline (µg per litre)	Noradrenaline (µg per litre)	Ratio of noradrenaline to adrenaline
♂	Plasma	22	1 18 ± 0 044	5 29 ± 0 233	4 69 ± 0 341
	Red cells	22	2 81 ± 0 065	2 02 ± 0 14	0 735 ± 0 058
♀	Plasma	21	1 46 ± 0 082	5 16 ± 0 16	3 81 ± 0 28
	Red cells	21	2 27 ± 0 14	3 77 ± 0 12	1 80 ± 0 13

Significance of differences

	t	P	t	P	t	P
♂ Plasma — ♂ red cells	20 9	< 0 01	12 0	< 0 01	11 4	< 0 01
♀ Plasma — ♀ red cells	4 98	< 0 01	6 95	< 0 01	6 5	< 0 01
♂ Plasma — ♀ plasma	3 01	< 0 01	0 46	0 65	2 0	0 05
♂ Red cells — ♀ red cells	3 51	< 0 01	9 5	< 0 01	7 5	< 0 01

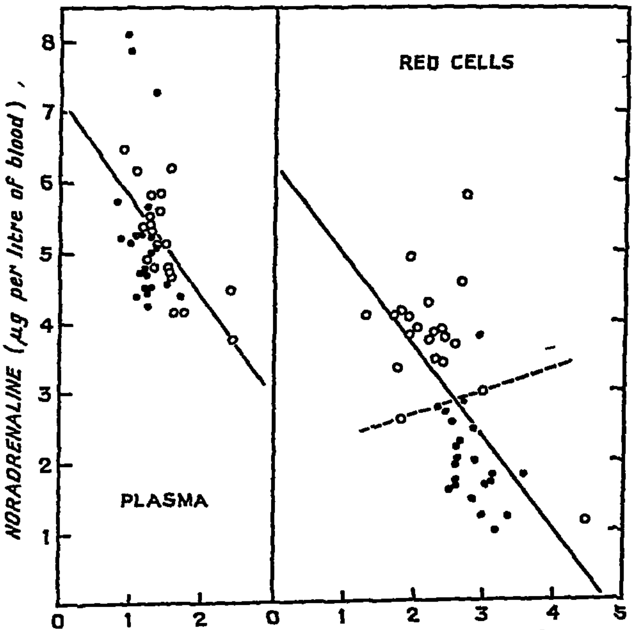

Fig 2—Concentration of adrenaline and noradrenaline in plasma and erythrocytes dots, males circles, females *straight lines, linear* regressions calculated on the pooled male and female samples

SPECIFICITY OF THE METHOD

It is pertinent to inquire whether the substances estimated by the method are in fact identical with adrenaline and noradrenaline, the more so as the errors of so many previous investigators have engendered a sceptical and even defeatist attitude of mind towards the problem of adrenaline estimation in blood We showed (Weil-Malherbe and Bone 1952a) that the fluorogenic substances in plasma were quantitatively destroyed by a preparation of amine oxidase at the same rate as added adrenaline To obtain further evidence some paper-chromatographic experiments were made In these, plasma samples from about 150 ml of blood were extracted with n-butanol The extracted amines were then re-extracted with 0 05 *N*-HCl, and the neutral concentrated solution was passed over a column of alumina After elution with dilute acetic acid and evaporation of the eluate the residue was transferred to paper with acid acetone and chromatographed by the method of Goldenberg et al (1949) Sections of the chromatogram were extracted with dilute HCl and the adrenergic amines estimated fluorimetrically in the extract

These experiments were done before the differential fluorimetric method was developed They are now being repeated by the new method, and the results, together with a more detailed account of the experimental procedure, will be published later Nevertheless the results so far obtained are worth mentioning at this stage

Both the extraction procedure and the chromatographic analysis involve losses, the recovery being 70–80% after either stage These losses are the same for added adrenaline as for the preformed fluorogenic material Results were calculated by applying the noradrenaline/adrenaline ratio determined by paper chromatography to the global value determined by the " direct " fluorimetric method on the same sample In five chromatographic experiments a mean concentration of 2 2 ± 0 06 µg of adrenaline and 6 8 ± 0 30 µg of noradrenaline per litre of plasma was found With a plasma volume of 60%, the figures translated into terms of µg per litre of whole blood would be 1 3 for adrenaline

Case 13.—A woman, aged 63, has had extensive lupus of the face since the age of 3. This had been treated with the Finsen and Finsen-Lomholt lamps as well as with superficial X rays. An epithelioma developed four years ago, which was successfully treated by radiotherapy.

On examination there was extensive scarring from former lupus, with a severe degree of ectropion of the right lower lid. Active nodules were present amidst the scar tissue, especially above the nose, on the cheeks, and below the chin. No evidence of active tuberculosis was found elsewhere. The E.S.R. was 11 mm. in 1 hour.

Treatment and Result.—Oral isoniazid 150 mg. was given daily for three weeks, followed by 300 mg. daily for twenty-six weeks. For the last five weeks isoniazid 200 mg. was injected twice weekly into the submental lesion, which has cleared, while all other active lesions have become considerably less scaly, with flattening of nodules. (2+.)

Case 14.—A man, aged 36, first developed lupus vulgaris behind the right knee at the age of 2. At 7 he started a three-year course of treatment with the Finsen lamp. Three years ago he reattended owing to a recurrence and was treated with the Finsen-Lomholt lamp but stopped attending six months ago owing to fractured ribs.

On examination there was a dark-red scaly area 16 × 11 cm. behind the right knee, with numerous nodules. There was no clinical evidence of tuberculosis elsewhere, and the E.S.R. was 6 mm. in 1 hour.

Treatment and Result.—For the first six weeks he was treated with weekly injections of isoniazid 50 mg. into a square measuring about a sixth of the total area affected. The injections were then increased to 100 mg. weekly for seven weeks and 250 mg. weekly for fourteen weeks. There was slow but steady improvement, especially at the site of injection, with flattening of nodules and decrease of scaling. However, after five months' treatment new nodules appeared on the medial border of the lesion. For the last four weeks oral isoniazid 300 mg. daily has been given in addition. Progress was considered to amount to moderate improvement. (2+.)

Case 15.—A man, aged 31, was born with a small white spot on the right cheek. His grandfather, father, and sister have similar lesions. At the age of 10 an attempt to remove the nævus with carbon-dioxide snow was followed by its enlargement and change of colour. The lesion has not received any further treatment and has remained unchanged in size for the past ten years. He has served in the Army for over six years, including a period in the Middle East.

Examination showed a solitary and slightly scaly lesion 3·5 × 2·5 cm. with "apple-jelly" nodules. General examination did not show any other active tuberculosis. The E.S.R. was 2 mm. in 1 hour.

Treatment was begun with oral isoniazid 300 mg. daily for nine weeks, with the addition of 200 mg. by injection twice weekly for the last three weeks.

Result.—Even after so short an interval the nodules were much flattened, with diminution in the depth of erythema. (1+.)

One further patient, a woman aged 29, had been irregular in her attendance for treatment of lupus of her nose and upper lip with the Finsen-Lomholt lamp. In consequence, the lupus had not improved, and she was given oral isoniazid 150 mg. daily for seven weeks. This caused diminution in erythema and flattening of nodules. She was given a further month's supply of 300 mg. daily but did not keep subsequent appointments and is therefore excluded from this survey.

TABLE II—COMPARISON OF DIFFERENT METHODS OF ADMINISTRATION

—	Oral	Local	Oral and local	Total
Cleared	1	..	..	1
Marked improvement.. ..	2	1	1	4
Moderate improvement ..	1	4	2	7
Slight improvement ..	1	..	1	2
No change	..	1	..	1
Total	5	6	4	15

Discussion

Isoniazid is relatively non-toxic. It can be given in doses up to 600 mg. daily without apparent ill effect. Minor subjective symptoms have been described (Brett and Braun-Falco 1953, Lucius 1952). They include nausea, palpitations, dizziness, flushing of the face, fatigue, headaches, paræsthesiæ of hands and feet, and constipation. Our patients have not complained of any of these. The only side-effect which was observed was mild urticaria in one patient treated with weekly injections, and it was by no means certain that the urticaria was caused by the isoniazid.

In addition to these minor symptoms, single reports have been made of purpura (Collins 1952, Lucius 1952), mild anæmia (Obermayer et al. 1952), sulphæmoglobinæmia (Feinmann 1952) and agranulocytosis (Varadi and Kelleher 1953).

Luntz and Smith (1953) report that the insulin requirements of diabetics receiving isoniazid may be increased; Robitzek and Selikoff (1952) reported a stimulating effect on the central nervous system, and Zabad (1953) has described psychosis developing during isoniazid therapy; but isoniazid seems to be far less toxic than calciferol, streptomycin, and *p*-aminosalicylic acid, with the reservation that time must pass before its possible delayed effects are known.

When we started this trial of isoniazid, there were no published reports of its use in skin tuberculosis, although several reports have since appeared in the Continental literature. Grütz (1952) treated 20 patients, most of whom had severe lupus vulgaris which had only shown temporary improvement on vitamin D and thiosemicarbazone. He obtained marked improvement after from six to twelve weeks' treatment, using daily oral dosages of 5–10 mg. per kg. of body-weight and considered a dose of less than 5 mg. per kg. of body-weight inadequate. Schoch (1952) found impressive improvement after seven or eight weeks' treatment in 11 out of 20 patients with lupus vulgaris and Bazin's disease, using doses of 100 mg. isoniazid thrice daily.

TABLE I—RESULTS OF DIFFERENT TREATMENTS WITH ISONIAZID

Result	Treatment										
	Oral only			Injections only			Oral and injections				
	Case no.	Weeks treated	Dosage (mg. daily)	Case no.	Weeks treated	Dosage (mg. daily)	Case no.	Weeks treated		Dosage (mg. daily)	
								Oral	Injections	Oral	Injections
Clinical clearance ..	1	32	150–300	..	..	..	..	..	..	..	..
Marked improvement ..	2	30	300	6	27	50–200	12	29	21	150–300	100
	3	14	300	..	..	..	..	..	..	..	..
Moderate improvement ..	4	18	300	7	27	50–100	13	29	5	300	400
	..	..	..	8	12	50	14	4	27	300	50-250
	..	..	..	9	17	100	..	..	..	..	..
	..	..	..	10	26	100	..	..	..	..	..
Slight improvement ..	5	28	300	..	..	..	15	9	3	300	400
No change	..	..	..	11	19	50–250	..	..	..	..	..

and 4 1 for noradrenaline The agreement with the results of the differential fluorimetric method is thus satisfactory

The important point shown by these experiments is that the fluorogenic material in plasma was concentrated in positions exactly opposite those of the adrenaline and noradrenaline spots on a reference strip (fig 3) Recent experiments in which the fluorescence was measured with different filters have further shown that the substance which has the same R_F value as noradrenaline also yields a fluorescence with the same spectral properties as noradrenaline, and similarly the substance with the R_F value of adrenaline produces a fluorescence with the spectral properties of the adrenaline derivative It has thus been established that the substances estimated in blood are identical with adrenergic amines in their affinity to amine oxidase, in R_F values, and in the fluorescence spectra of their derivatives

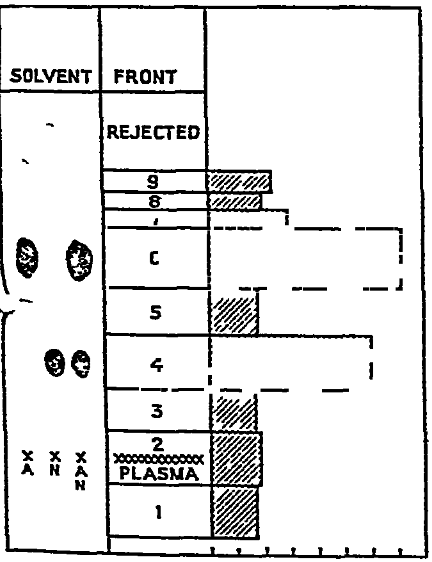

Fig 3—Paper chromatography of plasma extract on left, reference strip, after spraying with ferricyanide solution A, point of application of adrenaline solution N, point of application of noradrenaline solution , in centre, paper strip carrying plasma extract (crosses mark line of application after drying, paper was cut into sections as indicated) on right, bars indicate strength of fluorescence developed in extracts of corresponding paper section and measured with yellow filter only

SUMMARY

A differential fluorimetric method for the simultaneous estimation of adrenaline and noradrenaline in human plasma and red-cell extracts is described

Recovery experiments showed that the standard deviation from the true value is about 6–7%

The specificity of the method has been checked by paper chromatography, both methods gave similar results The two amines were identified on the chromatogram by their R_F values and by the spectral properties of their fluorescent derivatives

The mean concentration of adrenaline in plasma is 1–1 5 µg per litre of whole blood, and that of noradrenaline about 5 2 µg per litre of whole blood Red cells contain more adrenaline and less noradrenaline than plasma A significant sex difference was found in the intracellular distribution of adrenergic amines

We are greatly indebted to Dr W Jacobson, of the Strangeways Laboratory, Cambridge, who determined the fluorescence spectra of the adrenaline and noradrenaline derivatives, and to Mr J A. Mortimer, assistant engineer at Runwell Hospital who built the fluorimeter to our specifications We also wish to thank those members of the staff of Runwell Hospital who volunteered to give blood samples for this investigation.

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PNEUMOFLATOR FOR TREATMENT OF RESPIRATORY PARALYSIS

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B M Oxfd, F.F.A R C S
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The apparatus illustrated herewith is the prototype adaptation of a simple anæsthetic pneumoflator which has been in satisfactory use for several months It was shown at the recent conference on poliomyelitis at the Ministry of Health (Ministry of Health 1953)

Essentially this apparatus (fig 1) consists of a bellows mounted on a plain box chassis containing a motor and reducing gearbox These move the paddle of the bellows through a crank and connecting-rod The bellows have plain circular rubber valves uncovering a ring of holes and working atmospherically

At present R A F disposal motors and gearboxes, suitably adapted, are used, they are controlled by a rheostat For anæsthetic purposes the speed is regulated at about 23 r p m. The present motors have worked excellently—one for 200 hours—but there exist far superior types

The ideal, I think, is that supplied by Messrs Klaxon, 201, Holland Park Avenue London, W 11 (type HM 5CB2/WP 5, retail price £7 3*s* 6*d*) This delivers a torque at 23 r p m of 14 in lb—sufficient to produce a positive pressure in the existing machines of over 35 cm water With expansion of rubber tubing, leakage, &c, this amounts to a net inflation of over 20–25 cm, which is adequate

Owing to the nature of the motion the pressure cycle of the machine pauses at top and bottom "dead centres" Also there is a shift in the curve to the "pressure side," so that inspiration is about two-thirds the length of expiration

Further to mimic natural respiration, a later machine has been fitted with the device shown in fig 2 In this the cycle is interrupted at full inspiration and full expiration by separately adjustable stops, the rotary motion of the crank continuing unchecked by compressing the springs in the telescopic connecting-rod These springs must have a tension between the maximum thrust

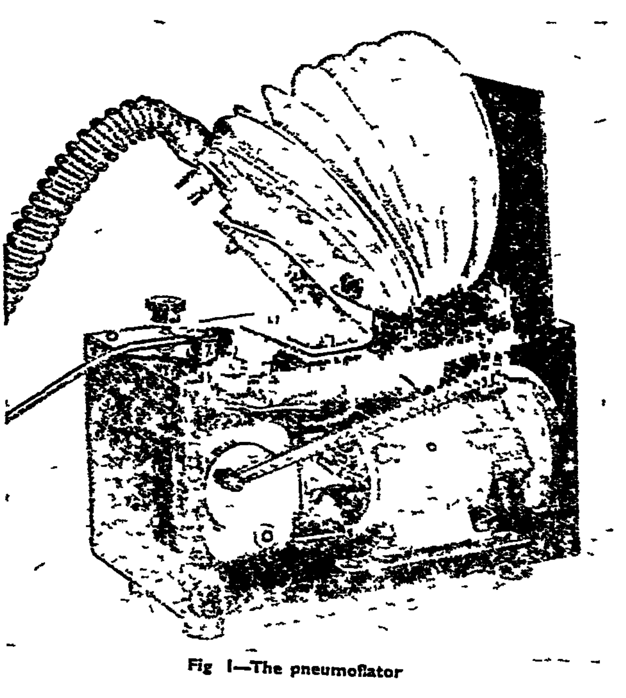

Fig 1—The pneumoflator

Since the course of untreated lupus is well known, and the number of cases suitable for treatment was limited, it was decided to dispense with controls.

Cases were distributed, so far as possible, equally between the three methods of treatment. Table I shows the results obtained by each method, and table II compares the results of those methods.

We believe that daily injections would prove as effective as, or even more effective than, the oral administration; but most patients with lupus are fully employed and daily attendances at hospital impose upon them too much financial loss to make this method practicable in most cases.

In pulmonary tuberculosis the development of isoniazid-resistant strains has been reported (Joiner et al. 1952, *Lancet* 1952). From the continuous and steady manner in which improvement has taken place in almost all our patients for up to thirty weeks we find no evidence to suggest that drug resistance has developed.

It is likely that isoniazid combined with calciferol will give better and quicker results than either drug alone, because the two drugs seem to act in different ways, isoniazid apparently having a direct action on the organisms, whereas calciferol seems to stimulate the host's powers of resistance in some undetermined way.

We consider that dosage should be at least 300 mg. a day for adults, and 400–600 mg. a day may prove to be optimal, giving maximal effect with minimal incidence of intoxication. We see no reason to estimate the dosage accurately in mg. per kg. body-weight except in children. Deviations from the average weights of adults largely depend on the amounts of fat and fluid in the tissues, for which adjustments in dosage are not needed. Nevertheless it is useful to remember that a dosage of 300 mg. daily for a woman of average build, weighing $9^1/_2$ st., provides 5 mg. per kg. body-weight, whereas a taller man of average build, weighing $12^1/_2$ st., should receive 400 mg. daily to obtain about the same dosage per kg. body-weight.

Weekly local injections are far too infrequent for a maximal response to be obtained with isoniazid, whereas in the case of calciferol weekly or fortnightly injections are effective. As with calciferol, there is a considerable increase of fibrosis after repeated injections, which makes their administration increasingly difficult.

The results obtained so far with isoniazid are impressive, but it remains as important as ever to pay attention to the patient's nutrition and environment and to try to improve them if they are defective. Calciferol still has a place in the treatment of lupus and is a valuable remedy both for systemic and for local use. General carbon-arc and mercury-vapour baths and the Finsen-Lomholt and Kromayer lamps also continue to be of value for selected patients in whom for one reason or another drug therapy is inadvisable.

Summary

15 cases of lupus vulgaris treated with isoniazid are reviewed.

Those treated orally were usually given 300 mg. daily, and those treated by injections into the lesions were given 50–250 mg. weekly. Where both methods were used the oral dosage was 300 mg. daily and the injected dose up to 400 mg. per week.

Apart from mild urticaria in 1 patient, there was no intolerance.

All the patients except 1 showed improvement, and in most of them this was progressive up to the time of writing.

We wish to thank Sister F. Hall for her great help in the study and treatment of these patients. Roche Products Ltd. supplied the solution of rimifon made up to our specific requirements, and E. R. Squibb & Sons supplied the hydrazid tablets.

References at foot of next column

LOCALISED MUSCULAR ATROPHY IN DIABETES

CEDRIC HIRSON
M.R.C.P.

LATELY MEDICAL SENIOR REGISTRAR.
WEST HERTS HOSPITAL, HEMEL HEMPSTEAD, HERTS

CHARACTERISTIC abnormalities in diabetics have bee noted in many of the body systems. In the six case reported here there were localised areas of muscula atrophy suggesting that a specific process independen of insulin atrophy was operating.

CASE-RECORDS

CASE 1.—A woman, aged 76, who had been diabetic for twelve years and controlled with insulin for four years, complained of pain, worse at night, in the arms with tingling in the feet and weakness of the arms for two years.

Examination showed areas of atrophy, which were not strictly symmetrical, in both forearms (fig. 1). The skin was normal, but muscle and subcutaneous tissue were involved in clearly defined areas extending from the lower borders of the deltoid muscles to the elbows. Fasciculation was absent, and the tendon reflexes were brisk in the arms though absent at the ankles. Cutaneous sensation was normal in the arms but impaired in the legs.

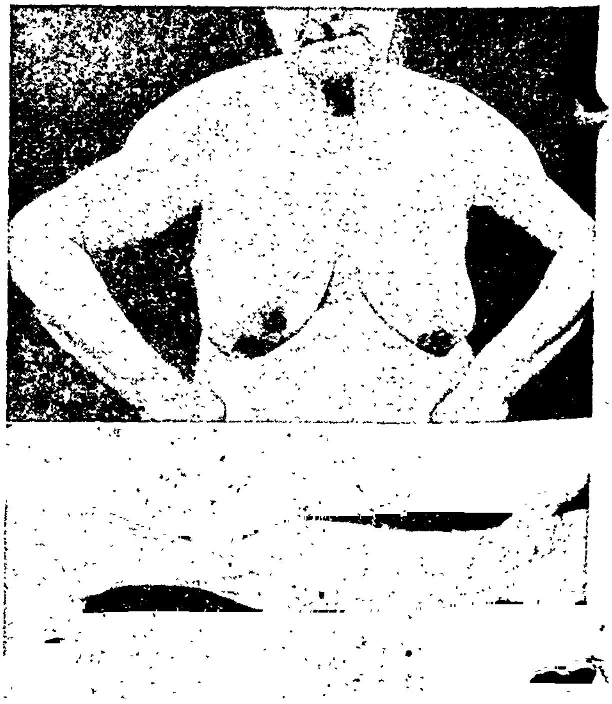

Fig. 1—Muscular atrophy of forearms (case 1).

The patient habitually injected insulin into her thighs, where the musculature was normal.

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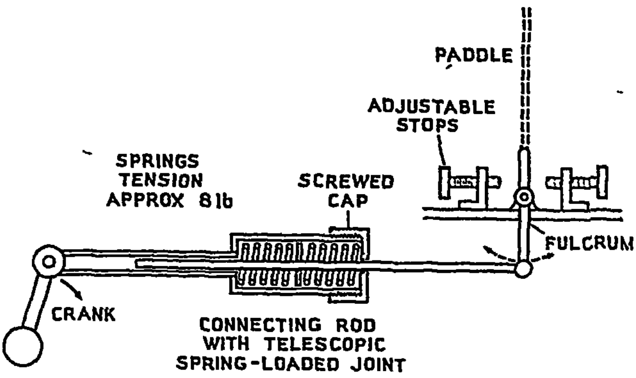
PADDLE
ADJUSTABLE STOPS
SPRINGS TENSION APPROX 8 lb
SCREWED CAP
FULCRUM
CRANK
CONNECTING ROD WITH TELESCOPIC SPRING-LOADED JOINT

Fig 2—Diagram of device for interruption of cycle

of the motor (15 lb) and the maximum thrust required to produce 25 cm water inflation pressure (8 lb)

The apparatus has been used extensively in the anæsthesia of patients for various thoracic surgical and neurosurgical operations in which paralysis was simulated with thiopentone and *d*-tubocurarine chloride so that controlled respiration was essential

Room air is supplied to the patient via the respirator, enriched with some 500 c cm oxygen per minute through a basal lead This was thought advisable, in order to eliminate excess nitrogen and ensure removal of carbon dioxide through the release valve, which is set to produce reasonable inflation No anoxæmia appeared when pure air was used, nor have there been any signs of hyperventilation at the end of 2–3 hours

No absorber has proved necessary

CONCLUSIONS

An attempt has been made to produce the simplest possible type of air-pump for continuous artificial respiration—the " mechanical student "

The cost should not exceed £20 , and, given a supply of motors, very large numbers can be produced in ordinary workshops at short notice

No compressed gas cylinders are necessary, but it is thought that a small basal oxygen enrichment is advisable

No absorber has proved necessary , the sole disadvantage is the noise of the expiratory valve

By immobilising the valves the machine can be used as an ordinary pneumoflator with absorber and basal lead , or, if thought advisable, a negative phase can be introduced into the respiratory cycle and suction as well as inflation applied

I should like to express my thanks to Messrs A Charles King for their continuing assistance, and also to Mr T Holmes Sellors, Mr Harvey Jackson, and others who have allowed me to develop these machines on their patients

REFERENCE

Ministry of Health (1953) Conference on Poliomyelitis, April 15 1953 See *Lancet*, 1953, i, 940

Preliminary Communication

ISONIAZID-RESISTANT STRAINS OF MYCOBACTERIUM TUBERCULOSIS

The recent observations of Fisher (1952), Barnett et al (1953), and Knox (1953) have prompted us to describe our experiences with virulent strains of *Mycobacterium tuberculosis* which have acquired resistance to isoniazid

Resistant variants of H37RV and of Ravenel RV were produced in the following way Serial $1^1/_2$-fold dilutions of isoniazid were made in tubes of the Youmans modification of the Proskauer and Beck medium, enriched by 5% human serum For the first passage, the inoculum for each tube consisted of 0 02 mg (wet weight) of a lightly ground three-week-old Lowenstein-Jensen culture suspended in Youmans medium The readings obtained at 14 and 28 days are shown in the accompanying table For the second passage and again for the third passage a mixed inoculum was made from the three tubes showing growth on the 28th day in the highest concentrations of the previous passage

HIGHEST CONCENTRATIONS (µG PER ML) OF ISONIAZID SHOWING GROWTH

Strain	First passage		Second passage		Third passage	
	14 days	28 days	14 days	28 days	14 days	28 days
H37RV	0 05	10 0	0 3	66 0	66 0	66 0
Ravenel RV	0 20	33 0	33 0	66 0	50 0	66 0

Particularly in the first passage, the major factor causing the apparent development of resistance in both strains during the 28 days was the inactivation of the isoniazid It is evident from the figures, however, that genuine resistance of a high degree had been produced during the second passage and to some extent during the first The drift between the 14th and 28th days, particularly in the tubes of the first passage, is greater than that reported by other workers who used Dubos-type media (Barnett et al 1953, Knox et al 1952, Mitchison 1952, Steenken et al 1952) It is possible that the ' Tween ' in their media enhances the activity of the isoniazid—as has often been shown for many tuberculostatic substances (Fisher 1948, Zetterberg 1949, Youmans and Youmans 1948, Williston and Youmans 1949)—and to such an extent that a greater proportion of the bacilli are rendered incapable of proliferation The result of this is that eventually, when the inactivation of the isoniazid has occurred on incubation, no growth appears in concentrations which under similar circumstances permit growth in Youmans medium Thus the absence of tween from the medium employed by us would also explain why we have encountered resistance arising more rapidly and to a greater degree than has been reported for tween media

In agreement with the observations of Fisher (1952), we have found that variants highly resistant to isoniazid, obtained in vitro and in vivo, do not grow in simple media in the absence of serum Fisher's explanation of this phenomenon is that isoniazid-resistant strains of tubercle bacilli require a growth factor which is supplied by serum, bovine albumin (fraction V), or yeast extract However, it has been shown in these laboratories that strong growth may be obtained in the unmodified synthetic medium of Youmans, provided that the medium has previously been treated with activated charcoal The charcoal was maintained at red heat for 1 hour and subsequently added to the basal medium in a concentration of 1 0% After 2 days it was removed by filtration and the resultant clear medium, in 5 ml volumes, was inoculated with approximately 0 02 mg of the resistant H37RV variant described above, which had been maintained on Lowenstein Jensen slopes containing 100 µg of isoniazid per ml

The isoniazid resistant variants of H37RV and Ravenel RV, isolated and maintained in this way, now show a very much reduced pathogenicity for guineapigs This agrees with the findings of Barnett et al (1953) Isoniazid resistant strains isolated from five cases of pulmonary tuberculosis and one of urogenital tuberculosis, as well as the resistant variants of H37RV and Ravenel RV mentioned above, have produced only minimal lesions on inoculation into guineapigs The lesions were confined to the site of inoculation and to the regional lymph nodes, eated with dextran, but tubarine was used as a muscle laxant, and no hæmatomata were observed. A further eck showed a correlation between the occurrence of ematomata and the use of gallamine in cases which ad not been treated with dextran, but the incidence as not so high as when dextran and gallamine were used gether. This is considered to be due to the mechanical ffect of the maintained blood-pressure rather than to a ormation of a gallamine-dextran compound.

SUMMARY

The use of macromolecular substances in supportive herapy is described.

Since it is now possible to prepare a solution of macro-nolecular substances possessing advantages over plasma tself, the term "plasma substitute" should be discarded.

Since the primary use of these substances is for the storation or maintenance of the circulating blood volume the term "blood-volume restorer" is suggested.

The criteria for an effective blood-volume restorer are: ease of infusion, freedom from undesirable effects, reproducible composition under manufacturing conditions, elimination from the body, and maintenance of a blood level of not less than 50% of the amount infused at the end of twenty-four hours.

These criteria could only be met by the development of a new type of dextran solution.

The steps in the development of the new material are described and its clinical advantages are discussed.

The number of people involved in this investigation makes individual acknowledgment impossible. We wish to thank everybody concerned, particularly members of the department of surgery and the nurses of Manchester Royal Infirmary, and Mr. W. A. Magauran, F.R.C.S., of the Lancaster Royal Infirmary, for their assistance in the clinical investigation; Mr. L. E. Martin for the physical chemistry; Mr. F. Fowler for the large-scale production of the various types of material; and Messrs. Bengers Ltd. for unlimited supplies of 'Dextraven.' The diagrams were drawn by the department of medical illustration of Manchester Royal Infirmary.

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REJECTION DYSPEPSIA

G. GLADSTONE ROBERTSON
M.D. Glasg.

THE considerable recent advances in the knowledge of body-mind relationships have sprung largely from the so-called psychosomatic approach, whereby the mental states of those suffering from various physical disorders and diseases are assessed and compared. Contributors in this field do not claim that disorders of the body are due to those found concurrently in the psyche or vice versa. They are generally psychiatrists or physicians with a psychological leaning, primarily motivated in outlook and training by a desire to improve mental health, and tend to lay emphasis on factors in the earliest years of life.

This paper is based on experience in general practice among ordinary people whose higher levels are intact, the girls who are the mothers of the future and the boys who marry them, folks who suffer from crops of boils one year and a succession of colds the next, those who get cancer of the breast and others who develop fibroids, women with dysmenorrhœa and men with peptic ulcer —in fact the whole range of the common afflictions acquired by mankind. The frequent occurrence of a sequence of different illnesses in the same person suggested that the affections were determined not in the earliest years but by variations in the later conditions of life. I do not claim originality for my method of approach or for many of my observations; but I believe that certain of my correlations are new, and that my interpretation of a common and troublesome disorder may be useful to practitioners and physicians who have not been working or thinking on the same lines.

These particular observations may be said to date from 1935, when the work of Halliday and others led me to consider emotional factors in the causation of the chronic disorders now termed psychosomatic. I began at that time to take histories from this viewpoint.

I found that many of my patients were women complaining of abdominal distension, eructations of wind and of small quantities of gastric secretion (usually termed "acidity"), nausea, and occasional vomiting. At first these symptoms would appear infrequently and pass off quickly, but later there would be acute exacerbations (often called bilious attacks), usually attributed to greasy food; and some patients rarely had a day free from belching or dyspepsia.

What struck me first was that it was very rare for *men* to have such symptoms and yet have no pain: typically the digestive troubles of the male began with pain and not nausea, whereas the female might have nausea but remain free from pain for years. I began to wonder, therefore, why only women—and they were almost always married women—were bilious in this way. I questioned them and got them to talk; but, though some of them mentioned their marital relations, these were not emphasised. Often the stomach disorder was mentioned only as a subsidiary complaint: the predominant symptoms might be those of an anxiety state, premenstrual tension, varicose veins, visceroptosis, uterine prolapse, gall-stones, hypertension, or rheumatism. I felt that there must be a definite answer; and then, as so often happens, the case turned up that provided the key to the others.

AN ILLUMINATING CASE

Case 1.—Mrs. A., aged 52, had had her first menstrual period at 16 years 3 months; she had been married 30 years but had never been pregnant.

Complaint.—Abdominal distension with noisy eructations of wind, burning abdominal pain, sensation of "stone" in the epigastrium, nausea, frequent vomiting unrelated to eating, constipation with occasional attacks of diarrhœa, frequent sore throats, palpitation and general nervousness, extreme irritability, falling sensation centred in the uterus and bladder.

Physical Examination.—Each organ system had been investigated in turn, to the limit of ordinary hospital technique, with negative result.

History.—The youngest of five siblings, she was shy and self-conscious as a child. Her relationship with her parents lacked warmth, affection, intimacy, and understanding. From her earliest recollection her mother, who was often confined to bed until she died at the age of 81, had required her help in the home. On this account her school work was poor and she became unpopular with teachers as well as classmates. The onset of headaches terminated her scholastic career at the age of 12. Sore throats commenced when she was 14, after the death of her only girl friend from diphtheria.

In 1916, at the age of 22, she married her fiancé while he had 48 hours' leave from military service. They did not live together until a year later when a varicose ulcer secured for him a month's convalescence. He joined her in Prestwick where she was spending a holiday. Within a few days of his arrival she began to feel bilious. Nausea and vomiting continued until her husband rejoined his unit. Her unfortunate indisposition was assumed to be due to sewage contamination of seawater at the bathing site. Next summer her husband, now stationed in the south of England, was released from duty owing to a recurrence of the leg ulcer. She decided to spend a few months with him, but the reappearance of nausea and vomiting soon after her arrival convinced her that the "air" did not suit her and led to a speedy retreat northwards. Once more separation from the husband was followed by instant recovery, but demobilisation ten months later brought her respite to an end

The nausea, wind, acidity, and bilious attacks which were her lot for 27 years she attributed to the irreparable damage sustained by her stomach and liver when in Prestwick in 1917 During these years she had sought relief from every source known to her, including general practitioners, hospital physicians, surgeons, and gynæcologists, osteopaths, Nature healers, homœopaths, physiotherapists, and chiropractors Surgical intervention had included fixation of floating kidney at 31, abdominal fixation of the uterus at 32, colopexy at 34, and cure of a ventral hernia at an operation scar at 35

Findings and Inferences—Her early life was characterised by lack of affection for her father with consequent inhibition of her erotic growth, retardation of menses, and inability to accept the male sex. Her association with her mother was made closer by the perpetual ill health of that parent She never experienced sexual desire or orgasm Flatulent dyspepsia, which first appeared with the commencement of marital relations, was always aggravated by coitus All her symptoms were accentuated during the premenstrual week

With the facts of this case so plain before me, I began to see the significance of the marital relations, the separations, and the divorces of so many of my previous patients As each old patient came back, and each new one arrived, it became apparent that the married woman with this syndrome either had always been frigid or had recently become so Here are some further examples

FURTHER ILLUSTRATIVE CASES

Case 2—First menstrual period at 15 years 5 months She had excellent health until her marriage at the age of 23, but then suffered from a vaginismus which rendered coital attempts difficult and painful Dysuria, nausea, flatulence, and bilious attacks followed Stretching of the vaginal introitus and dilatation and curettage of the uterus took place two years after marriage Her only pregnancy, which commenced in a few months, was associated with nausea and vomiting Within a year of the confinement colporrhaphy was performed because of bearing down pelvic discomfort Ten years later a colopexy was done Progressive increase in the severity of flatulence, acidity, nausea, and bilious attacks led to 16 radiological examinations being made between the ages of 38 and 46 On the last occasion a gall stone was discovered and the gall bladder removed In three years' time the persistence of her symptoms drove her to seek surgical aid yet again Once more it was given ungrudgingly, adhesions now being sepatated. When at the age of 53 she first consulted me her symptoms had abated but little Her meals were followed by noisy eructations of wind, very small amounts of fat provoked bilious attacks, while "chills" were blamed for her bouts of dysuria

Findings and Inferences—Like the first patient, she was sexually frigid and coitus seemed to instigate and maintain both her acute and chronic symptoms Gall stone deposit was preceded by many years of functional disorder The husband had contracted a duodenal ulcer within five years of marriage

Case 3—First menstrual period 13 years 2 months She was 69 years old at interview, having married at the age of 18 She grew up in a happy home with affection for both parents Her early relationship with her husband was exciting and satisfying, the first four pregnancies being uncomplicated by nausea and vomiting After the birth of the fourth child a proportion of coital acts took place in the absence of desire or orgasm on her part The incidence of sickness mounted in each of the succeeding pregnancies Following the seventh confinement she lost all sexual interest, but it was not until after the ninth that she began to suffer from nausea, wind, acidity, and bouts of vomiting in the intervals between pregnancies Two of her eighteen pregnancies terminated in miscarriage Dyspepsia was heightened at the menopause Her husband's death, eight years ago, was followed by slight improvement She had been an assiduous and faithful attender of outdoor hospital dispensaries, thereby increasing the running cost of these institutions over the last forty years by her consumption of roughly 1200 bottles of medicine

Findings and Inferences—In this case the maternal component of the patient's personality became dominant at the expense of the erotic, through mothering her own ever increasing family

Case 4—First menstrual period at 17 The eldest of s siblings, she was 51 years at interview, had married whe and had given birth to four children In childhood she h and feared her father, a habitual drunkard whose behav indicated dislike for his wife and children alike Dur adolescence she assisted her mother (who suffered from " weak stomach and biliousness") with housework and in t rearing of the younger children and protected her when poss from her father's abuse At marriage she professed affect for her husband, but admitted loathing for the sexual asp Within a year or two he seemed to lose interest in her a the home, eventually becoming a drunken character remin cent of her own father Her physical pattern closely appro mated her mother's—prolonged sickness in pregnancies w later a growing tendency to nausea, acidity, and bili attacks

Findings and Inferences—She illustrates the all too comm sequence of failure to acquire acceptance of the male own to hatred of the father and too strong attachment to th mother, the sequel being delayed menses, sexual frigidity, a drunken husband (his reaction to the problem), and final the likelihood of repetition in the lives of her children

Case-histories of this kind can be found at length in the books and journals (chiefly American) dealing w psychosomatic disorders, but in our standard textbook the clinical picture is discussed mainly under the heading of nervous dyspepsia, visceroptosis, and chronic chole cystitis No attempt is made to define the kind of emotion or the experiences likely to create it, and no explanation is offered for its rarity in the male

The underlying cause can, I think, be best indicated if we apply to it the term "rejection dyspepsia"

RELATION TO NAUSEA AND VOMITING OF PREGNANCY

In an earlier paper on nausea and vomiting in pregnancy (Robertson 1946) I drew attention to the ætiological significance of previous dyspepsia (cyclical biliousness in adolescent girls), mother attachment, sexual frigidity, and undesired coitus I believe it will be found that rejection dyspepsia is but a further stage in a disorganisation of function due to the same factors as pregnancy sickness The prevalence of both conditions is quite in keeping with published data on marital life and frigidity (Pearl 1938, Reich 1948) Reich gives a figure as high as 60% for the prevalence of frigidity in Germany I have failed to unearth a computation of female frigidity in this country, but of over 1000 pregnant women in industrial Glasgow whom I saw during about ten years, 12% had been completely frigid throughout their married lives, and in the others the degree and duration of sexual interest varied widely.

A SERIES OF CASES

The milder forms of rejection dyspepsia are encountered daily, and my records do not allow me to offer a representative sample, but I thought it might be of interest to analyse a series of 300 cases referred to me between 1938 and 1947 in which flatulent dyspepsia was the patient's chief complaint This series includes all patients treated by me during these years who suffered from or had suffered from "visceroptosis" or gall stones Many of the patients had endured multiple operations (e g, for uterine prolapse, rectocele, and cystocele) but none had suffered from peptic ulceration The accompanying table shows these 300 patients subdivided in respect of the factors which seem to me worthy of consideration from the ætiological standpoint

1 Mr I M Burdon and Mr J H Levack inform me that the ratio of 1 male to 57 females is in keeping with the average sex ratio of cases of gall-stones at the Victoria Infirmary and the Southern General Hospital, Glasgow

2 Of 300 patients with severe flatulent dyspepsia only 3 were single women Each of these had continued to reside with her mother for many years after reaching adulthood

3 The remaining 296 patients were married women, and they fall into three groups

and in some cases even these lesions were absent. No macroscopic disease was evident in the spleen or other organs. (The inoculum was approximately 0·5 mg. and the animals were sacrificed on the 86th day after inoculation.) In our experience, guineapigs injected with much smaller inocula of the parent strains show extensive disease in the usual organs within one month.

One of us (E. G.) is the holder of a Lasdon Foundation Research Fellowship of University College, Dublin.

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Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION

THE association's spring meeting was held in Dublin on April 23–25 under the presidency of Sir REGINALD WATSON-JONES.

Transfusion of Blood, Plasma, and Plasma Substitutes

Dr. W. E. R. HACKETT (Dublin) discussed the advantages of transfusions of blood, plasma, and plasma substitutes before and during surgical operations. In anæmic patients who required transfusion before operation it was important that the blood be given several days beforehand so that the body might benefit as fully as possible. Blood given during operation had its greatest usefulness in replacing blood lost: this was often more than was realised. A common unsuspected source of blood-loss was bleeding into the tissues, and this was an important cause of oligæmic shock after injuries such as fractures and extensive limb wounds. The risks of overloading the circulation by over-transfusion were small; a commoner error was not to give enough blood. With expert laboratory help reactions from mismatching were exceptional; mistakes, when they occurred, were more often due to clerical errors or confusion of patients with similar names than to mistakes in grouping. In practice the only rhesus factor of real importance was the D antigen. So far there was no true substitute for blood. So-called blood substitutes were really plasma substitutes, and none was equal to plasma itself. A perfect plasma substitute must have the same osmotic properties as plasma; this was very difficult to achieve. The best types at present available were the polyvinyl polymers such as 'Plasmosan' and the sugar polymers such as dextran.

Ocular Torticollis

Prof. L. E. WERNER (Dublin) recalled the significance of imbalance of the ocular muscles as a cause of tilting of the head in infants and young children. When due to an ocular imbalance, such tilting could be corrected by an equalising operation on the eye muscles, though in long-standing cases there might be secondary contractures of the neck muscles. Professor Werner classified torticollis as (1) purely ocular, (2) purely cervical, or (3) combined. From the orthopædic point of view it was necessary to determine as soon as possible in every case of torticollis whether there was an ocular element in the deformity, if necessary by referring the patient to an orthoptic clinic. If an ocular defect was overlooked orthopædic treatment directed to the neck would not be completely successful.

Fracture of Head of Radius

Mr. J. C. CHERRY (Dublin) had replaced the fractured radial head by an acrylic prosthesis in selected cases in which the head was badly comminuted. Mr. C. C. JEFFERY (Exeter) believed that the operation had a definite place, especially in cases of fracture where the radial shaft was displaced upwards; such fractures were, however, exceptional. Prof. BRYAN MCFARLAND (Liverpool) had found no tendency for the radial shaft to migrate upwards, even when the radial head had been excised in children. Mr. ST. C. STRANGE (Canterbury) recalled that the position of the radius depended upon the integrity of the interosseous membrane. If this was torn by the force of the injury the radius was displaced, but if the membrane remained intact displacement was not to be feared. Mr. PHILIP WILES (London) thought that it was necessary to know the late results of prosthetic replacement before determining the place of the operation. Mr. ARTHUR CHANCE (Dublin) believed that the radius might move upwards when weight was put on the wrist (e.g., leaning on a table) even though it appeared in normal position in routine radiographs. There was an established place for the operation, but if the capitulum was found to be badly damaged at operation acrylic replacement was better avoided. Sir REGINALD WATSON-JONES (London) had no doubt that the operation was appropriate for the rare but definite cases in which fracture of the radial head was associated with rupture of the interosseous membrane and marked upward displacement of the radius.

Treatment of Club-foot

Mr. A. T. FRIPP (London) discussed the treatment of relapsed or *neglected congenital club-foot in children aged six months to ten years*. In the past four years he had given an extensive trial to the Kite technique in which wedged plasters are used, and he had been impressed by the results. The technique aimed at gradual correction without harmful force and without anæsthesia. Each of the four components of the deformity (varus, inversion, equinus, and plantaris) was corrected successively by removing appropriate wedges from the plaster and closing the gap, the adjustments being made weekly. During treatment the foot became progresively more supple, and in most cases satisfactory correction was obtained. Professor MCFARLAND agreed wholeheartedly with the principle of gradual correction without the use of force. Such a method reduced, though it did not eliminate, the necessity for operation.

Pott's Paraplegia

Mr. H. J. SEDDON (London) remarked that in paraplegia of early onset the cord might be involved by an inflammatory lesion (fluid or solid), rarely by thrombosis of the vessels, and sometimes by mechanical collapse of the spine. Paraplegia of late onset was associated either with an inflammatory process or with pronounced bony deformity. The cord changes in paraplegia were of four kinds: simple compression, infective thrombosis, pachymeningitis (rare), and longitudinal shrinkage. With conservative treatment alone paraplegia of early onset persisted in about a quarter of all cases, and paraplegia of late onset in over half the cases. Operative treatment offered a good prospect of mechanical relief: fluid pus could be drained by costotransversectomy, but solid matter interfering with the cord was best removed by anterolateral decompression (except in the neck and in certain lumbar lesions, where laminectomy offered advantages). Operation was indicated: (1) when paralysis had become complete; (2) in all cases of late onset; (3) if continued improvement was not taking place under conservative treatment; (4) when paraplegia was associated with uncontrollable spasms of the legs; and (5) if paraplegia recurred after initial recovery. In older patients operation should be considered relatively early. In cases with a visible abscess shadow costotransversectomy should be tried first, but if this was unsuccessful anterolateral decompression should be undertaken.

Mr. D. LLOYD GRIFFITHS (Manchester) described the operation of anterolateral decompression employed by Mr. Seddon, Mr. R. Roaf, and himself. He emphasised that operation was not required in every case of paraplegia. It was a difficult, formidable, and hazardous operation and patients should not be submitted to it unnecessarily. Mr. Griffiths summarised the combined results in 48 patients operated upon by Mr. Seddon, Mr. Roaf, or himself. 34 recovered enough to walk normally; 11 recovered little or not at all; and 3 died. In successful cases recovery was often dramatic. Results were better in early cases with active disease than in late cases with much bony deformity. Spinal fusion was always advisable after anterolateral decompression.

was up by 20% or more and was characteristically very variable. In over 60% of the phæochromocytoma patients, the fasting blood-sugar level exceeded 120 mg per 100 ml. on at least one occasion. Glycosuria was less common. The cold pressor test[8] was normal in 60–70% of those with a functioning chromaffinoma but in only 22% of those with essential hypertension. The finding that about half the phæochromocytoma patients had postural hypotension and tachycardia (an increase of 20 beats or more per minute) is interesting, for these signs are rare in essential hypertension. The explanation presumably lies in the incompetence of the vasoconstrictor reflexes in the presence of overriding adrenaline and noradrenaline effects. Perhaps the most helpful feature is the characteristic paroxysmal nature of the episodes of hypertension in many patients with phæochromocytoma, but neurogenic paroxysmal hypertension has been described,[9] and the adrenaline release in spontaneous hypoglycæmia may closely mimic a paroxysm due to a phæochromocytoma. In children phæochromocytomas produce sustained rather than paroxysmal hypertension,[10] and in adults who have had symptoms for a long time the hypertension also tends to be continuous.

Another aspect that may help in both the diagnosis and the prognosis of phæochromocytoma is the presence of other conditions which are known to be associated with this tumour in a significant proportion of cases. Several workers[11 12] have noted, for instance, that between 10% and 20% of patients with phæochromocytoma also have manifestations of von Recklinghausen's disease; and if patches of skin pigmentation are regarded as heralding the complete form of von Recklinghausen's neurofibromatosis,[13] then this proportion is probably higher. Glushien et al.[12] describe 3 patients with phæochromocytoma, of whom 1 also had neurofibromatosis and the other 2 angiomatosis retinæ (von Hippel), which is another neurocutaneous disease and can be mistaken for the retinopathy of malignant hypertension. These workers suggest that the association of either von Recklinghausen's disease or angiomatosis retinæ with hypertension increases the chances that the cause of the hypertension is a phæochromocytoma, and they go so far as to prophesy that a connection will later be proved with other neurocutaneous diseases, such as tuberous sclerosis and angiomatosis of the Sturge-Weber type, with its visual defects, contralateral hemiplegia, migraine, epilepsy, and commonly mental impairment. It may be worth while inquiring for a family history of these conditions in known cases of phæochromocytoma. Von Recklinghausen's disease, it should be remembered, is very versatile in its manifestations,[14] which include single or multiple nodular or plexiform subcutaneous neurofibromata, patches of skin pigmentation, asymmetry of growth, scoliosis, radiological "cysts" in bones,[15] defects in hearing associated with acoustic neuromata, and mental impairment. Moreover, in the matter of prognosis, even if a phæochromocytoma is successfully removed and the hypertension relieved, there is still a more than even chance, according to Charpentier,[16] that a patient with von Recklinghausen's disease has mental impairment, and a fair chance, according to Hosoi,[17] that the fibromata will undergo sarcomatous change. And if the pessimist is to finish his say, the increased likelihood of malignancy of the breast when there are neurofibromata in it should be mentioned.[18] In angiomatosis retinæ blindness may follow, and there is a 20–25% chance of an angioma or a cyst elsewhere in the brain,[18] although it may show itself relatively late in life.

When all the clinical effects and the possible associations of a phæochromocytoma are considered, it seems that a correct diagnosis should be possible in a high proportion of cases; but in some of them the prognosis may be poorer because of the conditions which quite often accompany it.

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"PSEUDOLUETIC PNEUMONIA"

THE pneumonias are a group of diseases which we think of in many different ways. For instance, we consider lipoid pneumonia largely in terms of morbid anatomical appearances, while in staphylococcal pneumonia we include the bacterial cause of the histological changes and in aspiration pneumonia the mechanical cause. Other subdivisions rest only on clinical, anatomical, or even serological criteria. Thus, in 1936 Fanconi called an illness he had observed in children "pseudoluetic perihilar bronchopneumonia";[19] A similar condition has been named "Wassermann-positive lung infiltrations" by Hegglin,[20] and more recently "pseudoluetic virus pneumonia" by Herzog and Pulver,[21] who describe 37 examples of the "disease," diagnosed between 1940 and 1952. The common features were a short benign illness with respiratory symptoms, radiographic abnormalities in the lung fields, and a transiently positive Wassermann reaction. The bacterial population of the sputum is not recorded. Serological tests for virus infections were not carried out, and cold agglutinins were not demonstrated. There is, therefore, no acceptable evidence that the illnesses were due to a virus. The clinical and radiographic features alone do not distinguish these cases as a special group of the pneumonias. The only unusual feature is the positive W.R.; but, as Herzog and Pulver point out, a positive W.R. may occasionally be found in many other febrile conditions. The only infections that produce a relatively high proportion of positive W.R.s are syphilis, yaws, leprosy, and, to a less extent, malaria.[22] None are likely to have been the cause of these pneumonias; and it is highly improbable that a positive reaction would lead to a diagnosis of the cause of a pneumonia. The object in classifying the pneumonias should be to discover their causes; and a new clinical subdivision is only valuable if it promises to give such help. For this reason, "pseudoluetic pneumonia" seems a misleading title.

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THE LANCET, 7, Adam Street, Adelphi, London, W.C.2

Mr. F. W. Holdsworth (Sheffield) said that with the introduction of anterolateral decompression our ideas on the treatment of Pott's paraplegia had been revolutionised. Operation seemed strongly indicated in any case where recovery was not occurring with conservative treatment. Antibiotics had helped to make operation safer. Mr. Norman Capener (Exeter) suggested that operation should not be undertaken lightly. The operation he described was essentially the same as that recommended by Mr. Griffiths, but he thought it unnecessary to remove more than one or two ribs. Mr. J. Dobson (Wrightington) thought that anterolateral decompression should be done only in specially equipped centres. He emphasised the importance of treating the tuberculous patient as a whole by constitutional measures. Mr. R. W. Butler (Cambridge) believed that anterolateral decompression would greatly shorten the duration of paraplegia and would permit recovery in many patients who would not otherwise recover.

Treatment of Early Poliomyelitis

Sir Harry Platt (Manchester) remarked that a generation ago outbreaks of poliomyelitis were always small and children were almost exclusively affected. The main problem was to prevent and relieve crippling deformity. As a result of the greatly increased incidence of poliomyelitis and the frequent affection of adults, the subject had become even more important. The prevention of deformity was still one of the main problems. This could be tackled efficiently by the orthopædic surgeon only if the patient came under his care at an early stage. There was unfortunately a tendency for patients to be brought too late to the orthopædic surgeon.

Mr. D. M. Brooks (London) outlined a programme of treatment for patients with poliomyelitis. He recalled that the aims of treatment were to save life, to prevent deformity, to restore function, and to rehabilitate the patient. The orthopædic surgeon should have access to the patient at an early stage, and he should have a full knowledge of the complications that endangered life and of their management, including the use of different types of respirator. In preventing deformity the surgeon must remember its two causes—faulty posture and muscle imbalance. Faulty posture, which might be assumed in an attempt to minimise pain, was always preventable by appropriate splints. Muscle imbalance was more difficult to counteract, especially in children; when this was great, it was impossible to prevent deformity simply by external retentive apparatus. Relatively early tendon transplantation was often necessary. Active use of recovering muscles should be encouraged with relative caution; fatigue might be harmful during the early months. Electrical muscle tests were of value in determining at an early stage whether paralysis was going to be permanent. In general, if a muscle showed no sign of recovery within three months it was unlikely ever to recover. This knowledge enabled an early decision to be made on the question of tendon transplantation. Mr. H. H. Langston (Winchester) said that it was important that the orthopædic surgeon should have early access to patients with poliomyelitis. There was a tendency for too much delay. Professor McFarland believed that early orthopædic management would best be secured by the efforts of individual orthopædic surgeons in their own areas. Mr. R. I. Stirling (Edinburgh) suggested that in time of epidemics blocks of beds in fever hospitals should be put at the disposal of the orthopædic surgeons, who otherwise might be unable to accommodate the large numbers of cases in their own wards. Mr. J. C. Scott (Oxford) believed that in the early stages the ideal arrangement was close coöperation between orthopædic surgeons, pædiatricians, and infectious-disease physicians. Orthopædic surgeons should strive to contribute more to the solution of problems of the early phases of the disease.

Dupuytren's Contracture

Mr. J. I. P. James (London) recognised contracture of the fifth finger as a distinct clinical type in which the distal interphalangeal joint was not uncommonly flexed. He had found "knuckle pads" associated with Dupuytren's contracture in nearly a quarter of all his cases; the microscopic appearance of the pads was similar to that of the palmar fascia. Plantar involvement was also common. In the elderly subcutaneous tenotomy was occasionally justified, but for the ordinary case excision of the palmar fascia through a skin-crease palmar incision and through midlateral digital incisions was recommended. The greatest hazard was œdema of the hand. Of 84 cases reviewed the result was perfect or good in 64, and fair or poor in 20. Metacarpophalangeal contractures could usually be overcome, whereas interphalangeal contractures were very liable to persist.

Amputation of all Toes

Mr. K. I. Nissen (London) said that there was a place for amputation of all the toes in cases of gross deformity with rigid, functionless, but painful toes. Such a condition most commonly followed "burnt-out" rheumatoid arthritis; occasionally it was induced by peroneal muscular atrophy or by frostbite. The nature of the proposed operation should always be clearly impressed on the patient, whose written permission should be secured. After operation it was often possible for ordinary shoes to be worn, but special shoes might be required.

Tendon Transplants for Claw-toes

Mr. R. G. Taylor (Oxford) had studied the results, in 68 patients, of Girdlestone's operation of transplantation of the long toe-flexors into the extensor expansion for claw-toes. The results were almost uniformly good.

Colles Fracture

Mr. W. Doolin (Dublin) sketched the background against which Abraham Colles occupied with distinction the chair of surgery in Dublin. Colles was a man of exceptional modesty, admired by his colleagues and by students alike for his upright character and intense honesty.

Mr. G. N. Golden (Guildford) had studied the late results in 110 cases of Colles fracture treated one to twenty years before. Most fractures had been treated by junior residents, and the usual method had been manipulative reduction and immobilisation in plaster for four weeks. 15 fractures had required remanipulation for secondary displacement. Results were assessed on the basis of pain, functional disability, and deformity. Mr. Golden concluded that age alone was not an important factor in the result. The type of fracture was of some significance, the frequency of poor results being greater after comminuted fractures and especially after fractures complicated by radio-ulnar subluxation. There was a definite and striking relationship between the quality of the reduction maintained and the result. More stable reduction, and consequently improved results, might follow the use of above-elbow plasters. Dr. W. R. Harris (Toronto) said that one of the difficulties was to maintain reduction. He and his colleagues in Toronto believed that the use of plaster-of-paris was an inefficient method, especially in comminuted fractures. In selected patients a trial had been given to mechanical fixation by pin units of the Roger Anderson type. In 23 cases observed for from two months to five years after treatment there had been no recurrence of deformity and no patient had lost more than 5° of wrist movement. In 2 cases the pin fixation had to be abandaoned because of pin-track infection.

Median-nerve Compression in the Carpal Tunnel

Mr. J. S. R. Golding (London) recalled that pain and tingling in the distribution of the median nerve in the hand were commonly due to compression of the median nerve behind the transverse carpal ligament. He had studied the clinical features and results in 50 patients subjected to operation. Most patients were women in middle life, and in half the symptoms were bilateral. Tingling at night was prominent, and was often relieved by hanging the arm out of bed or shaking it. There was usually impairment of sensation, and sometimes there were motor weakness and wasting, which might be confined to the abductor pollicis brevis and opponens pollicis. The causes of the narrowing of the tunnel fell into two groups—non-traumatic and traumatic. Non-traumatic conditions included ganglion, tenosynovitis, changes in the transverse ligament itself (acromegaly, Leri's pleonosteosis), and idiopathic. The traumatic group included early lesions such as hæmatoma, carpal dislocation, and fractures with displaced fragments, and late lesions such as old fractured scaphoid and gross traumatic arthritis. The results of decompression by division of the transverse carpal ligament were good. The symptoms were almost always relieved. There was usually good or moderate recovery of sensibility, but motor impairment often persisted.

Edward Hallaran Bennett

Mr. W. Gissane (Birmingham) paid a tribute to the memory of Edward Hallaran Bennott (1837–1907), a former

Special Articles

HOSPITAL COSTING
ITS IMPORTANCE TO THE DOCTOR

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IT is probable that in the next year or two hospitals will adopt some form of departmental cost accounting in their official periodic statements of their financial position Three reports[1–3] have lately discussed ways of enhancing the value of this official information This is not a narrow affair of technical accounting procedure, on the contrary, the measures finally adopted on a national scale will affect all who work in the National Health Service, whether they be whole-time salaried personnel or part-time employees It is important therefore that doctors should know what is involved and that they should not think that "this is all too complicated" We shall get the administration we deserve, a little clarification now may help to avoid a good deal of mystery later

What is Costing ?

Historically, the origin of costing systems is to be found in the steady growth of complexity in the structure of industrial concerns The financial affairs of the private citizen and the one-man business can usually be comprehended by that citizen or that business man, so that a stocktaking and an estimate of how he stands can be made at any time without great difficulty He can analyse his expenditure and income so that he knows how he is spending his money—so much on rent, rates, electricity, gas, water, and so forth But when the business is large enough to have several departments, or is making an article which is complex enough to consist of many components and accessories, then new problems arise Is department A making a big profit, and department B a loss, so that the profit on the whole business is really concealing a loss on part of it ? Or is a component part costing more to make than it would cost to buy it ready-made by somebody else ?

Clearly, the answers to these questions demand that we analyse the costs of running the business so that we can separate the items of cost belonging to department A from those belonging to department B, or the items belonging to the job of making a component must be extracted from the records of expenditure of the business as a whole Consider, for a moment, this process of analysis in relation to departments A and B Some costs will be apportioned without difficulty the wages of employees wholly employed in department A, the materials used in department A, these items are easily extracted Together with other items (if any) directly and unequivocally *attributable to the department*, these constitute the so-called "prime cost" of department A. But the department also occupies part of the whole business premises, uses the services of the managers, directors, clerical staff, shares in the benefits accruing from advertising paid for by the business as a whole, and uses electricity and other power (maybe from a central power plant) All these items, whose precise apportionment between departments is not obvious, constitute a total mass of expenditure which has been called "oncost," or "overhead" expenditure The total cost of department A therefore consists of its "prime cost" plus its due share of the "oncost" or "overhead"

In industry, the aim of the analysis of costs is to determine the cost of producing X articles, so that a proper selling price can be established, or, given a pre-existing market price for an article, to establish how many articles must be sold at this price so that the excess of sales income over the prime cost of manufacture will cover the overhead costs and leave a given margin of profit

The Hospital's Problems

In hospitals, the output does not consist of homogeneous, tangible, countable units, but rather in a complex service which is partly measurable in quantitative terms (numbers of beds, patients, X-ray examinations) and partly assessable (but with great imprecision) in qualitative terms (professional skill, general efficiency, the human touch, kindliness)

In some respects hospitals have problems very like those in industry—e g, would it be more efficient to have the laundry done by an outside contractor rather than to run one's own laundry ? Are the circumstances of a particular hospital such that some departments (building and engineering, bakery) cost far more than they should in relation to general experience ? If so, is this unavoidable, or can it be rectified ? In any case, why is it so ?

The great defect of the present system of preparing accounts in hospitals is that it does not readily lend itself to an analysis which would answer questions of this kind In the days when many hospitals were autonomous units, there was no pressing need for comparison of detailed costs as between one hospital and another Each ran itself in the way which seemed best to those in charge, but the advent of public ownership and the necessity for Treasury control has compelled thought about the most intelligent way of allocating funds, and this implies the establishment of some yardsticks to measure the needs of different hospitals and to establish priorities within a limited budget

For the medical profession, the reasonableness of these yardsticks and the implications of their use are the most important aspects of hospital costing For the finance officers in each hospital, the labour involved in making the analysis of expenditure, and the degree of detail required are also important

Costing then, is basically an analysis of expenditure in relation to results—whether those results be a service, or the production of goods No form of analysis is entirely successful, some forms are more suited to certain types of production than to others One of the chief difficulties is how to apportion expenses which do not fall with precise divisibility on several departments of activity

Solutions of these problems of apportionment and suggestions for the detailed procedures of the routine recording of income and expenditure, so that departmental costs can be ascertained with the minimum of labour, are the basis of all published work on costing If this be remembered, no one need be mystified by the activities of the cost accountant It is not necessary to be familiar with double entry bookkeeping and accounting to appraise and criticise a method of classification of expenditure (or income) in relation to the purpose of that classification The criterion is simply—does the method of classifying (analysing) the figures bring out the maximum of meaning, with the least effort on the part of the reader ?

Subjective and Objective Analyses

The existing method of analysing expenditure into headings such as Salaries and Wages, Drugs and Dressings, has been described as a "subjective" analysis It has now been proposed[2] that this analysis by subject should be made *after* the items have been classified according to departmental headings—e g, Medical Inpatients, Medical Outpatients, X-ray Department

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1 Nuffield Provincial Hospitals Trust Report of an Experiment in Hospital Costing London 1952 See *Lancet* 1952, ii 1067
2 Costing Subcommittee appointed by the Committee of Regional Hospital Board Treasurers Second Report on Hospital Cost Accounting 1952 See *Lancet* 1952 ii 327
3 King Edward's Hospital Fund for London. Report on Costing Investigation for the Ministry of Health London 1952 See *Lancet* 1952, ii, 1067

professor of surgery in Dublin who described the injury now widely known as Bennett's fracture. Mr. Gissane said that the injury was now believed to be an adduction injury, and added that, although it might be reduced clinically without difficulty (as had been claimed by Bennett before the days of X rays), it was essential to maintain reduction under close radiographic control. Operative suture of the ruptured joint capsule might be required to prevent redisplacement; and, when necessary, this should be done early while the damaged tissues were still recognisable and easily handled. For late disability after inadequate reduction arthrodesis was preferable to arthroplasty.

AMERICAN ASSOCIATION FOR CANCER RESEARCH

THE forty-fourth annual meeting of the association was held in Chicago from April 9 to 11.

Tobacco Carcinogens

E. L. **WYNDER**, E. A. **GRAHAM**, and A. B. **CRONINGER** (St. Louis and New York) reported studies on the carcinogenicity of tobacco tars. Smoke from cigarettes, smoked in a manner simulating human smoking habits, was condensed in flasks immersed in dry ice and ethyl alcohol, and the resulting tars dissolved in acetone. One out of every two mice painted with this solution developed a papilloma, the earliest tumour appearing after 8 months; the average time required was 13 months. A carcinoma developed in one out of every six mice, the earliest after 10 months, and the average time of induction was 15 months. Some of these carcinomas metastasised to the lungs, and some were successfully transplanted for several generations. No tumours developed in the control mice painted with acetone alone.

Cancer of the Cervix

C. C. **ERICKSON** and his associates (Memphis, Tennessee) gave a preliminary report of the results of cancer screening of the general population: 20,000 women were examined by the vaginal-smear technique, and suspicious and positive smears were found in about 1·8% of women examined. Subsequent biopsies showed that about half of these women had intra-epithelial carcinoma of the cervix or invasive cancer.

S. C. **KASDON** and W. H. **FISHMAN** (Boston) reported work done since 1951 on the β-glucoronidase activity of the vaginal fluid of 386 cancer-free *pre*menopausal women: 88·6% had values below 400 units per g. Of the remaining 11·4%, the majority had gynæcological disorders such as preclinical cancer of the cervix, gonococcal and other infections, and ovarian dysfunction. Only 3 out of 16 premenopausal women with untreated primary invasive epidermoid cancer of the cervix showed vaginal-fluid β-glucoronidase activity below 400 units per g. But high vaginal-fluid β-glucoronidase levels were often found in *post*menopausal women and in those with deficient ovarian function who showed no clinical or other evidence of cancer.

Hydatid Mole

ROY **HERTZ** (Bethesda, Maryland) reported the absence of histidinuria of pregnancy in patients with hydatid mole, although high urinary gonadotrophin titres were found. As cortisone and A.C.T.H., but not progesterone, have been said to produce definite histidinuria, its absence in cases of hydatid mole may reflect a change in adrenal function. This deviation from the normal urinary findings in pregnancy may be a useful test for hydatid mole.

Cancer of the Prostate

W. H. **FISHMAN**, F. **LERNER**, and F. **HOMBURGER** (Boston) reported a method for estimating serum-acid-phosphatase of prostatic origin, which depended on the ability of *l*-tartrate to inhibit prostatic-gland acid-phosphatase.[1] This "prostatic" acid-phosphatase constituted 10–30% of the total serum-acid-phosphatase. In cases of disseminated prostatic cancer abnormal serum levels of this fraction were commoner than abnormal conventional acid-phosphatase levels. Some men, with normal conventional serum-acid-phosphatase and abnormal "prostatic" serum-acid-phosphatase were subsequently found to have cancer of the prostate, though there was no radiological evidence of bone metastases at the time of the phosphatase estimations.

Leukæmia

A. J. **ANLYAN** (New York) had studied the β-glucoronidase activity of the leucocytes of 46 leukæmic children under 13 years of age. The leukæmia was predominantly a "stem-cell leukæmia." The patients were divided arbitrarily into three groups: those with leucocyte enzyme activity below 2000 units per g. of buffy coat; those with between 2000 and 4000 units; and those with over 4000 units. The patients were equally divided among the three groups. It was found that the first group responded well to treatment, though the remissions were short and could seldom be achieved twice. The second group included many of the patients that survived a year or more and who had longer remissions than the other groups. The third group pursued a rapidly fatal course despite treatment.

Metastatic Tumours of Bone

JUDITH **BELLIN**, AGNES **HAUSINGER**, and HERTA **SPENCER** (New York) described experiments on the metabolism and removal of radiocalcium (Ca^{45}) in patients with osteolytic or osteoblastic metastases. Tracer doses were injected intravenously. The loss of Ca^{45} through the alimentary tract was similar in both groups, but the urinary excretion was 60–80 times greater in patients with osteolytic metastases than in those with osteoblastic metastases.

Tumour Growth

O. H. **PEARSON** and C. D. **WEST** (New York) discussed objective methods for the measurement of tumour growth in man. Lymphoid tumours and the myeloid tissue of acute leukæmia contained three times as much phosphorus per unit of nitrogen as muscle tissue, and thus growth or destruction of such tumours should be accompanied by a positive or negative balance of these elements in the same ratio as they exist in the tumour tissue. Slight changes in tumour mass of approximately 30 g. wet weight of tissue per day were detected in this way. Further, osteolytic tumours grew by destroying normal bone; it was assumed that growth of 1 g. of tumour caused destruction of 1 g. of bone, and hence a negative calcium balance of approximately 150 mg.; this amount of calcium loss per day was readily measured.

Chemotherapy

A new substance, 6-mercaptopurine, has recently been intensively studied at the Sloan-Kettering Institute for Cancer Research, New York. Some preliminary experimental and clinical results were presented by workers at the institute. D. A. **CLARKE** and his associates reported that this substance was a unique inhibitor of the transplantable mouse tumour, sarcoma 180. It was effective orally or parenterally. At first there was only moderate inhibition of tumour growth, but later most tumours became non-viable—i.e., unable to "take" when transplanted to normal mice. Survival-time was increased in treated mice and there was complete regression of the tumour in a significant number. J. H. **BURCHENAL** and his group gave details of some preliminary trials in over 100 patients with advanced neoplastic disease. The usual oral dose was 2·5 mg. per kg. body-weight until a therapeutic effect or a fall in the total leucocyte-count appeared. Children tolerated this dosage level for a longer period than adults. Particular caution was needed in patients with impaired renal function or very high leucocyte-counts, for difficulties in uric-acid excretion occurred when tissue-breakdown was too rapid. The main toxic sign was depression of the blood-count, but marrow examination showed none of the morphological changes characteristic of intoxication with folic-acid antagonists. 14 out of 45 children with acute leukæmia were temporarily improved, and 11 showed substantial improvement.

A. **GELLHORN** and his colleagues (New York) described laboratory and clinical studies of 1 : 4-dimethanesulphonyloxybutane ('Myleran'). This was a potent carcinostatic agent for the mouse mammary tumours 755 and E 0771, and for the Brown-Pearce carcinoma in rabbits. Clinically, they had confirmed recent observations[2,3] that the drug was useful in the management of chronic myeloid leukæmia.

S. **FARBER** and his colleagues (Boston) discussed the antimetabolite, antimalarial, and anti-cancer activity of a series of new dihydrotriazines. The monochlor and the dichlor compounds showed a definite but temporary effect in children with acute leukæmia resistant to folic-acid antagonists,

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[1] See *J. biol. Chem.* 1953, 200, 89.

[2] Haddow, A., Timms, G. M. *Lancet*, Jan. 31, 1953, p. 207.

[3] Galton, D. A. G. *Ibid*, p. 208.

Laboratories. This method is described as "objective" analysis, and the terms subjective and objective are used in contrast to each other, as if they were fundamentally different modes of approach. But the proposed method of classification is really an extension of the old subjective analysis, emphasising the purpose of the expenditure by subdividing it first into departmental heads. If objective analysis stopped short at the headings (X-ray Department, Medical Inpatients, &c.) without detailing, under these headings, the subjective items (Salaries and Wages, Materials, &c.) it would obviously be uninformative. Merely to be told that the laboratories have cost £*x* per annum is of little value unless we know something about how the £*x* was spent. I conclude that the word objective is used to mean functional; it is, I think, unfortunate that the descriptions of the old and new methods of analysis should employ the words subjective and objective respectively, for the time-honoured usage of these terms, as opposites in meaning, is different from their recent use in the context of hospital costing.

The accompanying table illustrates how the terms are used. The grand total in the bottom left corner is the whole expenditure of a given hospital for a given period; it is made up of the items listed vertically in the two left hand columns. If these items are apportioned between departments, as shown in the remaining columns then the total of each of these latter columns will give the whole expenditure on each department. It is clear that this diagram analyses expenditure under two different schemes—one, by subject, the other, by department. But it is also clear that the totals of columns A, B, C, D would not be worth knowing unless each were also divided by subjects. In other words, to obtain useful information both the subjective and objective directions of analysis are required. In practice, some items of expenditure are automatically separated as subjective headings by the very process of recording the expenditure—e.g., the salaries and wages paid by a management committee involving special withdrawals from a bank on that account—and these will then need to be apportioned between departments to give the complete analysis. Other items may obviously belong to a particular department—e.g., parts for a flame photometer for the biochemical section of a pathological laboratory—but the precise subjective heading (within that department's orbit) may not be immediately obvious—e.g., the items may be a new addition to equipment, or merely the repair of an existing instrument.

These illustrations show that setting-up a departmental costing system is not simply the substitution of so-called objective analysis in place of so-called subjective analysis; it is the extension of analysis so that the final subdivisions are subjective within objective (items 1, 2, 3, &c., within Department A in the table). It is a matter of practical convenience whether one begins by dividing any particular body of expense by headings 1, 2, 3, &c., or by headings A, B, C, &c.; in the end one has to arrive at A(1), A(2), and so on, down to D(6).

So-called subjective headings	So-called subjective totals in £	So-called objective headings			
		Dept A £	Dept B £	Dept C £	Dept. D £
Salaries and wages		(1)			
Provisions		(2)			
Staff uniforms &c		(3)			
Drugs and dressings		(4)			
Fuel light and power		(5)			
Maintenance of buildings &c		(6)			
Grand total	£	£	£	£	£

The number of headings has been restricted to six 'subjective' and four 'objective' but in practice the number would be greater than this.

How detailed the analysis should be must, in practice depend upon its value relative to the labour involved in making it. This brings us to the question of the function of costing.

Function of Costing

In the health service, costing analysis can serve several overlapping purposes. These can be discussed properly only in relation to the level of administration at which the figures are to be used. One can regard the service as comprising a series of levels of administration from the Treasury (or the Minister of Health), through the regional hospital boards, the hospital management committees (boards of governors of teaching hospitals) down to the main departments of individual hospitals, and finally to such individuals as ward sisters, heads of departments, &c.

At Ministerial level the total cost of the service is crucial; but comparative costs in different geographical areas, types of hospital, sizes of hospital groupings, are possible useful results of costing analyses. At regional hospital board level, the comparative costs are useful as also are more detailed figures of comparison within their own area. At hospital management committee level, the detailed departmental costs of a particular hospital are relevant, together with comparisons with regional and national averages. In wards or departments, the figures for expenditure controllable by the sister or departmental chief are useful.

Obviously no single statement can serve all these purposes. Any attempt to make such a statement would result in huge volumes of figures whose meaning would be obscure and whose value would be merely historical, for it would take so long to prepare such a statement that the whole thing would be months (or years) out of date before it was published.

The problem, then, is to establish criteria, appropriate to each level of administration from Minister to ward staff, to determine what information is displayed, and in how much detail. There is a perennial human tendency to present figures in a wealth of detail, for apparently their completeness enhances the æsthetic satisfaction with which the compilers contemplate the final results, a satisfaction which is absent from the minds of those whose acquaintance with the detailed material is measured in hours (or minutes) rather than months. Thus the administrators who have to act intelligently on the basis of the figures, are all too often simply bemused by the complications of the tabulated statements in front of them.

Such statements are costly to prepare, uninformative or even misinformative and a hindrance to good management. The proper way to present figures is to devise the simplest possible summary of the data essential to the purposes in hand, and to present this with supplementary analyses for special purposes, or, better still, to arrange that supplementary analyses are available—in the hands of their compilers, who should be present in person—to extract the nub of a matter on the spot.

If we apply this principle to the problem of costing in the hospital service, and if we start at the level of the ward staff in a hospital, we obtain a scheme roughly as follows.

Ward Staff

These people can exercise control over wastage of drugs and dressings, breakages of glassware and china, and economy in general housekeeping in the ward. A short summary of these items of expenditure in cash and quantity is all that is needed by the ward staff. Estimated proportions of overhead costs and suchlike are quite irrelevant, and indeed may militate against coöperation in household economy by looming large in a complete costing statement—dwarfing the items over

A.C.T.H., or cortisone. They also described further work on the effect of triethylenephosphoramide (T.E.P.A.) on malignant melanoma. Regression of malignant melanoma of the skin in patients without apparent visceral involvement has already been reported.[4] Complete regression of five tumours in one patient has now lasted for a year.

H. R. BIERMAN and his associates (Bethesda and San Francisco) discussed the importance of the "tissue contact time" (T.C.T.), with special reference to the effectiveness of nitrogen-mustard therapy. There was an enhanced effect after intra-arterial injection of nitrogen mustard, but increase of the T.C.T., by occluding the venous return and arterial supply of a neoplastic area, combined with arterial infusion of the drug, was more effective. The optimal T.C.T. for each tumour and parent organ varied considerably, but experience with 20 patients with various tumours indicated that it was about 10–14 minutes with doses of nitrogen mustard of from 5 to 30 mg.

Experimental Pathology

H. W. TOOLAN (New York) reported results of transplantation experiments with 100 human tumours (including epidermoid carcinomas and adenocarcinomas of the thyroid and alimentary canal). 90% of these tumours "took" when transplanted into cortisone-treated rats. It seemed that some of these tumours could be maintained indefinitely if transplanted into successive series of cortisone-treated rats; one tumour was transplanted through 8 generations and is now being carried by 150 rats. Dr. Toolan hoped that enough animals bearing human tumours would shortly be available to permit new therapeutic agents to be tested against human, rather than animal, tumours.

A. C. GRIFFIN and his colleagues (Stanford, California) found that hypophysectomised rats, fed with azo-dyes, did not have liver damage or tumours. Extensive liver degeneration and cirrhosis, however, occurred when these rats were treated with the pituitary gonadotrophin fraction. This suggested that the factor or factors involved in this carcinogenic process were present in this fraction.

F. E. RAY and M. F. ARGUS (Gainesville, Florida) described work on the distribution of radioactivity after administration of a S^{35}-labelled sulphonic acid (disodium fluorene-2,7-disulphonate) to A-strain mice bearing a transplantable squamous-cell carcinoma. 2 hours after administration the concentration of radioactivity was greater in the tumour than in any organ; 8 hours later the concentration was still greater in the tumour than in the liver, spleen, and muscles, although slightly less than in the kidneys and blood. This compound was more favourable than the dyes previously used, and it was concluded that localisation in the liver and spleen did not necessarily accompany localisation of sulphonic acids in tumour tissue.

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[4] See *Cancer, N.Y.* 1953, 6, 135.

Reviews of Books

Clinical Neurology

FRANK A. ELLIOTT, M.B., F.R.C.P., assistant physician, Charing Cross Hospital; BRODIE HUGHES, CH.M., F.R.C.S., professor of neurosurgery, University of Birmingham; J. W. ALDREN TURNER, D.M., F.R.C.P., neurologist, St. Bartholomew's Hospital, London. Editor: FRANK A. ELLIOTT. London: Cassell. 1952. Pp. 751. 42*s.*

THIS textbook by two neurologists and a neurosurgeon has been primarily written, the preface says, for postgraduate students. The first section deals with disorders of the motor system, somatic sensation, mental disorders, and speech disturbances and the like, ending with a short description of ancillary diagnostic procedures (including neuroradiology and electro-encephalography). A concise account of the principles involved in the electrodiagnosis of neuromuscular disorders is contributed by Dr. A. E. Ritchie. The second section covers individual diseases. The book is readable, well coördinated, and written in a clear and concise style. The aim has been "to present the common problems of neurology within a reasonable compass and to avoid the rare, the recondite, and the contentious," and by and large the authors have succeeded well in this, though there are occasional lapses.

In the section dealing with vertigo, no mention is made of benign positional vertigo and vestibular neuronitis, both common causes of this symptom. Again, though radicular disturbances due to cervical intervertebral disc degeneration are discussed in detail, only scattered references are made to the more important symptoms due to involvement of the spinal cord. Cervical spondylosis, being such a common and important condition, surely deserves fuller differentiation from the other neurological disorders it may closely resemble.

Within the limits defined by the editor, the book provides an accurate and up-to-date summary of contemporary neurological knowledge, and of the methods of investigation and treatment of disorders of the nervous system in current use in this country. We recommend it warmly to those for whom it is intended.

The Psychologist Looks at Sex and Marriage

ALLAN FROMME, D.PH. Kingswood, Surrey: The World's Work. 1952. Pp. 230. 15*s.*

THE relief of finding a first chapter in a marriage-guidance manual headed "Personal Maturity" would in itself excuse Dr. Fromme for adding to a congested literature, even if his contribution were not outstandingly good. This is, in fact, a sane and useful book. He emphasises social psychology rather than physiology (which dominates the older books). His approach to psychodynamics is eclectic, anthropological, and above all sensible, and he deals well with the physical side of sex hygiene. The device of summarising the text in a series of generalisations printed as paragraph headings is irritating to the continuous reader, but facilitates reference.

This is a book in line with humanistic ethics, acceptable to educated patients and to those who educate patients.

The Bile Pigments

C. H. GRAY, M.D., D.SC., M.R.C.P., F.R.I.C., professor of chemical pathology, University of London. London: Methuen. 1953. Pp. 142. 9*s.* 6*d.*

THIS, the third volume of Methuen's series of monographs on biochemical subjects, is well up to the high standard of its two predecessors, Davidson's *The Biochemistry of the Nucleic Acids*, and Albert's *Selective Toxicity*. The subject is undoubtedly a difficult one, the chemistry complex, and the nomenclature not easy to follow. Nevertheless, in 15 small pages an unusually clear account is presented of the structure of bilirubin, the steps by which this was ascertained, and the relationships with most of its important chemical derivatives and precursors. Useful sections on the preparation and determination of bile pigments are appended. The subject matter is by no means confined to pure chemistry, and the author's clinical interests are clearly shown in his expert discussion of the van den Bergh reaction, the clinical varieties of jaundice, and the problem of urobilin and its precursors in urine and fæces. The account of the biosynthesis of the bile pigments incorporates the results of recent work using N^{15}-labelled glycine, to which Gray has himself made significant contributions. According to the information on the cover, the "aim of this brief monograph is to provide a readable, useful and brief account of the bile pigments." It does even more: it provides an excellent guide through the maze of recent work on this complex subject.

Biological Hazards of Atomic Energy

Editor: A. HADDOW. London: *Oxford University Press.* 1952. Pp. 235. 35*s.*

THIS book records the proceedings of the conference on the biological hazards of atomic energy held in October, 1950, at the Royal Institution. The 24 short articles are by leading authorities in the United Kingdom, and by three distinguished foreign visitors. For those biologists interested in the implications of nuclear energy, biologists or otherwise, they form a useful reference book. They provide a good summary of British views in October, 1950; and few of these views will have changed much since then.

which sister has some control If she is asked to economise in items which are displayed as a small percentage of total costs she may well feel "what's the use?"

Departmental Chiefs

Similar argument applies here Quantitative criteria of output—beloved of the cost accountant—can be irritating if applied too rigidly It is more important that the chief and his staff should, in their relations with patients, be free from "the insolence of office," than that their output in items of service be x% greater than last year

Each departmental chief can agree with the local administration on the most efficient method of presenting costs in his department Again, the apportionment of overheads to each department is of minor interest to its chief, compared with figures relating to expenditure controllable by him

Hospital Management Committees

These are in a position to review the costs of the running of the group as a whole, and of running the various separate clinics and hospitals within their group Statements are therefore required to show how the total budget is distributed over the hospitals and departments, how the various quantitative criteria are being applied (inpatient days, outpatient attendances, &c), and how the group stands in relation to projected improvements, alterations in structure, developments of particular services, and so on

At this level, the modes of apportionment of overheads and general services expenditure are of relevance The details of use to ward sisters are only relevant in the form of brief summaries of costs (carbon copies of such detailed statements can be available if required)

Comparative statements of costs as between groups may be of interest, but these are not the main concern of the hospital management committee, its own quality of service per pound expended is the main thing

Regional Hospital Boards

In the distribution of funds to the hospital management committees in the region, the equity (or otherwise) of the bases for allocation is of paramount importance As the regions contain hospitals varying so widely in their architectural efficiency (converted public-assistance institutions with acres of stone-flagged corridors can be expensive to paint, to clean, and to heat), their internal accessibility (inadequate lifts are the rule in old-fashioned buildings), and their capacity to attract efficient labour (compare the portering staffs at different hospitals), there are many problems to be solved before costing comparisons can be made between groups of hospitals with sufficient validity to justify their application in any system of budgetary control This aspect is discussed by Topping [4] in an instructive paper

Limitations of Costing Systems

The main object of costing analysis is to help the management to exercise control over expenditure, not merely to economise, but to obtain the maximum value for money The claims which are sometimes made for costing systems—that they bring into being a "new approach" which enables one to plan the future in a new and more efficient way—are, in my opinion, not free from inflation with the wind of enthusiasm

A little reflection will show that, under the (admittedly not-fully-informative) system at present in use, management committees do in fact plan their future use of funds, assign priorities, and generally apply intelligent forecasting to the running of their hospitals The proposal to analyse costs a little further so that departmental costs will become available, will not revolutionise the situation, it will simply allow the accumulation of more detailed comparative cost-information How much use (or misuse) is made of this information will depend upon how much careful analysis is applied to the schemes of costing experts when these are examined in the administrative departments of the health service My object in writing this article is to provide a corrective to any too-enthusiastic adoption of detailed schemes

It will be necessary to urge some form of corrective restraint for the experience of the business world has shown that fashions for "systems" develop and hold sway for considerable periods, enthralling those who fall a prey to slogans like "budgetary control," and leading some (otherwise highly intelligent) people to think and believe that in some way the application of such and such a system will automatically reduce costs, increase income, abolish waste, and generally change the whole financial situation!

One kind of fallacy which can easily arise is well illustrated by a problem which occurred when a syringe service was being costed in the course of its planning on paper A centralised syringe service in a hospital removes from the wards and clinics the work of boiling-up syringes and needles, and substitutes centralised sterilisation with a collection and delivery service A simple calculation based upon the number of syringes used per day in each ward and clinic, and the value of the nurses' time thus saved, enables one to show that the annual saving thus effected goes far towards paying for the labour and materials required by the centralised packing and sterilising unit But is this a valid calculation? It is not A little thought will reveal that although indeed a large number of nurses will have a few minutes more time each day available for their other multifarious duties, this time saved will not affect the number of nurses required in any one ward or clinic, and so no *financial* saving will be made The proper way of describing the effect of the installation of the central syringe service is to point this out, and to recognise that the extra cost of the service has to be regarded as the price paid for greater assurance of sterility in the syringes and needles, and some slight reduction in the burden of work upon the nurses I would ask my colleagues to ponder this simple illustration, and to realise that this type of fallacy easily arises in discussions about comparative costs

A hospital laundry may be housed in part of the hospital premises, and its total costs, after charging to it a reasonable hypothetical rent for the premises occupied, may prove to be excessive compared with what would be charged by an outside contractor for the same volume of work. If, however, the premises once occupied by the laundry would in fact remain unused, if the laundry work were done by an outside contractor, then the result of the change might not be a saving, but a loss Nevertheless, it is entirely proper to charge the laundry with a reasonable hypothetical rent, for only thus can the total cost of the laundry be ascertained if comparison with outside contractors is desired Such a comparison may help to initiate inquiries as to the reasons why the costs, other than rent, are excessive

Summary

The introduction of departmental costing in the day-to-day accounting systems of hospitals will help to provide the additional information which is necessary before any rational comparisons can be drawn between expenditures at different hospitals

Such a change will in fact amount to an extension of the present system of analysis If adopted, it will not be a radical or revolutionary change, and it will not automatically solve major problems or cut costs, it will itself cost money

The application of the results of departmental costing will yield information of value, but the interpretation of the figures and the use made of them will call for close scrutiny by all involved—not least by the doctors

Such a scrutiny is perfectly feasible if the fundamentals be kept in mind, no one should be dissuaded from taking part merely because he feels himself a layman in respect of costing systems I would especially ask my colleagues to read what McLachlan [5,6] has written on the limitations of purely financial indices in the health service

Finally, I would plead for active coöperation between doctors and finance officers, so that the final forms of analysis adopted may reflect, not the wholesale application of an elaborate conventional costing system, but rather the recognition of the special problems of hospitals and the variety of indices which can prove helpful

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[4] Topping, A *Lancet*, 1936 ii, 807

[5] McLachlan G *The Accountant*, Oct 11, 1952

[6] McLachlan, G *Lancet*, 1952, ii, 1130

THE LANCET

LONDON: SATURDAY, MAY 16, 1953

Protection of Children

OUR most commonly used legal remedy for relieving an ill-used child is to take him away from his parents and put him with well-meaning strangers. The notion that the separation of a child from his mother is in itself an extremely damaging form of ill-usage is only just beginning to penetrate medicine, and will therefore take some time to influence the law. Under the Children and Young Persons Act, 1933, cruelty to persons under 16 is defined as follows:

> "If any person who has attained the age of sixteen years and has the custody, charge or care of any child or young person under that age, wilfully assaults, ill-treats, neglects, abandons, or exposes him, or causes or procures him to be assaulted, ill-treated, neglected, abandoned, or exposed, in a manner likely to cause him unnecessary suffering or injury to health (including injury to or loss of sight, or hearing, or limb, or organ of the body, and any mental derangement), that person shall be guilty of a misdemeanour . . ."

The Act does not make it clear whether "mental derangement" is confined to conditions accompanied by psychotic symptoms, or whether treatment likely to cause neurotic symptoms is also an offence. In the latter case, the court ordering separation must, on occasions, surely qualify as an offender. Nowadays cruelty need not even be "wilful": under the Children and Young Persons (Amendment) Act of 1952, a child may be removed by a court from his parents on grounds of ill-treatment, neglect, and so on, without its being necessary to show that his parents, or other custodians, have *intentionally* misused him. This means that the child may suffer not only the hardship caused by the offence, but the more severe and prolonged hardship of separation from a mother who may never have meant him—*or indeed even done him*—any harm. The Children's Officers Association, who have set out these facts and many others in a thoroughly sound memorandum, *Cruelty to Children*[1] (prepared at the request of a joint committee of the British Medical Association and the Magistrates' Association), say:

> "Our members know of cases where children have been brought before courts as being 'in moral danger' where the evidence was that the father bullied and terrified children and mother. In such cases the offender has gone unpunished and the very severe punishment of being taken away from their mother has been meted out to the children. In some cases the children (in spite of their alleged unhappy situation with their parents) have been known to scream and fight with the officers of the court who are removing them from their mother. Arrived at the institution they pine for their own homes. Such experiences may damage the children permanently."

The humane desire to protect children from cruelty began to show itself publicly in the last century, when the Industrial Revolution was causing growing numbers of children in mines and factories to suffer hunger, stunting, or disease, as well as bodily distress at the hands of hard masters or of despairing and drunken parents. Their suffering was occasioned mainly by *physical* violence, *physical* deprivation. The memorandum points out that this scene has now changed. The incidence of assault and undue restraint of children has diminished over the last half-century; it is mainly associated with drunkenness, which has also declined. Moreover the association believe that the machinery for detecting and combating physical violence against children is adequate. "The prevention of mental ill-treatment," they say, "is a much wider problem, and one in which a lead can only be given by the medical profession."

The law is certainly very uneven in its operation. Thus the mentally subnormal mother of a large family who loves her children but lets them get dirty and ill-nourished can be punished (for her incompetence rather than her fault) by imprisonment, or by having her children taken from her. In either case the children suffer harm. Excuses are found, however, for the unmarried father and mother who have a child and fail to arrange a secure upbringing for him. Again, a father can be convicted and imprisoned for a single blow delivered in a rare bout of drunkenness; but a father who wilfully spends his earnings on something other than the rent, and gets his family evicted and his children into institutions, at once becomes better off financially than his more responsible neighbours who still have children to keep. The children's officers, however, think something might be achieved immediately by a more flexible use of the law. Parents convicted of a first offence, especially of neglect, should be severely warned that another conviction will mean imprisonment, and then be sent home on probation. At present children are almost automatically committed to the care of a local authority whenever an offence is proved: the provision for placing them under supervision at home, and for taking recognisances from the parents, could, the association believe, be much more widely used. But if the parents have behaved so badly that the children *must* be taken away, then "a very substantial contribution to their maintenance" should be required from the parents. Sometimes the most constructive thing to do is to sentence the principal offender (who is usually the father) and send the children home with their mother. She will sometimes need help from the citizens' advice bureau in proceedings to ensure that the father never returns home; and she will often need the help of the domiciliary services—the health visitor, the home help, the school welfare officer, and perhaps the family service unit. Sometimes a neglectful mother can profit by the kind of training given in hostels such as the Brentwood and Mayflower homes, where she and her children can stay while she learns the rudiments of house management and child care. The first object, however, should always be to save the existing home, and keep the father and mother together, rather than to send either parent away.

This may sound a costly proceeding in terms of social services; but it would in fact, the children's officers point out, be a good deal cheaper than our present practice. To maintain one child for a week in a children's home may cost as much as £5; in an approved school more than £6; in a residential nursery as much as £8. One child in institutional care for fifteen years may cost up to £3000, and the outlay for a large family runs into five figures. "A tithe of

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[1] Copies available from A.S.N. Allison, 47, Full Street, Derby. Pp. 8. 5½d., postage paid.

INSTITUTE OF HOSPITAL ADMINISTRATORS

THE institute held its annual conference at Hastings from May 7 to 9.

Training of Administrators

In his presidential address, Mr. S C **MERIVALE**, secretary to the board of governors of the United Bristol Hospitals, examined the ways in which hospital administrators are at present learning their jobs The institute itself made arrangements for systematic instruction and examination for its diploma , and there was the Hospital Administrative Staff College in London, where King Edward's Hospital Fund provided special facilities for concentrated postgraduate study In addition certain hospitals throughout the country were working schemes for the instruction of one or more trainee administrators There were, Mr. Merivale thought various dangers in this situation For one thing, "private enterprise" schemes might remain both too "private" and too "enterprising" "too private" because such schemes would tend to turn out people purporting to be fully trained when they had had experience of working in only one hospital group or authority , "too enterprising" because such uncoördinated individual efforts might lead to over-recruitment of able people and a glut of "registrars" in the administrative branch of the service Another danger was that the Administrative Staff College might lose some of its effectiveness by an inability to link up the work which only it could do with approved practical work in the widest possible variety of hospitals and hospital authorities. The institute and its regional councils could play a big part in arranging in coöperation with hospital authorities and the staff college, training circuits to which people who were prepared to make the necessary sacrifices could enter from within the service These arrangements could and should be linked with the Recruitment Advisory Service which the King's Fund had already set up at the college

To overcome the difficulties involved in moving trainee staff about the country, Mr. Merivale proposed that there should be in every region a sort of Civil Service Commission for the administrative branch of the health service, containing representatives of the regional council of the institute and the employing authorities This body would approve appointments for designation [illegible] o six of which would be grouped [illegible] to provide the widest possible variety of experience These posts would be held for from six to twelve months each, and they would be linked with the staff college to ensure that a period of concentrated study and instruction was included in the normal progress round a training circuit The number of posts in each circuit should bear some relation to the ultimate prospects of their holders, bearing in mind the number of senior appointments that would be available As Mr Merivale pointed out, these proposals to some extent involved individual authorities voluntarily surrendering their present sovereign rights to make their own administrative appointments at "registrar" level. But if the administrative service was to compete successfully for its share of the best recruits, its training arrangements must bear comparison with those in other walks of life and the prospects of promotion must be fair and reasonable The need, therefore, was for some practicable and acceptable compromise between the present haphazard system and its opposite—promotion by posting

The Committee System

Mr **JOHN TREVELYAN** discussed the advantages and disadvantages of the committee system, with particular reference to its place in hospital administration Committees tended to discourage action as the anonymous cynic put it; "a committee is a group of men who individually can do nothing but collectively can meet and decide that nothing can be done." Sometimes, too, the power of decision on technical matters rested with the inexperienced On the other hand these were not always disadvantages for precipitate action was not always a good thing and in these days of specialists in every field often with competing claims, the judgment of the non-specialist might be valuable in maintaining a balance Moreover, history had taught us that the committee system, however cumbersome it might be, was an effective barrier to tyranny , and in our time we had to fight against the tyranny not of the autocrat, but of the bureaucrat In the hospital service executive responsibility was shared between the Ministry and the various committees—from regional hospital boards to house committees—in varying and not always clearly defined, proportions It produced the problem of how to blend central direction with decentralised committee administration , there was the danger of too much central direction largely in the form of a tight financial rein Remote control often led to standardisation and discouraged variations in individual hospitals

Turning to possible improvements in the system, Mr Trevelyan thought that there could usefully be more building from the perimeter to the centre For example, in the teaching hospital groups each board of governors might consist of some members appointed by the Minister and others elected by the house committees of the hospitals in the group Similarly, each regional hospital board might consist of a certain number of members appointed by the Minister and other members appointed by the hospital management committees in the region and each hospital management committee might be constructed in much the same way This process might be developed further by establishing a Central Hospitals Service Committee, with some members appointed by the Minister and some elected by boards of governors and regional hospital boards. Such a committee could represent the committee administration of the service in discussion with the Ministry and coöperate with the Minister in determining policy In this way all parts of the hospital service down to the committees concerned with individual hospitals could share in policy-making Further delegated authority should be progressively increased and should include as much financial responsibility as possible It was to be hoped that the new committee which was to investigate the cost of the N H S would see that the best way to save money on the hospital service was to trust the people who were running it The individual hospital committee should be given as much responsibility as possible, and it was no good having committees that had no responsible job to do In the details of committee work committees should consider what executive responsibility could be entrusted to their officers , it was up to the committees to see that they did not waste time discussing matters which could and should be dealt with by their officers. Mr Trevelyan summed up with the words of Anthony Ashton "The Committee is one of man's important social discoveries—like the use of money, the rule of law and the specialisation of labour—but it is not a panacea To solve problems it is not enough merely to set up committees They can moderate and guide the creative energy of individual men, but they can never be a substitute for it"

The Changing Function of the Hospital

Tracing the changes in the work of the hospital, Dr H W C **VINES** professor of pathology at Charing Cross Hospital Medical School, deplored the trend which was making the hospital more of an administrative unit and less of a place where patients were cared for The patient was being overlooked , and there was the money spent on maintaining neglected children in institutions apart from their parents could provide, throughout the kingdom, a first-class family service which would considerably reduce the incidence of neglect." The association offer some economic propositions which they regard as axiomatic:

> Children should not be removed from home simply for failure to attend school (it is less costly to send the school attendance officer to fetch them every day); or because their mother is ill (it is cheaper to put in a home help); or because their home is dirty (it is cheaper to put in a family service unit); or because the house is overcrowded or insanitary, or because there is no house (it is cheaper to provide a house); or because their mother is widowed, unmarried, or deserted and so has to go out to work (it is cheaper to pay an adequate allowance from National Assistance to keep her at home with them).

Their long-term remedies read, the association admit, like a prescription for the sickness of society. They are: to strengthen the churches and other organisations promoting the social virtues; to provide enough psychiatric and child-guidance and marriage-guidance clinics; to give people education in citizenship and parentcraft; to build enough houses; to extend domiciliary social services, services for unmarried mothers, health services for overburdened mothers, and educational services for handicapped children; and to ensure skilled social work in the matrimonial courts when families are breaking up, so that the court's decision is consonant with the welfare of the children. In cases of cruelty, the courts should always insist on exhaustive inquiries before breaking up the family; for "the removal of a child from his home is a dangerous and costly expedient which should only be resorted to after all other means of ameliorating his hardships have failed."

Cerebral Angiography

CEREBRAL angiography is now widely regarded as one of the most important accessory methods in the diagnosis of cerebral lesions. Percutaneous injection of contrast material into the carotid artery was first carried out by EGAS MONIZ,[1] to whom credit is due for much experimental work in angiography. In 1926, using a solution of 70% strontium bromide, MONIZ attempted cerebral angiography under local anæsthesia on four patients, but the results were unsatisfactory and thereafter he turned to injection after surgical exposure of the carotid artery. The introduction in 1931 of a colloidal suspension of the dioxide of thorium ('Thorotrast'), a non-irritant opaque contrast medium, gave further impulse to his work; and in 1932 the first carotid angiography in this country was done at the National Hospital, Queen Square, by MONIZ's pupil and successor, Prof. ALMEIDA LIMA. In the ensuing years cerebral angiography passed beyond the experimental stage; but it came under a cloud when NORTHFIELD and RUSSELL[2] and other workers demonstrated the potential dangers of thorotrast as a contrast medium. Thereafter for some years in this country carotid angiography was employed only when essential information could not be obtained by other methods. LIMA,[3] however, continues to use thorotrast as a contrast medium, on the grounds that it is non-irritant and will not produce vascular spasm. He claims that if the dose is limited to 16 ml. the risk from its radioactivity is negligible.

In Sweden interest in the subject continued during the war years and resulted in the establishment of a satisfactory percutaneous technique for injection of the carotid artery with diodone as a contrast medium. ENGESET[4] was largely responsible for this development, which revived interest in the procedure after the war. TORKILDSEN[5] described results in a series of over 2000 examinations, and BULL[6] in over 1000. LINDGREN[7] in Sweden, SUGAR et al.[8] in the U.S.A., and SUTTON and HOARE[9] in this country described the technique of percutaneous injection of the vertebral artery for the purpose of demonstrating lesions in parts of the brain not shown by carotid injection. RADNER[10] developed another technique for injection of the vertebral artery, by catheterising the radial artery. ECKER[11] and KRAYENBUHL and RICHTER[12] advocate the commoner percutaneous method, and claim that with efficient technique the risk is small. PETIT-DUTAILLIS et al.[13] have reviewed their own results with this method in over 1000 cases. They, too, believe that good technique will prevent untoward after-effects, and have observed "transitory and regressive incidents" in only 0·6% of their cases.

There is, however, some evidence that both method and contrast medium are not devoid of risk to the patient. Several workers have reported serious sequelæ. DUNSMORE et al.[14] feel less sure that technical efficiency is a guarantee against complications, and suggest that the delay in the appearance of the more serious reported complications points to their resulting from thrombosis following vasospasm, especially in patients with impaired circulation. These workers also point out the risk of injury to the cervical sympathetic chain if extravasation of the contrast medium occurs. After-effects of the intravenous injection of diodone have been described in these columns.[15]

Percutaneous cerebral angiography is an important diagnostic procedure, but its advantages should not obscure the fact that it involves the puncture of relatively small arteries by a "blind" technique and injection of a substance known to produce vascular spasm. Experienced workers admit that not uncommonly both walls of the artery may be punctured before the needle is surely in the arterial lumen. The subsequent effects on the arterial wall are still unknown. Until a non-irritant water-soluble contrast medium, which is rapidly excreted, is found the risk to a patient with arterial disease or a cerebral lesion likely to be aggravated by vascular spasm must be very carefully weighed against the value in treatment of the information likely to be obtained. The techniques of percutaneous arterial puncture and injection demand long training and continuous experience, not of a single

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even a danger that standards of hospital care would be determined by those who had never seen a patient and who would be no wiser if they did Professor Vines confessed that he was bored with the massive and uninformative financial statements that came from the hospitals, for they gave very little indication of the efficiency with which the patients were being cared for, and they certainly did not take into account the potential financial return achieved by the hospital service when it restored its patients to work—a return which was forgotten when urging economies in the service He could see no very vivid future for the hospitals now that the inspired service of their earlier days had given place to a mediocrity oppressed by bureaucracy

Emphasising the need for a more preventive approach, Professor Vines said that a large burden of national sickness had long been accepted as inevitable, and this burden was a measure of society's failure to provide for healthy living There was still little professional interest in preventive medicine, and the bed remained the chief operational tool of the hospital service On the administrative side, too many administrators thought that the care of inpatients was their only job, whereas in fact the outpatient department often afforded a much better chance of preventing serious deterioration in health But little money was spent on outpatient departments, and present conditions encouraged the admission of outpatients when a really efficient outpatient department might have saved a hospital bed and the expense of inpatient care It was said that we needed about 75,000 more hospital beds in this country to build and pay for these beds in the next fifty years was probably impossible, to staff them was almost certainly impossible, and it was very doubtful whether we could afford to maintain them even if we had them Professor Vines was sure that successful development did not lie along the unimaginative lines of building more and more beds These missing beds must be written off, and the bed must recede as a therapeutic weapon, while the outpatient department came forward We must reduce the no man's-land between health and disease by persuading the patient to seek earlier advice and by encouraging a more inquisitive outlook by the doctor More ambulant patients and more outpatient work should be the aim Along these lines, the polyclinic might become the centre of the hospital service This would involve a complete reorientation of medical thought, and the first step was a drastic overhaul of outpatient clinics—not just a bit of paint here and there, but replanning and rebuilding Many "hole-and corner" clinics would have to go No hospital should offer an outpatient service without adequate radiological and pathological facilities immediately to hand to save the time of both patients and staff Fluoroscopy rooms and pathological "sub stations," which would relieve the main departments of much routine work, could be usefully introduced into the plan As the emphasis of the hospital service moved from beds to outpatient clinics, more of the bedded hospitals might be situated in the outskirts of towns, leaving the unbedded clinics in the centre

Opening the discussion, Mr S W **Barnes**, secretary to the board of governors of *King's College Hospital*, said that no-one regretted the domination of administration, to which Professor Vines had referred, more than the hospital administrators themselves They did not like the cold, impersonal, centralised machine, and they were not responsible for it, it was the outcome of a central bureaucratic control which knew little of actual conditions in hospitals Commending Professor Vines's proposals for extending the outpatient service, Mr Barnes said that all would be wishful thinking unless the control of policy and finance by the Government could be reconciled with independence and variation in individual hospitals Mr W A **James** (Leamington) wondered whether advances in treatment might not help matters by enabling a reduction to be made in the number of beds for acute cases But Professor Vines was not sure that such a reduction would be an advantage, for the chronic sick of tomorrow were the treatable sick of today Mr F A **Weaver** (Windsor) suggested that the medical staff of the hospital service were terrified of making a diagnosis because of the threat of litigation They tended to "pass the buck" in a way which complicated the working of the service Mr S G **Hill** (Northampton) would have liked Professor Vines's criticisms to have been heard by the Ministry of Health, the local health authorities, and the doctors, for preventive medicine was not the business of the hospital administrators, or even of the hospitals, and the preoccupation with inpatient beds was the result of the Ministry's attitude

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JOINT CONSULTANTS' COMMITTEE

This committee met in London on April 29, under the chairmanship of Sir Russell Brain, F R C P

The committee again discussed the senior-registrar establishment, with particular reference to displacement Figures furnished by the Ministry of Health showed that the number of senior registrars did not now greatly exceed the establishment agreed with the committee in 1951 The number of senior registrars in their fourth or subsequent years, however, whose appointments were due to be terminated in the course of the next few months, substantially exceeded the expected consultant vacancies, and furthermore a large proportion of these senior registrars were in general medicine and surgery, in which specialties there were few new consultant appointments

Representatives of the committee had impressed upon the Ministry that many of these senior registrars were in fact undertaking consultant work, and that if they were dismissed a serious situation would arise They had again urged that the ultimate solution lay in the expansion of the consultant establishment, and they had made certain suggestions regarding immediate measures which the Ministry had received sympathetically It is hoped that a further statement on the subject will be available for publication shortly

The committee also considered a report from a subcommittee on discussions with representatives of the medical defence organisations on the increasing litigation involving members of hospital staffs

Pending further discussions with the Ministry, the committee expressed full agreement with a statement on the subject which had been drafted by the Central Consultants' and Specialists' Committee with a view to publication by the council of the British Medical Association The committee's attention was drawn to a statement on the furnishing of medical reports on hospital patients to solicitors, published in the *Law Society's Gazette* after discussions between the council of the Law Society and the Ministry The committee deprecated the issue of this statement without consultation with the medical profession, and the statement was referred to a subcommittee for detailed examination

Dr Peter Edwards, chairman of the tuberculosis and diseases of the chest group committee of the British Medical Association, attended the meeting to discuss matters of interest to chest physicians

Dr Edwards said that in most other specialties hospital boards often offered consultants an option of whole time or part time service, where the needs of the service permitted, and the group committee felt that this principle should be applied to chest physicians The Chairman explained that this matter had already been discussed with the Ministry, but there appeared to be certain difficulties connected chiefly with the duties carried out by chest physicians on behalf of local health authorities The matter was referred to a subcommittee for further discussion with the Ministry

Dr Edwards also expressed the views of his group committee on the shortage of nurses in sanatoria, and on the participation of chest physicians in the work of pneumoconiosis panels, and these matters also were referred for discussion with the Ministry.

operator but of a team comprising radiologist, radiographers, and nursing staff. Thus the method should be used only with due regard for its possible risks and in centres where the necessary skill and experience are available.

Ophthalmia Neonatorum

In 1884 the Ophthalmological Society of the United Kingdom reported that of the inmates of four representative institutions for the blind between 30 and 41% had lost their sight because of ophthalmia neonatorum. In the U.S.A. the percentage seems to have been somewhat greater, and in Continental countries much greater.[1] In 1922 a Ministry of Education survey of provincial schools for the blind showed that 30·4% of the inmates had been blinded by ophthalmia neonatorum: but by 1944, after twenty-two years of compulsory notification, the proportion had fallen to 9·2%.[2] In 1947 Sorsby[3] stated that in the years 1941–45 only 5 infants in England and Wales were known to have lost their sight in this way, and since then no case of blindness from this disease has been brought to the notice of the Ministry of Health. Ophthalmia neonatorum continues to be notified, though in decreasing numbers (4390 cases in 1940, 1935 cases in 1950); but serious ophthalmitis, and in particular gonococcal ophthalmitis, is now exceptional in maternity and eye hospitals in this country.

Benjamin Gibson, of Manchester, was one of the first to associate neonatal ophthalmia with maternal vaginal discharge. In 1807 he suggested[4] three steps to prevent it:

> "First, to remove, if possible, the disease in the mother during pregnancy; secondly, if that cannot be accomplished, to remove artificially as much of the discharge as possible from the vagina at the time of delivery; and third, to pay, at all events, particular attention to the eyes of the child by washing them immediately after delivery with a liquid calculated to remove the offending matter or to prevent its noxious action."

The elimination of blindness due to ophthalmia neonatorum is clearly the result of action such as Gibson advised, and the present low prevalence of maternal gonococcal infection must be the most important single cause. Local hygienic measures, which are undoubtedly valuable, are applied routinely; but prophylactic conjunctival instillations are no longer made universally. In 1948 a committee of the American Academy of Ophthalmology and Otolaryngology[5] reported unanimously in favour of such applications, preferably with silver nitrate; but in Britain practice has been changing. Elliott[6] found last year that in 50% of maternity units this step had been abandoned, and among 40% of local health authorities "no chemicals were in use as a routine measure." Impetus has been given to this trend by a bacteriological investigation at Queen Charlotte's Hospital in 1948: in their study of 220 infants Taylor and Calman[7] found that the rate of infection with any organism was not greatly different in eyes treated with silver nitrate from the rate in untreated eyes. These workers concluded that, in view of the effectiveness of modern treatment of established ophthalmia, it was probably unnecessary *in that hospital* to instil any form of eye-drops.

Silver-nitrate drops have an ill repute as a conjunctival irritant. When the solution is applied in the prescribed strength and amount, this irritation is usually mild and transient; but when by evaporation it becomes concentrated, or by actinic action decomposed, severe ocular irritation and serious damage may ensue. Several alternatives have been tried, including silver proteinate,[8] mercurochrome,[9] and acriflavine.[10] By far the most effective, however, is penicillin, which is now widely used on the Continent, in North and South America, and elsewhere. (In this country investigations have been concerned mainly with its value in established ophthalmia neonatorum.[8]) For prophylaxis an aqueous solution, usually in a strength of 2500 or 5000 units per ml., is instilled one or more times, either alone or after saline irrigation of the conjunctival sac. Sensitisation has not so far been noted; but repeated instillations call for increased nursing attention, and neonatal ophthalmia has not been wholly eliminated by them—it is perhaps too much, as Sorsby[3] has pointed out, to expect that a single drop of penicillin should sterilise the infected conjunctival sac. Intramuscular injection of penicillin has proved more successful: but this entails medical attention and a definite risk of sensitisation. Furthermore a fatal Herxheimer reaction may ensue: Woods[5] refers to 3 cases in which syphilitic infants died after prophylactic intramuscular injections of penicillin. Oily suspensions or ointments are more reliable, if their penicillin content is great enough. Davidson and his co-workers[11] at the Johns Hopkins Hospital compared the effect of an ointment containing 100,000 units per gramme, applied once at birth, with that of intramuscular injections of 10,000 units of penicillin, and of silver nitrate instillations. They found that the ointment was no less effective than penicillin given intramuscularly; and in the two groups treated by these two methods signs of conjunctival irritation or frank discharge were significantly less common than in the group treated with silver nitrate. The prevalence of maternal gonorrhœa at that time was estimated at 2·7%, but serious ophthalmia neonatorum was not encountered in any of the three groups. More recently Mallek and his co-workers[12] in Vancouver have come to similar conclusions. In one group of their series an ointment containing 2500 units per gramme was applied repeatedly. They attribute lid irritation seen in this group, but not in another treated once only with a more concentrated ointment containing 100,000 units per gramme, to trauma from repeated application.

There is thus good evidence that in prophylaxis, application of a potent penicillin ointment should replace silver nitrate; and the theoretical objections that not all organisms giving rise to neonatal ophthalmia respond to penicillin seems to weigh lightly in the opposite scale.

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Other matters considered by the committee included reports of discussions with the Ministry on the hospital medical staffing survey and security of tenure, and questions relating to medical advisory machinery and the domiciliary-consultation arrangements Points relating to terms and conditions of service were referred to the staff side of Committee B of the Medical Whitley Council

IMPERIAL CANCER RESEARCH FUND

THE Fund's fiftieth annual report has lately been published [1]

The many interesting lines of study that are being followed include experiments on the heterotransplantation of human tumours, where the possibility is being examined of culturing human tumours in the eye of the guineapig and in the mouse's brain, along the lines worked out by Greene at Yale The capacity for survival of the graft under such adverse conditions has been to some extent correlated with the malignancy of the tumour

Dr JAMES CRAIGIE, F R S , has continued his researches on ascites tumours One of the aims of this work is to make available transplantable tumours which can be studied in a more quantitative way

> An ascites sarcoma induced in a C_3H mouse by benzpyrene has been shown to be transplantable with doses of less than 100 cells, "the dose required to produce ascites tumours with S 37 or T 2146 is 10,000 to 100,000 times greater than this One sub line of this tumour has practically lost its ability to form solid tumour and peritoneal invasion rapidly follows subcutaneous inoculation "

Dr B D PULLINGER is studying spontaneous mammary carcinoma in the R IIIb strain of mouse, which is carried on *without* the intervention of the milk factor

Work on fowl tumours has been started once more in the Fund's laboratories

> The incidence of neoplastic diseases is greater in the fowl than in man, and is the most important cause of death in fowls in countries with highly developed poultry industries "A large-group of these diseases, known as the leukosis complex, includes a great variety of neoplastic conditions which arise from alterations of cells of the blood, bone marrow, reticulo endothelial and lymphatic systems In some ways they are analogous to the leukæmias of man " Experiments are under way on a still undecided question—whether fowl lymphomatosis is transmitted by the living lymphoid tumour cell, or by a highly labile virus which so far has eluded all attempts at isolation

Mr P C WILLIAMS has been investigating the response to œstrogen of spayed mice of the C_3H, Strong A, and C_{57} strains, he finds that the vaginal œstrogen sensitivity is inversely related to mammary cancer incidence in these three strains Moreover, there is no obvious correlation between vaginal opening and mammary development, for the vagina opens earliest in the Strong A mice, but their mammary glands develop latest

Dr J STRATTON YOUNG and Dr G D LUMB have undertaken a study of human breast cancer from anatomical, histological, and cytological aspects, and by an examination of the hormonal status of postmenopausal patients with the disease

Dr L M FRANKS found, from a study of 150 prostatic glands removed post mortem, that histological evidence for malignancy could be shown in one third After œstrogen therapy of well established primary carcinoma of the prostate, insensitivity developed in the cells of the growth, which reverted to its former malignant structure The epithelium of the prostatic urethra, however, continued to show the metaplastic change induced by the œstrogen

Mr W H W JAYNE has been using tissue culture technique in order to determine the real nature of the cells in pleural exudates in suspected bronchial cancer

Mr H G CRABTREE has continued his studies on azo-dye carcinogenesis

> The effect of diet on the induction of liver tumours by various azo compounds, particularly 4 dimethyl amino-azobenzene (" butter yellow "), has been the basis of many investigations into the nature of the dietary factors giving protection against this form of carcinogenesis Attention was from the first focused on the B group of vitamins, since tumours originally described by Japanese workers were induced by the azo compounds in animals maintained on a diet of polished rice It was soon evident that aneurine alone was not the protective factor Yeast and liver-extracts were found to be protective, and Kensler showed that riboflavine (vitamin B_2) had a definite protective action against butter yellow carcinogenesis in rats maintained on diets of medium protein content but not on low protein diets The nature of the protective action appears therefore to be complex, and it is now realised that vitamins, proteins, and fats may all be involved

In this year's report Crabtree describes experiments which, he suggests, implicate yet another member of the vitamin-B group

> His work on the relative carcinogenic activity of amino azotoluenes led him to the conclusion that those compounds of this series which failed to induce liver tumours in rats are metabolised in the liver to *p* toluidine, which then gives rise to *p* aminobenzoic acid *p* Aminobenzoic acid is probably a precursor of folic acid, and the suggestion is that the *p* aminobenzoic acid, or more probably folic acid, is a protective factor against azo dye carcinogenesis Experiments to test this idea were described in last year's report, and more complete results are now given *p* Aminobenzoic acid itself failed to protect, but it is thought that effective concentrations of the vitamin in the liver may not be obtained by its addition to the diet, and Crabtree has fed animals with azo compounds designed especially to be metabolised in the liver to yield *p* aminobenzoic acid, thus producing a high concentration of the vitamin in that organ These azo compounds, when added to the food of rats in conjunction with butter yellow or *o* aminoazotoluene, significantly retarded the average rate of induction of liver tumours by these carcinogens

The results are interpreted by Crabtree as evidence " that the metabolism of *p* aminobenzoic acid (and possibly folic acid) may have particular significance for the mechanisms of carcinogenesis "

PROVINCIAL TEACHING HOSPITALS

Boards of Governors

THE Minister of Health has made the following appointments, to fill vacancies caused by the retirement of a third of the members, to the boards of governors of the ten provincial teaching hospitals in England and Wales Out of 92 appointments, 61 are reappointments of retiring members , 2 appointments are still outstanding Those now appointed will hold office until March 31, 1956 The names of medical members are given in bold type

UNITED NEWCASTLE UPON TYNE HOSPITALS

Reappointed Prof **R V Bradlaw,** O B E , F R C S , L D S , Edward Foyle Collingwood, C B E , J P , Prof **R Bramble Green,** F.R C.S , Prof **F J Nattrass,** F R C.P , Edward Colgan

New members **Norman Hodgson,** F.R C S , Rev R E Robson, J P , Miss A M Truesdale, B SC , G Hodnett, **James Hendry,** L R C P E

UNITED LEEDS HOSPITALS

Reappointed Alderman D Beevers, O B E , LL D , J P , Prof **A M Claye,** F.R C O G , Councillor W Maldwyn Jones , J E Rusby, M C , J P , Miss E G Lupton, M A , LL D , J.P , Prof **T Talmage Read,** F R.F P S , F D S R C S **Donald Watson,** F.R C S

New member Prof **P J Moir,** M C , F.R C S

UNITED SHEFFIELD HOSPITALS

Reappointed A R Martin , T Pearson, J.P , **H. R Vickers,** F R C.P , Prof **E J Wayne,** F.R C.P , J M Whittaker,

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[1] Imperial Cancer Research Fund Fiftieth Annual Report, 1952–53 Published by the Fund Royal College of Surgeons Lincoln's Inn Fields London W C 2

Annotations

RADIOGRAPHIC ENLARGEMENT

In ordinary radiography the sharpest definition is obtained by placing the film as close as possible to the object that is being radiographed, and the X-ray tube a good distance away from the object—hence the term "teleradiography." By moving the film away from the object a radiographic enlargement can be obtained, but use of an ordinary X-ray tube with a focal spot 1·0 sq. mm. for making such an enlargement entails a loss of definition. However, with a focal spot 0·3 sq. mm. —i.e., practically punctiform—and with both the X-ray tube and the film 24–30 in. from the body (and on opposite sides thereof) definition is remarkably good. Bronchograms taken by this method, which the French call "*radiographie en gros plan*" (a term borrowed from the cinematograph trade), have been exhibited in Paris,[1] and some excellent examples have been published.[2] Part of the secret of such bronchography is to use, as the radio-opaque medium, a mixture of 'Lipiodol' and either sulphanilamide or pure talcum powder, which fills the bronchial tree slowly and leaves on the bronchial wall a thin layer that shows up the smallest folds of mucosa. Apart from bronchography twofold radiographic enlargement can be applied to the lungs with advantage, both rendering the details much clearer than in ordinary radiographs and making more transparent the shadows of the intervening ribs. It is therefore especially useful in depicting miliary lesions and scars; but in the study of cavities tomography still reigns supreme.

Radiographic enlargement must not be confused with photographic enlargement; the former enlarges the X-ray shadows before they are fixed on the film, whereas the latter enlarges the picture already fixed on the film and therefore enlarges also the emulsion grains of the film and any flaws in it. Barclay[3] got over this difficulty in photographic enlargement of X-ray films by using film emulsions of very fine grain; but such long exposures were necessary that the method, though useful for depicting histological specimens, proved unsatisfactory for routine radiography of patients.

Now it is suggested by Layani et al.[4] that the two methods of enlargement, radiographic and photographic, should be combined. These workers first obtain threefold enlargements by direct radiography and then make threefold photographic enlargements thereof, thus obtaining ninefold enlargements altogether, examples of which they publish.

TREATMENT OF LYMPHŒDEMA

In lymphœdema there is chronic swelling of the superficial soft tissues, owing to accumulation of extracellular fluid rich in protein. This may arise as a congenital, and rarely familial, disorder in which a sponge-like lymphangectasia distends the soft tissue; or it may follow damage to the lymphatic system by recurrent streptococcal infections (elephantiasis nostras streptogenes), surgical intervention, or filarial or neoplastic disease. Often, however, no cause can be found in young women in whom there develops a progressive, painless, firm œdema of the lower limbs—a disturbance termed lymphœdema præcox.

The treatment of the lymphœdematous leg in the early, and often reversible, stages of the swelling is by firm support, preferably by a rubber bandage over a lisle stocking. Foot hygiene must be strict, and every effort made to eliminate recurrent streptococcal lymphangitis and interdigital fungus infections. Too often, however, the surgeon finds a massive limb which, in addition to its mechanical and cosmetic disadvantages, is recurrently attacked by a hæmolytic streptococcal infection.

Many ingenious operations have been designed to increase the drainage of lymph from the subcutaneous tissues, either into the deep tissues or into the abdominal wall. All have proved disappointing. Operations designed, not to repair the physiological disorder but to excise as much as possible of the abnormal tissue, have proved more successful. The original Kondoleon operation has been modified by Sistrunk,[1] Homans,[2] Macey,[3] and others. In principle, these procedures consist in a staged excision of the thickened abnormal tissue between the muscle or the deep fascia and the skin. The skin is widely undermined for exposure and finally turned back on the denuded muscle or fascia as a graft. These operations should not be undertaken lightly, for the blood-loss and traumatic shock may be great and skin healing is often tardy, and subsequent recurrence of the swelling and streptococcal cellulitis are not uncommon.

Recently Pratt[4] has introduced a further modification of the Kondolen procedure by which, after preliminary reduction of the swelling by postural drainage, the skin over the swollen limb is removed with an electric dermatome to a depth of 0·43 cm. This thickness, he believes, removes epithelium but not the lymphatic-bearing portion of the skin. After radical excision of all remaining hypertrophied tissue, the skin grafts are stitched together and replaced on the denuded muscle. When healing has taken place, bandage support is continued. Pratt has done 25 such operations in the last three years, and in none has the swelling recurred. Unfortunately he does not give details of the types and the severity of the cases selected. Possibly this skin-graft technique will find a place in the treatment of some lymphœdematous legs, but we need more precise correlation of results with ætiology and pathology.

WORLD HEALTH ASSEMBLY

Last Monday the sixth World Health Assembly, in Geneva, elected Dr. M. G. Candau, of Brazil, to be the new director-general of the World Health Organisation. Dr. Candau is at present deputy director of the W.H.O. regional office for the Americas; and for two years up to March, 1952, he was assistant director-general of W.H.O. in charge of the department of advisory services.

When the Assembly opened on May 5 the delegates paid homage to the Burmese delegation, composed of Dr. U Ba Maung and Dr. C. C. Po, who were killed in an aircrash near Calcutta on their way to Geneva. In his valedictory address to the members, the outgoing president, Dr. Juan Salcedo, jun. (Philippines), drew attention to dangers facing the Organisation—namely, the delay by some countries in the payment of their contributions, and the cut of nearly half in the U.N. Technical Assistance Funds for W.H.O. Dr. Murched Khater, minister of health of the Syrian Republic, who is the president of this year's assembly, spoke of his election in these words:

> "Has not this election upheld before the whole world the principle of equality as between large and small States, and demonstrated the spirit of true democracy? . . . up to the present, no-one from my part of the world had been honoured with this presidency; and so, in order that the principles

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3. Barclay, A. E. Micro-arteriography. Oxford, 1951. See also *Lancet*, 1951, i, 1006.
4. Layani, F., Fischgold, H., Perles, L. *Bull. Soc. méd. Hôp. Paris*, 1953, 69, 8.

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1. Sistrunk, W. E. *J. Amer. med. Ass.* 1918, 71, 800.
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3. Macey, H. B. *Proc. Mayo Clin.* 1940, 15, 49.
4. Pratt, G. H. *J. Amer. med. Ass.* 1953, 151, 888.

D SC, F R S, J Madin, J P, P Malby, Councillor A. Wilde, A O'Connor Fenton

New member **C S O Flynn,** M B

UNITED CAMBRIDGE HOSPITALS

Reappointed Prof **A Leslie Banks,** F R C P, Lady Elizabeth Rook, T C Wyatt, O B E, A M I C E, Lady Bragg, M A, J P Mrs E Hephor, E C Webb, PH D

New member **T J Fairbank,** F R C S

UNITED OXFORD HOSPITALS

Reappointed **C W Carter,** B M Colonel C B Krabbe, O B E, J G Robinson, M B E, Miss Rosemary Spooner, R E Warrell

New members A W Dent, **A S Till,** M CHIR **W Ritchie Russell,** C B E, F R C P, one vacancy to be filled

UNITED BRISTOL HOSPITALS

Reappointed Mrs Helen Bloom, H K Campbell, Prof **A I Darling,** M R C S, F D S R C S, Miss Iris M Lobb, Alderman J J Milton, J.P, Sir Philip Morris, C B E, LL D, Lady Mary Sinclair, Colonel H Bland Stokes, M B E, J P

New member **G K McGowan,** B M

UNITED CARDIFF HOSPITALS

Reappointed Alec Johnson, M P S, J P, Edward Tompkins, J P, **James Walker,** M D

New members Prof **Lambert Rogers,** F R C S, **J Tudor Thomas,** F R C S, Prof **Fred Grundy,** M D, Eddi Jones, J P, Harold M Meredith, J P, W J Canton, LL B

UNITED BIRMINGHAM HOSPITALS

Reappointed Alderman A F Bradbeer, J P, **Ernest Bulmer,** C B E, F R C P, W J G Sperryn, D Bulgin, J F Crowder, LL B

New members W L Barrows, J P, Prof **J M Smellie,** O B E, F R C P, Humphrey Humphries, O B E, M C, LL B (until Sept 30, 1953), one vacancy to be filled

UNITED MANCHESTER HOSPITALS

Reappointed L G M Crick, **Ogilvie Duthie,** F R C S, Graham Halbert, Prof Mansfield Cooper, LL M, H E Newbold, Sir **John Stopford,** F R C P, F.R S, G C Sumner, J P

New members Prof H G Radden, F D S R C S, Colonel F J Gidlow Jackson Lady **Stopford,** M B, and Charles A Miller (until March 31, 1954), Prof **Walter Schlapp,** M B (until March 31, 1955)

UNITED LIVERPOOL HOSPITALS

Reappointed J H Bromfield, J.P, **Sir Henry Cohen,** F R C P, J P, Richard Davies, Councillor H S Dickson, J P Miss Mary Jones, O B E, George Leather, J P

New members **P E Gorst,** M D, R R P Roberts, **P H Whitaker,** M D

Medicine and the Law

Alleged Negligence in Injection

In a recent claim against a Glasgow doctor for £10,000 damages for his alleged negligence[1] the issue was perhaps unusually simple Mr James Reid attended the outpatient department of the Western Infirmary, Glasgow, for treatment for boils in the neck He was given, he said, an injection of penicillin on two successive days, the first time in the hip and the second in the right buttock As he was going home by tram after the second injection, he suddenly became aware of a complete loss of power and sensation in his right foot He was brought home with difficulty and suffered great pain for many hours the right leg had been helpless ever since, and amputation might be necessary His own doctor had come to the conclusion that at the second injection the syringe must have been thrust into the main sciatic nerve It was claimed that the injury, which would be *permanent*, was due to a negligent and reckless plunging of the needle into the nerve at a point fully six inches above the classical site for such an injection

For the defending doctor it was contended that, if the main nerve had been penetrated as suggested, the reaction of pain would have been immediate, had this occurred, the doctor would at once have investigated the cause of the pain, he had no recollection of any such occurrence Lord Blades, giving judgment in the Court of Session, said he had made up his mind without hesitation that he accepted the authoritative and convincing evidence, based on expert knowledge and wide experience of the very subject matter of the case, given by the two doctors called for the defence, in preference to the evidence given by the two doctors called for Mr Reid It was impossible for the court, upon that view of the evidence, to hold that Mr Reid had discharged the onus of proving his claim One might add, perhaps, that the defendant doctor must have been at some disadvantage in dealing with an allegation relating to treatment in an outpatient department six years ago

The Economics of Litigation

Another claim for damages based on charges of negligence has been brought to an end because, in the words of one of the Queen's Counsel engaged in the litigation, the profit would be almost exclusively to the lawyers In Basford *v* Board of Charing Cross Hospital and Others[2] the plaintiff's case was that in 1947, suffering from pain in his arm, he was treated for fibrositis at the Maida Vale Hospital for Nervous Diseases A year later he had headaches and worse pain and was sent to Wembley Hospital There the director of physiotherapy diagnosed a displaced spinal disc but took no X ray photographs Electrical treatment was given In 1949 a radiograph showed no evidence of a displaced disc, but the shoulder and arm were not photographed The patient received radiant heat and massage, went back to the Maida Vale Hospital, and was put down for radiography—but again, it was alleged, for the wrong place His employer then sent him to Sir Hugh Griffiths He was found to have a swelling as big as an orange on the upper arm and another on the shoulder, the growth had spontaneously fractured the bone Damages were claimed for the failure to make a sufficient examination of his condition at the proper time and to take X ray photographs, had the photographs been taken, it was contended, a malignant tumour or cancer would have been disclosed in the upper left arm and there would have been a reasonable chance of saving the limb The electrical treatment, radiant heat, and massage, it was said, were the worst possible treatment for a growing malignant tumour

Sir Hugh Griffiths stated his opinion that the growth would have been disclosed by radiography and, he thought, by palpation, definite diagnosis was difficult, the witness communicated with the Medical Research Council and the Atomic Research Council, a remarkable amount of investigation was carried out for this purpose After other evidence had been called and the case for the defendant director of physiotherapy had been opened, a settlement was announced on the third day of the trial Plaintiff's counsel said that proposals had been made which were satisfactory to his client and which provided for the plaintiff's costs In the circumstances he did not desire to pursue the allegations of negligence against any of the defendants Counsel for the latter agreed to the settlement while not admitting the allegations As four Q C s and four juniors were engaged on behalf of the various parties, the expense of an inevitably long hearing with much expert evidence, was an obvious deterrent The defendants, however, may well feel at a disadvantage inasmuch as the plaintiff's case was fully reported while their own had no chance of publicity

A Successful Action for Libel

Dr William Mervyn Crofton was awarded £2000 damages for libel in the action in which he complained of social justice might prevail, the great nations, which could easily have tilted the balance in whichever direction they chose, stood aside and renounced the presidency in favour of the small States.

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[1] *Glasgow Herald*, May 2

[2] *Times* May 5–7

Dr. Brock Chisholm, the first director-general of the Organisation, who is retiring on July 21, presented his report for 1952,[1] which shows clearly how, during his tenure, the organisation has acquired stability and how it continues to meet international needs, which are becoming better defined.

Communicable diseases still present new problems, ever changing with the social and economic development of the people. Malaria control remains foremost, but in many parts of the world, notably in Asia, national governments are taking over and expanding schemes originally laid down and started by international consultants and teams. On the other hand, in tropical Africa malaria control is still in its early days and is attracting more and more attention. Tuberculosis comes second on the list of infectious diseases, and over 38 million young people have been tuberculin-tested and 18 million non-reactors vaccinated with B.C.G. The setting up of the international laboratory in Copenhagen for tuberculosis immunisation research is an important recent development. The international yaws campaigns seem to be steadily crushing the enemy and bear witness to the competent planning of the general staff behind them.

Education plays an increasing part in the work of W.H.O., and a total of 1147 fellowships were awarded in 1952. Of these, 487 were for group training; and W.H.O. organised 26 courses and assisted in 18 more, including those on Engineering Aspects of Public Health in London, Yaws Control in Bangkok, Anæsthetics in Copenhagen, Nursing Education in Taiwan, and Brucellosis in Santiago. Of the fellows, 666 were studying health organisation and services, 348 communicable diseases, and 131 clinical and medical sciences and education. In the organisation and execution of this programme, as in all W.H.O.'s work, there has been an increasing amount of decentralisation to the six regional offices. The regional office for Africa, directed by Dr. F. Daubenton, moved from Geneva to Brazzaville in October last and, despite recruiting difficulties, has begun a full programme in which the training of African doctors and medical auxiliaries plays a large part. The flourishing work of the South-East Asia regional office, under Dr. C. Mani, continues; here India seems to provide a model for the proper use of international aid and international experts. Much good work is also being done under very difficult circumstances in Burma, Indonesia, and Thailand.

The total assessments of the 71 member countries for the year totalled just under $9 million. The largest subscribers are the United States ($2·8 million), the United Kingdom (1·0), and France (0·5). Of the total subscriptions, 80% have already been paid, and most of the remainder is due from countries with Communist governments who continue to be "inactive members."

An important decision was taken at the Fifth World Health Assembly, when the increase and control of world population were discussed. There was considerable disagreement on the question of whether this was or was not properly a medical problem, and the assembly ultimately decided that no action should be taken. Many doctors in all countries must regret this decision, but clearly no international organisation can proceed without a substantial measure of agreement amongst its constituent members.

Any public-health report inevitably contains a large mass of factual data and details of organisation, which are not easy reading. The difficulty in presenting this work in an imaginative way is great, but W.H.O. has set an excellent example by including many fine photographs of its workers in the countryside, in hospitals, and in laboratories. These add immensely to the value of the report, especially for the non-technical reader.

After six years W.H.O. has a reliable and efficient secretariat, and an executive board which is capable of thinking internationally rather than nationally and which is thus capable of carrying out major international plans. These achievements are in no small measure due to Dr. Brock Chisholm's vision and energy.

EARLY SURGERY IN SKELETAL TUBERCULOSIS

It happens not uncommonly that an important advance in surgery, though long foreseen, depends for fruition on developments in another field of science. The internal fixation of fractures by metal—an idea that had been cherished since the early days of aseptic surgery—had to await the development of biologically inert metals. A parallel situation is seemingly evolving in the early surgical treatment of skeletal tuberculosis; in this case the accessory is the development of effective antibiotic drugs.

Long before the introduction of antibiotics the idea of a direct surgical attack on a tuberculous focus in bone or joint had seemed theoretically attractive to orthopædic surgeons, and such operations were occasionally practised. But the results were often discouraging: dissemination of the disease to other organs and the formation of chronic discharging sinuses with secondary infection were common sequels. Consequently the attitude of most surgeons towards skeletal tuberculosis became strictly conservative, especially in Britain. Operative treatment was seldom undertaken except in the quiescent phase of the disease, and even then the surgeon sought to avoid cutting directly into diseased tissue. The introduction of antibiotic drugs—especially streptomycin—has led to reconsideration of the possible advantages of a bolder policy. Many surgeons now believe that, with the greater security against unfavourable complications afforded by streptomycin, direct operation on tuberculous lesions of the skeleton may prove, after all, to be advantageous. Johnson et al.[1] suggest that certain lesions can be tackled surgically with impunity and probably with benefit to the patient; and Wilkinson[2] makes it clear that similar observations are being made in Britain. In following up this development orthopædic surgeons must beware lest their enthusiasm carry them too far. A proper note of caution was struck in the British Orthopædic Association's discussion of Pott's paraplegia, summarised on p. 799. Whatever its local manifestations tuberculosis is a systemic disease. Therefore constitutional treatment must continue to be the first method of attack: to advocate surgical treatment without proper constitutional measures is to court disaster.

Johnson and his collaborators emphasise the value of operation in diagnosis. Important though this may be, it is mainly in the hope of hastening the healing of the lesion that British surgeons are investigating the possibilities of surgery. So far, early operation has been undertaken mainly for the thorough evacuation of abscesses and the removal of tuberculous debris by curettage, especially in spinal disease. Synovectomy is also under trial in selected joint lesions. Such operations should create favourable conditions for rapid healing; and in spinal disease drainage of paravertebral abscesses will help to prevent extension of the infection along the of language used in the report of a tuberculosis conference which he had attended at Hackney in June, 1950 The report after describing claims he made at the meeting for the success of his own method of treatment and the statements of his supporters "including several patients whom he had brought with him to demonstrate so-called 'cures'" went on to say that "the conference, however, soon recognised the language of the quack remedy advertisements and passed on to discuss tuberculosis problems in East London" Dr Crofton complained that these words meant that he had falsely claimed to have effected cures, was not fit to be on the Medical Register, was advertising himself in an unprofessional manner, was a pedlar for his own profit of cures which he knew to be valueless, and had conspired with others to deceive the public The defendant denied those implications, but admitted that the words could mean that the plaintiff was advertising himself unprofessionally, in that sense said the defendant, the words were true in substance and in fact in so far as they were matters of opinion they were fair comment without malice on a matter of public interest The jury found that the words were defamatory that they were not true in substance and in fact, and that they meant that Dr Crofton was a charlatan, not fit to be on the Register, dishonest in falsely claiming to have effected cures advertising himself in an unprofessional manner and peddling a method of cure which he knew to be valueless, for his own profit In further answers to the judge's questions the jury said that if the words meant only that the plaintiff was advertising himself in an unprofessional manner, they were untrue, that they were not fair comment and that the defendant was actuated by malice in publishing them

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[1] The Work of W.H.O. Annual Report of the Director-General, 1952. W.H.O., Geneva, 1953. Pp. 204. 9s. Obtainable from H.M. Stationery Office, P.O. Box 569, London, S.E.1.

[1] Johnson, R. W., Hillman, J. W., Southwick, W. O. *J. Bone Jt Surg.* 1953, 35A, 17.

[2] Wilkinson, M. C. See *Ibid*, 35B, 150.

Dr Crofton, in the witness-box, explained that his method was to take a culture from tuberculous patients' sputum and so produce immunisation There was no secret about it, he had publicised it as much as he could After his attention had been drawn to the report, and its author had been identified, he received a private letter of apology, but, three days later, the defendant had put on record in the present action his plea that the words were true and that he meant them to imply advertisement in an unprofessional manner Mr Justice Finnemore, in his summing up to the jury distinguished between a doctor saying "Come to me and I will cure you" and saying "Here is a method which any doctor can use and which, if used, will eliminate tuberculosis"

The law of libel in England is a remarkably flexible instrument for deciding a dispute If the judge and jury in Dr Crofton's case were not exactly performing the function of the Medical Research Council or the Ministry of Health in assessing the merits of his system of treatment, they were in some degree deputising for the General Medical Council in passing judgment on his professional conduct

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Parliament

Priority for the Mental Health Services

REPLYING to a debate on the adjournment in the House of Commons on May 7, Miss PATRICIA HORNSBY-SMITH said that the number of inpatients who were mental defectives at the end of 1952 had risen to 53,066 as against 51,194 in 1951 But there was still a growing waiting-list, and a large proportion—about 4000 out of 8714—were children These children were mostly in the age-group 4–7 when it was difficult to keep them at home But progress in staffing beds had been made At the beginning of January 1952, there were 2145 unstaffed beds in mental-deficiency institutions At the beginning of 1953 there were 1587 unstaffed beds The first problem was more nurses and the second more buildings

The Minister of Health had repeatedly said that priority must be given to the mental side in capital expenditure In the Leeds area for example, in the two-year programme, out of an expenditure of £190,000 the sum of £102,000 was going to mental deficiency and in East Anglia £49,000 was being allocated out of £181,000 for the 1953–54 programme The largest project on hand was Greaves Hall, near Southport, which would cost £3 million, take five years to complete and provide 1040 beds In the last two financial years £899 000 had been spent on improvements in the purchase of buildings and adaptations for mental-deficiency work.

The staff in 1948 were 6000 full-time and 50,000 part-time and at the end of 1952 the figures were 6610 full-time and 54,665 part-time, but she agreed that they still needed many more

QUESTION TIME

Accommodation for Mental Defectives

Mr B R BRAINE asked the Minister of Health if he would give the figures of recognised bed space set aside for mental defectives in England and Wales and the number of beds not used for lack of staff or other reasons—Mr IAIN MACLEOD replied On Dec. 31 last, including certified institutions and approved homes outside the National Health Service, the bed figures were as follows recognised bed space, 50,401 out of use, 1921, occupied, 53,914

Mental-deficiency Nurses

Mr BRAINE asked the Minister what steps had been taken on the advice of the Mental Health Advisory Committee and others to recruit additional staff for mental-deficiency nursing—Miss M. P HORNSBY-SMITH replied The Standing Mental Health and Nursing Advisory Committees have not yet completed their study of the problem, but they have tendered interim advice to the Minister of Health in the light of which he hopes to issue a memorandum of guidance to the management committees concerned in the course of the next few weeks. He is also considering, with the Minister of Labour, the desirability of devoting the resources available for recruitment publicity in the current financial year largely to the recruitment of mental, and mental deficiency nurses

National Health Service Cost

Major TUFTON BEAMISH asked the Minister of Health what extra cost would fall on the Exchequer in this financial year if the National Health Service were made free in all respects—Mr MACLEOD replied. It is, of course, difficult to estimate the level of demand that would result if charges were removed, and therefore no accurate estimate is possible; but I think that the extra cost in a full year would be at least £40 million.

Committee on N.H S Costs

Mr SOMERVILLE HASTINGS asked the Minister what knowledge and experience of the work and management of hospitals was possessed by the members of the committee that was to inquire into the cost of the health service—Mr MACLEOD replied The inquiry is to be independent and objective, the members appointed have, therefore, no direct connection with any part of the health service The committee will decide their own procedure, but I have no doubt they will wish to take evidence from organisations and individuals with knowledge and experience of the working of the service

Mr HASTINGS Does not the Minister feel that some knowledge of the work of a hospital is necessary for those whose job it is to assess the value of what is spent on that hospital?—Mr MACLEOD Frankly, I disagree If we once start having representatives of hospitals, in any sense of the term, I should have to have representatives of doctors consultants, dentists local authorities, opticians, and the rest I wanted this problem to be examined by a committee of five wise men, or four wise men and one wise woman—whatever we like to call it I think we shall get the best result from that

Mr ARTHUR BLENKINSOP Could the Minister say why he has by-passed the central advisory committee, which is there surely to give him advice on this and other matters?—Mr MACLEOD For the very reason I have just explained, because the Central Health Services Council is representative of all the interests in the health service For that reason, in my view, it is the wrong body for this kind of inquiry.

Junior Hospital House-officers

DR BARNETT STROSS asked the Minister whether he was aware of the difficulty experienced by some hospitals in spinal column. It is not yet known whether the beneficial effects of operation are due solely to efficient drainage of pus and debris or also to some other mechanism; some believe that the mechanical disturbance of tuberculous tissue in some way stimulates the resistance of the body to the disease. More will certainly be heard in coming months of the surgical treatment of skeletal tuberculosis.

THE LIND BICENTENARY

IN 1753 the naval surgeon, James Lind, a graduate of medicine of Edinburgh University and a native of the town, published his *Treatise of the Scurvy*. This weekend in Edinburgh, Town and Gown combine with the Royal College of Physicians and the Nutrition Society to celebrate the bicentenary. Visitors from the U.S.A., France, Belgium, and Holland have come to attend the official receptions, to take part in four symposia on modern aspects of vitamin C and scurvy, and to listen to a Lind oration from Surgeon Vice-Admiral Sir Sheldon Dudley, F.R.S. The Edinburgh University Press has reprinted the original first edition of the treatise, together with additional notes on Lind and his contemporaries and on the chemistry and physiology of vitamin C.[1]

The modern reader will soon find that this reprinting is more than a proper act of filial *pietas*. The layout of this 200-year-old monograph is essentially modern and includes chapters on epidemiology, diagnosis, prognosis, prophylaxis, and treatment, together with a discussion of the history of the disease and a good bibliography. The book is written in elegant English, characteristic of the great age of Edinburgh literature which was just about to begin. There is little of the topical professional jargon, which mars so many medical books in all ages.

The clinical description of scurvy remains, without doubt, the best available to the student. Lind, like many of his generation of naval surgeons, had a clinical experience of thousands of cases, and certainly no modern physician can write with such personal authority. His clinical trial of oranges and lemons, together with other remedies of repute at the time, was carried out at sea in H.M.S. *Salisbury* in May, 1747. Today it is still a model of how to plan and conduct a therapeutic trial. This experiment established beyond any doubt that these fruits, alone out of many recommended remedies, were capable of curing the disease. Lind was also well aware that a supply of fresh fruits and vegetables was of fundamental importance in the prevention of the disease during long sea voyages. But modern nutritionists will be interested to find that he thought that the stresses and strains of the life of the sailor, and especially the repeated exposures to damage and cold, played an important contributory part in the onset of the symptoms of scurvy.

Five years after the publication of the treatise Lind was appointed chief physician to the new R.N. hospital—Haslar Hospital, at Portsmouth. At the time this was probably the largest hospital in Europe and could receive 2200 patients. In his first two years of office 1146 cases of scurvy were admitted. Lind held this post for twenty-five years; yet such are the delays in the introduction of new knowledge that he did not live to see scurvy eradicated from the Navy. James Cook was indeed able to complete his second great voyage to Australia in 1772–75 without a single case, but not until 1795, a year after Lind's death, did the Lords of the Admiralty supply lemon juice to the sailors at public expense, "which acted so speedily that in less than two years it became extinct." A miracle in the preservation of sailors was thus effected. Sir Gilbert Blane, a pupil of Lind, was largely instrumental in bringing the Sea Lords to this decision. The additional notes to the reprint include an account by Dudley of the Lind tradition in the Royal Naval Medical Service. Largely through his pupils, the aristocratic Blane and Thomas Trotter, who like Lind had started as a surgeon's mate, he was able to secure immense improvements in the conditions of life at sea. After the introduction of lemon juice Blane wrote: "One of the most distinguished sea officers that ever lived declared to me that it was his conviction that two ships are now equal to four of former times." Dudley adds that a man who could double the striking force of the King's Navy with no increase in the "naval estimates" or use of that dread instrument the press-gang was worth half a dozen ordinary admirals. In fact Lind's influence effected much more than the prevention of scurvy and extended far beyond the Navy. In directing his naval medical colleagues towards attempts to preserve the health of the seamen in addition to their regular duties of treating their diseases, Lind was a pioneer of modern public health and social medicine.

The editors have carried out their work unobtrusively, and the beautiful printing is a credit to modern Edinburgh craftsmen. Those who read this book will find a fascinating mixture of medical science and naval history.

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[1] Lind's Treatise on Scurvy: A bicentenary volume containing a reprint of the first edition of *A Treatise of the Scurvy* by JAMES LIND, M.D., with additional notes. Edited by C. P. STEWART, PH.D., D.SC., and DOUGLAS GUTHRIE, M.D., F.R.C.S.E. Edinburgh: University Press. 1953. Pp. 440. 45s.

PHÆOCHROMOCYTOMA

FOR a long time phæochromocytoma was largely a post-mortem diagnosis, but now there are methods of investigation which afford a greater opportunity for early recognition of the tumour. Adrenolytic drugs such as benzodioxane ('Piperoxane')[1] and phentolamine ('Rogitine')[2] are amongst the useful diagnostic tools, although both may give misleading results. And, as Dr. Cobb and his colleagues report on an earlier page of this issue, benzodioxane can also be used to control the rise in blood-pressure during an operation on a phæochromocytoma; and phentolamine can be used for the same purpose. In diagnosis, provocative drugs such as histamine,[3] methacholine ('Mecholyl')[4] and tetraethylammonium bromide[5] may precipitate severe hypertensive attacks and are probably better avoided. A still more direct investigation is the measurement of the urinary excretion of catechol amines,[6] the results of which have proved almost uniformly reliable. This assay, however, is at present performed in only a few centres, so that it is well to consider how far it is possible to diagnose phæochromocytoma using simpler tests. Smithwick and his colleagues[7] collected detailed information on the many patients referred to them for splanchnicectomy for hypertension. Amongst these patients there were 11 with phæochromocytoma, in most of whom the tumour was not diagnosed before operation. A subsequent analysis of all the clinical data of these 11 cases, together with those of 107 reported cases and of 100 unselected cases of essential hypertension, showed a number of differences which served to identify those of phæochromocytoma. A high proportion of the patients with phæochromocytoma gave a history of excessive sweating or vasomotor disturbances, such as coldness or blanching of the extremities. At least 70% of them, as against 10% of those with essential hypertension, had unexplained rises in body-temperature of 1°F or more; and in over 60% the basal metabolic-rate

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obtaining candidates for junior house positions, what was the extent of this problem, and whether he would consider increasing the payment for locums for these positions from the present rate of £8 per week.—Mr MACLEOD replied: I am aware that this problem is widespread, particularly in the remoter hospitals. I am considering how it can be solved, but I do not think a solution can be found on the lines suggested.

Dr STROSS: Does the Minister recall that I wrote to him about a hospital which is not remote and which has 1000 beds in Stoke-on-Trent where I think that four out of the five surgeons have no assistance? Does he not think that increasing the remuneration above £8 per week might help them to get locums?—Mr MACLEOD: One of the difficulties about the scale was that it was only promulgated in November, 1952. The second difficulty seems to me to be that to encourage people to take locum jobs is not right from the long-term point of view. The best solution may well be secured by seeing what happens as a result of the preregistration Act which has come in this year.

Specialists and Merit Awards

Dr JEGER asked the Minister how many merit awards had been made each year since the system was instituted.—Mr MACLEOD replied: 1740 awards were made in England and Wales for 1948–49, 439 new or higher ones for 1950, and 229 for 1951. Recommendations have not yet been received for 1952.

Mr BLENKINSOP asked the Minister the total number of full-time specialists now employed in the N.H.S., as compared with the number twelve months ago.—Mr MACLEOD replied: There were 2149 whole-time consultants and senior hospital medical and dental officers at the end of 1950 and 2445 a year later.—Mr BLENKINSOP: This will give some satisfaction because of the rather anxious reports which have been put out by many full-time consultants that there has been a great falling away of that service. But, nevertheless, it is very much more costly to encourage recruiting of part-time specialists than to encourage further full-time appointments.—Mr MACLEOD: Those figures only take us up to a little more than a year ago. I have not the 1952 figures—which will be interesting—but I hope to have them by about the end of the month.

Atmospheric Pollution

On the motion for the adjournment in the House of Commons on May 8 Mr A. E. MARPLES, parliamentary secretary to the Ministry of Housing and Local Government, stated that the Government had decided to appoint a committee under an independent chairman to undertake a comprehensive review of the causes and effects of air pollution and to consider what further preventive measures were practicable.

Public Health

Smallpox

A FURTHER 3 cases of smallpox have been reported from Yorkshire, bringing the total of confirmed cases in the outbreak to 30, with 7 deaths. The daughter and son of the Leeds mortuary attendant who was admitted to hospital on May 2 are now known to have smallpox. The girl, who was vaccinated for the first time on May 2, fell ill on May 6, and the boy, who had his primary vaccination at the same time, on May 10. The third new case is that of a miner, aged 19, who lives at Baildon and works in a colliery at Gomersall. He was not under surveillance as a contact, but he lives 3 or 4 miles from one of the earlier patients. He fell ill on May 1 and was admitted to hospital on May 5.

Death from smallpox may take place in the pre-eruptive stage or when there are only sparse focal rashes. The patient may be desperately ill—perhaps comatose—on reaching hospital, and in the absence of any rash his condition may easily be attributed to some other acute medical or surgical illness, such as uræmia or an abdominal condition requiring laparotomy. A patient who has been very ill in the early stages of smallpox does not necessarily develop a definite rash later. Thus smallpox enters into the differential diagnosis of any unexplained fever and toxæmia, particularly with hæmorrhage or petechiæ. When there is the slightest doubt material should be kept for virological examination, and the medical officer of health notified.

In England Now

A Running Commentary by Peripatetic Correspondents

I RAN the Pathologist to earth in a rather small dirty room. He was smoking a cigarette, his glasses were pushed up on his forehead, and he didn't seem too busy. "Can you tell me, sir, please," I asked, "why differential white-cell counts are always given as percentages of the total whites? ... I mean, the different white cells don't bear any particular relation to each other, do they, sir?" He appeared to be trying to take this in, so I was encouraged to make it a bit simpler. "Supposing you enumerated all the different objects in a living-room for instance," I said, "within normal limits you might expect one grand piano, half a dozen chairs, two or three tables, a few rugs, curtains, vases, pictures, and, say, a couple of hundred books. Your percentage of grand pianos would average about 0·3% and would depend largely upon the number of books. It might be as low as 0·15% in a library or as high as 2% in a studio. Right? Very well, but supposing there were *two* grand pianos in the room, sir—" He took me up promptly. "There are people who would need two. Rawicz, for instance. And Landauer, too, I wouldn't mind betting." "So that they could visit each other, turn and turn about?" I hazarded. "And Sellick and Smith?" "Oh, but they are married, aren't they, sir?" He nodded sagely, and went on with enthusiasm. "And there's that thing of Bach's that old H. J. was so fond of at the Proms that takes *three* grand pianos. He used to give it to his students. My niece played in the team one year, I remember. Outside right, I think she was." "Really, sir? Then I may have seen her." I persevered, "But my point is that more than one grand piano in a room has a definite significance. Half a dozen would be pathological." He agreed, "Half a dozen would be excessive. ... Didn't they have four in *Les Noces*, up on the stage?"—"No, two I think. Four voices, or was it eight, but only two pianos. But lots of percussion." He nodded happily, "Yes, lots of percussion." I ploughed on, "Well, people can have from one to three grand pianos in the room and still keep within the normal percentage range, so long as there are enough books and vases and things to balance them up, or do I mean dilute them?" "I can't see anything wrong in that," he replied after deliberation. "Good," I said. "Now, sir, some of your white cells—I can't remember their names—are as scarce as grand pianos, and their actual number can be doubled and trebled without anyone paying much attention if their number is expressed merely as percentages of the white-cell count. In fact, I'm surprised you don't lump in the reds as well and divide the number of thingummy cells by five million odd. ..." "I dare say we could do that for you. It would only mean dividing by five and shifting the decimal point. Would that help you?" "No, no, sir," I exclaimed hastily. "Not a bit. Quite the contrary in fact. I'd like you to divide each cell quantity by its own particular normal so that your path. report would read—Polys normal, Lymphos two-thirds normal, Thingummy cells five times normal." There was a pause and then the telephone rang. With heavy deliberation he took up the receiver and listened. With his right hand he drew on his blotter an Aberdeen terrier balancing a sugar-lump on its nose, putting in the shading very carefully. A laboratory assistant barged in, noisily dumped a basket of test-tubes on the desk, looked at me pityingly (I thought), and barged out again. The telephone earpiece cackled and burred. "All right," said the Pathologist, "I'll hang on," and went on with the shading. I crept out.

* * *

The remarks of your non-psychiatric, but without doubt psychologically eminent, peripatetic correspondent (April 4) who has designed a de-luxe body for his 10 h.p. car reminds me of an awkward situation which I successfully overcame in my youth (1939). I had an ancient 1926 Austin Seven of which I was inordinately proud. It was, however, always embarrassing, especially when there were young ladies aboard, to hear a stream of scurrilous and derisory remarks whenever I stopped at a garage. There was one garage hand, a large, lanky, ginger-haired coarse youth, whom I particularly disliked,

a) *Not Frigid.*—Although not frigid by definition, these 6 tients had all experienced coitus far in excess of their sires or their capacity to attain orgasm.

(*b*) *Frigid Throughout Marriage.*—This, the largest group, mprised 162 women. A history of undue mother attachment s given by 83% while 23% developed gall-stones.

(*c*) *Frigid After Marriage.*—There were 128 in this section. itus, which had been completely or partially gratifying ring the early years of marriage, ceased to be desirable satisfying at a later period, usually in conjunction with a owing family (case 3 is a typical example). The percentage gure of 14 with mother attachment at marriage approximates that of the general community. Gall-stones occurred in 2·5%.

LASSIFICATION OF 300 PATIENTS WHOSE CHIEF COMPLAINT WAS FLATULENT DYSPEPSIA

Cases	Frigidity	Total	Mother-attached	Gall-stones
Married women	Not frigid	6	0	3
	Frigid throughout marriage	162	135	37
	Frigidity acquired after marriage	128	18	16
Single women		3	3	1
Male		1	—	1

4. The findings among single women, and the proportion exhibiting mother-attachment in group 3(*b*) (namely 83%), lead to the inference that not only does an undue attachment to the mother predispose to flatulent dyspepsia but in accentuating the maternal component of womanhood it interferes with erotic growth and thereby contributes to female frigidity. The development of maternal qualities through the rearing of a family seems to have a similar effect.

My own conclusion from these 300 cases and from many hundreds of milder cases and of various control groups is that in general the severity of the disorder is in direct proportion to the frequency of unappreciated coitus.

MECHANISM

In speculating on why the revolt against unwanted coitus should express itself in apparently remote symptoms, several factors need consideration.

The Conditioned Reflex.—Pavlov showed that a stimulus, as it travels from sense receptor to end-organ, leaves in its wake a change of some permanence in the cerebral hemispheres. The response to further similar stimuli is intensified or widened in scope by the summation of past stimuli, so that a conditioning may reveal itself as a profound response to a comparatively slight stimulus. Of the many emotions evoked by the physical act of submission to an unloved husband, disgust, fear, anger, and displeasure are most readily recognisable in the sequelæ of flatulent dyspepsia, nervousness, hypertension, and rheumatism. Women conditioned by this ordeal may yet enjoy a remarkable state of well-being during a respite in hospital or at a holiday resort; but rapidly relapse in the environs of their homes and husbands.

Endocrine.—The decisive influence of parental associations in early life on personality structure and character formation are well known but their effects on female hormonal activity are still largely uncoördinated. From observations made in our practice the following generalisations seem to be emerging:

When the growing girl enjoys much of her father's company and forms a strong affection for him (especially if the mother's influence is small), the menses tend to appear early. The girl shows a vivacious temperament and an urge to mix socially with the male sex in adolescence. Sexual difficulties in marriage are rare. Nausea, vomiting, and varicose veins are absent or very slight, at any rate in early pregnancies.

When the father is indifferent, strict, harsh, or drunken, there is an average relative delay of two to three years in the onset of menstruation. The girl adheres to the mother, assisting her in the home, is bashful and diffident in mixed company, and has a low male acceptance, often amounting to complete sexual frigidity on marriage.

On this basis the influence of the father during childhood and adolescence is towards promoting erotic growth and acquiescence in pleasurable sensations, whilst that of the mother is towards promoting motherliness and a stoical acceptance of work. These rôles are antagonistic but complementary and find their counterpart in the sequence of mating and pregnancy and also in the follicular and luteal phases of ovarian function. Indeed, if the clinical observations are correlated with the endocrinological data, the following broad classification emerges:

(*a*) The strongly erotic female has relatively high œstrogen levels and usually menstruates early, vigorously, and regularly. She often suffers from dysmenorrhœa and may have an inadequate milk secretion after parturition.

(*b*) A strong motherly component coupled with a weak or inhibited eroticism results in a relative preponderance of progesterone-relaxin values. Menstruation appears at a later average age and is unattended by dysmenorrhœa. Subject to the appropriate conditions in later life, there are found in this group temporary amenorrhœa, anorexia nervosa, nausea, vomiting, and varicose veins in pregnancy, adequate lactation after parturition, premenstrual tension, visceroptosis, uterine prolapse, herniation at operation scars, flatulent dyspepsia, and gall-stones.

Gastrohepatic Function.—Though the association between disgust and vomiting is common knowledge, the precise consequences of this emotion on stomach and liver function are still largely undetermined. Women who suffer from flatulent dyspepsia have a low fat-tolerance, are immune from peptic ulceration, and are inclined to be hypochlorhydric and to develop gall-stones.

HUSBANDS AND WIVES

The assertion that love, while playing but a part in the life of man, is woman's whole existence, is one of these misleading half-truths; for, whereas the erotic requirements of the female are intermittent and transitory, the male is enslaved by his need of female affection throughout his span of life. On finding in marriage the futile pretence, passivity, or protest in lieu of subtle caress and passionate embrace, he is by no means unhurt; but the emotions engendered by this threat to his security are of a very different nature from those of his frigid wife.

The husbands of the greater part of this series of 296 married women were still alive during investigation, and a number were known to me. Unfortunately, my attention was not drawn to them until 1944 when many of the patients had drifted beyond my reach. The data obtained from just over two-fifths of them indicate their more typical reactions. Roughly, 25% became addicted to alcohol and 20% contracted peptic ulcer, while an unknown but substantial proportion found solace in the arms of other women. Many compensated through vocational diligence in gaining positions of influence and responsibility in the community.

The process of growing up involves a transition in habitude from the all-play to the purposive; but even the lives of the fully mature require a leavening of joy to maintain health.

Clinical experience teaches that a grossly overworked housewife will eventually show minor or major rheumatic manifestations. These will come into being the sooner if the fundamental pleasure principle normally associated with marriage is substituted by other emotions. When her reaction to a drunken husband is dominantly one of anger and hostility, hypertension looms ahead, probably via a sympathetico-renal mechanism. If sexual disgust has played a substantial part in her life, the result will be the gastrohepatic disorder here called rejection dyspepsia.

Whether in detail I am right or wrong in these interpretations, I am certain at least the habits, the emotions, the endocrine imbalance, the bodily changes and social repercussions of the mass of sexually maladjusted women constitute a challenge of the first magnitude to the doctor of today At present their endless complaints are usually dealt with mechanistically Drugs are administered to counter their states of mind, to balance their endocrines, and to interfere in the function of their bodily parts When structural changes are deemed irreversible, operation follows The poor reward attending these therapeutic efforts can readily be traced to the continuance of the noxious emotional factors in their lives and to the difficulty in destroying a conditioned reflex once established

SUMMARY

A syndrome entitled "rejection dyspepsia" is described Among the commonest complaints met with in adult life, it is largely confined to married women and probably has the same origin as the nausea and vomiting of pregnancy and gall bladder disorders Predisposition depends on factors in early life, notably lack of affection for the father and over attachment to the mother with consequent erotic inhibition and female frigidity Precipitating factors include a continuance of association with the mother, marital incompatibility, a rapid succession of pregnancies, and the frequency of ungratifying coitus

I am deeply indebted to my partners, Dr G Ronald Anderson, Dr Gordon J Ker, and Dr Norman D Ker, for their help in the assessment of clinical data, to Dr I Anderson and the biochemical staff of the Victoria Infirmary Glasgow for carrying out many urinary pregnanediol assays in women who had had varicose veins in pregnancy, and to Dr Ranyard West and Dr Peter L McKinlay for helpful criticism in the preparation of this paper

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URINARY EXCRETION OF PEPSINOGEN IN GASTRODUODENAL ULCERATION

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THE existence of a pepsin-like enzyme in the urine has been known for more than ninety years (Brücke 1861) Despite the discovery of the inactive pro enzyme of pepsin, pepsinogen (Langley 1881), it was thought that this urinary enzyme was free pepsin, and Benderskoy (1890) called it uropepsin Evidence which has accumulated since then has shown that this urinary enzyme is free pepsinogen Final proof of its identity came from the experiments of I A Mirsky et al (1948) in which intravenous injections of pure pepsinogen increased the urinary excretion of enzyme, whereas pepsin, either injected or given by mouth did not do so The term "uropepsin" is therefore incorrect and should give way to the more precise term "urinary pepsinogen"

The enzyme originates in the peptic cells of the stomach (Langley 1881) The persistence of pepsinogen in the leucocytes sometimes for years, after total gastrectomy indicates that these cells probably elaborate some pepsinogen endogenously, but this accounts for very little of the urinary enzyme

The relation between the level of urinary pepsinogen and gastric secretory activity is uncertain Varró et al (1952) deny any such relationship, but Gottlieb (1924) and Janowitz and Hollander (1951) claim that there is a close relationship The evidence presented by the latter workers is the more convincing

Pepsinogen diffuses into the blood directly from t stomach wall, none being reabsorbed from the g lumen (Mirsky et al 1948) The enzyme is filter through the *renal glomerular membrane* and part reabsorbed in the tubules, as will be shown in a pap to be published elsewhere

Before X-ray diagnosis of gastroduodenal disea came into general use, the diagnosis of carcinoma o the stomach was sometimes based on the estimation o urinary pepsinogen, but for this purpose the test valueless (Rothschild 1930) By the time radiograph diagnosis became general, about 1930, work on urinar pepsinogen had been dropped

Since the introduction of the more reliable and accurat hæmoglobin method of peptic assay by Anson and A E Mirsky (1932), and its application to urinary peptic assay by Bucher (1947), the investigation has been applied in cases of gastric and duodenal ulcer by Podor et al (1948) and by Janowitz et al (1950), who have tried to show a difference in urinary excretion of pepsinogen *between normal people and those with peptic ulcer*

I describe here the disturbances of urinary excretio of pepsinogen in patients with gastric and duodena ulcers

TABLE I—AGE DISTRIBUTION AND MEAN URINARY PEPSINOGE IN CONTROLS

—	Sex	Age group (yr)					Tota
		15–29	30–39	40–49	50–59	60 or more	
No of persons	M	7	6	7	8	8	36
	F	2	5	8	4	5	24
Total		9	11	15	12	13	60
							Mea
Mean urinary excretion of pepsinogen ([P U]^{Hb} per hr)	M	216	277	183	103	205	19
	F	160	213	243	267	236	21
Mean		248	246	215	157	217	215

METHODS

The hæmoglobin method of peptic assay modified from Anson and Mirsky (1932) was used

Dilute a 10 ml aliquot of a timed measured output o urine (a twelve hour or a twenty-four hour sample) to 12 5 ml with 0 33 *N* hydrochloric acid Of this incubate 1 ml (≡ 0 8 ml of urine) for ten minutes at 37°C with 5 ml o acidified 2% hæmoglobin substrate (≡ 0 1 g of hæmoglobin) † Add 10 ml of 0 3 M trichloracetic acid and filter A parall blank estimation is made, the urine being added to the tri chloracetic acid to inactivate the enzyme before the sub strate is added The filtrate of each is dealt with similarly— i e , to 2 0 ml of filtrate add 1 2 ml of 1 3 diluted Folin Ciocalteau reagent, and then add 4 ml of 0 5 *N* sodium hydroxide and shake immediately A blue colour develops which is most *intense between five and twenty minute* The colour is measured in a spectrophotometer at 560 mμ, and the difference between the blank and the incubated specimen is compared with the colour produced by a standard aqueous solution of 1 tyrosine containing 2×10^{-4} m eq in 2 0 ml

1 unit is that amount of enzyme which will release the spectrophotometric equivalent of 1×10^{-4} m eq of 1 tyrosine from 0 1 g of hæmoglobin substrate in a ten-minute digestion at 37°C (modified from Janowitz et al 1950) The results are all expressed as units per hour, which is a more reliable index of urinary excretion in the individual than concentration (Gottlieb 1924 Bucher 1947, Mirsky et al 1948), and for each patient in this report represents the average of two or more specimens of urine To conform to the standard usage

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[*] In receipt of a Medical Research Council grant

† Armour's bovine hæmoglobin enzyme substrate powder was mad up as a 2% solution in 0 15 N hydrochloric acid (Anson 193) *This acts as a buffer of moderate strength the pH of the incubate then varying only from 1 8 to 2 1*

and there was one young lady whom I especially wished to impress, and I laid my plans carefully.

With my young lady aboard I stopped at the garage; the lanky ginger youth came forward his nose in the air, and would no doubt have made some rude comment had I not forestalled him with a peremptory command to fill her up (1½ gall.). He bent down, unhitched the decrepit bonnet and threw it up. His mouth fell open, his eyes popped out, and he jumped to his job with a promptness and civility I had never before experienced. With aluminium paint even an ancient Austin Seven engine can be made to look like one of the shining gleaming aero-engines we sometimes see on display during the Battle of Britain week.

* * *

I sat with my hand immersed in hot wax and looked round for entertainment. The physiotherapy department is a small building separate from the main hospital, and this morning it was nearly empty. "My" therapist, who sometimes has time to chat, had completed her duties—namely, handing me a clean towel on arrival—and disappeared to another patient at the far end of the corridor; a young boxer brooded alone over his biceps in another cubicle. My mind began to occupy itself with a door across the passage marked OCCUPATIONAL THERAPY, apparently always locked and never seen to admit or let out anyone. So when Sister rustled along to smile at me, I seized the opportunity to ask when the room was used. I hoped to be shown (when disentangled from the wax) a room full of busy patients integrating their egos with raffia or sublimating with poster paints. "They come to dinner," said Sister surprisingly. "How odd," I remarked. "Yes, it *is* odd," replied Sister thoughtfully. "They come every day to dinner. I suppose they like the food better here than at the other places." I mused a little. "Of course," I observed, "eating is an occupation and it is often therapeutic, but to come here. . . ." "I think it peculiar myself," said Sister dryly and rather disapprovingly. "They have their meals and then get into their cars and go." "Where do they go?" I inquired fascinated. But instead of saying "Home," she mentioned the names of places here and there in the county, mostly unknown to me. It seemed odder still until the word "cars" returned to me and light dawned. "Do you mean the Occupational Therapists?" I asked. "Yes," replied Sister; "they all come here for meals." "But the patients," I faltered; "when do they come?" "Oh, the patients!" Sister dismissed them disdainfully. "I don't know when *they* come. I really don't know anything about them" she added after some thought, and rustled away.

* * *

When first we met, about three weeks ago, he had just killed a blackbird in my garden, and I was much upset. Perhaps that is why my aim was so good: he got a wallop on the back of his head that stunned him. I was completely unnerved, having missed every target since boyhood and having no intention of hurting a living thing. "Poor puss," I muttered as I stroked him back to normality, "you're just a cat."

Whether or not it was my best bedside manner I cannot say, but I haven't been able to get rid of Archibald since. No-one has answered my expensive advertisements about his having been found, and the local R.S.P.C.A. man tells me that the only home he might find for him would be a "long" one. Archibald, in other words, has adopted me, just as I, somewhat against my judgment, have adopted him. I comfort myself with the reflection that in a mixed practice one can't have everything. There are patients and patients. The birds are my first love, my old established friends who have learned to trust me. I am not sure what they think, but Archibald, rapscallion that he is, is now on my list and shows no wish to transfer to another doctor. For my own peace of mind, I am putting a nice wire-netting fence round the birds' pond and giving them a more elaborate feeding-tray. I only hope that Archibald appreciates my difficulties.

* * *

News from Hospital.—Our geriatrist has recently been warded with a virus pneumonia. After a few days we were relieved to read the report of our Jamaican night nurse that "Doctor complains of feeling all right today."

Letters to the Editor

HOSPITAL COSTING

SIR,—I was surprised at two examples "Administrator" gave last week to make his point that large-scale extravagancies exist within the hospital service: he instances that losses of bed-linen included sums of £6963 and £8150 at two large hospitals, and that farms and gardens run by hospitals showed a national deficiency of £614,033. There appear to be important fallacies in relation to such losses of linen; for it seems that, in stocktaking, ward deficiencies are taken into account, but not any excesses. When complete stocktaking of the entire hospital is taken on a single day, it has been found that apparent discrepancies may largely melt away. It does appear that the stocktaking system in hospitals needs overhauling.

It is entirely unfair to consider the cost of gardens in this context. In my opinion hospital gardens should be rated in the same category as hospital catering. They are essential for the well-being of the patient; some contact with trees, flowers, and lawns makes a very real therapeutic contribution, particularly for those who have to stay in hospital more than a few days. A distinguished American whom I was showing round a hospital commented that in his country they could not afford such gardens. He may have been a keen hospital economist, but I think his remark revealed a pathetic lack of any knowledge of the psychology of the average patient, at least in this country. With regard to hospital-farm accounts, I remain profoundly unimpressed by deficiencies based on internal book transactions.

There is actually one large-scale extravagance, which has so far escaped comment, revealed by the Ministry's Annual Report on Hospital Costing, which also gives figures for bed-occupancy rates. A general community hospital should have at least 90% bed-occupancy, and it is perfectly feasible to achieve a 93% bed-occupancy; and yet, up and down the country, there are many hospitals with only 80% occupancy and some substantially lower. Indeed, on the basis of the figures reported, there cannot be said to be any over-all shortage of hospital beds in this country. It is likely that low bed-occupancy rates reflect old-fashioned, inflexible systems of bed allocation. I am certain that attention to detail concerning this point could effect an impressive increase in the efficiency of the hospital service and a reduction in waiting-lists. A special study of this subject by the independent medical foundations—e.g., Nuffield or King's Fund—would be most opportune.

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F. AVERY JONES.

SIR,—In his letter of May 9 Mr. McCarthy suggests that those who are now attempting to compare the maintenance costs of hospitals would do well to read Dr. Topping's article.[1] I agree, however, not for the reason given by Mr. McCarthy, but because they would be convinced of the utter futility of making comparisons of costs calculated under subjective headings of expenditure. If comparisons are to be worth anything at all, like must be compared with like. If this were done it would reveal not only such differences as Mr. McCarthy mentions but also the cost of these differences. This was, in my opinion, the basic argument of Dr. Topping's excellent article.

ADMINISTRATOR.

DIAGNOSIS OF ACUTE MENINGITIS IN INFANCY

SIR,—I wish to support the findings of Dr. Haworth in his article last week. He has done well to draw attention to the paucity of signs and symptoms in this condition. I also have been interested in this problem,

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[1] Lancet, 1936, ii, 807.

73	38	2	+	0	+	+	+	0	+	++	+	+	0	0	56	0	+	+	+	67		27	0	0	1	G	0	+	0	0	0	7	Good
74	28	2	0	0	Cy	0	0	0	+	+	+	0	0	0	52	+	+	0	0	60	60	1	0	0	1	F	0	0	0	0	0	6	Good
75	36	20	1	0	0	0	0	0	++	+	+	0	0	0	18	0	+	0	0	26	59	9	0	0	1	F	0	0	0	+	0	6	Good
76	20	4	0	0	0	0	+	0	++	+	+	++	1	+	65	0	++	++	+	36			0	0	1	G	0	+	0	+	0	6	Fair
77	27	5	0	0	0	0	0	0	++	N	+	+	0	0	60	0	+	0	0	17	24	4	0	0	2	F	0	0	0	0	0	6	Good
78	19	4	0	0	+	0	0	0	N	+	+	0	0	0	56	+	+	0	0	10	18	15	0	0	1	F	0	0	+	+	0	6	Good
79	10	10	+	0	0	+	0	+	0	++	0	+++	+	+	79	+++	+++	++	+	55		29	+	0	1	G	0	0	+	+	+	0	Died
80	29	1	0	0	0	0	0	0	0	++	0	++++	0	+	63	+	++	+	+	50		22	+	0	1	F	0	0	0	0	0	6	Good
81	27	18	+	0	0	0	0	0	+	+	+	0	0	0	12	0	N	0	0	23	10	3	0	0	2	F	0	0	0	0	0	5	Good
82	23	1	+	+	Cy	0	0	0	++	+	+	0	0	0	60	+	+	0	0	13		12	0	0	1	G	0	0	+	+	0	5	Good
83	51	25	0	0	+	0	0	0	++	++	+	+	+	+	68	0	++	++	+	66			+	0	2	G	0	0	0	0	0	5	Good
84	35	5	+	+	+	0	+	0	++	+	+	0	0	+	53	+	+	+	+				0	0	1	F	0	0	0	0	0	5	Good
85	20	4	0	0	0	0	0	0	++	+	+	0	0	0	16	+	+	0	0	31	12	8	+	0	1	G	F		0	+	0	5	Good
86	17	7	0	0	+	+	0	0	++	+	+	+++	+	+	67	+	+++	+	+	70		13	0	0	1	G	F	F	0	+	0	5	Good
87	58	7	+	0	0	0	0	0	N	++	0	+++	+	+	56	+	++	0	+	56	71	2	+	0	1	G	0	0	0	0	0	0	Died
88	18	1	+	0	0	0	0	0	++	++	+	0	0	0	51	+	++	+	0	18	68	13	0	0	2	F	0	0	0	0	0	4	Good
90	52	1/2	+	+	0	+	0	0	++	++	+	+	0	+	50	0	++	0	0	23	10	7	+	0	1	G	0	0	0	0	0	4	Good
92	37	8	+	0	+	0	0	+	++	+	+	0	+	0	58	+	+	+	0	12	68	17	+	0	1	G	0	0	0	0	0	3	Good
93	11	2	+	+	0	0	0	0	++	N	0	++	0	0	50	0	++	0	+	68		26	+	0	1	F	0	0	+	0	0	3	Good
94	25	13	+	0	Cy	+	0	0	N	N	+	+++	+	+	68	+	+++	++	0	26		7	+	0	1	F	F	0	0	0	0	3	Good
95	11	6	0	0	0	0	0	0	+	+	+	++	0	+	51	0	++	+	+	52	76	24	+	0	1	F	0	0	0	+	0	3	Good
96	31	12	+	0	+	+	0	0	+	++	P	+++	0	+	63	+	++	++	+	71		16	+	0	1	F	0	0	0	+	0	0	Died
97	31	8	1	1	+	+	0	0	+	++	0	+++	0	0	60	+	++	++	+	80			0	0	1	G	0	F	+	+	0	3	Good
98	52	11	+	0	0	+	0	0	+	N	+	0	+	+	59	+	++	+	0	11	64	13	0	0	1	F	F	F	+	0	0	3	Good
100	46	4	+	0	0	0	0	0	0	N	+	0	+	+	57	+	+++	++	+	36	80	15	+	0	1	G	F	0	0	0	0	Follow up less than 3 months	
101	12	7	+	0	1	0	0	0	+	+	+	0	0	0	18	+	++	+	0	10	72	2	+	0	1	G	0	0	0	0	0		
102	40	10	+	0	0	0	0	0	+	+	+	0	+	+	69	0	++	+	+				+	0	1	G	0	0	0	0	0		
103	31	25	0	0	+	0	0	0	+	+	+	0	+	+	72	+	++	+	0	36	69	11	+	0	1	G	0	0	0	0	0		
104	12	12	0	0	0	0	0	0	+	++	P	0	0	0	57	0	++	+	+	60		29	0	0	1	G	0	0	+	0	0		
105	11	7	0	0	0	+	0	+	++	+	+	+++	+	+	61	0	++	++	0				0	0	2	G	0	0	0	0	0		
106	20	1/2	0	0	0	0	0	0	++	+	+	+	0	0	18	+	+	+	+				+	0	1	F	0	0	0	0	0		
108	30	6	0	0	+	0	0	0	++	+	P	0	0	+	53	+	+	0	0	17		20	0	0	1	G	0	+	+	0	0		
109	32	8	+	0	+	0	+	0	++	+	+	0	0	+	51	+	+	+	+				0	0	2	F	+	0	0	0	0		
110	36	15	0	0	Cy	+	+	+	+	+	+	0	+	+	66	+	++	++	0	51		20	0	0	1	G	0	0	0	0	0		
111	21	1/2	+	0	0	0	0	0	+	+	+	0	0	0	57	0	+	0	+				0	0	2	G	0	0	0	0	0		
112	30	13	1	0	1	0	0	0	++	+	+	0	0	0	50	+	++	0	0				0	0	1	G	0	0	0	0	0		
113	37	10	1	0	0	0	0	0	++	+	+	0	+	+	58	+	+	+	+				+	0	1	G	0	0	0	0	0		
114	38	17	0	0	0	+	0	0	N	++	+	+++	+	+		++	AN	0	+	(34)			0	0	2	G	+	+	+	0	0		Died
115	28	1	+	0	0	0	0	0	N	+	+	++	0	0	51	0	+	++	0				0	0	2	G	0	+	0	0	0		
116	50	7	0	0	0	0	0	+	N	+	+	++	+	+	63	++	++	++	0				+	0	1	F	+	++	+	0	0		Died
117	37	5	+	0	+	+	0	0	N	N	0	++	0	0	55	+	+	+	+				+	0	1	F	0	F	+	0	0		
118	35	7	+	0	0	1	0	0	+	++	+	0	0	+	16	++	++	0	0	17	75	20	0	0	1	F	0	+	0	0	0		
119	37	8	+	0	Cy	0	0	0	+	N	P	++	0	+	16	0	+	0	0				0	0	2	F	+	+	0	0	0		
120	10	10	0	0	0	0	0	0	++	++	+	++	+	+	61	N	+++	++	+				0	0	1	F	0	0	+	0	0		
3	47	0	0	0	0	+	0	0	N	+	0	+++	+	+	73	+	+++	++	+				0	+	3		++		0	0	0		
20	32	9	0	0	+	0	0	0	N	++	0	+++	0	+	55	+	+++	+	+	26	10		0	0	3		++		0	0	0		
24	27	2	0	0	0	0	0	0	N	++	0	++	0	0	59	0	++	+	+	35	11	8	0	0	3		++		0	0	0		
33	37	5	+	0	0	1	0	0	+	N	0	++	+	+	61	0	+++	0	0	27	16		0	0	3		++		0	0	0		
34	41	3	0	0	+	0	0	0	0	++	0	+++	0	0	61	0	++	+	+	28	50	4	0	0	3		++		0	0	0		
35	33	1/2	0	0	0	0	0	+	+	+	P	++	+	+	49	+	+++	0	0	18	22		0	0	2		++		0	0	0		
38	23	1/2	+	0	0	0	0	0	N	++	0	0	0	0	51	+	+	0	0	30	18		0	0	2		++		0	+	0		
39	30	7	0	0	0	0	0	0	+	N	0	++	0	0	51	0	N	0	+	26	17	1	0	0	3		++		0	+	0		
40	27	1	+	+	0	0	0	0	N	++	0	++	0	0	61	0	++	0	+	30	10	10	0	+	3		++		0	0	0		
41	30	2	0	0	0	0	0	+	0	+	0	+++	+	+	59	++	+++	+	+	26	16	1	0	0	3		++		0	0	+		
49	27	1	0	0	+	+	0	0	N	++	0	+++	0	0	57	0	++	+	+	52			0	+	3		++		0	0	0		
51	17	7	+	+	0	+	0	0	0	+	0	+++	+	+	54	0	+++	+	+	37	15	11	0	0	2		++		+	0	+		
60	58	4	+	+	0	+	0	0	N	N	0	++++	+	+	67	0	++	++	+	30	18		0	+	3		++		0	0	0		
73	20	2	0	0	0	0	0	+	N	+	0	+++	+	+	61	++	++	++	+	22	15	7	0	0	3		++		0	+	0		
91	37	2	0	0	+	+	0	0	N	+	0	+++	+	+	58	0	++++	+	+	19	72		0	0	3		++		0	+	0		
99	10	8	0	0	0	0	0	0	0	+	0	++++	+	+	61	+	++	+	+	28	10	12	0	0	3		++		0	0	0		
107	20	5	1	0	+	0	0	0	0	+	0	+++	0	0	50	+	+++	+	++	12	75	13	0	1	3		++		0	0	0		

Each feature recorded here is discussed in the text. Serial numbers refer to the order in which the 120 patients were operated on. Three cases have been omitted from the statistical analysis: case 9 had a vestigial auricle and valvulotomy was not done; case 13 (thoracotomy only) is the same patient as case 10 (pericardial graft); case 15 (first valvulotomy) is the same patient as case 89 (second valvulotomy). Above the line are 100 consecutive patients with predominant stenosis subjected to valvulotomy alone; below it are 17 consecutive patients who had mitral stenosis but in addition significant incompetence, and in all except case 3 a pericardial graft was inserted below the mitral valve with or without previous valvulotomy.

“Left sided enlargement” is placed between inverted commas because, as explained in the text, true enlargement of the left ventricle is not differentiated from displacement of the left ventricle. Preoperative and postoperative jet refer to regurgitation felt before and after division of the commissures. The symptoms are noted as: 0, absent; +, present; 1, present on one occasion only; Cy, present only during pregnancy; Tb, tuberculosis. *Mitral 1st and pulmonary 2nd sound*: 0, not heard; N, normal; +, ++, +++, ++++, accentuated in increasing degree. *Opening snap*: 0, not heard; F, faint; +, clear. *Mitral systolic murmur*: 0, not heard; +, ++, +++, ++++, increasingly loud; AS, aortic stenosis; T, tricuspid disease. *Auricular fibrillation*: 0, not present; +, present; P, paroxysmal. Radiology of *pulmonary artery* and *left atrium*: 0, not convex; +, ++, +++, ++++, increasingly enlarged (PA + = probably within normal range; AN = aneurysmal enlargement). *Right sided enlargement* and *left sided enlargement*: 0, not observed; +, ++, increasingly great. *Intracardiac pressures*: the numerals in parentheses are right ventricular and not pulmonary arterial pressures. *Right* and *left ventricular hypertrophy*: 0, no evidence; +, ++, increasingly great. *Mitral orifice*: 1, admitting no more than finger tip; 2, admitting more than tip but no more than the third phalanx; 3, admitting more than third phalanx. *Valvulotomy*: G, good, at least one commissure was completely divided; F, fair, partial division of one or both commissures. *Preoperative* and *postoperative jet*: 0, not felt; F, faint; +, present. *Clot, calcification,* and *embolism*: 0, not present or did not occur; +, present or did occur. In all columns — indicates observation not recorded.

because most of the cases I have seen have not shown the well-known signs described in the textbooks.

I have personally treated 12 cases of acute meningitis in children under five years of age in the past three years at Dr. Steevens' Hospital; of these, 6 were aged one year or under. 2 cases were meningococcal, and 3 were pneumococcal; in 5 no organisms were isolated; and 2 were acute lymphocytic. There were no deaths.

Only 7 of these cases showed neck rigidity. Kernig's sign was never present; neither was Brudzinski's sign, being a sign only in advanced cases. Most cases had some lassitude or drowsiness, but this was not of great value diagnostically. However, in 10 cases (including those in which there was no neck stiffness) there was a definite history of vomiting.

In Dr. Haworth's series of 50 cases, vomiting occurred in 31. Vomiting appears to be the most constant early clinical manifestation of meningitis in young children. It seems reasonable to conclude that if a child (especially an infant) is vomiting with no physical signs to account for it, and is persistently unwell, a diagnostic lumbar puncture should be performed without delay.

Dublin. P. B. B. GATENBY.

OBSERVATIONS ON PEPTIC ULCER

SIR,—Peptic ulceration, as Sir Heneage Ogilvie implies (March 21), is a disease of civilisation, and major scientific advances have contributed few clues to its exact ætiology.

Perhaps this continuing ignorance is due to our failure to bear in mind the dual aspect of the disorder. This duality manifests itself by a rhythmic swing of the symptoms, which patient and physician alike accept as pathognomonic. The active phase takes the form of distinct "attacks" with a sharply defined onset: the diurnal epigastric discomfort, with its daily peaks related to certain phases of the digestive cycle, usually increases to a maximum after 2–3 weeks and then diminishes to disappear completely after an average of 6 weeks in untreated cases. The subsequent intermissions, in typical and uncomplicated cases, are free from epigastric discomfort related to the time of eating. Often an ulcer crater previously demonstrated by radiography can still be seen; and the impression is that the symptoms remit with or without treatment and that the discomfort then cannot be provoked, in spite of the persistence of the ulcer crater. Most observations and methods of treatment are based on the apparent chronicity of peptic ulceration, while the active stage and the periodicity are seldom considered.

The following observations on treatment are related to the unexplored active phase; it is doubtful whether they have a direct bearing on the healing of peptic ulcer in the sense of restored anatomical structure. These observations were made over a period of 5 years on 37 patients with chronic peptic ulceration who were unsuitable for, or rejected, accepted forms of medical or surgical treatment. The average history of chronic peptic ulceration was $11^{1}/_{2}$ years.

Treatment consisted in daily intramuscular injections of 500 international units of chorionic gonadotropin. A rational background to this form of treatment was provided by Harvey Cushing's writings on the hypothalamus and the parasympathetic nervous system; by the experiments of Sandweiss and his colleagues on the ulcer-preventing effect of pregnancy-urine extracts on the experimental jejunal ulcer of the Mann-Williamson dog (gastrojejunostomy and diversion of the pancreatic and biliary secretions from the duodenum to the ileum); and by the known rarity of attacks of peptic ulceration during the second half of pregnancy. No other medicines were prescribed; no dietary or other instructions were given; and the patients were told nothing of possible time or evidence of improvement.

The patients fell into three groups. The first group (28 patients) had during past attacks had adequate medical treatment (rest, Sippy diet, powders, and belladonna) but were reluctant to subject themselves again to a prolonged régime because the recurrences had become more rather than less frequent; the average length of history of peptic ulceration in this group was 11·1 years, and the average number of recurrences in each of the two preceding years 2·1; 22 patients had pronounced deformity of the duodenal cap. The second group (5 patients) wished to try one last form of medical treatment before agreeing to surgery; the average length of history in this group was $14^{1}/_{2}$ years. The third group (4 patients) were by temperament and occupation unsuited for a medical régime; the average length of history was 1 year. All 37 patients had at the time of treatment the typical ulcer pain, and the crater was in all cases radiologically demonstrated. On the 4th day of treatment (i.e., after the third injection, that is 48–72 hours from the first) 34 of the 37 patients volunteered that, having noticed no change after the first two injections, they now had complete relief. With 1 exception, these 34 patients abandoned spontaneously all customary medicines, rules, and dietary precautions. In 6 of the 34 patients the symptoms recurred after a few days, but 28 patients remained free from symptoms and unaffected by what they had known in the past to provoke pain.

Of the 28 patients who experienced lasting relief 18 have been observed for 2–5 years. These 18 (15 duodenal ulcers, 3 gastric ulcers) had an average history of 9·6 years; in 12 there was distinct deformity with a crater. The average number of recurrences in each of the two previous years was 3·4; in the 2 years following treatment it was 0·31. The results by way of lasting relief were significantly, but by no means decisively, related to the type and severity of the case. The improvement or disappearance of the radiographic signs was not always in relation to the clinical improvement.

The optimum therapeutic effect was produced by the minimum number of injections that gave relief. At the start of this investigation it was felt that injections should be continued at least until the radiological signs had disappeared. Some patients, however, had a return of the symptoms while still receiving daily injections; and they attributed further exacerbation to the injections themselves. The injections were discontinued, and the symptoms cleared. In later cases (24) a maximum of three consecutive daily injections was given.

Experience has shown that the effect of the injections cannot be enhanced by increasing the dosage or by prolonging the treatment. Three or fewer injections, given during the active phase, produced sudden and more or less lasting improvement; but when given during the phase of improvement or remission, they seemed to reactivate the ulcer process. The pattern of the response seemed constant in each individual patient. Renewed courses of treatment produced the same pattern of reaction in the 6 patients who had lost their symptoms on the 4th day but who had relapsed within a fortnight. Further courses in the 3 cases which did not respond to the initial course also failed to relieve the symptoms.

These observations suggest that the active phase of peptic ulceration is a functional aberration of the feed-back mechanism in the autonomic system, similar in principle to Gasser's classical diagram of reverberating circuits, which also was histologically demonstrated and experimentally proved by Lorente de Nó.

There are established instances of brief endocrine stimuli evoking a "step" function in the nervous system and of substances acting on the transmission of autonomic nerve impulses producing a similar endocrine effect.

T. CSATO.

London, W.1.

Auscultation

Sir Thomas Lewis said that one should learn to recognise certain murmurs as one would the bark of a dog By auscultation mitral stenosis can often be detected in a few seconds In the diagnosis of associated mitral incompetence and similar problems the quality of the heart sounds and of added sounds and murmurs may give more information than accessory methods of investigation We believe that, when patients are being assessed for operation, more attention should be paid to the details of auscultation than has been customary in the past

HEART SOUNDS

A sudden, loud, slapping *first heart sound* at the apex is a confirmatory sign that mitral stenosis is the predominant lesion The absence of these qualities suggests either predominant incompetence, of which other evidence should be sought, or tight stenosis with a rigid valve It should be possible on other grounds to differentiate between these extremes When the first sound is obscured by a murmur, its features should be assessed by auscultation towards the mid-axillary line Towards the sternum the sound produced at the tricuspid valve may be mistaken for the mitral sound

Accentuation of the *second heart sound* in the pulmonary area is widely believed to reflect the degree of pulmonary hypertension Table II shows that in this series, whereas a loud pulmonary second sound was usually associated with severe pulmonary hypertension, there was sometimes a considerable discrepancy, and pulmonary hypertension was in some cases associated with a normal second sound The loudness of the sound may vary widely in the same person with exercise and with emotion—e g, on examination for the first time or by a new examiner, especially a surgeon It also varies with respiration and is loudest when the breath is held in expiration

Splitting of the second heart sound in the pulmonary area may be heard in healthy people, especially in youth It may also be heard in patients with mitral stenosis, particularly if the right ventricle is enlarged and there is delay in closure of the pulmonary valve More often apparent splitting is due to the opening snap of the mitral valve, which is often audible in this area although loudest at the lower left sternal border This has been proved to our satisfaction by the study of simultaneous phonocardiograms at the apex, at the left sternal border in the fourth intercostal space, and at the left sternal border in the second intercostal space (fig 2)

True *triple rhythm* is rare in patients with mitral stenosis, and is apt to be confused with an opening snap Pathological triple rhythm is of serious prognostic importance, whereas the opening snap bears no such significance It was not recorded in this series

Reference has recently been made to the significance of the *opening snap of the mitral valve* in determining whether mitral stenosis or mitral incompetence is the predominant defect when both are present (Logan and Turner 1952b) It is an *important* physical sign It may be heard more often than not in cases of mitral stenosis, whether there is normal rhythm or auricular fibrillation, and bears no relation to complications such as cardiac failure We believe that the opening snap may be absent in cases of tight stenosis with rigid or calcified cusps, but the chief points to emphasise are that in our experience, when a snap is heard, mitral incompetence is unlikely to be the predominant defect at the mitral valve, and that weakness or absence of this sound should lead to a search for other signs of mitral incompetence In the differentiation of an Austin Flint murmur from the diastolic murmur of mitral stenosis the detection of an opening snap signifies that mitral stenosis is present in addition to the aortic incompetence

The Present Series

In this series of 100 patients shown at operation to have predominant mitral stenosis a snap was heard in 87 The remaining 13 had a narrow rigid valve Of the 16 patients operated on for mitral incompetence the snap was not heard in 15, and was faint in 1 who also had moderate stenosis

HEART MURMURS

The grading of murmurs is subjective, so there can be no precision in recording their qualities Throughout the series the grading has been agreed on by the same three persons and is probably, therefore, reasonably uniform

Diastolic

The characteristic *mid-diastolic* and *presystolic* murmurs of mitral stenosis do not require detailed description here Unless tachycardia makes precise timing impossible, a distinct gap can be appreciated between the end of the second heart sound and the beginning of the mid diastolic murmur The murmur often appears to begin with the opening snap referred to above We have not found the presystolic murmur important Since it depends on auricular contraction it is absent in auricular fibrillation

An *early diastolic* murmur beginning immediately after the second heart sound is due to either aortic or pulmonary incompetence The murmur of aortic incompetence is best heard along the left sternal border, and is often audible at the apex If there are no signs of free aortic regurgitation, this murmur may be difficult or impossible to differentiate from the Graham Steell murmur of pulmonary incompetence The Graham Steell murmur is found only when there is severe pulmonary hypertension and therefore is often associated with an accentuated second sound and signs of right ventricular hypertrophy It is rarely so loud or so long as the early diastolic murmur of aortic incompetence, and is not conducted to the apex It may appear superficial in origin, and may be inconstant

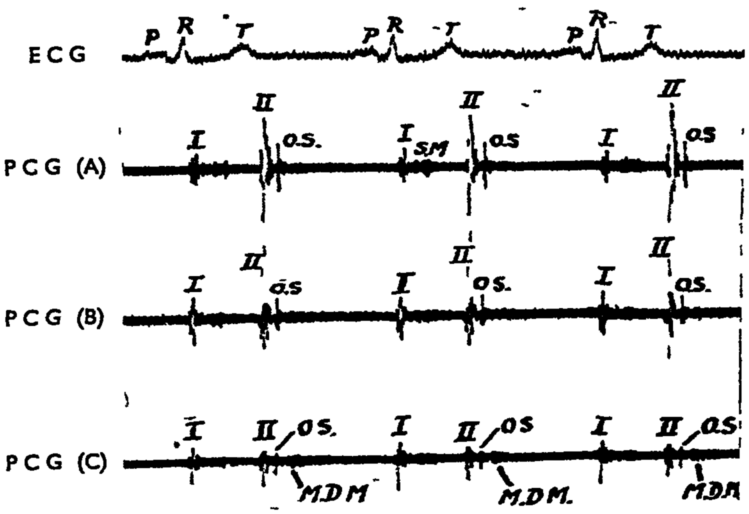

Fig 2—Phonocardiograms showing apparent splitting of pulmonary second sound due to mitral valve s opening snap, which is usually maximal at lower left sternal edge and immediately precedes mid-diastolic murmur at apex (*Frequencies were adjusted to show heart sounds clearly and not murmurs*) E C G electrocardiogram lead II, P C G (A), phonocardiogram 2nd left interspace, P C G (B), phonocardiogram 4th left interspace, P C G (C), phonocardiogram apex, I, first heart sound II, second heart sound, O S, opening snap M D M, mid-diastolic murmur S M, systolic murmur

THE ILLEGIBLE CANDIDATE

SIR,—All examiners appreciate only too well what an extra burden is imposed on them by candidates whose writing is difficult to read. There must be an unconscious prejudice against bad and illiterate handwriting, but all the examiners I have ever worked with have made it a point of honour to try to decipher what has been written and to avoid any deliberate penalisation for handwriting.

It has been left to our youngest Royal College—that of Obstetricians and Gynæcologists—to express openly the view that handwriting may lead to loss of marks. This is stated in so many words in the preamble to the examination paper for the Diploma in Obstetrics in March, 1953.

It is to be feared that candidates for higher medical examinations have already stabilised their handwriting to such an extent that not even a ukase from one or even all the Royal Colleges is likely to produce any striking improvement. Many must regret the mushroom growth of diplomas, but if these are to be made a test of handwriting as well as of a knowledge of the subject in question, the burden on doctors will be heavier than it is already.

Guy's Hospital,
London, S.E.1. J. J. CONYBEARE.

TRICHOMONAS VAGINITIS

SIR,—I have been following with interest the correspondence on this subject, and should like to state some of my observations about this common condition.

My view is that the disease is in most cases self-communicated. Every gynæcologist must have noted the unclean state of the perineum and perianal region in many women, especially the parous. A dry cotton-wool swab, drawn across the perineum, will show a faint fæcal smear even when the skin appears clean. This is especially common in women who have external pile tags, and who, either through obesity or tight low corsets, are unable to cleanse the anus efficiently after defæcation. In some women with slack anal sphincters, this fæcal contamination occurs even as a result of passing flatus. From this contaminated site the infection is carried into the vagina either by the fingers, by rubber occlusive pessaries, by masturbation, or by coitus.

Suitable instructions, including the washing of the anus with soap and water after defæcation, will prevent relapses.

London, N.W.2. M. E. LANDAU.

PHARMACEUTICAL ADVERTISEMENTS

SIR,—I should like to add to the correspondence about support of medical research by private firms in this country by drawing attention to what is done in the U.S.A. This information has been given by Deignan and Miller.[1]

The principle generally accepted in that country is that the support should be "in conformance with the research potential"—in other words that full use should be made of the research-workers available and qualified to investigate a given problem. The burden is divided between government and private sources. In the years 1946–51 a total of $135,044,125 was awarded for medical research, of which $51,933,454 (38·5%) was from private sources. Furthermore the funds from private sources increased materially towards the end of the period.

In this country it seems difficult to obtain authoritative information on this subject. Sir Reginald Watson-Jones (April 11) appears to know more than the Association of British Pharmaceutical Industry. They were unable to provide the statistics required, stating that "the financial details would normally be confidential to the firms themselves." It is unfortunate that they should be kept secret, since, as long as this is the case, suspicion and controversy are possible. Many commercial firms in this country have research laboratories of world-wide reputation, and this is certainly a good way to support research. At the same time the provision of more funds to workers in other laboratories would undoubtedly benefit the firms themselves. This is not a matter of charity: medical research is the life-blood of the pharmaceutical industries. The great expansion of their transatlantic rivals is due to a more longsighted policy.

The paper by Deignan and Miller describes a survey made by the Medical Sciences Information Exchange in America. The research potential in this country is undoubtedly great, and it would be a good thing if research-workers here could find out in a similar way about funds made available by British commercial firms.

London, S.W.18. PAMELA JEWELL.

INTESTINAL OBSTRUCTION IN INFANTS

SIR,—Dr. Sweetnam in his letter (April 4) agrees with the remark in your annotation (March 7) that the mortality from surgical conditions in children has been greatly reduced. He does not go on to acknowledge the part played in this improvement by just those special centres which he decries.

His use of intussusception and intestinal obstruction of the newborn as examples of these surgical conditions seems to me to point to the source of confusion which underlies much discussion on this subject. Intussusception is a fairly common condition in which a general surgeon operating in the excellent pædiatric units now established throughout the regions will soon obtain the experience necessary for efficient treatment. It is one of the important class of illnesses of childhood (others are pyloric stenosis and appendicitis) which are relatively frequent and for which there is an established and largely effective treatment.

Neonatal obstruction, however, is much less common. A peripheral unit is unlikely to have sufficient material to become efficient in the special techniques necessary for operation and management. It is an example of a group of conditions that are mainly congenital abnormalities and mainly require treatment in the neonatal period. Œsophageal atresia, congenital anorectal malformations, diaphragmatic hernia, and spina bifida may be cited as other conditions in this class. They are less common and their management is not yet settled. The usual surgical textbooks and teaching give little guidance in this respect. These are the cases in which the special clinics have made such great progress.

The foremost consideration is the survival of the patient. The next is the collection of knowledge about these difficult conditions. Does Dr. Sweetnam believe that either aim will be realised more frequently when these babies are cared for by surgeons who see only a few cases?

Many of these cases are urgent, and Dr. Sweetnam rightly points out the necessity for early diagnosis. Once this is achieved the few hours needed for transfer in this small country are insignificant. For instance, when intestinal obstruction is diagnosed a tube can be passed and the stomach emptied; and the baby will then withstand a journey surprisingly well.

The pædiatric surgeon is not an ultra-specialist. Rather does he extend the scope of the general surgeon to include proctological, urological, plastic, thoracic, and orthopædic conditions within this special age-group. Overlapping is inevitable, and personal interests and talents must affect individual arrangements; but in principle the completely different problems set by these patients seem to me to justify the approach.

The general surgeon has become largely a specialist in alimentary conditions. Nevertheless his older patients' behaviour will not guide him far in treating obstruction

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[1] Deignan, S. L., Miller, E. *Science*, 1952, 115, 321.

Dr. Robert Heilig Library
S. M. S. Medical College
[illegible] JAIPUR

Systolic

A systolic murmur at the apex is often heard in patients who also have signs of mitral stenosis and always signifies the possibility of predominant mitral incompetence. A systolic murmur was present in 59 of the 120 patients in the combined series.

We have limited ourselves to differentiating five grades of murmur. Grade five is rare and was not recorded in this series. Comparison has been made between the systolic murmur heard preoperatively and the regurgitant jet felt at operation (see table II). In most cases a systolic murmur presumably means that there is mitral regurgitation but this may be too faint to be appreciated by the gloved finger, and occasionally it is attributable to aortic or to tricuspid disease.

An attempt was made, by noting the qualities of the murmur, to estimate the degree of regurgitation likely to be met at operation. Of 17 cases in which a strong regurgitant jet was felt a systolic murmur of grade four intensity had been heard in 2; of grade three in 9, of grade two in 5; and in 1 case no murmur had been recorded. A loud presystolic murmur together with tachycardia sometimes makes the detection of a faint systolic murmur difficult. An apical systolic murmur was heard in 29 out of 75 cases in which no jet was felt. The absence of a palpable jet may have been due to the temporary weakening of cardiac action, which sometimes occurs during the operation. The loudness of the murmur in this group was recorded as grade one in 13 cases and as grade two in 12 cases. In 4 cases a murmur of grade three or four was recorded in spite of fairly tight stenosis, and in these the murmur, although loud, was finer and higher-pitched than the murmur of significant regurgitation.

We think that a fine high-pitched apical systolic murmur unaccompanied by other signs of mitral incompetence can be ignored. If the murmur is long, loud and harsh significant incompetence is more likely, but in our experience such a murmur is not necessarily a sign of predominant incompetence rendering the patient unsuitable for valvulotomy if in addition there is a loud slapping first heart sound or a clear opening snap.

A harsh systolic murmur at the apex is often present *in aortic stenosis* but does not mean that this is the predominant lesion. Other evidence of aortic stenosis should be sought particularly in the peripheral circulation. The aortic second heart sound is often weak or absent. The murmur of aortic stenosis may occasionally be loudest at the apex, but the same harsh systolic murmur can be recognised to the right of the upper sternum. It is usually conducted into the vessels of the neck and accompanied by a systolic thrill. An early diastolic murmur of aortic incompetence may also be heard.

A pregnant woman, aged twenty six, was seen because of severe paroxysmal pulmonary œdema. A harsh systolic murmur was heard at the apex. This murmur was loudest in the aortic area, conducted into the neck, and accompanied by a systolic thrill. It was interpreted as being due to aortic stenosis. An early diastolic murmur of aortic incompetence was also present. The aortic second sound was normal. The first heart sound at the apex was accentuated, and a mid-diastolic murmur of mitral stenosis could be distinguished. The opening snap of the mitral valve was easily heard. There were no dynamic signs of aortic incompetence in the peripheral circulation, and the pulse was of normal volume. The blood pressure was 100/60 mm Hg. At fluoroscopy in the postero-anterior view the heart was of normal size, and in the right anterior oblique view there was slight enlargement of the left atrium without systolic expansion. There was no left ventricular enlargement. The electrocardiogram indicated auricular but not ventricular hypertrophy. The mean pressure in the pulmonary artery was 28 mm Hg and there was a sharp rise on gentle exercise.

It was concluded that mitral not aortic valvular disease was the more important lesion, and that the paroxysmal dyspnœa was not due to left ventricular failure. At operation tight mitral stenosis was found and after valvulotomy her condition has been greatly improved.

Tricuspid lesions are difficult to detect, and may occur without characteristic pulsation in the veins of the neck and in the liver. If the right ventricle is enlarged, a careful search should be made for evidence of tricuspid disease, especially if the pulmonary arterial pressure is unexpectedly low. It cannot be concluded that a systolic murmur is due to tricuspid disease because it is loudest near the sternum. A study of necropsy material has shown that such a murmur may be due to mitral valvular disease when the valve is much deformed and calcified. The only means of confirmation of tricuspid incompetence during life may be by digital examination of the tricuspid valve through the right auricle, but this would be justified only by the belief that there was also enough tricuspid stenosis to require valvulotomy. One of our patients with tight calcific mitral stenosis had a loud harsh systolic murmur audible to the right of the lower sternum and maximal over the sternum. She died, and at necropsy no tricuspid lesion was evident. However, that functional tricuspid incompetence existed in life cannot be proved or disproved by examination after death.

The points to be emphasised are that there are causes of a loud apical systolic murmur other than mitral incompetence, and even a loud mitral systolic murmur does not necessarily mean that there is mitral regurgitation of dynamic significance.

Palpation

The position of the *apex-beat* is a rough and ready guide to the size of the heart, but anyone who regularly compares his clinical and radiological findings will soon be disillusioned about the accuracy of palpation in this respect, at least in cases of rheumatic heart disease.

Palpation is a valuable guide to ventricular hypertrophy, which may be present in considerable degree without much radiological evidence of enlargement of the heart, especially when hypertrophy results from increased work against resistance, as in cases of valvular stenosis. The deliberate apical thrust of left ventricular hypertrophy is unmistakable. Right ventricular hypertrophy has been said to give rise to a tapping apical impulse but many find difficulty in appreciating this quality and we consider that right ventricular hypertrophy is more readily detected by a thrust high in the epigastrium under the left costal margin or by a parasternal heave. The apical impulse may have a tapping quality without other signs of right ventricular hypertrophy, and right ventricular hypertrophy may be severe without a tapping impulse.

A *diastolic thrill* is a familiar accompaniment of the presystolic or mid-diastolic murmur of mitral stenosis. If, in addition, a *systolic thrill* is palpable it signifies that both stenosis and incompetence are present but gives no guidance as to which is the predominant lesion. A diastolic thrill from sclerosis of the cusps may be associated with a widely incompetent valve, and a systolic thrill may accompany tight mitral stenosis. The presence or absence of a thrill is of no material value in the assessment.

The Pulse

In patients with pure mitral stenosis of severe degree the pulse is characteristically small in volume. This is probably related both to the diminished cardiac output and to compensatory vasoconstriction. The hands are usually cold, and a "poor circulation" is a common complaint. If the pulse is not of this type, some complication should be sought, notably aortic or mitral incompetence. In pregnancy the pulse may be of relatively good volume, probably because of the increased blood volume.

in the newborn. For instance, indwelling gastric tubes have to be so small that they cannot be reliable. They are tolerated variably and may produce œsophageal hæmorrhage. Intravenous therapy has to be controlled on the assumption that renal function will be inefficient. The ordinary technique of two-layer anastomosis will not often be applicable. Peristalsis may be found to persist in the presence of peritonitis, and muscle-guarding to be absent under the same conditions. Experience of underlying lesions, such as errors of rotation and cystic fibrosis of the pancreas, cannot be gained from surgical treatment of adults; and yet such lesions require diagnosis by observation at laparotomy if treatment is to be adequate.

General surgical principles are the essential foundation in this as in other branches; but the foundation alone is not enough—a superstructure of experience of the individual variations of these cases is also required.

Harrow, Middlesex. H. H. NIXON.

CONTRACEPTIVE TECHNIQUE

SIR,—May I correct the misapprehensions expressed by Dr. Marie Stopes (May 2) with regard to my company's announcements on 'Preceptin Vaginal Gel'?

As international manufacturers and distributors of contraceptive jellies and creams and vaginal diaphragms, we are naturally aware of the limitations of the chemical contraceptives hitherto available, when used as a sole preventive against migration of spermatozoa through the os. These limitations are due to the inability of vegetable gums and emulsified fats to adhere closely to a secreting surface and so provide the necessary "barrier" to the cervical os. For this reason the "diaphragm and jelly" technique has been accepted as hitherto the most effective measure because the diaphragm provides both a physical barrier and a means of holding a sufficient quantity of the spermicide close to the cervix. But there are cases where the diaphragm either cannot or will not be used. Further, any means of conception control depends on intelligent use. Acceptability to the patient is no small factor in success.

More than eight years' research in the Ortho Research Foundation was concentrated on the development of a simpler method that would be at least as effective as the use of a diaphragm. The release of preceptin vaginal gel was preceded by two years' study involving thousands of patients, and the resultant high degree of success reported in these earlier studies has since been widely confirmed in many countries. The preparation succeeds, where other chemical contraceptives have failed, because it is neither a jelly nor a cream but is compounded in a base of unique synthetic materials having the ability to adhere tenaciously to a moist secreting mucosal surface. It provides its own "barrier" when 5 ml. is deposited at the cervix. The synthetic base also has the power to release the active spermicidal system more rapidly than has been possible even with such highly spermicidal compounds as 'Ortho-gynol' jelly, which is compounded in a vegetable gum base.

Mechanical devices solve only part of the vast problem of contraception. The acceptance of the mechanical barrier as the final achievement of science takes no account of such resources as those of the Ortho Research Foundation, with which my company is associated.

REGINALD GEORGE
Managing Director,
Ortho Pharmaceutical Ltd.

High Wycombe,
Bucks.

ANTICOAGULANT DRUGS

SIR,—Are anticoagulant drugs a benefit or otherwise to our patients? I am prompted to ask this question owing to the wide divergence of opinion held by two great schools in their treatment of acute deep-vein thrombophlebitis.

On the one hand, the Swedish school presents us with statistics showing a great diminution in the occurrence of embolism, and a speedy resolution of thrombophlebitis, when heparin and drugs of the dicoumarol series are employed. On the other hand, the Manchester school takes an opposite view. Professor Boyd suggests that anticoagulants have no place in the treatment of acute thrombophlebitis, and he is of the opinion that dicoumarol is an extremely dangerous capillary poison which, when administered to patients with ischæmia, may cause eruptions of the skin followed by sloughing. He tells me that recently in six cases he has had to amputate legs which might have been saved had this drug not been given. He makes the suggestion that heparin tends to loosen recently deposited soft clots, and in support of this view states that in twenty-five years he had never found bona-fide embolism following deep vein thrombophlebitis, but in recent years has come across such cases in patients receiving anticoagulants. Cases of acute deep-vein thrombophlebitis in their earliest stage are treated by the Manchester school by means of paravertebral block, and all anticoagulants are anathema.

This makes me ask the question—are anticoagulants our friends or our foes? Your readers' views on this most important subject would be valuable. It is fully time that the treatment of deep-vein thrombophlebitis was standardised, since all will agree that crippling sequelæ are all too common. The country has a vast population of patients with severe ulceration of the legs, which might well not have arisen had the antecedent condition of deep-vein thrombophlebitis been promptly and correctly treated.

London, W.1. R. ROWDEN FOOTE.

SUCKLING

SIR,—To suckle is a transitive verb meaning to give suck to (*Concise Oxford Dictionary*). In your leader on Puerperal Mastitis (May 2) you state that a procedure "allows the baby to . . . suckle normally"—which is a wrong use of the verb. Your next sentence uses it correctly in speaking of "pain on suckling"; for suckling is what the mother who feels the pain does. The infant feeds, takes the breast, or sucks.

Guy's Hospital, London, S.E.1 RONALD MAC KEITH.

UTERINE CANCER AND VAGINAL SMEARS

SIR,—Like Dr. Osborn (May 2) I was surprised at the misapprehensions in your leading article of April 18, and I was glad to find such support for cytology from a pathologist. We too have passed the 5000 mark, and the assessment of results of 3000 is shortly to be published.

I agree with Dr. Osborn in nearly every respect. But I believe that expansion of this work, which many of us have come to regard as essential, depends on its being largely carried out by technicians, if for no other reason than that there are not enough pathologists. This has been abundantly shown in the U.S.A., and there is no doubt that it is perfectly feasible. The negative smears are screened out by technicians, who can achieve this competence in six months, and the difficult and positive ones are kept aside. The laboratory is in the gynæcology department, and we cater for the pathology in this subject for the whole region.

I should have liked to see Dr. Osborn divide cancer of the uterus into its two types—cervical and corporeal. We find that our most useful contribution is in cervical cancer, where we can show just under 1% of women coming to our gynæcological clinics to have a cancer not suspected by the gynæcologist after speculum examination. But in the matter of body carcinoma, well known to be more difficult, we find it almost impossible to compete with curettage, which is usually so speedily arranged that we contribute very little, though we have had a few discoveries.

With Miss Mary Egerton I also agree—the value of the method is not assessable by the cost of working hours. And it is usually forgotten that the 499 patients who

Examination of the Lungs

When there is pulmonary œdema, or soon after hæmoptysis, crepitations may be heard in the lungs. There may be no crepitations although there are signs of congestive cardiac failure in the peripheral circulation. Abnormal signs may be caused by pulmonary infarction or by hydrothorax secondary to either infarction or cardiac failure. Attacks of acute bronchitis are common in patients with mitral stenosis, quite apart from the signs of "bronchitis" in the form of rhonchi which may accompany œdema.

We have been struck by the infrequency of radiological signs of hilar congestion or of congestion in the peripheral parts of the lungs in patients with mitral stenosis. This may be related to the fact that "hilar congestion" is usually due not to increased vascular markings but to pulmonary œdema; and in mitral stenosis this is rarely present except in acute attacks, whereas in left ventricular failure it may be chronic. Pulmonary arteriosclerosis, which is often present in mitral stenosis, may perhaps prevent or mask pulmonary congestion. Possibly the volume of blood in the lungs is not increased as is commonly supposed.

Cyanosis

Cyanosis may be central or peripheral in origin. Central cyanosis does not occur unless the disability is very severe and of long standing. It is due to deficient oxygenation of the blood as a consequence of the alveolar changes of prolonged pulmonary congestion. Peripheral cyanosis is due to stagnation secondary to vasoconstriction, and the arterial oxygen saturation is normal. Cyanosis is not in itself a sign of cardiac failure; when it is accompanied by clubbing of the fingers, some complication unrelated to rheumatic heart-disease should be sought. In 1 patient in this series cyanosis was due to a shunt in bilateral congenital arteriovenous aneurysms in the lung (case 57).

Auricular Fibrillation

Sooner or later, auricular fibrillation develops in most patients with mitral stenosis. Of 100 patients operated on for predominant stenosis 40 had established auricular fibrillation or had experienced paroxysmal attacks. In 17 cases with predominant incompetence auricular fibrillation was present in 9. The exact cause is obscure, and we have been unable to demonstrate any close relation with other factors, such as the severity of the stenosis, the degree of pulmonary hypertension, and the size of the left atrium. On the other hand, the incidence of fibrillation increases as age advances, and it is common in those with large hearts. Involvement of the myocardium by the rheumatic process is probably the most important cause. Precipitating factors include exacerbations of rheumatic carditis, acute infections, and sometimes, apparently, exertion. The onset of fibrillation may be shortly followed by acute cardiac failure, thrombus formation in the heart, and pulmonary or systemic embolism. The heart-rate should be rapidly controlled. When a precipitating factor can be identified the question of attempting to restore normal rhythm will sometimes arise. In most cases this is not worth while, because of the likelihood of an early return to fibrillation.

Paroxysmal fibrillation usually means that fibrillation will shortly become established. Repeated episodes of fibrillation are distressing to the patient, and established fibrillation with the rate controlled by digitalis is often preferable. Fibrillation, however, means a less competent heart and a greater likelihood of embolism. In some cases it is possible to prevent further attacks and to postpone the establishment of fibrillation by the regular administration of quinidine.

If acute carditis can be excluded, the onset of auricular fibrillation is an indication for considering operation on the grounds that it is evidence of progression of the disease; and, in theory at least, the mechanical disadvantage of auricular fibrillation will be to some extent offset by reduced obstruction at the mitral valve. Cardiotomy may offer the opportunity of emptying the auricle or the atrium of clot, and thus of diminishing the risk of systemic embolism. Moreover, when it is known that no clot remains in the atrium, the restoration of normal rhythm may be considered.

The problem of whether to restore normal rhythm in cases of recent auricular fibrillation in patients considered suitable for operation also arises. In recent years it has been widely believed that the risk of embolism after restoration of normal rhythm with quinidine has been exaggerated, and that the risk of further thrombus formation and embolism is greater while auricular fibrillation persists. Statistically this may be true, but one is bound to be influenced by the individual case.

A patient referred from another hospital was first seen three weeks after the onset of auricular fibrillation and put on the waiting list for admission with a view to assessment. In the meantime it was recommended that normal rhythm should be restored with quinidine. This was achieved without difficulty, but forty-eight hours later he developed a hemiplegia from cerebral embolism.

In such cases, when operation is necessary it is probably better done before an attempt is made to restore normal rhythm, so that any loose clot is removed from the auricle and atrium.

Although auricular fibrillation is usually a sign of severe myocardial damage, and predisposes to the formation of clot which may be dislodged into the systemic circulation during operation, it is not in itself a contra-indication to operation.

After successful valvulotomy the question of restoring normal rhythm again arises. In most of our patients with well established fibrillation before operation we have not thought this advisable. In 2 the attempt was successful, but in 2 the arrhythmia proved resistant even to high dosage of quinidine (4 g. per day). If age and rheumatic myocarditis are the principal causes, the arrhythmia will soon return. Of the 40 patients with auricular fibrillation who were subjected to valvulotomy 25 were aged more than forty. However, if there is a history of embolism, and the auricle and atrium are found at operation to be free from clot, and the valvulotomy is satisfactory, restoration of normal rhythm may be a reasonable prophylactic measure against further embolism.

Patients with auricular fibrillation do not have electrocardiographic evidence of right ventricular hypertrophy as often as those with normal rhythm. Although tight mitral stenosis was present in 34 of the 35 patients with auricular fibrillation in whom pressures were recorded, pulmonary hypertension was moderate in most cases, and severe in only 4. This may explain why recurrent hæmoptysis and paroxysmal dyspnœa were rare in this group. Attacks of breathlessness associated with paroxysmal fibrillation did occur but *not* typical paroxysmal nocturnal dyspnœa or pulmonary œdema.

9 of the 17 patients with predominant incompetence had auricular fibrillation and of these none had electrocardiographic evidence of right ventricular hypertrophy and 2 had evidence of left ventricular hypertrophy.

Postoperative auricular fibrillation in those who previously had sinus rhythm is common and occurred in 19 of this series. It was not a cause of *immediate* anxiety, because the heart rate was readily controlled with digitalis; but we feared that it might predispose to thrombus formation in the heart, especially on the auricular suture line. We therefore took steps to restore sinus rhythm with quinidine as soon as possible, and this was achieved in all cases. One patient, who reverted to fibrillation after returning home, died from cerebral have negative cytology are benefited to some degree, as well as the 500th who has a positive answer and is successfully treated.

Department of Obstetrics and
Gynæcology,
University of Edinburgh. A. F. ANDERSON.

TUBERCULOSIS IN GLASGOW

SIR,—It is incredible that Dr. Horace Joules can expect anyone to take seriously his letter in your issue of May 2 criticising tuberculosis administration in Glasgow on the basis of a fleeting visit and a view of one "unselected" patient suffering from pneumonia. Before he presented evidence, it appears to us that he would have been well advised to consult the senior administrative medical officer of the Western Regional Hospital Board and the medical officer of health of the city. This might have prevented him from making inaccurate statements. He says: "I learn that no consultant in tuberculosis has yet been appointed to the whole region of South-West Scotland, of which Glasgow is the centre." This is not true, as there are no fewer than 14 tuberculosis consultants in the area, of whom 6 are within the City of Glasgow itself, and the board are at present in process of appointing 3 further consultants for Glasgow.

Dr. Joules also failed to make inquiry regarding the B.C.G. scheme which is the largest and most progressive in the United Kingdom, nor did he ascertain that the city had the best and purest milk-supply in the country.

We can certainly agree when he says that it may be thought impertinent for someone from the South of England to make comments on the situation. The impression he has left in this city is that as an authority on Glasgow Dr. Joules may justly claim a status approximately equivalent to that of the gentleman who moralised on the problems of India, inspired by personal experience of them acquired from a conversation held on his doorstep in the Gorbals with a Hindu pedlar who spoke broken English.

For your readers who are interested in the progress which the city is making towards the eradication of tuberculosis, the following figures are offered as evidence:

Year	*Deaths from pulmonary tuberculosis*
1949	1093
1950	930
1951	674
1952	556

No-one denies that the housing problem in Glasgow is extremely serious, the reason being that over the last century the population of the city has quadrupled. Since 1919 Glasgow Corporation have constructed over 80,000 houses, which, considering that the period included the war years, is no mean effort.

The standard of work in the tuberculosis service in Glasgow is high, but the problems which have to be met are extremely difficult. Thoughtless and uninformed criticism is no helpful contribution.

STUART LAIDLAW
Medical officer of health

J. S. GEMMILL
Glasgow. Principal medical officer (tuberculosis).

SIR,—It is not impertinent for Dr. Joules (May 2) to make comments on the housing situation in Glasgow and its effects. What is lamentable is that he does not know that successive Governments in London have failed to do anything about it. The Government elected in 1945 preferred to fritter away its energies on a Festival Hall for London, whilst the amount of timber in London today is surprising in view of the housing shortage. I feel that in "Government circles" there is lacking any will to tackle this problem, and if there is ever to be any real improvement in Scottish housing it must be made by a Parliament sitting in Edinburgh. I commend this solution to Dr. Joules.

AN ARDENT SCOTTISH NATIONALIST.

POLIOMYELITIS

SIR,—Dr. Ritchie Russell (May 2) pleads with his orthopædic colleagues "to widen their thoughts beyond muscle resting and the avoidance of deformity"; he is in no doubt that the current orthopædic practice is to discourage activity in weak muscles for several months after the onset of poliomyelitis. As a plan is afoot for comparing the results of treatment under different physiotherapeutic régimes, I asked him to give me the name of any orthopædic hospital or department in the country where this is the practice. Alas, he was unable to give me the name of one; perhaps some reader of THE LANCET may be able to help, since we are anxious to know something about the progress of recovery in patients treated by surgeons who are persuaded of the value of rest for muscles weakened or paralysed by poliomyelitis.

Dr. Ritchie Russell is under the erroneous impression that such opposition as there has been to the strenuous treatment he advocates is due to the rigid conservatism of orthopædic surgeons. My own criticism of the treatment recently described in his book, shared by many of my brethren, is simply that he has failed to produce any evidence of its value. The experiments he describes were uncontrolled, documentation was sketchy, and the most favourable conclusion that can be drawn from the account of his work is that the patients suffered no harm. The onus of proof is on him, and he may be confident that if he can show that exercise to the point of complete fatigue of a weak muscle is better than other forms of neuromuscular re-education, we shall be no less grateful to him than we already are for his convincing work on the rôle of fatigue in aggravating the extent and severity of damage to motor neurones during the stage of invasion.

Dr. Ritchie Russell seems to be driving himself too hard in endeavouring to refute evidence that casts doubt on the safety of the method of treatment he champions. In his letter of April 25 Mr. Geoffrey Hyman described a case in which violent exercise appeared to aggravate the paralysis during the stage of recovery. Dr. Ritchie Russell suggests that this relapse was caused by a second attack of poliomyelitis, the virus being of a different strain from that causing the initial attack. If it really is possible that poliomyelitis viruses of different strains hunt in packs, then he should be the first to discourage violent therapeutic exercise, for he has shown how harmful it can be at the onset of the first attack—and why not the second?

In 1948 Dr. Ritchie Russell and I went together to the first international conference on poliomyelitis in New York. In a discussion on methods of treatment during the phase of recovery, I referred to a few patients, treated at the Wingfield-Morris Orthopædic Hospital in 1947, whom I had allowed to get up early and exercise themselves fairly freely, though to nothing like the extent he advocates. The affected muscles were examined at weekly intervals and a number of them, but not all, became much weaker. The tempo of exercises was then reduced, and walking was forbidden; the muscles slowly returned to their former state, and in the course of time became a little stronger than before. At that time he did not suggest that these patients must have suffered second attacks of the disease; he said nothing at all. The chairman at this discussion knew me well enough to say that the only cause for surprise was that I had been unwise enough to embark on the experiment at all. Since then I have been more cautious, yet even so we have several more fully documented cases in which muscles have lost power when the load on them (we should say on their neurones) was rapidly increased.

Royal National Orthopædic Hospital,
London, W.1. H. J. SEDDON.

embolism. At necropsy clot was found in the auricle although none had been observed at operation.

Radiography

THE HEART AND VESSELS

The size of the heart cannot be accurately estimated by clinical examination alone. Since the left atrium is at the back of the heart no information can be obtained about the size of this important chamber without radiography. To estimate the degree of cardiac enlargement as slight, moderate, or considerable is to formulate a rough impression of the severity of the underlying cardiac disease. This estimate of general enlargement usually refers to the transverse diameter of the heart—i.e., to the shadow of the right atrium, right ventricle and left ventricle. It is not, however, sufficient to say that the heart is enlarged; one must decide which chambers are enlarged and to what degree.

The condition of the aorta, of the pulmonary artery and its main branches, and of the lung fields should be noted.

When severe mitral stenosis develops early in life, the *aorta* is much smaller than normal. Presumably this is related either to failure of development or to "disuse atrophy" from the diminished output of the left ventricle. When there is also aortic incompetence the aorta may be enlarged and may show excessive pulsation.

The size of the *pulmonary artery* does not reflect closely the degree of pulmonary hypertension (table II). Duration of the hypertension is probably important. In this series, when the artery was considerably enlarged, mitral stenosis was usually severe and the pulmonary arterial pressure was high. In only 3 cases was the pulmonary artery enlarged to the degree commonly seen in other conditions, such as interatrial septal defect.

The prominence on the left cardiac border next below the pulmonary artery in the postero-anterior view is formed by the *left auricle* (auricular appendix) and not, as is still widely believed, by the outflow tract of the right ventricle (fig. 3). Visibility of the auricle suggests that an easy approach to the mitral valve will be available, and in some cases in which the characteristic convexity has been absent the small size of the auricle has prevented the use of the auricular route. The shadow of the left atrium can nearly always be seen behind the right atrium in the anterior view, and in this position its size may sometimes be better appreciated than in the customary right anterior oblique position. We have not found that the size of the left atrium is a reliable guide to whether mitral stenosis or incompetence is likely to be the predominant defect.

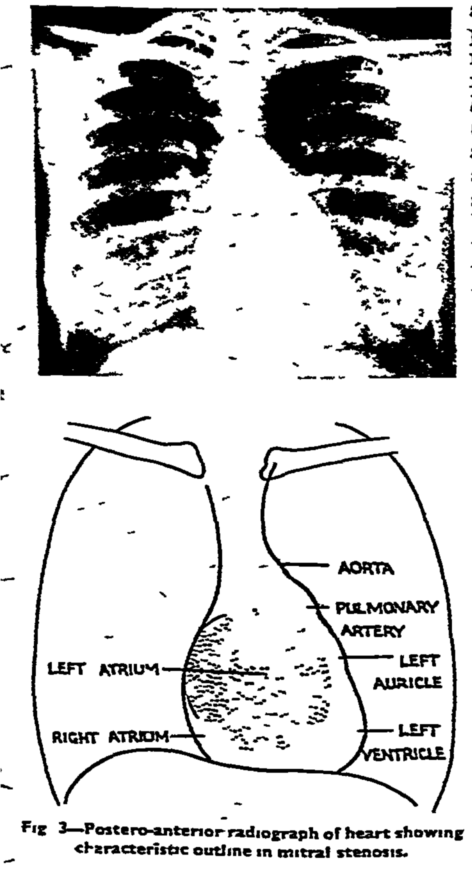

Fig 3—Postero-anterior radiograph of heart showing characteristic outline in mitral stenosis.

With increasing experience we have found it less and not more easy to differentiate minor degrees of enlargement of the various cardiac chambers. The size of the *right atrium* is best noted in the postero-anterior view, and that of the *right ventricle* in the left anterior oblique view. The right ventricle may be considerably enlarged when there is no electrocardiographic evidence of hypertrophy. The right atrium may be displaced to the right by an enlarged right ventricle. When these two chambers are both enlarged, fusion of the two curves in the left anterior oblique view may make their differentiation impossible. We now usually refer to the presence or absence of right-sided enlargement. When right-sided enlargement is marked there is probably considerable pulmonary arteriolar resistance, tricuspid disease or severe myocardial damage. When the right ventricle is enlarged, as is often the case, it may be difficult to differentiate enlargement of the *left ventricle* (as in mitral incompetence) from displacement of the left ventricle to the left in the postero-anterior view or backwards in the left anterior oblique view by the right ventricle. In these circumstances radiology is of less value than clinical or electrocardiographic assessment.

In other cases we have sometimes thought that considerable left ventricular enlargement made the differentiation of right-sided enlargement impossible, but for obvious reasons such cases are not usually under consideration for valvulotomy.

Calcification may be detected in the cusps or in the ring of the valve. Advantage may be taken of this to compare the movement of the mitral valve with that of the barium-filled œsophagus outlining the posterior border of the left atrium in the right anterior oblique view. Movement in the same direction in patients with pure mitral stenosis has strengthened our conviction that upward movement of the anterior cusp of the mitral valve into the atrium contributes to systolic expansion of the atrium, which is not therefore necessarily a sign of mitral incompetence as has been claimed.

So-called *systolic expansion of the left atrium* has already been discussed in some detail (Logan and Turner 1952b). Systolic expansion should be sought on the right and left cardiac borders in the anterior view, and in the right and left anterior oblique views, and by noting whether in the anteroposterior view the right atrium and barium-filled œsophagus move in opposite directions and, when the opportunity offers, whether the calcified mitral valve and the posterior border of the left atrium move in the same direction. Severe systolic expansion certainly suggests the presence of mitral incompetence, but the diagnosis can then readily be made on other grounds. We have observed gross expansion in all views in a patient with pure stenosis. Moderate systolic expansion may be observed in mitral stenosis, in mitral incompetence, and when these two defects are combined. Slight systolic expansion may be present in mitral valvular disease and occasionally in people with apparently normal hearts, and is of no value as a radiological sign.

THE LUNGS

We have found that radiological signs of pulmonary congestion, by which is usually meant increased vascular markings, are uncommon in patients with mitral stenosis and are of little help as a guide to pulmonary hypertension or cardiac failure. We have come to appreciate that the range of normal is wide.

It must be remembered that the depth of lung tissue in the anterior view is greatest towards the hilum; this may explain why the characteristic hazy opacities

Obituary

ROBERT GEORGE ARCHIBALD

Kt., C.M.G., D.S.O., M.D. Edin., Major R.A.M.C. retd

ALL those interested in tropical medicine or tropical agriculture will have read with regret the announcement in our columns last week of the death of Sir Robert Archibald on May 2.

He was born in 1880, the son of the Rev. W. F. Archibald of Edinburgh, a well-known Presbyterian chaplain to the Forces. From Dollar Academy he went on to Edinburgh University, where he graduated M.B. in 1902. After holding house-appointments in Liverpool, he entered the R.A.M.C. in 1906 and in the following year he was seconded for service under Sir David Bruce on the Royal Society's commission on sleeping-sickness. In Uganda he found himself in congenial company and he spent many eventful days with his fellow officer, Captain A. E. Hamerton, in hunting big game. Soon afterwards he was transferred to the Sudan, where he had his first taste of active service in operations on the Blue Nile. The next seven years he spent as a regimental medical officer with Sudanese troops, and it was this experience that gave him his knowledge of Arabic and insight into the character of this virile people.

At the outbreak of the first world war Archibald was recalled to the regular Army and in 1915 he was posted as chief of the laboratories at Mudros with the rank of major. The results of his investigations into the epidemics of dysentery and enteric in Gallipoli were published in two detailed papers in 1916. His chief problem was the correct diagnosis of the devastating dysenteries which assumed such formidable proportions. He concluded that both amœbic and bacillary forms were present, the former prevailing from June to October, and that after October the epidemic became entirely bacillary. The extensive studies on the paratyphoid fevers which he also undertook paved the way to the introduction of T.A.B. as a prophylactic vaccine.

In 1920 Archibald retired from the Army to become director of the Wellcome Research Laboratories in Khartoum, and eight years later he took over the new Stack Research Laboratories also in that city. When he left the Sudan in 1936 on reaching the age-limit he returned to Britain, and during the late war he worked in a public-health laboratory in Dorset. But once again Egypt called and though he was in his sixties, in 1947 he accepted an invitation to become professor of bacteriology in the Farouk University at Alexandria. During the last three years he had moved to the parasitological department.

During his time in the Sudan Archibald published over forty papers dealing with the diseases of that region.

Attracted at first by the problem of kala-azar, he described some coccal bodies, in association with leishmania, and he succeeded in transmitting the disease to cercopithecus monkeys. Later, he described its treatment with tartar emetic and recorded a fatal case after antimony, as well as one spontaneous recovery. In 1917, on an expedition to Darfur in the South Sudan, he observed some cases of seven-day fever. About this time he became interested in fungus diseases, and he described the pathology of mycetoma with special reference to "Russell's bodies." In 1922 he discovered the presence of *Trypanosoma rhodesiense* in the South Sudan. From 1932 to 1934 he studied the epidemiology of schistosomiasis, verified its treatment by tartar emetic, as established by Christopherson, and described the minute anatomy of the cecariæ of *Schistosoma hæmatobium* and *S. mansoni*. He also discovered the molluscicidal properties of a tree (*Balanites ægyptiaca*) which flourished in irrigated areas: its nuts and branches give out a substance lethal to fresh-water snails which promised a practical means of controlling the spread of schistosomiasis.

Perhaps his most important literary work was his editorship, together with his fellow officer and colleague, W. B. Byam, of that authoritative work the *Practice of Medicine in the Tropics*, to which he contributed the section on laboratory methods. Agricultural parasitology in the Sudan owes much to his investigations on the black-arm disease of cotton and the sulphuric-acid treatment of cotton-seed. His services were recognised by the government, and he was awarded the order of the 4th class Medjidieh and the 2nd class Nile. He was also appointed D.S.O. in 1917 and C.M.G. in 1928, and he was knighted in 1934.

P. H. M.-B. writes: "Archibald was a handsome, friendly, and imposing Scot, a typical healthy outdoors man, fond of all manly sports. No-one could fail to recognise the great qualities which marked him out as one of that select band who created the modern Sudan, and in this he followed in the footsteps of his friend and predecessor, Sir Andrew Balfour."

O. F. H. A. writes: "Archie, as he was universall called, and I served together in the Sudan for 26 years During the last 11 years of this time we worked in clos collaboration, he as director of the Wellcome Research Laboratories and I as director of medical services. I was during this latter period especially that I learnt to value his great qualities of unremitting methodical work and tireless devotion to duty, and in all eventualitie to rely on his friendship—a friendship readily extended to all. I think few men in the Sudan have gained such respect and affection as were given to him. In the seclusion of his laboratories and work he became to those who had never seen him an almost legendary figure."

He married, in 1919, Olive Chapman, only daughter of Arthur Cant, and they had two daughters.

Births, Marriages, and Deaths

BIRTHS

BENIANS.—On April 27, at Bradford, to Edith, wife of Dr. Richard Benians—a daughter.

DUFF.—On May 5 to Audrey (née Heaton-Smith) wife of Dr. A. Dewar Duff, 5, Tanza Road, N.W.3—a daughter (Elizabeth Anne).

GILL.—On April 27, at Godalming, to Aileen, wife of Mr. W. G. Gill, M.A., M.CHIR., F.R.C.S.—a daughter.

DEATH

MACBETH.—On May 9, Alison Nicol Macbeth, M.B., B.S., aged 56.

Appointments

ARCHER, NORA, M.A., D.M. Oxfd, D.P.H.: asst. M.O.H. and school M.O., Bristol.

CUTHBERT, J. M., M.B. Glasg., D.P.A.: medical superintendent to the boards of management for the Angus hospitals, and the Stracathro and Brechin hospitals.

DAVIES, J. B. M., M.D. Lond., D.P.H.: deputy M.O.H. and deputy port M.O., Liverpool.

DONELAN, M. J., M.B. N.U.I., D.P.H.: senior asst. M.O., Derbyshire County Council.

FRANCIS S. G. M., M.B. Edin.: group medical superintendent, Royal Infirmary of Edinburgh, and associated hospitals.

HALL, T. S., M.B.E., M.D., B.SC. Belf. D.P.H., D.OBST.: M.O.H. and school M.O., Salop County Council.

HOARE, R. D., M.B. Lond., D.M.R.D.: neuroradiologist, The Hospital for Sick Children, Great Ormond Street, London.

KEAY, K. R., M.D. St. And., M.R.C.P.E.: appointed factory doctor, Kirriemuir, Angus.

MAUGHAN, J. H., M.B. Durh., D.P.H.: deputy M.O.H. and deputy school M.O., Bournemouth.

MORRISSEY, W. J., M.B. N.U.I., D.P.H.: asst. M.O., Derbyshire County Council, and M.O.H., urban districts of Ashbourne and Belper and the rural district of Belper.

SMITH, THOMAS, M.B. Glasg., F.R.C.S.E., M.R.C.O.G.: part-time consultant obstetrician and gynæcologist, Jessop Hospital for Women, Sheffield.

SUTTON, DAVID, M.D. Manc., M.R.C.P., D.M.R.D.: (consultant) asst. director, diagnostic radiological department, St. Mary's Hospital, London.

WHITEHEAD, J. P. S., M.R.C.S.: asst. pathologist (S.H.M.O.), hospitals in the Scarborough, *Bridlington, Malton,* and Whitby H.M.C. group.

Sheffield Regional Hospital Board:

ADDIS, H. S. C., M.A., M.B. Camb., M.R.C.P.: consultant chest physician, Sheffield area.

BROWNE, MARGARET, M.B. Edin., D.A.: consultant anæsthetist, hospitals in the Nottingham area.

LETT, ZOLTAN, M.D. Czechoslovakia, D.A.: asst. anæsthetist, Mansfield area.

TANENBAUM, JULIUS, M.D. Paris: asst. chest physician, Mansfield area.

TOWNSHEND, R. H., M.B., B.SC. Manc., M.R.C.P., D.T.M.&H.: consultant chest physician, Sheffield area.

of pulmonary œdema are usually densest in the circumhilar region These opacities are important to recognise because, except in pregnancy, they signify severe mitral stenosis. Radiological signs may persist for several days or longer after the clinical attack of pulmonary œdema is over

If pulmonary hypertension is of long standing, the pulmonary artery and its main branches may increase in size and become denser

Some patients in this series showed radiological changes compatible with mild hæmosiderosis, which was confirmed histologically in operation specimens, but this study is incomplete Changes due to pulmonary infarction—e g , irregular or linear opacities, high diaphragm, and pleural effusion—will not be discussed further Mottling due to blood in the alveoli may be seen after hæmoptysis Hydrothorax may be secondary to cardiac failure

Electrocardiography

A detailed electrocardiographic study is being made of the patients in this series, but in summary it may be said that, although electrocardiography may not give information of material value in making the assessment for operation, sometimes it gives useful supporting evidence Since the left ventricle is never hypertrophied in pure mitral stenosis, electrocardiographic evidence of such changes, however slight, means that there is some important complication usually aortic valvular disease, mitral incompetence, or systemic hypertension For reasons which are still obscure, even clinically manifest ventricular hypertrophy may not give electrocardiographic signs In this series changes indicating pure right ventricular hypertrophy were found in 36 patients, all of whom had tight stenosis (fig 4*a*) An important corollary is that evidence of pure right ventricular hypertrophy has meant that predominant mitral incompetence was not present despite other suggestive signs such as a loud systolic murmur Patients in this group are most suitable for valvulotomy, and after operation there may be a progressive decrease in the electrocardiographic signs of right ventricular hypertrophy (fig 4*b*) Sometimes there is evidence of old rheumatic myocarditis Signs of auricular hypertrophy were present in 95% of those with sinus rhythm

Cardiac Catheterisation

Most of the patients in this series were subjected to cardiac catheterisation as part of the assessment for operation By this technique it is possible to measure the pressures in the right atrium and the right ventricle, in the pulmonary artery and its main branches, and in the pulmonary capillaries It is generally held that the capillary reading, which is made with the catheter inserted as far as possible into a branch of the pulmonary artery, reflects the approximate pressure in the left atrium (fig 5), and a sample of blood withdrawn while the catheter is in this position is arterial in oxygen content The cardiac output can be estimated according to the Fick principle From these findings can be calculated the resistance to blood flow at the mitral valve and in the pulmonary arterioles, and the approximate area of the mitral orifice Some consider that the shape of the capillary-pressure curve may provide evidence of mitral incompetence, but we have found this unreliable The blood volume and the circulation rate can also be measured To do all this with accuracy requires not only time but also organisation and technical assistance of a high standard It is important that these observations should be made in a few cardiac centres where equipment and staff are adequate to further our understanding of the hæmodynamics of valvular heart disease From the patient's point of view little more is entailed than the minor discomfort of venesection

We have usually restricted ourselves to simple measurements of pressure It was considered desirable to form our own conclusions about the value of this procedure The opportunity has been taken to correlate various physical, radiological, and electrocardiographic signs with the degree of pulmonary hypertension

Early in this series mean pressures were measured with a saline manometer Now systolic, diastolic, and mean pressures are measured with an electromanometer and recorded photographically

The pulmonary arterial pressure was recorded at rest and, if hypertension was not severe, after exercise Although patients with mitral stenosis are restricted in their activities, most of them are not at rest throughout the day, and it is the range of pressure which is important. Exercise consisted in pedalling against motor-cycle pumps and was stopped if the pressure rose promptly, because it was desired to determine only whether the pressure would in fact rise, there being no rise on exercise in normal people Since the exercise was not graded and patients vary considerably in the vigour with which they carry it out, these figures are not comparable but serve as a rough guide Probably several minutes should be allowed for a steady level to be reached , and, although this may be necessary for strictly comparable studies to be made, it was not necessary for our purpose in this series The pulmonary artery-pulmonary capillary gradient was used as a measure of pulmonary arteriolar resistance The importance of this is discussed below

With a view to allaying anxiety, '*Sodium amytal*' gr 3–6 was given to many of our patients, perhaps unnecessarily since none was obviously distressed by the procedure The effect of sedation, even when the dose was adjusted to the body-weight, varied greatly Some patients became so sleepy that pressures must indeed have been basal, and the patients were with difficulty persuaded to exercise In others some latent anxiety may not have been allayed , and, since we have found that emotion has a great influence on pulmonary arterial pressure, comparable results may not have been obtained The sodium amytal may also have had some effect in reducing a raised pressure, but this point was not determined Now we do not give a sedative as a routine

Because of these inconstant factors much attention should not be paid to the exact pressures recorded in comparing one patient with another, and patients are best divided into three groups according to whether pulmonary hypertension is mild, moderate, or severe The pressure may vary from day to day , it is certainly raised by exertion, emotion, coughing, straining, and discomfort Quinidine was given, before catheterisation, to diminish the risk of precipitating an arrhythmia

From these studies we have acquired much useful information and gained insight into many aspects of mitral valvular disease A decision whether to operate or not can often be made on clinical grounds supplemented by the readily accessible ancillary methods of radiology and electrocardiography Sometimes, however, the decision has been materially influenced by knowledge of the pulmonary arterial pressure A higher pulmonary arterial pressure at rest than had been expected, or a pressure which rose promptly on mild exertion, supported a decision to advise valvulotomy in a patient about whom we were uncertain on clinical grounds, whereas a low pressure that did not rise on exertion had the opposite effect We have not recommended operation in patients with a normal pulmonary arterial pressure which does not rise on exertion Except in 1 instance (case 49) no patient with predominant mitral incompetence has had a mean pulmonary arterial pressure above 50 mm Hg and in only 2 was the pressure above 40 mm Hg

Pulmonary Hypertension

Pulmonary hypertension is one measure of the severity of mitral stenosis and is probably a guide to prognosis In our experience patients with high pulmonary arterial pressures have been severely disabled, many pursuing a rapid downhill course, but they have also shown the most gratifying results after valvulotomy The highest pressures are not found in those with the largest hearts

Notes and News

ROYAL DENTAL HOSPITAL

At the 36th annual clinical At Home of the Royal Dental Hospital, held last Saturday, the demonstrations covered all aspects of dental surgery, and reflected much recent progress in orthodontic diagnosis. Methods of treatment have been modified now that a clearer picture has been gained of the factors—e.g., skeletal and muscle patterns, and the bad habits of thumb and lip sucking—which make for an unfavourable prognosis. A new type of appliance, introduced from the United States, and known as the edgewise arch, was shown by Mr. J. J. Tittle. It is obviously a useful method of dealing with certain types of malocclusion, but its capabilities cannot be properly assessed for a year or two, since it has been in use in this country for only a few months.

Excellent and technically beautiful radiographs of the temporomandibular joint were shown by Dr. S. Blackman, director of the X-ray department. These pictures, which reveal the true shape of the condylar head and give an accurate anteroposterior view of the ascending ramus, were taken by his new technique, details of which are to be published shortly. It is hoped that the already well-equipped department will soon be provided with the apparatus necessary for tomography.

Dr. J. E. Garside presented the results of an investigation into the cutting hardness of stainless-steel dental chisels. His results are interesting because they support the opinion of many dental surgeons that carbon steel is harder and more resistant to abrasion than the stainless variety.

During the morning session, demonstrations of oral surgery under general anæsthesia were given by Mr. M. P. Graham at the hospital's inpatient unit in the Grove Hospital, Tooting. Further clinical cases were shown in all departments during the afternoon session, which ended with the ever-popular brains trust, now in its third year. The team consisted of Mr. B. W. Fickling, Dr. A. B. MacGregor, Mr. H. M. Pickard, and Mr. W. E. Earle, under the chairmanship of Mr. N. J. Ainsworth. As in previous years, the questions with which they had to cope extemporaneously ranged from the slightly frivolous to the completely serious—from a question on whether parents should be warned of the high marriage-rate among women dental students to one on maintaining the high standard of dental teaching. As before, too, the team took these diverse matters in their stride, and provided an entertaining hour in which wit was nicely blended with many sound and useful opinions.

POLTERGEIST AND ZEITGEIST

Poltergeist phenomena, those ebullitions of china-smashing, stone-throwing, arson, and other extravagances, while so far remaining inexplicable on the physical plane, are beginning to make some kind of psychological sense. In a new book,[1] Mr. Hereward Carrington summarises the history of the poltergeist through the ages, and Mr. Nandor Fodor reviews some actual cases in the light of modern psychology. These phenomena, it has long been recognised, are usually associated with the presence of an adolescent child in the house; and the behaviour of the supposed spirit has much in common with that of an aggressive adolescent. On occasions, moreover, the ghost provides itself with a voice; and its conversation —as reported in the case of the "Bell witch," who in 1817 terrorised a family in Tennessee, or the "Saragossa ghost," who talked down a Spanish stove-pipe in 1934—is apt, like that of some young delinquents, to be abusive and grandiloquent. In short, supposing a disturbed adolescent with some form of hysterical dissociation were able—without direct physical contact—to wreak changes on his environment, these are very much the kind of changes he might wreak. The fact that poltergeist phenomena usually disappear as the associated young person matures lends additional colour to the theory.

A natural corollary would be to suppose that ghosts in general have a like origin; and this possibility led Mr. Fodor (who was formerly a psychical researcher and is now a psychoanalyst) to treat a lady whose house was haunted not for her ghost but for her complexes—with excellent results. Neither she nor the friend who shared the house was troubled by further visitations. This promising line of treatment suggests that in time we may be able to dispose of hauntings altogether; but it would be a pity if they became extinct before we have discovered what source of energy such disturbed patients are able to release from within, or tap from without, in order to engineer physical events which are apparent to others. By transferring the subject from the realm of the occult to the relatively respectable field of abnormal psychology Mr. Fodor may well have relieved investigators of some of the embarrassment which has so far hindered inquiry in this field.

University of Oxford

On April 30 the following degrees were conferred:

D.M.—J. V. Garrett, J. M. Jefferson.
B.M.—W. H. Allchin.

University of Cambridge

On April 25 the following degrees were conferred:

M.Chir.—P. G. Somerville.
M.B., B.Chir.—*E. J. Stacey.

* By proxy.

University of Leeds

Prof. Sydney Sunderland, professor of anatomy in the University of Melbourne, will give a lecture at Leeds General Infirmary, on Friday, June 12, at 8.15 P.M. He will speak on the Applied Anatomy of Peripheral Nerve Trunks.

Royal College of Physicians of Edinburgh

Queen Elizabeth, the Queen Mother, has accepted the honorary fellowship of the college.

At a meeting of the college held on May 5, with Dr. W. A. Alexander, the president, in the chair, the following were elected to the membership:

D. S. Nand, G. R. B. Kumarakulasinghe, W. MacLeod, S. N. Wanchoo, L. K. Ganguli, W. D. L. Fernando, N. Y. McCallum, E. W. Moore, M. Hasan, R. A. Gulmohamed, I. F. Sutherland, D. A. I. Grewar, B. Senior, N. Feldman, Y. Ho, Q. G. Quah, S. K. Biswas, W. S. A. Allan, T. H. Maniar, K. Z. Hasan, M. M. Baig, W. L. F. Hatchuel, A. Sandler, I. N. Marks, A. T. Lambie, J. K. McKechnie, C. Nwokolo.

Institute of Child Health, London

Three guest lectures are to be given at the institute at The Hospital for Sick Children, Great Ormond Street, W.C.1. On Thursday, May 28, Prof. S. van Creveld (Amsterdam) will speak on the Clinical Significance of New Clotting Factors; on Thursday, June 25, Dr. W. C. Davison (Duke University, N. Carolina), on Childhood Cancer; and on Thursday, July 2, Prof. G. Fanconi (Zürich), on Renal Dwarfism. All the lectures are at 5 P.M., and admission is free.

Education for Parenthood

The National Association for Maternity and Child Welfare has chosen this subject for discussion at its annual conference, to be held at St. Pancras Town Hall, Euston Road, London, N.W.1, on June 10, 11, and 12. The speakers will include Dr. Jean Mackintosh, Dr. John Burton, and Dr. Catherine B. Crane. Tickets (21*s.*) may be had from the secretary, N.A.M.C.W., Tavistock House North, W.C.1.

Workmen's Compensation and Sickness Benefit

From May 7 totally disabled persons receiving Workmen's Compensation are no longer to have their sickness benefit reduced on that account. The regulations making this change have been made by the National Insurance Joint Authority with the approval of the National Insurance Advisory Committee. (S.I. 1953. No. 765. H.M. Stationery Office. 2*d.*)

Harveian Society of London

This society's Buckston Browne—Gray Hill dinner was held at the Royal College of Surgeons on May 6. The Dean of St. Albans, proposing The Society, declared that custom outlives rule; and he urged members to keep the society alive for the future, which, judging by present signs, would see a spiritual revival and renewed initiative. In his reply, Dr. Tom Hare, the president, said that Sir Buckston Browne always spoke with pride of the address he gave to the society on his method of crushing stone. The President extended a special welcome to Dr. G. F. Abercrombie, chairman of the foundation council of the College of General Practitioners. Dr. D. A. Imrie spoke generously of the guests. Mr. Justice Danckwerts, in his response, remarked that Harvey's work on the circulation occupied 52 pages; and he commended this example of brevity to modern scientists. Dr. Abercrombie reported that the support for the new college was very gratifying.

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[1] The Story of the Poltergeist down the Centuries. London: Rider. 1953. Pp. 216. 16*s.*

probably because the increase in size is the end result of rheumatic myocarditis rather than simple hypertrophy due to work They are found in those with relatively little enlargement but with clinical and electrocardiographic evidence of right ventricular hypertrophy In a few there has been no radiological evidence of enlargement of the heart Patients in this group tend to die young from "pulmonary failure"—i e , severe congestion and œdema, often with infarction

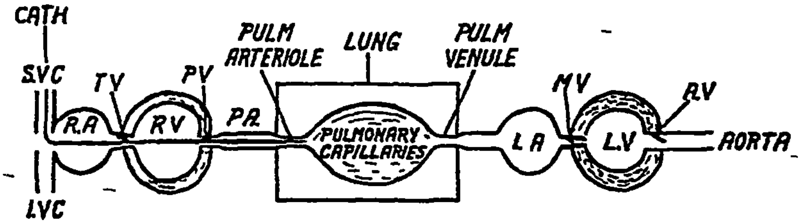

Fig 5—Position of cardiac catheter recording pulmonary capillary venous pressure When catheter tip is withdrawn into main pulmonary artery, pressure rises by resistance of pulmonary arterioles A V, aortic valve Cath, catheter, I V C, inferior vena cava, L.A, left atrium L.V, left ventricle M V, mitral valve P A, pulmonary valve, R.A right atrium, R V, right ventricle, S V C, superior vena cava, T V tricuspid valve

We have found that the degree of pulmonary hypertension cannot always be determined even approximately except by cardiac catheterisation There may be a striking discrepancy between the pulmonary arterial pressure recorded by the manometer and that deduced from the loudness of the pulmonary second sound or from the size of the pulmonary arterial shadow Although it is true that, when the pulmonary second sound is very loud or the pulmonary artery is much enlarged, pulmonary hypertension is usually considerable, the converse does not hold

Analysis of the cases of 24 patients with the highest pressures, excluding 2 who were pregnant, shows that all were severely disabled by dyspnœa on exertion and were liable to breathless attacks on slipping down in bed, but none had experienced an attack of acute pulmonary œdema All 12 patients in whom pulmonary capillary-venous pressures were recorded had evidence of considerable pulmonary arteriolar resistance This increased pulmonary resistance may explain why 20 of the 24 patients had electrocardiographic evidence of right ventricular hypertrophy All had tight mitral stenosis Only 5 had established auricular fibrillation, and they were aged more than forty One man, aged thirty-four, had an episode of fibrillation shortly before operation following catheterisation 15 gave a history of hæmoptysis

The increased pressure in the pulmonary artery in patients with mitral stenosis is due partly to the resistance at the narrow mitral valve, and partly to that in the pulmonary arterioles, which are narrowed by intimal proliferation and medial hypertrophy It is probable, although unproved, that arteriolar resistance may also be affected by vasoconstriction If the mitral valve is narrowed, the blood-flow can be maintained or increased on exertion only by a rise of pressure in the left atrium Since there are no valves between the mitral valve and the pulmonary capillaries, pulmonary hypertension results Narrowing of the pulmonary arterioles (fig 5) may be regarded as a protective phenomenon in that it tends to reduce the blood flow from the right ventricle, and so to prevent the lungs from being flooded On the other hand, an increase in pulmonary arteriolar resistance increases the work of the right ventricle, and will contribute to its eventual failure It will be appreciated that the patients with mitral stenosis who are in danger of pulmonary œdema are those with tight mitral stenosis, relatively little pulmonary arteriolar resistance, and a strong right ventricle The symptoms of mitral stenosis are those of pulmonary hypertension and reduced blood-flow, the first causing dyspnœa on exertion, orthopnœa, paroxysmal dyspnœa, and hæmoptysis, and the second weakness, fatigue, and lassitude

The opinion has been expressed that very high pressures are a contra indication to operation on the grounds that they show irreversible changes in the pulmonary arterial tree Our results in this particular group have been most encouraging, and a regression of electrocardiographic evidence of right ventricular hypertrophy suggests that the changes resulting from severe stenosis are not in all cases irreversible (fig 4) Soon after valvulotomy much or little improvement may be noted, but in either case gradual improvement may continue over many months Initial improvement is tentatively ascribed to the relief of valvular obstruction, and the later gradual improvement to regression of the arteriolar changes

The limitations of pressure recordings without calculation of blood flow are appreciated, but in most of the cases in which the pressures were relatively low mitral stenosis was not very severe—i e , the valve would just admit the terminal phalanx of the index finger On the other hand, a relatively low pulmonary arterial pressure may be due to severe myocarditis affecting the right ventricle Case 94 is a good example of this

A girl, aged twenty five, had, on arrival from a long journey, congestive cardiac failure with gross œdema and ascites and a large heart (cardiothoracic ratio 68%) She responded well

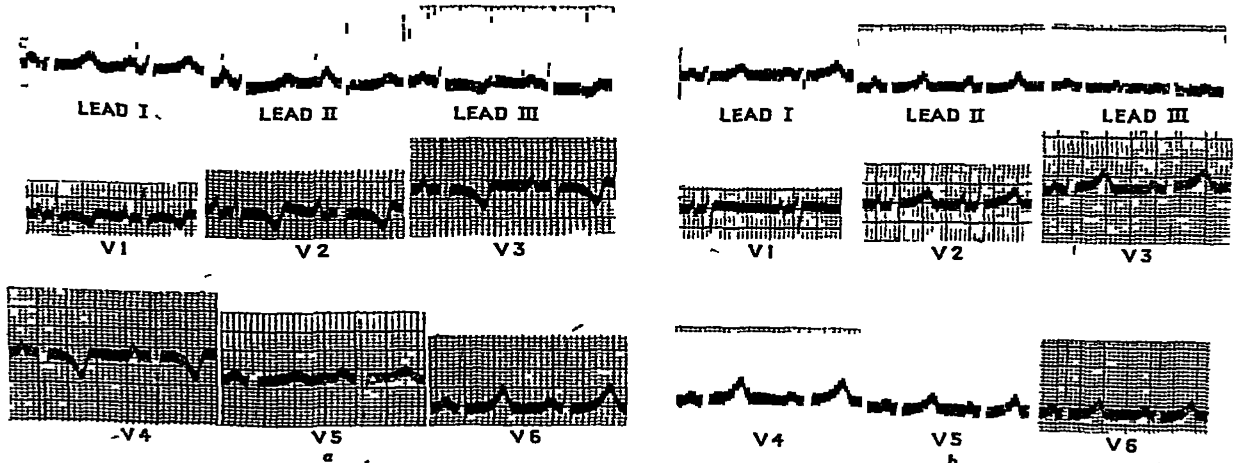

Fig 4—Electrocardiograms a pattern of right ventricular hypertrophy (tall R waves and negative T-waves in leads recorded over right ventricle), b recession of signs of right ventricular hypertrophy in same patient sixteen months after valvulotomy

American Otological Society

The 1953 award of merit and gold medal of this society has been presented to Dr. Julius Lempert.

Royal Medical Benevolent Fund

The annual general meeting of the Fund will be held on Tuesday, June 9, at 5 P.M. at 11, Chandos Street, London, W.1, with Lord Webb-Johnson, the president, in the chair.

Liverpool Medical Exhibition

At 11.30 A.M. on Monday, May 18, Dr. E. N. Chamberlain will open this exhibition at St. George's Hall, Liverpool. It will be open daily from 11 A.M. to 6.30 P.M. till May 22.

British Association for the Advancement of Science

Sir Henry Dale, O.M., F.R.S., will take the chair at a meeting of this association on Thursday, May 28, at 6 P.M., at the Royal Institution, Albemarle Street, London, W.1, when Sir Harold Hartley, F.R.S., will deliver the Alexander Pedler lecture on the Life and Times of Sir Richard Gregory.

British Association of Sport and Medicine

At a meeting of this association at the Westminster Hospital Medical School, Horseferry Road, London, S.W.1, on June 24, at 5 P.M., Sir Adolphe Abrahams and Dr. A. McEldowney will open a discussion on the Doping of Athletes.

R.A.F. Appointments

Air Vice-Marshal V. S. Ewing has been appointed principal medical officer, Home Command; and Air Commodore R. H. Stanbridge principal medical officer, Middle East Air Force, with the acting rank of air vice-marshal.

Health Exhibition at Deptford

An exhibition showing the work of the personal health services in Deptford, Greenwich, and Woolwich is to be held at the Health Centre, Amersham Road, Deptford, from noon to 6 P.M. on Friday, May 15, and from 10 A.M. to 6 P.M. on Saturday, May 16.

International Scientific Film Association

The seventh congress of this association will be held in London from Sept. 18 to 27, in the National Film Theatre and Royal Festival Hall. Special meetings and film shows will be devoted to the technique and application of films in medicine. Further particulars may be had from Dr. R. C. Mac Keith, the vice-chairman of the medical committee, Guy's Hospital, London, S.E.1.

Anglo-French Exchange Bursaries

The following have been awarded bursaries for special studies in France:

F. B. COCKETT, senior lecturer, professorial surgical unit, St. Thomas's Hospital, London.

R. H. GORRILL, senior lecturer in bacteriology, University of London.

A. MACDONALD, reader in bacteriology, University of Liverpool.

A. MCPHERSON, 1953 Laming-Evans research fellow of the Royal College of Surgeons.

J. W. F. SCRIMGEOUR, senior registrar in obstetrics and gynæcology at St. Mary's Hospital and Crumpsall Hospital, Manchester.

E. C. TURTON, consultant psychiatric physician in charge of the department of electro-encephalography and electrophysiology, Barrow Hospital, near Bristol; tutor in electro-encephalography, University of Bristol.

Society of Chiropodists

The annual dinner of this society was held at the Park Lane Hotel on May 7. Responding to Sir Henry Souttar's toast of The Society, Mr. J. H. Hanby, the president, said that the prevention of foot disabilities came first in the society's programme, and the regular inspection of school-children's feet was one of the most important preventive measures. The seriousness of the matter was shown by the high proportion —about 70%—of the community who had abnormal feet. To enable the public to know where it could obtain scientific chiropodial treatment, a State register of chiropodists was essential, and the society would continue to urge the Government to establish one. Mr. S. Coates, vice-president of the society, welcomed the guests, among whom were Lord Webb-Johnson, Lord Hollenden, Sir Cecil Wakeley, Sir Heneage Ogilvie, Sir Harry Platt, and Sir Zachary Cope. In his reply, Sir Zachary commended the society for insisting on a State register, and he hoped that the combined efforts of all the medical auxiliaries would shortly induce the Government to act.

Prof. C. A. Wells has spent a week in Syria lecturing for the British Council. He is on his way to Hong-Kong to act as external examiner at the university.

Diary of the Week

MAY 17 TO 23

Monday, 18th

UNIVERSITY COLLEGE, Gower Street, W.C.1
4.45 P.M. Sir Rudolph Peters, F.R.S.: Inhibitors and Intracellul Chemical Dissection. (Last of four lectures.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.1
4 P.M. Prof. R. V. Christie: Dyspnœa.
MANCHESTER MEDICAL SOCIETY
9 P.M. (University of Manchester.) *Section of General Practic* Dr. R. H. Titcombe: The General Practitioner and Pos graduate Education. (Presidential address.)

Tuesday, 19th

NEWSHOLME LECTURE
5.15 P.M. (London School of Hygiene and Tropical Medicin Keppel Street, W.C.1.) Prof. Alan Moncrieff: Chil Health and the State—Infant Welfare and the Ministry Health. (First of three lectures.)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Stree W.C.2
5.30 P.M. Dr. S. C. Gold: Lupus Erythematosus.
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospita Medical School, W.2
5 P.M. Brigadier J. S. K. Boyd, F.R.S.: Bacteriophage Typin and Epidemiology. (Almroth Wright lecture.)
SOUTH WEST LONDON MEDICAL SOCIETY
8.30 P.M. (Bolingbroke Hospital, Wandsworth Common, S.W.11. Dr. Benjamin Barling: Diseases of the Thyroid.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Medical School, Small's Wynd, Dundee.) Dr. C. G. Kin (New York): *Aspects of Nutrition.*

Wednesday, 20th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
6.30 P.M. Prof. A. M. Boyd: Dextran—The New Narrow Fractio (First showing of the film.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. F. O. MacCallum: Laboratory Diagnosis of Viru Diseases.
ROYAL SOCIETY OF MEDICINE
5 P.M. *Section of Comparative Medicine.* Sir William Ogg, PH.D., Mr. G. C. Ainsworth, PH.D., Dr. D. P. Cuthbertson, Sir James Scott-Watson, D.SC.: Organic Manures and Fertilisers and Production and Composition of Food for Man and Animals.
8 P.M. *Section of General Practice.* Mr. Melford Stevenson, Q.C.: The Medical Witness.
NEWSHOLME LECTURE
5.15 P.M. (London School of Hygiene and Tropical Medicine.) Professor Moncrieff: School Health and the Ministry of Education. (Second of three lectures.)
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. O. Oliver: Pathology of Lupus Erythematosus.
MIDDLESEX HOSPITAL MEDICAL SCHOOL, W.1
4.30 P.M. Prof. E. C. Dodds, F.R.S.: Chemicals and Food—A Reconsideration. (Sanderson-Wells lecture.)
ROYAL COLLEGE OF SURGEONS OF EDINBURGH, 18, Nicolson Street, Edinburgh, 8
3.30 P.M. Dr. R. B. Cattell (Boston): Carcinoma of the Pancreas.

Thurday, 21st

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. E. S. Clarke: Cerebral Circulation.
NEWSHOLME LECTURE
5.15 P.M. (London School of Hygiene and Tropical Medicine.) Professor Moncrieff: The Deprived Child and the Home Office. (Last of three lectures.)
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. J. C. Broom: Leptospirosis in Tropical Countries.
LONDON JEWISH HOSPITAL MEDICAL SOCIETY
8.30 P.M. (11, Chandos Street, W.1.) Prof. David Slome: Experimental Surgery.
SOCIETY FOR ENDOCRINOLOGY
9.30 A.M. (11, Chandos Street, W.1.) Symposium on the Determination of Adrenal Cortical Steroids and their Metabolites.
NORTH-WESTERN TUBERCULOSIS SOCIETY
5 P.M. (Manchester Royal Infirmary.) Dr. W. Robinson: Air Cysts of Lung. Dr. G. Penrhyn Jones: Pulmonary Adenomatosis.
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. M. W. Paterson: Abnormalities of Optic Disc.
UNIVERSITY OF ST. ANDREWS
5 P.M. Prof. Harold Scarborough: Purpura.

Friday, 22nd

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr. F. Masina: Diagnosis and Surgery of Bladder Tumours.
4 P.M. Dr. B. M. Wright: Inhalation and Retention of Aerosols.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. W. N. Goldsmith: Xanthoma, Necrobiosis Lipoidica and Granuloma Annulare.
INSTITUTE OF OBSTETRICS AND [illegible] W.6.)
2 P.M. (Queen Charlotte's [illegible] is in Dr. J. Purdon Marti [illegible] Pregnancy and Puerperium.

The fifth and latest issue of *Prescribers' Notes* has now been sent to executive councils for distribution to doctors taking part in the National Health Service. Hospital boards are invited to apply for copies for members of their medical and pharmaceutical staffs.

to treatment. Her mean pulmonary arterial pressure was 26 mm Hg (systolic pressure 38 mm Hg, right ventricular filling pressure 5 mm Hg). She had tight stenosis.

Cardiac Failure

It might be thought easy to decide whether or not a patient has cardiac failure, but in practice, for lack of a simple clinical definition, it may be difficult. The customary objective criteria include crepitations at the bases of the lungs, peripheral œdema, distended neck veins, and enlargement of the liver, and when these are present the diagnosis is clear. Judged by symptoms (dyspnœa, pulmonary œdema, hæmoptysis, tiredness, and weakness) the heart may fail to provide an adequate output for the needs of the body, although the above-mentioned signs are absent. To ascertain whether cardiac failure has occurred in the past is still more difficult. A history of œdema of the ankles is common in women, especially if their day includes much standing; it often comes on during pregnancy. This œdema is mistaken for cardiac œdema, even when the heart is healthy; and if the heart is known to be diseased the inference is harder to avoid. A single sign, such as œdema, occurring without supporting evidence requires critical interpretation.

In the assessment of the severity of rheumatic heart-disease, cardiac failure occurring once at the onset of auricular fibrillation should be distinguished from cardiac failure occurring otherwise. The sudden change of rate and rhythm imposes a severe strain on the heart; but, if initial treatment is adequate and digitalisation is maintained, failure may not recur for many years.

Every effort should be made to secure freedom from cardiac failure before deciding on operation. In some patients this is impossible because their disease has progressed too far and the myocardium is severely damaged. Others have tight mitral stenosis and yet little enlargement of the heart, because the myocardium has not been injured by the rheumatic process and has responded by simple hypertrophy. They usually have normal rhythm, gross pulmonary hypertension, and electrocardiographic evidence of right ventricular hypertrophy. Pulmonary congestion is severe. The size of the mitral orifice is insufficient to permit an adequate cardiac output even under basal conditions. Valvulotomy may be followed by early relief of symptoms and later regression of the signs of ventricular hypertrophy. It is important to operate on this group of patients without delay, for they may become unfit for valvulotomy within a few months because of progressive cardiac failure or pulmonary infarction from thrombosis in the pulmonary arteries.

POSTOPERATIVE CARDIAC FAILURE

30 patients in this series developed signs of congestive cardiac failure within two weeks of operation and before being allowed out of bed. No patient developed failure after being allowed up. Cardiac failure in those in whom operation is believed to carry a serious risk was not surprising, but sometimes it occurred unexpectedly in patients who had never previously experienced it. In no case was it severe, and in most it amounted to no more than slight peripheral œdema or congestion of the neck veins. The few in whom treatment was considered necessary responded to the customary measures of restriction of salt intake, injections of mercurial diuretics, and digitalis. 5 patients experienced a mild attack of cardiac failure after returning home. In 2 this could be attributed to giving up digitalis prematurely, and in 2 to an attack of rheumatic fever. One (case 2) was a patient whose condition was not materially influenced by operation.

Pregnancy and Mitral Stenosis

We shall not discuss here the way in which pregnancy may aggravate mitral stenosis, or the general management of mitral stenosis in pregnancy except in relation to valvulotomy.

It is usually stated that there is no evidence that pregnancy permanently aggravates rheumatic heart disease, but we have been impressed by the frequency with which patients date the onset of their symptoms or of material deterioration of their condition to pregnancy. This matter requires further study.

In pregnancy the blood volume increases by 25–40% between the third and eighth months, and this increase may explain the change in symptoms and signs which takes place in patients with mitral stenosis. The circulatory effects of moderately tight mitral stenosis in pregnant patients are similar to those of very tight stenosis in the non-pregnant. Undue breathlessness on effort and discomfort on lying flat may be appreciated for the first time or be greatly aggravated. Such symptoms may be evident within two or three weeks of the start of pregnancy. Paroxysmal dyspnœa, pulmonary œdema, and hæmoptysis are liable to occur in patients who previously were not materially disabled. Auscultatory signs which before pregnancy were hard to detect may be striking. Pregnancy might therefore be considered a good test of the severity of the underlying heart disease, but this may be fallacious. Even severe signs and symptoms may regress after the confinement, and the patient may remain well for several years.

Nevertheless during pregnancy, as early as the second or third month, symptoms may become severe enough to compel a choice between termination of the pregnancy, continued observation in hospital, and valvulotomy. Natural delivery at term is generally considered to carry less risk than termination of pregnancy after the fourth month. It sometimes happens that attacks of pulmonary œdema or hæmoptysis occur without a known precipitating factor and continue although the patient is kept at rest; and it is in such circumstances that valvulotomy should be considered. There is no reason to suppose that the risk of operation is increased in early pregnancy.

The cases of 2 patients in this series who were operated on during pregnancy as an alternative to termination have already been reported (Logan and Turner 1952a). They remained well throughout the ensuing months, and each was safely delivered of a healthy child at full term. A 3rd woman was observed during a severe attack of acute pulmonary œdema with hæmoptysis which took three days to resolve.

During treatment in hospital two less severe attacks of pulmonary œdema and further hæmoptysis occurred. There was no reason to suppose that these attacks would not continue and even, since the blood volume would further increase, become more severe. The resting pressure in the pulmonary artery was high (45 mm Hg), and accordingly valvulotomy was advised. At operation the lung was found to be heavy with œdema, and there was a hydrothorax of more than 300 ml. The mitral valve just admitted the terminal phalanx of the index finger, and the valvular orifice was satisfactorily enlarged.

We do not suggest that valvulotomy in pregnancy is often required. With few exceptions, patients in whom mitral disease complicates pregnancy can, by careful medical treatment, be safely carried to term, and whenever possible this is the better way.

(*To be concluded*)

> “But I have the hardihood to believe that there is little in the content of real science that cannot be made clear to the ordinary man *in* ordinary plain English. That technical terms and certain unfamiliar words must of necessity be introduced I freely admit; but that any man’s views on life—its modifications and even its meanings—cannot be transmitted in plain and familiar terms to his fellow men *I do not* believe.”—Prof. F. WOOD JONES, F.R.S. *Trends of Life.* London, 1953; p. 191.

MITRAL STENOSIS

DIAGNOSIS AND TREATMENT

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SURGICAL treatment has brought new life and new hope to many who were incapacitated, in varying degree, by mitral stenosis. Valvulotomy provides an illuminating method of investigation as well as effective treatment and has given impetus to the study of the natural history of the disease.

Not long ago most physicians were content merely to make a diagnosis of mitral stenosis. Cardiologists then began to differentiate certain groups of patients, for example, the "œdematous" group of Gallavardin (1934), which corresponds to the patients described below who have tight stenosis, little cardiac enlargement, normal rhythm, and attacks of paroxysmal dyspnœa. Today it is important to assess in each case not only the degree of mitral stenosis but also the state of the myocardium and lung, the resistance in the pulmonary arterioles, the degree of mitral incompetence and aortic valvular disease, if present, and the rate of progression of the disability. The surgeon can improve only the degree of mitral stenosis, and occasionally perhaps the valvular action of the mitral cusps. Now that precision in diagnosis is important, and the clinical assessment can be confirmed or confounded at operation, it is desirable for clinicians to re-examine their present views in the light of the findings at operation.

The experience of only one other hospital has so far been reported from this country (Baker et al. 1950, 1952). Since experience everywhere is limited, we decided not to review published work but merely to describe our own.

MATERIAL

Of 200 patients subjected in the past two and a quarter years to thoracotomy for mitral valvular disease 130 came from one medical unit. This paper is principally concerned with the study of the first 100 of these 130, who had pure or predominant mitral stenosis for which valvulotomy was performed (table I). Of the remainder 17 had predominant mitral incompetence, and 16 of these were treated by a different operation ; 11 have already been reported (Logan and Turner 1952b).

TABLE I—AGE, SEX, AND CARDIAC RHYTHM

Age (yr.)	Total no. of patients	Male	Female	Auricular fibrillation
10–19	1	0	1	0
20–29	22	2	20	7
30–39	36	7	29	9
40–49	27	4	23	17
50–59	14	4	10	7
Total	100	17	83	40

Early in our experience 2 patients were found at operation to have predominant mitral incompetence although this had not been suspected preoperatively. One patient had a thoracotomy only, because the auricle was found to be vestigial and too small to admit the surgeon's finger. One had her valvulotomy repeated later because of unsatisfactory progress.

Except when otherwise stated, all the statistics cited refer to the 100 patients with predominant stenosis.

Each patient was studied in detail, and there was seldom a case which did not present some new facet of the diagnosis or treatment of mitral disease, or provide information of value for the future. Most of the patients stood the operation well, made a satisfactory convalescence, although not without occasional incident, and returned home well pleased.

The group of patients is representative of the whole range of mitral stenosis, except for mild lesions not known to be progressive, and those with large hearts and uncontrollable cardiac failure. Ages varied from sixteen to fifty-nine. More than a third had auricular fibrillation, and almost a third had experienced cardiac failure. Many gave a history of pulmonary œdema or of hæmoptysis. Many had large hearts. If it was believed that improvement could be obtained, patients were accepted in spite of considerable operative risk, since the only alternative was rest, further restrictions, and digitalis, without prospect of sustained symptomatic relief.

Symptoms

Mitral stenosis is recognised primarily by the auscultatory findings, but these do not indicate the degree of stenosis or the severity of the functional incapacity. Attention must be paid to the history, a detailed clinical examination, and an analysis of the radiological and electrocardiographic findings. In addition useful information may be obtained by cardiac catheterisation, although in many cases this is not essential.

We shall consider here chiefly those features which are important in the assessment for operation.

DYSPNŒA

It would not seem difficult to ascertain how breathless a patient is ; but *dyspnœa on exertion* may be purely subjective, and patients vary widely in their appreciation of its severity. In the absence of special apparatus the degree of dyspnœa may be roughly assessed by accompanying the patients up one or more flights of stairs. Some belittle what is, to the observer, clearly a considerable disability, and others make much of a slight limitation of their activity. Especially in young people there is danger of attaching too little importance to a complaint of dyspnœa, since tight mitral stenosis and pulmonary hypertension may be present although the heart is of normal size and there is no manifest congestion of the lungs at the time of examination. In such cases data obtained by cardiac catheterisation may be of value.

Dyspnœa which is progressive is an indication for considering operation.

Orthopnœa

Orthopnœa is a sign of severe pulmonary congestion, and therefore either of tight mitral stenosis or of severe myocardial damage. If the myocardium is much damaged, the heart is usually much enlarged.

Acute Paroxysmal Dyspnœa

Patients with mitral stenosis often suffer from acute paroxysmal dyspnœa. The attacks are unpredictable, and there may be long intervals between episodes of great severity. Why they occur in some patients and not in others who have a similar degree of mitral stenosis is unknown, but one factor is probably the degree of pulmonary arteriolar resistance (see below). During the attack the pulse-rate is usually rapid, and the pounding of the heart may be seen through the clothes and heard several feet away. In a sense the attacks are due to left atrial failure—i.e., they are precipitated by any factor which temporarily increases the cardiac output with the result that the right ventricle pumps into the lungs more blood than the left atrium can accommodate and pass on to the left ventricle. As a result severe congestion of the lungs develops.

TROUBLESOME TAPEWORMS

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THE title is chosen deliberately to emphasise that apeworms are troublesome, both because they cause ymptoms and because they can be difficult to treat apeworms in this country are often considered as a oke, and regarded as more suitable for examination uestions than *for consideration of their clinical* importance I have not been able to find any article on beef apeworms published in British medical literature in he last ten years

Since 1943, in the routine practice of a general hysician, I have seen thirteen patients with the beef apeworm (*Tænia saginata*), which shows that such nfestation is not a great rarity Of these thirteen atients six complained of general symptoms before hey noticed they were passing segments, and in some ases these symptoms were severe In a case of obscure bdominal pain the diagnosis of tapeworm is worth onsidering Tæniasis, though certainly not a common ause of abdominal pain, is probably as important as orphyria, tabetic crisis, Addison's disease, and other are but well-known causes of abdominal pain

CASE-RECORDS

The following case records illustrate the symptoms that beef tapeworm can cause

Case 1 —A hospital sister, aged [illegible], began in 1942 to have attacks of colicky central abdominal pain in bouts lasting 2 or 3 days At first there were intervals of about a week with no pain, but after 6 months the pain became more frequent and more severe till it occurred almost daily At that time she noticed that her appetite was increased, and particularly at midday or last thing at night she had a sudden craving for food which, when satisfied, considerably improved her abdominal pain After 9 months she began to vomit two or three times a week about 2 hours after food, this made the pain worse, and she began to feel "really rotten" (as she put it), though normally she was a most cheerful and active person

10 months after her first symptoms she was diagnosed as having chronic appendicitis and operated on, but, though the appendix was reported as chronically inflamed, her pain and vomiting persisted unchanged after its removal A fortnight after the operation she happened by a lucky chance to look at her motions and saw moving white segments At that time she was severely incapacitated by her pain, she had lost 1½ st in weight, and could hardly carry on her nursing duties After routine treatment the complete worm was found, and all her symptoms disappeared next day She has been perfectly well ever since

She admitted that since she had been given bits of raw meat "to play at shops with" as a child she had acquired a taste for it, and that she regularly used to eat raw meat

Case 2 —A housewife of 34 was admitted in 1949 For 9 months she had mild indigestion, and 8 months before admission she had been in bed for a fortnight with "gastric flu" characterised by severe sickness whenever she got out of bed, and diarrhœa For 2 months she had felt worried and miserable She had severe colicky "rolling" pains worse in the mornings, and slightly eased by her midday meal Sometimes these pains were so severe that when doing her housework she would have to stop sweeping hold on to her broom, and groan aloud Her friends noticed that she looked ill and pale, and she lost enough flesh for her to have to alter the buttons on her stays and her skirt The pain continued unabated till her admission Though her appetite became rather poor throughout this illness, she used to get sudden bouts of hunger, particularly in the evenings

8 months after the *onset of* her *symptoms* she noticed "small white pieces which moved" in her motions She took some worm powders that her chemist gave her and then passed several feet of worm, but the symptoms and the passage of segments continued till she was referred to hospital for treatment After routine treatment the whole worm was recovered, and her symptoms disappeared straight way and have not returned She told us that she often ate beef sausages completely raw

Case 3 —A Lebanese nurse, aged 25, was admitted in 1952 with a month's history of increased appetite, giddy feelings, and central abdominal cramps The hunger was worse in the mornings, but she couldn't eat as much as her appetite was asking ' The abdominal pain came in short attacks lasting 2 seconds but was severe while it lasted The giddiness was bad enough to make her feel very unsteady when she first got out of bed in the morning A fortnight later she noticed that segments came out from the anus even when she was not defæcating she inspected her motions and noticed more She was admitted 2 weeks later After routine treatment the whole worm was recovered, all her symptoms ceased forthwith, and she has remained completely well

She said that her people (the Lebanese) habitually eat all their meat raw, and she had recently been on holiday in Lebanon eating raw meat

ANALYSIS OF THE THIRTEEN CASES

Of the nine patients who were asked, eight admitted to eating raw meat, so this appears to be an important factor

There were eight women and five men No children were affected Four of the patients had received previous courses of treatment elsewhere, and the worm had grown again One of these patients, a man of 40, had had sixteen ineffective courses of treatment, the other patients had received from one to four courses All the cases were cured the head of the worm being found and identified in twelve cases and in the remaining patient, though the head was missed, a clinical follow-up 5 months later established that there was no recurrence Infestation varied from 5 days to 6 years, but the commonest length of infestation was about 6 months

DIAGNOSIS

Tapeworm is rarely diagnosed before the patient notices segments, but in cases of obscure colicky abdominal pain, with bouts of unexplained hunger or giddiness, it is worth *asking the patient to inspect the motions* When segments are present they are easily seen, for the mature proglottides are a distinct whitish yellow colour, and they move, changing their shape from ▭ to ▯. Affected patients have told me that they never pass more than three motions without seeing segments, and these are usually present in every motion Sometimes segments migrate from the anus spontaneously, this is pathognomonic of *T saginata* and does not happen with *T solium* Often a patient says he has a tapeworm when he has roundworms or threadworms, and it is wise to ask the patient to draw rough pictures of the alleged segments or, better still, to bring up some for laboratory examination, so that he is not admitted for a course of treatment until it is certain he has a tape worm Patients may have had previous inadequate courses of treatment followed by the passage of several feet of the worm which makes the diagnosis certain on the history alone

TYPES OF WORM

In this country if a patient has a tapeworm it is almost certain to be a beef tapeworm. There are however, three possible infestations—by beef tapeworm, by pork tapeworm, and by fish tapeworm As the treatment for these is the same, it is of academic interest to decide which worm is present before treatment

Microscopy of the proglottides or of the ova can settle the matter, and there are also clinical differences The beef tapeworm is more likely to produce clinical symptoms, such as abdominal pain, hunger, and giddiness and the proglottides often migrate from the anus independent of defæcation The pork tapeworm rarely produces clinical symptoms, and its proglottides rarely migrate from the anus In England it is much rarer than the

TABLE II—ANALYSIS OF CASES

		Symptoms							Signs						Radiology					Intracardiac pressures (mm. Hg)			E.C.G.		Operation								
No.	Age (yr.)	Duration of symptoms (yr.)	Paroxysmal dyspnœa	Pulmonary œdema	Hæmoptysis	Cardiac failure	Pulmonary infarction	Systemic embolism	Mitral 1st sound	Pulmonary 2nd sound	Opening snap	Mitral systolic murmur	A. fibrillation preoperative	A. fibrillation postoperative	Cardiothoracic ratio (%)	Pulmonary artery	Left atrium	Right-sided enlargement	"Left-sided enlargement"	Pulmonary artery (resting)	Pulmonary artery (after exercise)	Pulmonary artery-capillary gradient	Right ventricular hypertrophy	Left ventricular hypertrophy	Mitral orifice	Valvulotomy	Preoperative jet	Postoperative jet	Clot	Calcification	Systemic embolism (postoperative)	Follow-up (mos.)	Result estimated on clinical grounds
1	27	13	+	0	+	0	+	0	++	N	+	++	0	0	59	+++	++	0	0	90	..	..	+	0	1	G	0	..	0	0	0	28	Good
2	28	2	0	0	0	+	0	0	+	+	0	++	P	+	62	0	++	++	+	41	(37)	..	0	0	1	F	F	..	0	+	0	28	Poor
4	35	13	0	0	+	0	0	0	++	++	+	AS	0	0	55	+	++	0	+	(20)	(37)	..	+	0	1	G	0	..	0	0	0	25	Good
5	31	11	+	+	0	0	0	0	+	+	0	+	0	0	46	++	++	0	0	30	39	..	0	0	1	F	F	+	0	0	0	25	Good
6	20	8	0	0	Cy	0	0	0	+	+++	+	+	0	+	48	++	+	++	0	64	..	..	+	0	1	G	F	..	0	0	0	25	Good
7	16	2	+	+	+	0	0	0	++	+++	+	0	0	0	60	+	+	+	0	(20)	(39)	..	+	0	1	F	F	F	0	0	0	25	Good
8	40	6	+	+	0	0	+	0	+	+	+	++	P	0	40	++	++	0	0	(28)	(39)	..	+	0	2	F	F	..	0	0	0	24	Good
10	37	10	+	+	0	0	0	0	++	++	0	+	0	+	45	+	+	0	0	75	..	..	0	0	1	F	0	..	0	0	0	23	Good
11	42	16	0	0	1	1	0	0	+	+	+	++	+	0	52	+	++	0	0	30	53	..	+	0	1	F	0	0	0	0	0	23	Good
12	45	1	+	0	0	0	0	0	++	N	0	0	0	0	49	+	+	+	0	48	64	..	+	0	1	F	+	+	0	+	0	22	Good
14	50	24	0	0	0	0	0	0	++	++	+	+	0	0	56	+	++	0	0	37	52	..	0	0	1	F	0	0	0	0	0	22	Good
15	27	9	+	0	+	0	+	0	+	++	+	+	P	+	50	++	+	0	0	46	54	..	+	0	1	F	0	0	0	0	0	21	Poor
16	23	2	0	0	+	0	0	0	+	++	+	+	0	0	49	+	++	0	0	30	62	..	+	0	1	F	0	0	0	0	0	21	Good
17	36	3	+	0	0	0	0	0	++	++	+	+	0	0	52	++	+	0	0	51	60	..	+	0	1	F	0	0	0	0	0	19	Good
18	31	20	0	0	0	0	0	0	+	++	+	++	P	+	42	++	+++	+	+	33	52	..	0	0	1	F	0	0	+	+	+	19	Good
19	42	5	0	0	Tb	+	0	0	+	+	+	++	+	+	57	0	++	+	0	(18)	(20)	..	0	0	1	F	0	0	0	0	0	19	Good
21	37	20	0	0	0	1	0	0	+	+	+	0	+	+	48	0	+++	+	0	51	62	..	0	0	1	F	F	F	0	+	0	18	Good
22	30	13	0	0	+	0	0	0	++	++	+	0	0	+	60	+	+++	+	0	51	63	..	0	0	1	F	0	0	0	0	0	18	Good
24	37	11	0	0	1	0	0	0	+	++	+	++	0	+	48	0	++	0	0	(26)	(33)	..	0	0	2	G	+	+	0	+	0	17	Good
25	27	7	+	0	0	0	0	0	++	+	+	0	0	0	46	+	++	0	0	54	60	8	0	0	2	F	0	0	0	0	0	17	Good
26	43	12	0	0	0	0	0	0	++	+	+	0	0	0	46	+	++	0	0	22	30	12	0	0	2	G	0	0	0	0	0	17	Good
27	26	5	+	+	0	0	0	0	++	++	0	AS	0	0	49	+	+	+	0	23	(28)	3	0	0	1	F	0	0	0	0	0	17	Good
28	31	6	+	+	+	0	0	0	++	+	0	0	0	+	49	+++	+	0	0	77	..	..	+	0	1	F	0	0	0	0	0	17	Good
29	38	3	0	0	0	0	0	0	++	N	+	0	0	0	45	0	+	0	0	15	22	..	0	0	2	F	0	0	0	0	0	16	Good
30	46	8	0	0	0	+	+	0	++	N	+	+	+	+	54	+	++	+	0	22	32	5	0	0	1	F	0	0	0	0	0	15	Good
31	40	30	0	0	0	0	0	0	+	+	+	0	0	0	49	+	+	0	0	22	30	2	0	0	2	F	0	0	0	0	0	15	Fair
32	31	1	1	0	0	0	0	0	++	++	+	0	0	+	49	0	+	0	0	28	38	..	0	0	1	G	0	0	0	+	0	15	Good
36	29	3	0	0	Cy	0	0	0	++	++	+	0	0	0	48	+	+	0	0	33	41	7	0	0	1	F	0	0	0	0	0	14	Good
37	47	4	0	0	1	0	0	0	+	++	+	0	+	+	65	+	++	+	0	55	75	23	0	0	1	F	0	0	0	+	0	14	Good
41	59	1	+	+	0	0	0	0	+	N	+	0	0	+	49	N	+	0	+	15	24	3	0	+	2	F	0	0	0	0	0	2	Died
42	51	2	0	0	0	+	0	0	+	++	0	++	0	+	63	++	+	++	0	51	60	34	0	0	1	F	0	0	0	0	0	13	Good
43	52	4	+	0	0	+	+	+	++	+	+	+	+	+	57	0	+	+	+	23	30	1	+	0	1	F	0	0	+	0	+	0	Died
45	50	7	+	0	+	0	0	0	++	+	+	0	+	+	55	0	+	0	0	41	54	13	0	0	1	G	0	0	+	0	0	13	Good
46	49	16	0	0	0	+	0	0	++	+	+	0	+	+	58	0	++	0	0	37	46	11	0	0	2	G	0	0	0	+	0	13	Good
47	25	7	0	0	1	0	0	0	++	++	+	+++	0	+	51	+	++	+	+	55	67	25	+	0	1	G	F	+	0	0	0	12	Good
48	43	16	+	0	+	0	0	0	++	+	+	+++	+	+	62	++	++	+	0	..	..	..	0	0	1	G	F	..	+	0	+	12	Good
50	42	2	0	0	+	+	+	0	++	++	+	0	0	0	68	+	++	+	+	52	67	21	+	0	1	F	0	0	0	0	0	11	Good
52	42	14	+	0	+	0	0	0	++	++	+	0	0	0	48	++	+	0	0	62	75	25	0	0	1	F	0	0	0	+	0	0	Died
53	29	2	0	0	0	0	0	0	++	+	+	++	+	+	56	+	++	+	0	20	38	7	0	0	1	F	F	F	0	0	0	11	Good
54	58	2	0	0	0	1	0	0	+	+	+	++	+	+	57	+	+	+	+	33	55	13	0	0	1	F	F	0	+	+	0	10	Good
55	38	3	+	+	+	+	+	0	++	++	+	++	P	+	49	+	0	0	0	15	24	1	0	0	2	G	+	+	0	0	0	10	Fair
56	53	1	+	+	+	+	0	+	+	++	+	+	+	+	62	+	++	++	+	32	51	1	0	0	2	F	F	F	+	++	0	10	Fair
57	30	2	0	0	+	0	0	0	++	+	+	++	0	0	44	+	+	0	0	26	46	3	0	0	1	F	F	0	0	0	0	10	Fair
58	32	10	0	0	0	+	0	0	++	+	+	++	0	0	54	+	+	++	0	90	..	..	+	0	1	F	0	0	0	0	0	9	Good
59	31	3	0	0	+	0	+	0	++	++	+	0	0	0	59	+	++	+	+	75	..	..	+	0	1	F	0	0	0	0	0	9	Good
60	33	10	+	0	+	+	+	0	++	++	+	T	0	+	55	+	++	++	+	75	..	40	+	0	3	G	0	0	0	0	0	9	Good
61	48	2	0	0	+	0	0	0	++	+	+	0	0	+	48	+	+	0	0	46	61	20	0	0	1	F	0	0	0	0	0	9	Good
62	41	14	0	0	+	0	+	0	++	+	+	+	0	0	59	+	+	+	0	48	61	8	0	0	1	F	0	0	0	0	0	9	Good
63	42	11	0	0	0	+	0	0	++	+	+	0	+	+	53	+	0	+	0	75	..	..	+	0	1	F	0	0	+	0	0	9	Good
64	42	20	+	+	1	0	+	+	++	++	+	0	+	+	52	+	+	+	0	35	48	11	0	0	1	F	0	0	+	0	0	7	Good
65	56	10	0	0	+	+	0	+	++	+	+	0	+	+	59	++	++	++	+	71	..	7	0	0	1	F	0	F	+	+	0	7	Fair
66	50	10	0	0	1	0	0	0	++	++	+	0	+	+	57	+	++	+	+	26	33	9	0	0	1	F	0	0	0	+	0	7	Good
67	43	9	0	0	0	0	0	+	+	++	+	0	+	+	56	+	++	+	+	22	33	3	0	0	1	F	0	0	0	0	0	7	Good
68	37	5	+	0	0	0	0	0	++	++	F	++	0	0	57	0	+	++	+	38	55	1	0	0	1	F	+	+	0	+	0	7	Good
70	27	8	+	0	0	0	0	0	++	+	+	0	0	0	52	0	++	+	0	21	40	6	0	0	1	F	0	0	0	0	0	7	Good
71	45	20	+	0	0	0	0	+	+	++	+	++	+	+	78	0	++	0	+	37	56	4	0	0	1	F	0	+	+	0	0	7	Good

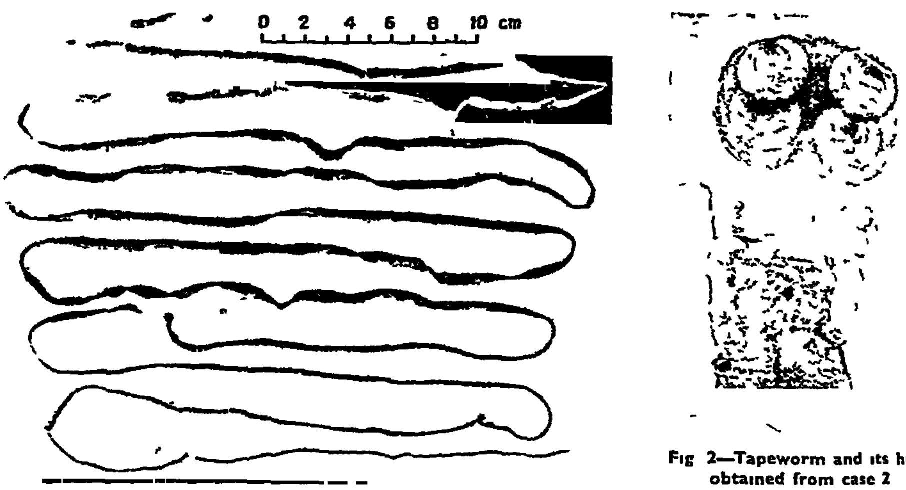


Fig 2—Tapeworm and its head obtained from case 2

beef tapeworm, but it is a much more dangerous parasite, because the host can infect himself (or others) with the cystic stage of the parasite if the ova he passes reach the mouth (via food, fingers, or flies) This general cysticercosis may cause only muscular pains and fatigue if confined to the muscles, but if it involves brain or eyes it may cause fits, mental deterioration, or blindness (Dixon and Hargreaves 1944) Fig 1 shows numerous cysticerci in muscles from a patient with cerebral cysticercosis

The fish tapeworm is very rare in this country and occurs mostly around the Baltic, near the freshwater lakes of Europe It has a complicated life-cycle, passing through a one eyed water-flea and a fish, and sometimes causes an anæmia resembling pernicious anæmia, by interfering with the reaction between extrinsic and intrinsic factors Harland et al (1950) reported a case in this country in a Finnish servant

LIFE-CYCLE OF BEEF TAPEWORM

Man is the only definitive host for the beef tapeworm, and the cow the only intermediate host Therefore it is astonishing that the cycle persists, for, to acquire cysticercus bovis, a cow has to eat grass contaminated by the fæces of a tapeworm-infected man, and this cow has to be eaten partly raw by another man—whose fæces must then reach a cow-inhabited field if the cycle is to continue It might have been thought that with modern sanitation and cooking the parasite would become extinct in this country, but it is certainly not becoming less common The 13 cases I report here are distributed in the last ten years as follows

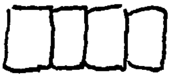
1943–48	4 cases
1948–52	9 cases

TREATMENT

A standard course of treatment was used in all these cases as follows

Preparation—The patient is admitted to hospital and kept on an entirely fluid diet for 3 days On each of these days he is given mist alba $^1/_2$ oz in the morning and mist cascaræ $^1/_2$ oz in the evening The purpose of this is to make the fæces completely fluid, so that the passing of the worm and the finding of the head shall be easier If the motions are not sufficiently liquid by the 3rd day, the dose of mist alba and mist cascaræ should be doubled, and an enema given in the evening

Day of Treatment—On the 4th day the patient is allowed nothing by mouth apart from the medicines At 7 A M he is given 1 oz of mist alba, and at 8 A M he starts taking capsules of 15 minims of male fern every quarter of an hour for eight doses At 11 A M a warm saline enema is given The worm will probably come away with the result, if not another enema should be given an hour later The nurses are firmly instructed that no motions are to be thrown away until the head has been found and its authenticity confirmed by the doctor They are also shown a drawing of the size of the head • and of the segments near it to show their extreme smallness compared with the mature segments



It is wise to award half a crown to the finder of the head With the naked eye one can be reasonably certain of it, but confirmation is easily obtained with a pocket magnifying glass or an auriscope without its speculum Fig 2 shows the worm and its head obtained from case 2

RESULTS

Twelve patients were cured at the first attempt with the standard course just described The remaining patient had harboured his worm for 6 years and received sixteen previous courses of treatment at other hospitals The standard course produced several feet of headless worm, then the parasite grew again The man, being rather desperate, was treated with a second course of rather heroic proportions After 4 days' fluid diet, with twice the standard doses of purgatives he was given eight doses of 30 minims of male fern at quarter hour intervals, and oil of chenopodium 1 ml and carbon tetrachloride 3 ml made up to 1 fl oz with liquid paraffin The complete worm was then passed Such a course would be dangerous to anyone in poor health, this patient, a healthy man aged 34 was quite ill for 24 hours after treatment However, "the man recovered from the dose, the worm it was that died"

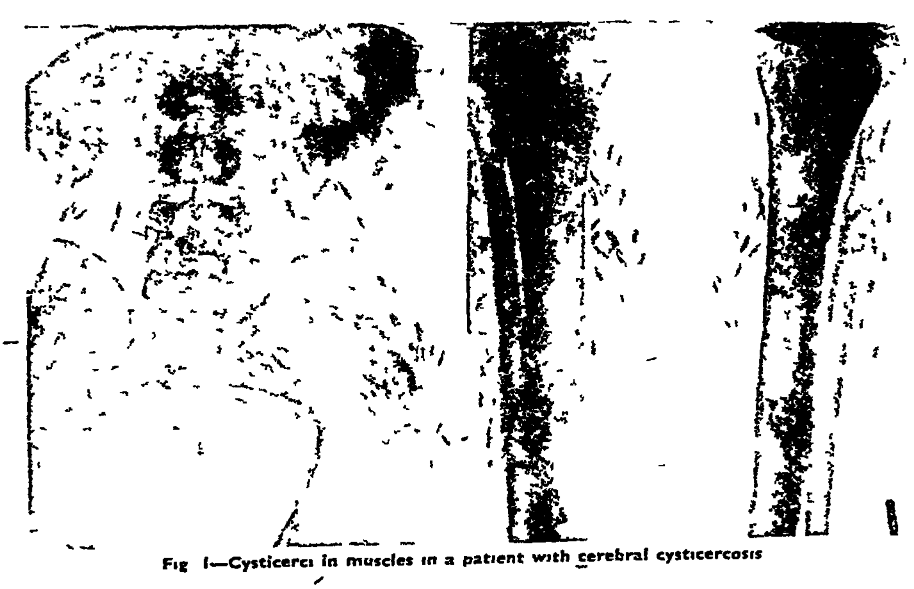


Fig 1—Cysticerci in muscles in a patient with cerebral cysticercosis

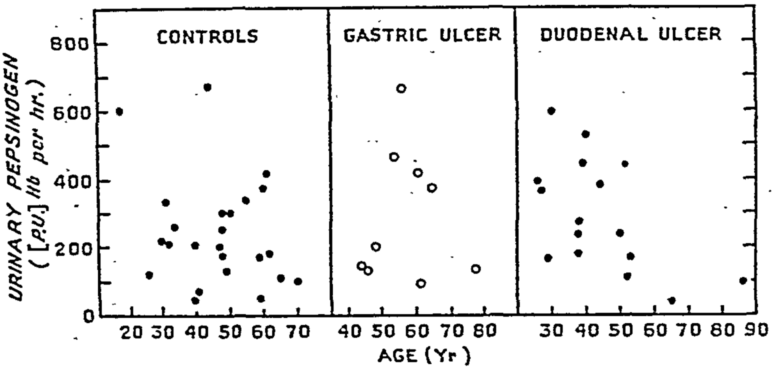


Fig. 1—Amount of pepsinogen excreted in urine of females according to age.

suggested by Northrop (1932) the symbol [P.U.]^{Hb} is used to mean peptic units in a standard hæmoglobin assay.

RESULTS

149 persons of either sex were studied: there were 60 controls free from dyspepsia, 61 patients with duodenal ulcer, and 28 patients with gastric ulcer.

Controls

These 60 persons, 36 males and 24 females, aged 15–88, comprised ambulant patients in hospital and hospital staff, chosen to correspond approximately to the duodenal-ulcer group in age. As will be seen from table I the age-distribution was similar between the sexes, and age appeared to have no consistent effect on the urinary excretion of pepsinogen. The average urinary excretion of pepsinogen in the 36 males was 195 [P.U.]^{Hb} per hour (S.D. ± 132), and in the 24 females 244 [P.U.]^{Hb} per hour (S.D. ± 154). This difference is not significant at the 5% level ($t = 0{\cdot}415$, $0{\cdot}05 < P < 0{\cdot}10$).

Peptic Ulcer

It soon became apparent that in patients with peptic ulcer certain differences existed within the group. These differences are related to sex of the patient, the site of the ulcer, and the length of history of dyspepsia.

Sex differences.—In the presence of an ulcer, irrespective of the site and length of history of dyspepsia, females excreted normal amounts of pepsinogen in the urine (fig. 1). In confirmation of previous results (Podore et al. 1948, Janowitz et al. 1950) it was found that in males there was a difference between the controls and patients with peptic ulcer, whether gastric or duodenal (fig. 2), though within these groups other factors seem to play a part (see below). Further observations deal with males only.

Site of ulcer.—The 19 male patients with gastric ulcer could be divided into two categories: (1) the 12 patients with the ulcer on the lesser curvature excreted normal amounts of pepsinogen (average 234 [P.U.]^{Hb} per hour); and (2) the 7 with the ulcer at or beyond the lesser curvature excreted an average of 597 [P.U.]^{Hb} per hour, thus resembling the 45 male patients with duodenal ulcer who excreted an average of 435 [P.U.]^{Hb} per hour (table II). Therefore, on this criterion of gastric function, gastric and duodenal ulcers may be grouped functionally into two groups: (1) those of the lesser curvature of the stomach in patients who excrete normal amounts of urinary pepsinogen; and (2) those at or beyond the lesser curvature—i.e., antroduodenal ulcers—in patients who excrete amounts significantly greater than normal.

TABLE II—AVERAGE URINARY EXCRETION OF PEPSINOGEN IN MALES

Group	No. of cases	Pepsinogen ([P.U.]^{Hb} per hr.)	S.D.
A, controls	36	194	± 132
Gastric ulcer:			
B, on lesser curvature ..	12	234	± 155
C, beyond lesser curvature ..	7	597	± 295
D, duodenal ulcer	45	435	± 379

By "t" test: difference between A and B $0{\cdot}05 < P < 0{\cdot}10$
" " A " C $P < 0{\cdot}001$
" " A " D $P < 0{\cdot}001$
" " B " C $P < 0{\cdot}01$
" " B " D $0{\cdot}02 < P < 0{\cdot}05$
" " C " D $0{\cdot}05 < P < 0{\cdot}10$

Length of history.—The length of history is taken as the continued presence of symptoms, complications, or radiological signs of an ulcer without complete intermission of longer than five years. In this group of 45 duodenal ulcers and 7 prepyloric ulcers it was clear that the urinary excretion of pepsinogen increased progressively with the length of history (tables III and IV).

To prove that this increase in urinary pepsinogen in patients with duodenal ulcer was solely related to the length of history of dyspepsia and not to age, which increases with the increasing length of history, a partial correlation was made between urinary pepsinogen (u), age (a), and history (h):

Correlation coefficient $r_{uh\cdot a} = 0{\cdot}639$ $P < {\cdot}001$
$r_{ua\cdot h} = -0{\cdot}0296$ $0{\cdot}5 < P$
$r_{ha\cdot u} = 0{\cdot}445$ $P < {\cdot}001$

This showed that there was a highly significant correlation between pepsinogen and history, and between age and history, at the 0·1% level, but no correlation at all between pepsinogen and age, leaving the third factor out of account in each instance. With less than a five-year history the urinary excretion of pepsinogen was within normal limits, but was increased with longer histories (table IV). The differences between duodenal ulcers with histories less than five years and duodenal ulcers with histories more than five years are highly significant statistically at the 0·1% level. A similar analysis for ulcers of the lesser curvature in males and for

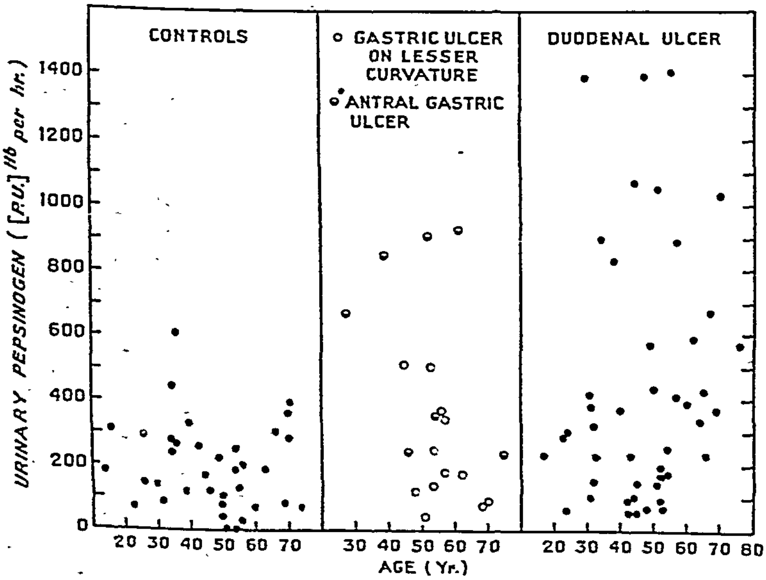


Fig. 2—Amount of pepsinogen excreted in urine of males with different kinds of peptic ulcer and of controls.

TABLE III—ANTRODUODENAL ULCERS IN MALES ARRANGED ACCORDING TO LENGTH OF HISTORY (NUMBER OF CASES)

Urinary excretion of pepsinogen ([P U]^{Hb} per hr)	Duodenal ulcers							Prepyloric ulcers	
	Dyspeptic history (yr)							Dyspeptic history (yr)	
	<2	2–4	5–9	10–14	15–19	20–24	25 or more	<5	> 5
1000–1500	—	—	—	2	1	1	2	—	—
750–999	—	—	2	—	—	1	—	—	3
500–749	—	—	—	—	1	2	1	—	1
400–499	—	1	—	1	2	—	—	—	—
300–399	3	1	1	—	1	1	—	—	1
200–299	2	1	1	1	—	1	—	2	—
100–199	3	5	—	—	—	—	—	—	—
0–99	5	1	—	—	—	—	1	—	—

gastric and duodenal ulcers in females did not reveal any relation between urinary excretion of pepsinogen and length of history, the excretion being similar to that in the controls

DIAGNOSTIC SIGNIFICANCE OF URINARY PEPSINOGEN

Apart from the physiological significance of disturbed urinary excretion of pepsinogen in patients with peptic ulcer, it was originally hoped that this test might prove to be of some value in the diagnosis of peptic ulcer Table v shows that this hope was not sustained by the findings that in all cases, except in male patients with antroduodenal ulcers with a history of more than five years' dyspepsia, the amount of pepsinogen excreted in the urine was no different from that excreted by the controls *The estimation of urinary pepsinogen therefore seems to have a very limited application in routine* gastroduodenal diagnosis

DISCUSSION

From the results of estimations of urinary pepsinogen in patients with gastric or with duodenal ulcer and in controls, points of difference emerge which have not been commented on by previous workers

In the controls age and sex seem to play no part in the regulation of pepsinogen excretion In patients with peptic ulcer, however, several *factors seem to* affect the urinary excretion of pepsinogen—namely, the sex of the patient, the site of the ulcer, and the length of history of dyspepsia

Podore et al (1948) studied males only and did not differentiate gastric from duodenal ulcers Janowitz et al (1950) did not comment on any sex difference and, while separating *gastric from duodenal ulcers, reported* only 4 gastric ulcers; they also included stomal a jejunal ulcers with duodenal ulcers Results in 6 patie with stomal ulcers in the present study (but not i above) showed normal urinary excretion of p Neither Podore et al (1948) nor Janowitz et al (195 reported any correlation with the length of histor of dyspepsia Varró et al (1952) reported normal urinar excretion of pepsinogen in their few cases of duodenal ulcer

TABLE IV—ANALYSIS OF RESULTS IN ANTRODUODENAL ULCERS ACCORDING TO LENGTH OF HISTORY (MALES)

Length of history (yr)	No of cases	Mean length of history (yr)	Mean age (yr)	Mean urinary excretion of pepsinogen ([P U]^{Hb} per hr)	—
Duodenal ulcer					
0–4	22	1 34	13 2	186	*a*
5–9	4	6 7	34 0	594	*b*
10–19	9	13 9	47 7	694	*c*
20 or more	10	25 5	59 2	688	*d*
Total	45	10 52	46 6	435	*e*
Prepyloric gastric ulcer					
0–4	2	0 15	60 5	237	*f*
5 or more	5	7 8	46 2	741	*g*
Total	7	5 6	50 0	597	*h*

By t test difference between *a* and *b* $P<0\ 001$
,, ,, *a* ,, *c* $P<0\ 001$
,, ,, *a* ,, *d* $P<0{\cdot}001$
,, ,, *h* ,, *e* $0\ 02<P<0\ 10$
,, ,, *f* ,, *g* $0\ 2<P<0\ 5$

It is abundantly clear that sex differences are considerable, *in that females all excrete normal amounts* of pepsinogen, irrespective of the presence of an ulcer (fig 1) or of the length of history of dyspepsia

In males ulcers may be divided functionally into those on and those beyond the lesser curvature of the stomach. Males with the ulcer on the lesser curvature excrete normal amounts of pepsinogen in their urine, whereas those with the ulcer beyond the lesser curvature—either prepyloric gastric or duodenal ulcer—excrete significantly increased amounts of pepsinogen

In males with an antroduodenal ulcer the amount *of urinary pepsinogen is normal initially* with a history of dyspepsia less than five years and increases progressively with the increased length of history, even as the gastric acidity in duodenal ulcers increases with the length of history (B I Hirschowitz and T D Kellock, unpublished data)

TABLE V—CASES SUBDIVIDED BY SEX, SITE, AND LENGTH OF HISTORY AND ARRANGED ACCORDING TO AMOUNT OF URINARY PEPSINOGEN

Urinary excretion of pepsinogen ([P U]^{Hb} per hr)	No of males				No of females		
	Con trols	With gastric ulcer on lesser curva ture	Antroduo denal ulcer		Con-trols	Gastric ulcer	Duo denal ulcer
			<5yr	> 5yr.			
0–99	10	3	6	1	4	1	2
100–199	11	4	8	—	7	4	4
200–299	8	1	5	3	5	—	3
300–399	5	2	4	4	5	1	3
400–499	1	—	1	3	1	2	2
500–749	1	2	—	5	2	1	2
750–999	—	—	—	6	—	—	—
1000–1500	—	—	—	6	—	—	—
Total	36	12	24	28	24	9	16

The increase in gastric activity shown both by the urinary excretion of pepsinogen and by the gastric acidity in the long-continued presence of an antroduodenal ulcer in men suggests that gastric hypersecretion may be an effect rather than a cause of the ulcer, or that both may be the result of a common stimulus This concept is not new (cf Shay et al 1942), but it has received little general support

In view of the reports of Podore et al (1948) and of Janowitz et al *(1950) I hoped that this test* might prove to be of some diagnostic value However, the finding of normal values in females, in males with a gastric ulcer in the lesser curvature, and in many males with an antroduodenal ulcer, makes it valueless in *the routine* diagnosis of peptic ulcers—*a conclusion reached* by Benderskey (1890)

SUMMARY

Pepsinogen, arising from the gastric mucosa, is excreted in the urine Its measurement is used for indirect assessment of part of the secretory activity of the stomach

The urinary excretion of pepsinogen was measured in 149 patients—60 controls, 61 patients with duodenal ulcer, and 28 with gastric ulcer

Females, with or without an ulcer, all excreted normal amounts of pepsinogen in the urine

All male patients with a gastric ulcer on the lesser curvature excreted normal amounts of pepsinogen in

OLD WIVES' TALES

It is interesting that many patients have a lore of their own concerning the clinical features and treatment of tapeworm.

One woman had been told by her grandmother how to treat the worm. "First," she said, "you must starve yourself till the worm is very hungry, then you open your mouth, hold a piece of bacon in front of you, take a pair of scissors in one hand and wait. Then the worm will make a leap for the bacon and you can cut off its head." I confess with regret that the thirteen cases reported here were treated by the orthodox ritual of purgation and male fern, rather than the more sporting methods advocated by the grandmother.

Other superstitions are that if the host drinks enough gin this makes the worm "turn its head the other way and come away natural." Also it is believed by some that the increased hunger occurring in certain cases of tapeworm infection is due to the voracious appetite of the worm and that if the host does not eat enough to satisfy his unwelcome guest the worm in its desperate search for food "may come up in your throat and choke you," or worse still "it may eat away your inside." Stranger still is the widely circulated story that many of the pills sold to reduce weight are in reality tapeworm eggs and that to ensure they are safe the pills should be left overnight in a little water, when, if they are eggs, they will have hatched into a worm by the morning.

SUMMARY

Thirteen cases of infestation by beef tapeworm are described.

Six of the patients complained of symptoms, consisting of sudden abdominal cramps, giddiness, and hunger, which in three cases were severe. The majority of them had eaten raw meat.

Infestation by tapeworm should be included in the differential diagnosis of obscure abdominal pain.

There is no evidence that infestation by tapeworm is becoming less common in this country.

A standard course of treatment with filix has cured twelve of the patients. The remaining patient responded to a second and stronger course with added carbon tetrachloride and oil of chenopodium.

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EFFECT OF A.C.T.H. AND CORTISONE ON VITAMIN-C METABOLISM AND ON THE WEIGHT AND COMPOSITION OF THE LIVER

IN GUINEAPIGS AND OTHER SPECIES

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THE investigations recorded here began in 1950 in an attempt to throw new light on the puzzling problem of the apparent interrelation between adrenal function and vitamin-C metabolism.

Presumptive evidence for the existence of this interrelation is afforded by such facts as the following: (1) the silver-staining properties of the adrenal cortex (Szent-Györgyi 1928) attributable to vitamin C, which is present in remarkably high concentrations both in the cortex and in the medulla (Harris and Ray 1932, 1933); and (2) the action of adrenocorticotropic hormone (A.C.T.H.) in bringing about a transient fall in the concentration of the vitamin within the adrenal (Sayers et al. 1944).

Our original object in these experiments was to ascertain whether the repeated administration of large doses of A.C.T.H. to guineapigs would lead to so great a loss of vitamin C from their adrenals as to increase the effective requirement for the vitamin, and thereby to hasten the onset of scurvy in guineapigs kept on diets deficient in it. Although the answer to this question was substantially negative, some unexpected observations were made—particularly the fact that, in the guineapigs given these repeated injections of A.C.T.H. there resulted a remarkable and continuous increase in the weight of the liver. As we have published hitherto only brief summaries of our conclusions (Bland et al. 1952, Hughes et al. 1952, Harris 1953), it seems desirable to give some typical numerical examples of our actual data; and we are also taking the opportunity, at the same time, to present some of our later results.

EXPERIMENTAL

Unless otherwise stated, the findings given below relate to experiments in which young guineapigs weighing 300–350 g. had a course of intramuscular injections of A.C.T.H. (2 mg. of Armour standard L.A.1.A., four times daily). The standard "basal diet" consisted of Sussex ground oats 650 parts, bran 144, dried egg-yolk 80, dried brewers' yeast 108, and salt mixture 18, supplemented with 25 mg. of ascorbic acid daily (omitted for experiments with scurvy), 4 drops of halibut-liver oil weekly, and water ad lib. In other tests a "natural" diet was used instead, consisting of Sussex ground oats 1000 parts, and bran 220, supplemented with 15 g. of cabbage per animal per day, water and hay ad lib., and roots when available. None of our guineapigs was subjected to hypophysectomy. Rats, when used, were kept on the standard "synthetic" diet used in this laboratory, and rabbits on the above-mentioned "natural" diet, with cabbage ad lib.

RESULTS

(1) *Effect of A.C.T.H. on Vitamin-C Metabolism*

Contrary to our expectations, it was found that the vitamin-C economy of the body as a whole was not appreciably changed. Although the concentrations of ascorbic acid in the liver and adrenals of the guineapigs were diminished, the total quantities of ascorbic acid in these two organs (both of which were enlarged as a consequence of the treatment) were not substantially affected (fig. 1). The administration of A.C.T.H. did not hasten the onset of scurvy in guineapigs on the deficient diet; nor did it increase the rate of depletion of ascorbic acid from the liver or the adrenals during the development of deficiency.

(2) *Effect of A.C.T.H. on A.A.: D.H.A.A. Equilibrium in the Adrenals*

After a single injection of A.C.T.H. no substantial change was found in the relative proportion of dehydroascorbic acid to ascorbic acid present in the adrenals of guineapigs, although the concentration of ascorbic acid was temporarily depressed.

(3) *Liver Weights*

In the young guineapigs given the standard course of injections of A.C.T.H. (see above) a remarkable increase was seen in the weight of the liver, which was already apparent after only two days and continued thereafter day by day—e.g., up to ten days—when the increase had reached a value of about 50%, compared with the controls (fig. 2). This increase in weight has now been observed repeatedly in nine series of tests extending for over twenty months and involving over 350 animals, and is statistically highly significant ($P = < 0{\cdot}01$).

THE LANCET

LONDON SATURDAY, MAY 23, 1953

Antibiotics in Action

REVIEWING problems affecting the search for micro-organisms that produce antibiotics, ROUTIEN and FINLAY[1] forecast that unsolved problems will continue to attract research-workers to this subject. A satisfactory agent against the smaller viruses has not yet been discovered; possibly an antibiotic might be useful in the treatment of cancer; and better agents against mycobacteria and protozoa are much needed. The resources of industrial firms are well organised and skilfully directed in the search, which seems for the present to be largely concentrated on the rewarding genus streptomyces. Many programmes of systematic exploration are being undertaken, chiefly on a great variety of soils from all parts of the world but also on such varied material as growing plants, culture collections, waters, muds, bogs, composts, decaying leaves, earthworms from graveyards, sewage, fermentations, and anthills. Studies have been made, too, of bacteria from human infections undergoing resolution,[2] and there have been attempts to induce antibiotic-producing mutants among micro-organisms by X-ray and ultraviolet irradiation.[3] The search for new antibiotics is largely empirical, and individual workers with few resources should not be discouraged, for an acute observer whose mind is prepared and whose approach is flexible may still hope to meet and recognise one of the lucky chances which have so often led to great discoveries.

Empirical methods, however, are not enough. The important developments of chemotherapy have naturally been followed by explanations of the properties of antibiotics in terms of their chemical reactions with living matter. Speculation and research on this topic began with EHRLICH's side-chain theory, and new reports continue to appear at short intervals. Since we last commented on this subject[4] much of the recent knowledge has been reviewed in a symposium arranged by the Society of American Bacteriologists.[5] Clearly, many different biological properties of bacteria are affected by some of the antibiotics, and it is extremely difficult to devise critical experiments to show which of the interactions between bacterium and drug is of real importance and whether the resultant modifications of bacterial metabolism affect the organism directly or indirectly. SMITH[6] named forty-nine bacterial metabolic processes and enzyme systems which have been studied for their sensitivity to chloramphenicol, but he considered that only two of these were clearly significant as causes of growth inhibition—namely, interference with utilisation of amino acids and with the metabolism of fats and esters. He cited work by GALE and PAINE[7] which suggests that chloramphenicol may possibly act by inhibiting protein synthesis because of its action in preventing the formation of combined glutamate and the utilisation of ammonia. An important point about chloramphenicol inhibition of esterase activity is that this action is found with esterases isolated from tissue cells as well as with bacterial esterases, but that intact tissue cells—of horse-liver for example—possess a mechanism which prevents the antibiotic from inhibiting the esterase activity of the host cells. HOBBY,[8] reviewing work on aureomycin and terramycin, mentioned evidence for their action on the phosphorylation system on the metabolism of tricarboxylic acids and α-ketoglutarate, and on the oxidation of glycine, glutamic acid, and aspartic acid. She referred to AJL's[9] view that the actions of terramycin and aureomycin are similar, and that the site of their action may involve the initial step in acetic-acid oxidation. The hypothesis that antibiotics stimulate animal growth simply by inhibiting intestinal organisms is now in some doubt, because growth responses have been observed with doses of antibiotics which are too small to act on the intestinal flora; it appears that the drugs may act by increasing absorption of nutrients as well as by inhibiting drug-sensitive pathogens.

OGINSKY[10] discussing the mode of action of streptomycin drew attention to its inhibition of aspartate and amino-acid oxidation by *Bacterium coli* and to other respiratory effects causing increased acetate formation. In bacterial cells capable of oxidising acetate, no streptomycin inhibition of the oxidation of pyruvate and oxalacetate could be demonstrated, but the oxidation of these substrates was much inhibited if acetate oxidation was slight or absent. Studies of the action of streptomycin on the tubercle bacillus indicated that the oxidation of the long-chain fatty acids is sensitive to the drug, but that oxidation of the short-chain fatty acids is not, suggesting that their metabolism by the organism may also be different.

PRATT[11] drew attention to changes in the morphology and staining reactions of penicillin-treated organisms. These changes are the same as those described by STEARN and STEARN[12] as characteristic of "starving" bacteria, which fits in with the knowledge that penicillin prevents staphylococci from absorbing glutamic acid and various inorganic substances and generally interferes with the ability of

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[1] Routien, J B, Finlay, A C *Bact Rev* 1952, 16, 51

[2] Rountree, P M., Barbour, R. G H *J Path Bact.* 1951 63, 313

[3] Kelner, A *J Bact* 1949, 57, 73

[4] Leading article *Lancet* 1952 ii, 374

[5] *Bact Rev* 1953, 17, 17

[6] Smith, G N *Ibid* p 19

[7] Gale, E F, Paine, T F *Biochem. J* 1950, 47, xxvi; *Ibid*, 1951 48, 298

[8] Hobby, G L *Bact Rev* 1953, 17, 29

[9] Ajl, S J Unpublished data.

[10] Oginsky, E L *Bact Rev* 1953, 17, 37

[11] Pratt, R *Ibid* p 41

[12] Stearn, A E. Stearn, E W *J Bact* 1930, 20, 287

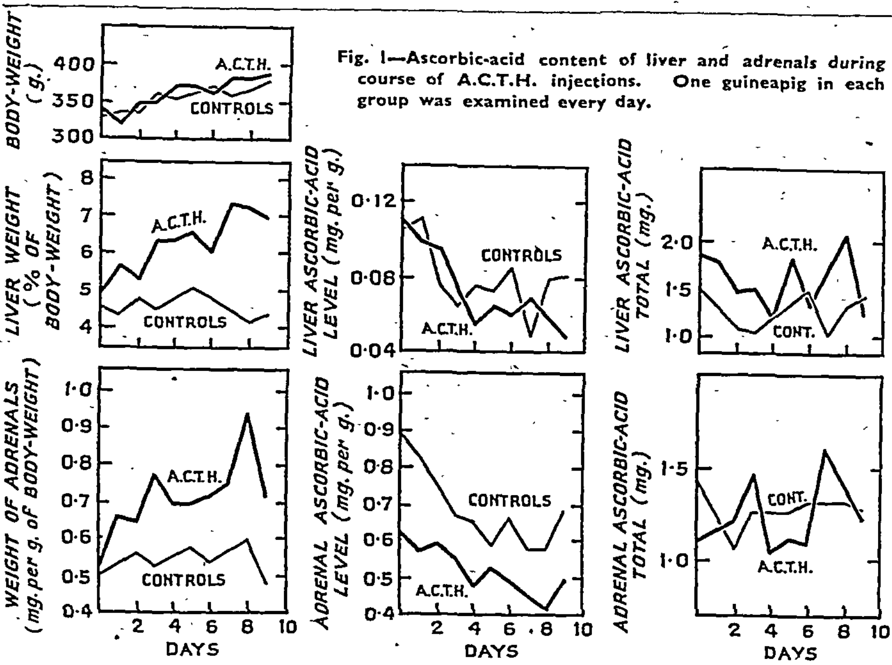

Fig. 1—Ascorbic-acid content of liver and adrenals during course of A.C.T.H. injections. One guineapig in each group was examined every day.

In adult guineapigs A.C.T.H. had a similar effect to that in young growing ones in causing a great increase in the liver weight (av. = 39%, after 10 days, statistically highly significant).

(4) *Liver Weights : Dose-response Curves*

Dose-response curves have been constructed, relating the increases in liver weight observed to the size of the dose of A.C.T.H. administered (fig. 3). It seems likely that our findings may have possible uses in biological assay, as in characterising the action of different hormones —e.g., the various A.C.T.H. fractions (see also below under *Cortisone*).

(5) *Composition and Structure of Enlarged Liver*

Analyses were made of the fat, protein ("Kjeldahl-nitrogen"), carbohydrate, and water contents of the enlarged liver, and the composition of the "increment" was calculated by difference (fig. 4). It will be seen that during the first day or so the increased weight of the liver was due essentially to extra glycogen and water but thereafter there was also an appreciable addition of protein. Histological examination by Dr. C. P. Cherry, at the Strangeways Research Laboratory, showed that there was an increase in the size of the liver cells, which was attributable to an increased volume of the cytoplasm and was equivalent in magnitude to the increase observed in the weight of the whole liver.

Under the conditions of our experiments the A.C.T.H. caused a diminution in the percentage of fat in the liver and not a rise (as might perhaps have been expected from previous reports relating to other species). There was little effect on the concentration of sulphydryl compounds (including glutathione) in the liver.

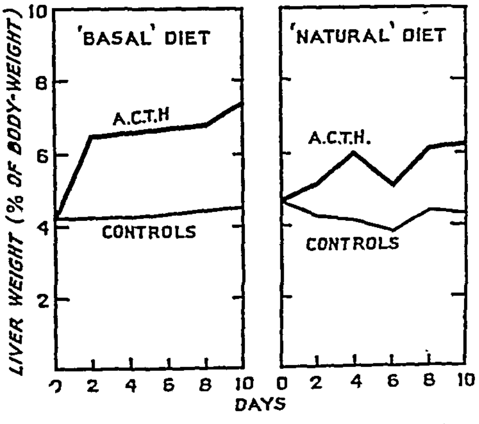

Fig. 2—Weight of liver (average of group) during a course of A.C.T.H. injections.

(6) *Long-term Injections*

When the injections of A.C.T.H. were continued for longer periods, up to forty days, the general effect on the chemical composition of the liver was similar—i.e., a further increase in the amounts of water, protein, and glycogen (absolute weights) in the liver, compared with the controls (or, in terms of percentages, an increase in glycogen, but some decrease in the protein and fat, and little change in the water).

(7) *Result of Discontinuing the Treatment.*

When, after ten days, the injections of A.C.T.H. were discontinued, there followed a sharp fall in the weight of the liver, with the result that two days thereafter it weighed no more than the control (and, from three to thirty days subsequently, was about 10% smaller). The glycogen in the liver decreased to within the normal limits, of the controls, within about a couple of days, and the protein some days later.

(8) *Effect of Cortisone on Liver Weight and Composition*

In young guineapigs cortisone had an effect similar to that of A.C.T.H. in increasing the weight of the liver, but to an even greater degree. For example, after ten days' treatment with intramuscular cortisone acetate 7·5 mg. per day in two doses, there was an average increase in weight of 50% ; and with 15 mg. per day (see fig. 5) an average increase of 72% after four days, or of 123% after ten days ($P = \leqslant 0{\cdot}01$).

The effect of cortisone on the proximate chemical composition was similar to that observed with A.C.T.H. (fig. 4).

Incidentally, the injections of cortisone and A.C.T.H. had the effects, as expected, of diminishing and of enlarging, respectively, the weights of the adrenals (cf. figs. 1 and 5).

(9) *Effect of Cortisone on Weights of Other Organs*

In the young guineapigs given the repeated injections of cortisone there was no significant change in the average weights of the pancreas, lungs, heart, thymus, or spleen. There was, however, an increase in the average weight of the kidneys, amounting to 8% after 7·5 mg. of cortisone per day for 10 days, or of 20% after 15 mg. per day, these figures being statistically "significant" ($P = 0{\cdot}05$) and "highly significant" ($P = \leqslant 0{\cdot}01$) respectively. A possible effect on the weights of the testes seemed less consistent, and needs further study (33% increase in weight after 7·5 mg. of cortisone acetate per day, with $P = 0{\cdot}05$—i.e., "significant"—but no significant effect after 15 mg. of cortisone acetate per day).

(10) *Species Differences*

In young rats, contrasted with guineapigs, A.C.T.H. had no important effect on liver weight, and cortisone caused some loss in the weight (absolute) of the liver, in place of a rise. (At the higher levels of dosage of cortisone, with the consequent decline in body-weight, the liver of the rats lost somewhat less weight than did the body as a whole, and there was thus some increase in the relative weight of the liver, although not in its absolute weight.)

Again, in chicks and mice given A.C.T.H. no important changes were observed in liver weight.

organisms to retain such substances as lipoids, fatty-acid hydrolysates, and nucleotides It appears that penicillin, ribonuclease, and cobra venom exert many similar actions on bacteria , and this supports the idea that penicillin may interfere with the phosphorylation of important nucleotides and that its effect on bacteria may depend on excessive dehydrogenation of reduced substances—probably those bearing sulphydryl groups If these assumptions are correct, penicillin will be most effective at a concentration which accelerates the transfer of hydrogen from —SH or other reduced groups without seriously hindering the activity of hydrogen acceptors On this basis it would be expected that the most efficient and rapid antibacterial effects would follow the use of the least concentration capable of producing irreversible injury to the bacteria At an appropriate lower concentration than the optimum, penicillin might be expected to act as a growth stimulant, and at concentrations much higher than the optimum the drug might so impair the activity of hydrogen acceptors as to give some protection to the hydrogen donors against the rapid, irreversible dehydrogenation on which its action may depend There is clinical and experimental evidence for the view that bacteria are less efficiently killed by concentrations of penicillin and other antibiotics above and below the optimum[13]

Isoniazid has not yet been so intensively studied as the other antibiotics, but an explanation of its mode of action might be particularly interesting since it is active only against mycobacteria **Barclay** et al ,[14] using isoniazid labelled with C^{14}, studied the uptake of drug and its effect on bacterial growth in a normal culture and in a culture of a drug-resistant variant of the same strain of *Mycobacterium tuberculosis* (H37RV) Isoniazid did not halt growth immediately , the tubercle bacilli continued to multiply, at first quite rapidly, but then more and more slowly until growth ceased at a point when the bacterial population had approximately doubled The isoniazid effect was not influenced by bacterial numbers or phase of growth, or by changes in concentration of drug within the range 0 05–100 µg per ml The organisms whose growth was arrested retained some enzyme activity and were neither killed nor lysed Those subjected to low concentrations of drug resumed growth in about two weeks and were then resistant to the concentration of drug in the medium All this contrasted strikingly with the effects of streptomycin, which arrested growth almost at once, stopped enzyme activity, killed the organisms, and led to perceptible lysis of the culture in three days Resistant organisms eventually appeared, however, and growth was resumed The radioactive isoniazid clearly showed that the sensitive strain of bacteria took up the drug, whereas the resistant strain did not Isoniazid action thus has points in common with sulphonamide action, which may suggest that absorption of the drug interferes with the formation of an essential metabolite

Reviewing problems of combined chemotherapy, **Garrod**[15] has declared that we still do not know enough about the mode of action of antibiotics to explain with certainty why the use of two drugs helps to prevent the development of resistant bacteria Probably the second drug blocks the metabolic pathway developed by a resistant organism to circumvent the effect of the first drug Since so many combinations of drugs are effective in this way, **Garrod** suggests that by studying their effects it may be possible to discover more about the points of attack of individual drugs Clearly, a great deal of laboratory work lies ahead Some of this, as **Garrod** points out will be extremely laborious—work on a case of enterococcal endocarditis which he studied occupied well over 100 hours of laboratory time—and much of the work, as **Wyss**[16] has said, resembles groping in the dark Nevertheless the recent contributions show that we have a considerable body of new knowledge about the biochemistry and physiology of micro-organisms

Children in Road Accidents

Our predecessors fenced off those dangerous trains, and forbade the public to invade the permanent way Motor-cars do not run at fixed times, do not announce their approach as noisily as trains, and are just as dangerous to life and limb , yet we all share the same roads—young and old, halt and spry, motorists, cyclists, and pedestrians alike—and we look like doing so for the rest of this century Road accident figures are so monotonously high that those who wish to sting us into some sense of responsibility have to use devices to touch the imagination—telling us, for example, that on our roads during 1951 at least one child was killed or injured in every fifteen minutes This fact alone should make us *demand to know the ages of the children*, and what they were doing at the time , and an important study[17] along these lines has just been published by the Economic Research Council for the Children's Safety Crusade Trust, founded by the late Mr **Gordon Stewart** The trust have presented their report to the National Federation of Women's Institutes, who gave them substantial help in deciding on age span groupings of children, and offered many opinions which the subsequent analysis of figures proved to be shrewd and sound

With Prof **Harry Jones** as chairman, the study group[18] have discussed their findings in terms of " risk-rates " These are calculated to represent the risk of injury per 10 million children per day within each age-group, and are therefore strictly comparable thus, if the risk-rate of a 12-year old boy on a June schoolday is 20, and that of a 4-year old on a similar day is 150, the risk to the younger boy is $7^1/_2$ times greater than the risk to the elder The study group have taken it that a risk-rate of 20 (the average risk of a child as *passenger* on the road) is probably as

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[13] Gould J C , Bowie J H Cameron, J D S *Lancet* Feb 21, 1953 p 361 See also leading article, *Ibid* March 7, 1953 p 475

[14] Barclay, W R Ebert R H , Koch Weser, D *Amer Rev Tuberc* 1953, 67 490

[15] Garrod L P *Brit med J* May 2, 1953, p 953

[16] Wyss, O *Bact Rev* 1953 17, 17

[17] The Child on the Road. Economic Research Council, 18, South Street, London, W 1 Pp 70 4*s*

[18] The members were Prof J Harry Jones, LL D , author of *Report on Road Accidents* for the Ministry of Transport in 1946 , Miss Enid Blyton, author of books for children Lieut Colonel G T Bennett, M I C E , and Mr Eric Farmer, M A , both members of the Road Research Board , Mr G Prys Williams, F I S , economist and statistician , and Mr Harold S Goodwin, secretary of the Economic Research Council

With rabbits, on the other hand, the effect of A.C.T.H. on the liver was similar to that in guineapigs, the increase in weight being very pronounced (48% increase, after ten days, on 24 mg. of A.C.T.H. daily, in 3 doses per day), and statistically "highly significant" (P =0·01).

COMMENTS

A.C.T.H. and Vitamin-C Metabolism

Our findings on A.C.T.H. in relation to vitamin-C requirements have been essentially negative. Previous published reports have been somewhat conflicting, some observers—e.g., Hyman et al. (1950), Eisenstein and Shank (1951), and Long (1947)—reporting that A.C.T.H. may apparently "spare" vitamin C, and others—e.g., Clayton and Prunty (1951)—noting an absence of any such effect.

There have been indications also (Stewart et al. 1953, Cornforth and Long 1952, Loxton and Le Vay 1953) that both A.C.T.H. and cortisone may affect the equilibrium between ascorbic acid and dehydroascorbic acid in the blood. Under the conditions of our own tests we found no change in A.A. : D.H.A.A. ratio, so far as the adrenals were concerned, following on the injections of A.C.T.H.

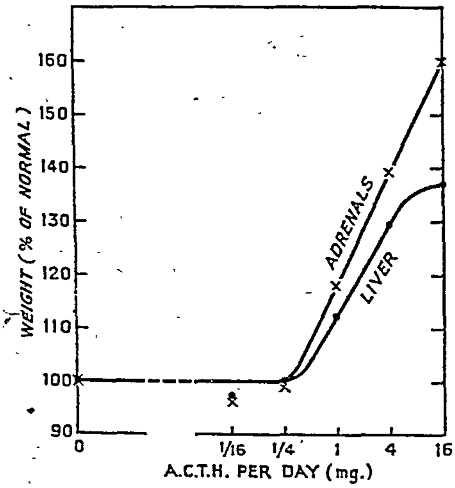

Fig. 3—Dose-response curve, showing increase in weights of liver and adrenals (after 10 days) depending on amount of A.C.T.H. administered daily (log. scale).

Liver Enlargement

It is remarkable that the massive increase in liver weight in guineapigs after A.C.T.H. does not seem to have been noted by previous investigators. The explanation perhaps is that the guineapig has not been the animal most usually employed in research on A.C.T.H. Also, other unusual features in our experiments were the prolonged course of injections and the absence of hypophysectomy.

It seems clear from our results that this action of A.C.T.H. on the liver is to be attributed largely if not entirely to its influence in stimulating the production of cortisone. In terms of proximate components, the enlargement is associated with an increase in the absolute amounts of glycogen, water, and protein—i.e., Kjeldahl-nitrogen. The effect of cortisone in stimulating glycogen production is, of course, already well known. The more novel feature in our results is what we may term the "intracellular œdema." The fact that there is some increase in the protein in the liver, but that it is not in full proportion to the total increase in weight of the liver, can perhaps be most easily interpreted as representing the result of an increased passage of lymph into the liver. We cannot, however, rule out the possibility that some gradual building up of extra protein may take place as the functional response of the liver to the increased activity put upon it, under the stimulus of the cortisone. More detailed analyses of the various nitrogenous fractions, in place of the simple Kjeldahl-nitrogen determinations here recorded, are obviously needed to throw further light on such questions.

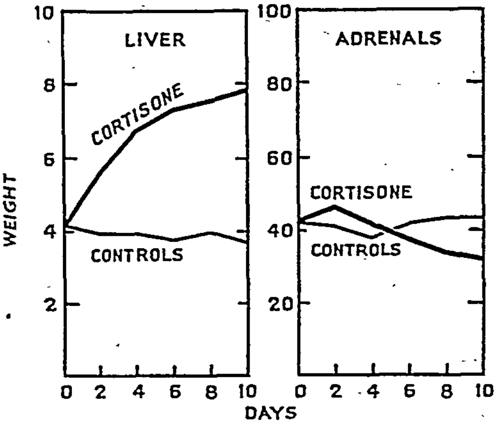

Fig. 5—Weights of liver and adrenals (average of group) during a course of cortisone injections. (Liver weights in g. per 100g. body-weight; adrenal weights in mg. per 100g. body-weight.)

Species Differences

The cause of the species difference in the liver enlargement is uncertain. Guineapigs, together with primates, are unique, it is true, in being the only species known to need vitamin C in their diet, other species being able to synthesise it. However, the general negative trend

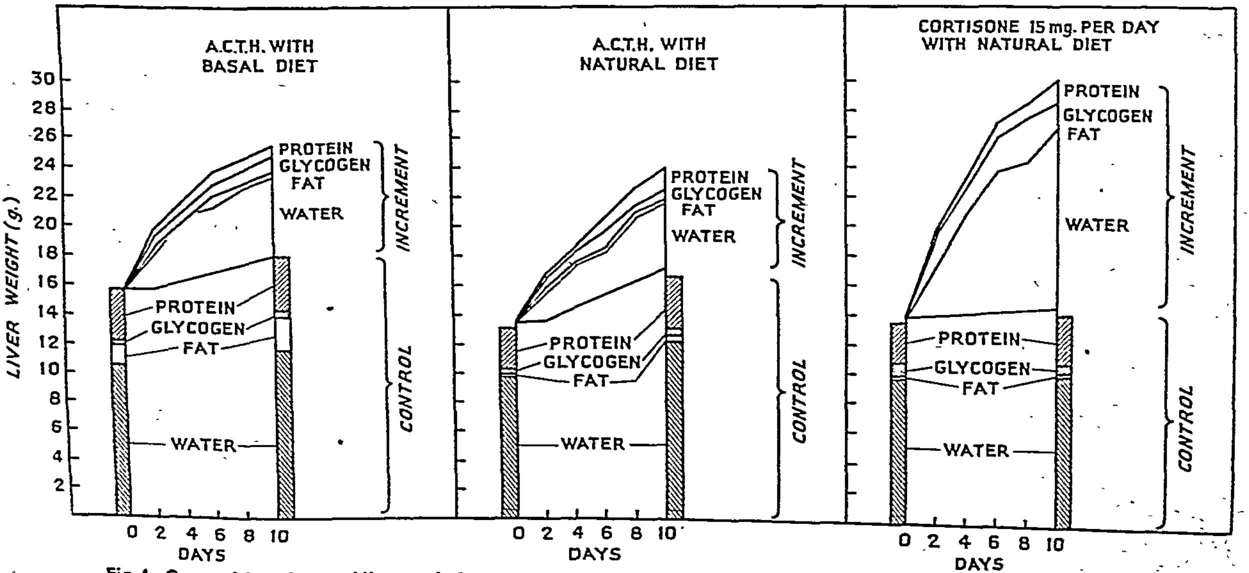

Fig. 4—Composition of normal liver, and of newly formed "increment," resulting from action of A.C.T.H. or of cortisone.

low as it is possible to get it and they grade risk-rates of 20–80 as "serious" of 80–140 as "tragic," and over 140 as "catastrophic."

It should perhaps be noted that children as "passengers" are classed as those boarding, alighting or falling from a vehicle, sitting or standing inside a vehicle, or stealing a ride, and it is odd to notice that though none of these occupations carries a great risk for children easily the highest figures—ranging up to 31—fall in the columns for those sitting or standing inside a vehicle, where no blame can possibly attach to them.

The study group have analysed the 1951 figures for child casualties so as to show risk-rates at different ages at different times of the year, at different times of day, in school term-time and during the holidays, for boys and girls, for child pedestrians, passengers and cyclists and according to what the child was doing at the time. One finding is new and outstanding. It has long been recognised that the risk-rate for young children just starting school and perhaps using the roads unattended for the first time, is very high indeed—well into the tragic class for both sexes, and for boys often (indeed usually) in the catastrophic class. Thus the risk-rate for boys aged 5–7 during term time in 1951 ranged from 150 to 220. It has not been generally realised that the rates for boys of 15–16 the safest *pedestrians* in the country, are far in excess of these—even at some seasons of the year, twice or thrice as great. And the cause of these towering risk-rates is the bicycle.

The ironically named safety-bicycle is now so much a part of our civilisation that we have not perhaps observed that for modern road conditions it is growing dangerously out of date. Two-thirds of the child cyclists injured or killed in 1951 were doing nothing calculated to bring them to harm: they were riding straight ahead, neither overtaking nor turning. As this report says:

> "The child cyclist precariously balanced and unprotected is allowed to go on our heavily trafficked roads untrained, inexperienced, with his back to following faster, heavier vehicles, with no means of seeing what is overtaking him or of signalling unless he turns his head and takes one hand off the handlebars. Of course he swerves. And of course he pays the heaviest toll of the road."

As the study group point out on the next page at some age or other, and in some way or other, most of us nowadays—or anyhow most men—have to become efficient and responsible drivers on the road. But it is astonishing to find the group advocating the bicycle as the perfect tool for the prentice road user. 'Could we in fact devise any more suitable instrument for the beginning of their training than the bicycle?' they ask. The answer is surely "yes." Could we indeed have devised a worse one? Their own earlier paragraph makes it hard to believe that we could.

The truth is that the writers of this report, like the rest of us, are ambivalent about the bicycle: we have all gone through the stage, which they describe, in which it was a symbol of freedom and growing up—an exciting means of locomotion, our first real piece of machinery, stage one in the process of graduation to control of a mechanical vehicle on the roads. What asses we thought those careful seniors, urging caution. But the roads are very different now: every decade (war-times apart) makes a great and dangerous difference in the roads. It is true that the boy who learns to manage a bicycle safely in modern traffic has acquired road sense, but it is surely an extraordinary principle to allow the beginner to ride the most dangerous vehicle on the roads the moment he has learnt to keep a wobbling balance on it. The N.F.W.I. suggest that no child should be allowed to ride a bicycle on the road unless he has passed a test as to his own fitness and the fitness of his machine, and the study group supplement this with the sound proposal that a driving-mirror should be made part of his necessary equipment, as well as a simple direction indicator which he could operate without taking a hand off the handlebars.

In his introduction to the report Professor JONES urges that an efficient road system would do much to protect not only child cyclists but all road users: for though in nine out of ten accidents human error is the immediate cause, the true cause, he says, lies in "a combination of circumstances that create the situation in which the critical error is made." Such circumstances may be the poor lighting of a road, a hidden turning, a bad road surface, and the like. Again, *ignorance can contribute to accidents*: pedestrians walking in the roads without sidewalks often do not know that they should face the oncoming traffic, and van-drivers are seldom made aware of the risk of backing on to children playing behind them. Children are nowadays carefully taught kerb-drill in school, and at many school crossings patrols have been established to see them over at the appropriate times. But the parent or teacher finds it difficult to train children to keep on the pavement when for want of playgrounds they normally play in the street, and therefore hardly notice whether they are on or off the pavement: in 1951 nearly half the accidents to children aged 5–10 were the result of the child stepping, walking, or running off the pavement, and most of the rest happened to children crossing the road. Nevertheless, much could still be gained by better instruction of the public in the avoidance of accidents—not, as the group point out, in the flabby "do be careful" sense, but in specific risks at particular ages, as well as in the pedestrian's rule:

Keep to the left on the footpath,
Keep to the right on the road.

The writers make many ingenious suggestions for using existing channels of communication: the mother seeking maternity benefit should find road-safety advice on the forms of application; the infant-welfare centre could hang up posters; the family-allowance forms could carry information related to the exact ages of the children in a family; renewers of driving licences should be confronted with useful warnings about the types of vehicle they use; petrol stations might display items from the Highway Code; transport cafes would certainly use posters if asked; insurance companies might be induced to take a leading part in road-safety education (as they do in America); and buses might advertise the fact that 88% of accidents to people getting off London buses happen at places other than official stops. To these suggestions we should like to add another—that this mechanically minded age should develop a form of transport as cheap, handy, swift, and convenient as the bicycle, but without its murderous instability.

of our results on vitamin C, together with the additional fact that rabbits (not known to need vitamin C) behave like guineapigs argue against any explanation based on the difference of species in their vitamin-C metabolism. Nor can a species difference in regard to the release of cortisone after A.C.T.H. be held responsible, for in rats both A.C.T.H. and cortisone were equally ineffective in producing any liver enlargement. The possibility remains that guineapigs and rabbits are more liable than are other species to develop œdematous changes after A.C.T.H. (the addition of water being, as we have seen, an essential feature of the liver enlargement in our experiments); but, if that is so, it does not seem to have been hitherto reported.

In any event this spectacular effect on the liver seems of sufficient interest to warrant further study, in view of both the many side-effects produced by these hormones and the importance of the liver as the seat of so many diverse chemical activities.

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MYSOLINE IN THE TREATMENT OF EPILEPSY

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FOR fifteen months 'Mysoline' (5-phenyl-5-ethyl-hexahydropyrimidine-4 : 6-dione) has been used in the treatment of epilepsy at St. David's Hospital, following favourable results obtained by Handley and Stewart (1952) at the David Lewis Epileptic Colony.

The patients selected for treatment were 58 sane male epileptics whose ages ranged from 20 to 66 and whose fits were not satisfactorily controlled by phenobarbitone, soluble phenytoin, 'Mesantoin,' phenyl-methyl-malonyl-urea, bromides, belladonna, amphetamine sulphate, or combinations of these.

The transition to treatment with mysoline was effected gradually, the existing medication being continued for the first two days, and then reduced step by step as the dose of mysoline was increased over a period of about a fortnight. Table I shows the dosage given in 0·25 g. tablets.

TABLE I—DOSAGE OF MYSOLINE USED

No. of patients	Daily dose of mysoline (g.) in divided doses
3	1·0
7	1·25
13	1·5
3	1·75
3	2·0

Almost all the patients complained of slight drowsiness or listlessness during the first day or two, especially before breakfast. 1 man complained of nausea. 2 became slightly ataxic, and 1 had slurred speech. 8 patients continued to feel drowsy, and in these cases, after a trial on reduced doses for periods varying from a fortnight to three months, the treatment was discontinued.

No other toxic symptoms or signs have been observed, and in most cases no complaints were made after the first few days. Urine and blood have at no time shown any abnormality.

In 29 cases treatment with mysoline was discontinued because of failure to reduce the number of fits and/or complaints of drowsiness.

During the period under review 2 patients died, neither fatality being in any way attributable to the medication.

Table II shows the results obtained.

As will be seen, 50% of the patients have benefited from the treatment, 35% of them because of a reduction in the number of their fits, and 15% because, although their fits were not reduced, they have felt better than when taking other drugs, such as phenobarbitone and soluble phenytoin. It has to be remembered that the therapeutic dose of soluble phenytoin is only narrowly separated from the toxic dose; and the preference for mysoline, a drug of low toxicity, evinced by these 15% of patients is not likely to be merely fanciful.

TABLE II—RESULTS OF TREATMENT OF GRAND MAL WITH MYSOLINE

Degree of improvement	Percentage of patients
100 %	3
75 %	10
50 %	15
25 %	7
No improvement in incidence of fits, but "feeling better"	15
Treatment discontinued	50

Of the 29 patients still being treated 20 are taking mysoline only; 2 are having mysoline plus malidone (because of petit mal); and the remaining 7 are having mysoline plus soluble phenytoin.

A slighter improvement in the incidence of petit mal was also recorded. In all, 23% of patients have experienced an average reduction of just over a half of their petit-mal attacks. A reduction of grand-mal attacks was not necessarily accompanied by a corresponding improvement in the petit-mal incidence, or vice versa.

The only patient in the series with psychomotor attacks has shown great improvement.

As has been mentioned, all 58 patients originally selected for treatment had, at different times, had full doses of other anticonvulsants or combinations of them. They were, in fact, the worst cases of idiopathic epilepsy from the point of view of treatment; and much surprise and gratification were evoked by the fact that as many as 20 of them were helped by mysoline alone. Less severe cases of epilepsy might well respond much more satisfactorily.

SUMMARY

Of 58 epileptics treated for grand mal with mysoline for fifteen months 50% derived benefit.

Most of the patients complained of drowsiness for a day or two. In 8 cases persistence of this symptom necessitated the withdrawal of the drug. Apart from this, toxic symptoms and signs were few and transitory.

Petit-mal attacks were reduced by half in 23% of the cases. One patient with psychomotor attacks has shown great improvement.

The Imperial Chemical (Pharmaceuticals) Ltd. supplied the mysoline.

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Annotations

MISDIAGNOSIS

A GREAT proportion of road accidents are due wholly or mainly to hurry and lack of care; only a few are unavoidable. Similarly, in diagnosis most mistakes can be attributed to the same two causes. It is old teaching that incomplete physical examination is the most important cause of misdiagnoses, and it is probable that lack of care is more often a factor than lack of knowledge. Present day opinion is perhaps tending more than ever to stress the value of a detailed history with full laboratory and other investigations, and to belittle the significance of physical signs. What, say many, is the value of the stethoscope in the diagnosis of early pulmonary tuberculosis when radiography has shown that it alone can detect the really early stages of this disease? True, replies the clinician, but radiography is not always available or of high standard, and therefore it cannot replace clinical examination. It is certainly a just demand of the general practitioner that chest radiography should be available to him directly, without the need for hospital outpatient or dispensary consultation. At the same time, the quality of the radiograph and the skill with which it is interpreted must be of high standard, or errors may easily be increased. Laboratory investigations, too, if used as a substitute for clinical examination, may have dangerous sequelæ; results are not always known before the patient has either died or recovered, and not uncommonly they are equivocal. Free access to laboratory diagnosis is not without some serious drawbacks, for it is not always realised how big the variations may be between different laboratories in the estimation of such things as, say, the blood-urea.[1] There is often a tendency to discard strong clinical evidence because of a negative laboratory report, just as an X ray finding is sometimes too easily accepted to the exclusion of a clinical diagnosis. Certainly many peptic ulcers are missed because a typical clinical history is at once discounted when the radiologist reports "no ulcer seen."

Mistakes are also very likely to arise when a diagnosis is made on the response to some special form of treatment. Thus, when the histidine treatment of peptic ulcer was in vogue it became fairly widely accepted that a dyspepsia was not due to an ulcer if it did not clear up under histidine injections—a disastrous conclusion. This type of error—diagnosis *ex juvantibus*, as Prof M Bürger terms it in a recent book[2]—is matched by diagnosis *e nocentibus*, in which worsening under a special treatment is taken as evidence for a particular diagnosis. Both are subject to many fallacies.

In recent years, both the accuracy of diagnosis and the stage at which it is made have become more important, largely owing to advances in therapy, and in particular to the rapidly enlarging field of surgical treatment. Once it was perhaps of mainly academic interest to detect, for instance, the exact type of a congenital heart lesion, or a mitral stenosis at its early stage; but it is now a matter of surgical urgency. Mistakes in diagnosis must, of course, be judged in great degree by their effect on treatment, and too much emphasis ought not to be laid on diagnosis as an end in itself. Little practical harm, for example, may be done if a leather-bottle stomach is missed in its early stages, since its growth may be slow, pain may be slight, and prospects of radical surgical cure at any stage are bad. But the public—perhaps rightly—will not appreciate such distinctions, and there is no doubt that the layman is less tolerant today of diagnostic failures than he was in the past. So much, indeed, is this the case that the fear of medico-legal proceedings is becoming a problem of very serious import in doctors' minds.[3] The young casualty officer threatened with a law case soon spreads alarm among his newly qualified friends, and it is possible that increasing difficulty may arise in finding young men willing to accept clinical responsibility unless they are encouraged and supported, more than has sometimes been the case, by their seniors and more experienced colleagues.

Bürger describes some of these difficulties in diagnosis, basing his discussion of them on 170 cases which at post-mortem examination were found to have been wrongly diagnosed. He writes clearly and with wisdom of these "failures," dividing them into different categories, but in every case posing five direct questions to the clinician who has been mistaken: (1) was a thorough physical examination of the patient undertaken? (2) were diagnostic investigations carried out—and which? (3) was the history properly assessed? (4) were the signs correctly evaluated? (5) were there superadded symptoms obscuring the diagnosis?

It might be a good rule for clinicians, whenever they make a mistake, to ask themselves these same five questions, even though they need not necessarily hold themselves equally to blame in every case if the answers are "no."

THE INCONTINENT WOMAN PATIENT

INCONTINENCE of urine is troublesome for both nurse and patient, tiring the one and humbling the other. One of the best achievements of modern geriatrics has been to show that many patients incontinent after a stroke can, if they are given training, recover sphincter control. Nevertheless there will always be a proportion who are unable to respond to such training. The men among them can usually use a bottle, and so protect their bedding; but women are not so fortunate, and there are still hospitals where the disagreeable task of sluicing the wetted sheets before sending them to the laundry is added to the already heavy assignment of the nurses. Any device which would reduce this burden seems worth trying, and the suggestion has lately been made to us that cushions of sphagnum moss, which could be thrown away after use, would not only protect bed linen, but would add greatly to the comfort of these patients.

Sphagnum was used on a large scale in the 1914–18 war, and its virtues were much discussed at the time; but when, with the coming of peace, the need for absorbent dressings diminished, sphagnum was allowed to drop out of use. This seems a pity, for its absorptive powers are remarkable, far in excess of those of cotton wool; and it grows so abundantly on moors throughout the country that its cost need only be trifling. During the late war we drew attention to its value,[4] and noted that methods of preparing it had advanced considerably.[5]

Botanically, sphagnum lies between the true mosses and the liverworts, and its large cells, perforated with small pores, absorb fluid rapidly and act as reservoir. It is much more efficient mechanically than cotton wool, which consists of cellulose tubes of small diameter, usually collapsed and twisted by drying, and so incapable of filling by capillary attraction like the moss cells. It grows in great profusion, and is so easily recognised that in the 1914–18 war it was collected by school children. But it is heavy when wet, and the gatherer must resist the impulse to wring out the water and so damage the cells; only gentle squeezing is permissible. The moss should be spread out to dry in an attic or outhouse; for though oven drying is quicker it makes the moss brittle. Foreign bodies such as twigs and dead leaves should be picked out and the dry moss packed in muslin bags

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[1] Wootton I D P King F J Lancet March 7 1953 p 470 Leading article *Ibid* p 476

[2] Klinische Fehldiagnosen Stuttgart Thieme 1953 Pp 480 DM 58 50

[3] See leading article *Lancet*, May 2 1953 p 887

[4] *Ibid* 1940 ii 753

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PERINEAL TESTIS

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PERINEAL testis was first described by John Hunter in 1786, when he reported 2 cases and also gave his classical description of the gubernaculum, which he believed was responsible for the descent of the testis.

Ricord (1843) reported 2 cases, and Vidal (1844) observed 2 more. Curling (1856) was the first to operate for this condition, on an infant aged 4 weeks which later died of sepsis. Partridge (1858) and Adams (1871) were the next to operate, both with fatal results due to sepsis. The first successful operation was done by Annandale (1879).

Weinberger (1899) reported that 74 cases had been published, Klein (1906) found 81, and Campbell (1936) brought the number up to 102. Jones and Lieberthal (1938), Cecil (1947), and Wattenberg et al. (1949) each added 1 case.

I report here 3 more, bringing the total to 108 cases, and discuss the anatomical development giving rise to this condition.

CLASSIFICATION OF ECTOPIC TESTIS

The only mammals in which the testes are found in the scrotum at birth are man and the chimpanzee. In man, as is well known, the testis may not always reach the scrotum but may be arrested along its normal path of descent—the condition called cryptorchidism. If, however, the testis migrates from its normal channel of descent, it is known as an ectopic testis. This condition is very rare, but five types of ectopic testis have been described, of which perineal testis is one. The standard classification is as follows:

(1) *Interstitial.*—After the testis has left the external ring it passes upwards and laterally towards the anterior superior iliac spine and comes to rest on the aponeurosis of the external oblique muscle. This is the most common variety of ectopic testis.

(2) *Pubopenile.*—Here the testis passes out through the external inguinal ring and comes to lie on the base of the dorsum of the penis and the overlying os pubis. Only 6 cases have been recorded (Popow 1888, Poupart 1897, Forsyth 1924, Bernhard 1925, Kausch 1925, Kaufman 1943).

(3) *Femoral or Crural.*—Here the testis is found in the medial portion of the femoral triangle.

(4) *Transverse.*—Both testes descend in the same inguinal canal and are therefore found lying in the same side of the scrotum. Hertzler (1916) recorded 16 cases.

(5) *Perineal.*—The testis, having passed through the external inguinal ring, descends to the perineum and comes to lie near the ischial spine and is often attached to it.

An important feature from the surgeon's point of view emerges from the anatomical facts of these conditions. The spermatic cord of an ectopic testis is of a normal length, whereas in cryptorchidism it is shorter than usual.

DEVELOPMENT OF TESTIS

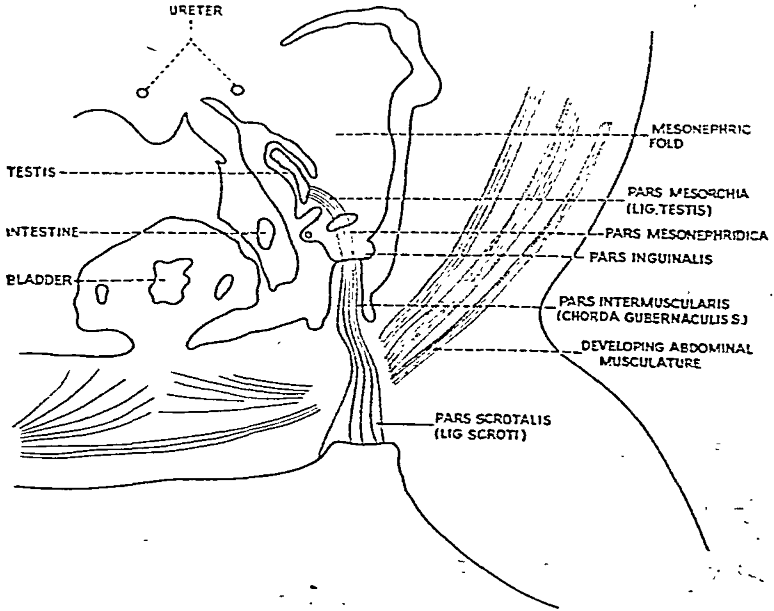
The testis develops in the genital fold on the medial side of the excretory apparatus. At first the genital gland lies in the upper part of the body cavity. It is often taught that the testis moves to the region of the iliac fossa, but it is now thought probable that there is no active descent but rather a degeneration of the cranial end of the gland and a growth at the caudal end, the two processes taking place pari passu, with the result that the testis occupies a lower position in the body cavity. At the seventh week of fœtal life the lower pole of the testis lies at the brim of the true pelvis.

The caudal end of the testis is attached to the mesonephric fold at the brim of the pelvis. Here the genital fold of mesenchyme condenses to form a cord composed of connective tissue and plain-muscle cells. This will form part of the gubernaculum, which corresponds to the ligament of the ovary in the female.

In the meantime the urogenital fold becomes connected to the anterior abdominal wall at the crista inguinalis. There is from the outset a compact cord of mesenchyme present in the crista long before the muscles of the abdominal wall are differentiated. When later this musculature begins to develop it grows round this cord, which is also a part of the gubernaculum. At the external oblique muscle this cord becomes continuous with a further mesenchymatous cord extending to the integument. Lastly a further mesenchymatous cord develops in the mesonephric fold, connecting the cord at the lower pole of the testis with that in the abdominal wall. A complete gubernaculum has now been formed extending from the testis to the scrotum (see figure).

John Hunter was the first to describe the gubernaculum, and in the opinion of McGregor (1929) his description is still the best. It is as follows:

> "The testicle is connected in a very particular manner with the parietes of the abdomen. This connection is by means of a substance which moves down from the lower end of the testis to the scrotum. At present I shall call it the ligament or gubernaculum testis, because it connects the testis with the scrotum and directs its course in its descent. It is of pyramidal form; its large bulbous head is upwards and fixed to the lower end of the testis and epididymis, and its lower slender extremity is lost in the cellular membrane of the scrotum. The upper part of this ligament is within the abdomen, before the psoas reaching from the testis to the groin, or to where the spermatic vessels begin to pass through the muscles. Here the ligament runs down into the scrotum precisely in the same manner as the spermatic vessels pass down in adult bodies and is there lost. It is hard to say what the structure or composition of this ligament may be. It is certainly vascular and fibrous, and the fibres run in the direction of the ligament itself. It is covered by the fibres of the cremaster or musculus testis, which is placed immediately behind the peritoneum. This is not easily ascertained in the human subject, but is very evident in other animals, more especially those where the testicles remain in the cavity of the abdomen after the animal is full grown" (Hunter 1786).


URETER
TESTIS
INTESTINE
BLADDER
MESONEPHRIC FOLD
PARS MESORCHIA (LIG.TESTIS)
PARS MESONEPHRIDICA
PARS INGUINALIS
PARS INTERMUSCULARIS (CHORDA GUBERNACULIS S.)
DEVELOPING ABDOMINAL MUSCULATURE
PARS SCROTALIS (LIG SCROTI)

Formation of gubernaculum.

which can then be sterilised. Steam was used for this purpose in the 1914–18 war, but it reduces the absorptive power by hardening the walls of the cells. A later method, described in detail at the time,[6] was to impregnate the moss with corrosive sublimate. The bags were then usually flattened in a hydraulic press, the thin sheets thus produced being easier to pack and handle. The absorptive power of the moss, however, was impaired by the pressure; and it is best used in the form of loose pads. These should be peculiarly convenient for the use of the incontinent, and for patients without bedsores sterilisation of the moss should hardly be necessary. Cushions of sphagnum, capable of taking up 12–19 times their own weight in fluid, would not only reduce the work of the nurses, but would restore to patients some of the confidence and self-respect which lying in a wet bed, even for a few minutes at a time, so quickly destroys.

THE TREASURES OF BARTS

St Bartholomew's Hospital for its first four hundred years was an ecclesiastical institution, and for its second four hundred years a Royal Hospital administered by its own board of governors. Under the Act of July, 1946, it started a new career as part of the national hospital organisation; which seems to augur well for the durability of the National Health Service. In the splendid 18th century great hall was displayed last week an exhibition of fine portraits, ancient documents, prints, and archives, and as well as the superb 17th-century flagons, chalices, and patens of St Bartholomew's the Less, the parish church of that unique parish, the hospital. It is a collection that spans much of the story of medicine. The earliest document is a deed sealed in 1137 by Rahere, founder of the hospital and priory, and himself first prior and master of the hospital; his very bones lie just outside the precincts in his own priory church, St Bartholomew's the Great. A few centuries after he sealed it—some time between 1420 and 1468—Brother John Cok, the hospital renterer, sat down to copy exquisitely into his illuminated *Cartulary* all the deeds in the possession of the hospital in his time; and more than half of these original deeds are still in the hospital's care. How much he would have valued—if he had lived another hundred years to see it—the indenture signed and sealed by Henry VIII giving the hospital to the Mayor and Commonalty and Citizens of London and their successors for ever, for the relief of the "poor, aged, sick and impotent people . . ." The seals on ancient Royal documents are things to marvel at, so rich are they in design, so finely coloured and so very large—about as big as a Camembert cheese. St Bartholomew's has documents sealed by Edward II, Elizabeth I, Edward III, and a good many others. In this exhibition James I, in armour, mounted and waving his sword, gallops across a flowery mead, a hound at his side, and a Tudor rose at his back. Next to him Queen Victoria sits sedately bolt upright on a stout Victorian horse.

Thomas Vicary, William Harvey, Sir James Paget, and many other famous old Barts' men appear here; and the portraits of Percival Pott by Sir Joshua Reynolds and of John Abernethy by Sir Thomas Lawrence are national treasures, quite apart from their medical interest. Then there are prints showing the hospital in former times, Rowlandson's cartoon of Bartholomew Fair (which was still being held less than a century ago), and records of martyrdom in Smithfield market, just outside the hospital gates. From the last century bills and ward reports have survived, and records of patients—including the case of Elizabeth Brookes, who had led a seafaring life and been used to drink raw rum in the West Indies. Somehow she makes modern patients seem rather tame.

BRUSH AND PASTE

Some years ago a favourite slogan in dental propaganda was: Clean Teeth Do Not Decay. Much depends on what was meant by "clean," but the inference presumably was that brushing would ward off caries. This is not true, as any dental surgeon—and many patients—will admit. A patient with a mouth never touched by a brush, although he probably has gingivitis or perhaps pyorrhœa, may have caries free teeth, while another whose oral hygiene is beyond reproach may need conservative treatment every three months. Nevertheless, for æsthetic reasons if for no others, cleaning the teeth seems desirable—at any rate for civilised man, whose diet might have been designed to leave the maximum amount of debris on and around the teeth.

The practice of cleaning the teeth by mechanical means is not new. Hindu writings dating from about 400 years ago refer to the use of myrtle twigs[1] for this purpose—a method still used in some parts of the world, especially among Mohammedans. The bristle brush seems to have been introduced about 1640.[2] The earlier advertisements for these brushes often referred to them as gum brushes; "toothbrush" is a much newer appellation—and a worse one, since the brush can play a most useful part in massaging the gums. Now, however, one of the leading firms of brush manufacturers has adopted the term "mouthbrush," which, though sounding strange, at least indicates the brush's function.

Present day views on the shape and material of brushes are described by Bryan Wade,[3] who cites the results of a postal survey by a manufacturing company. The dental profession favour a medium-texture bristle (rather than nylon) brush set on either a bayonet-shaped or an angled handle. At least two smaller sizes of brush should be made for children, and all brushes should be narrow to avoid laceration of the buccal mucosa, which may result from enthusiastic application of a wide brush. A suggested maximum width is 9 mm. The dental profession's preference for bristle seems to have little rational foundation.[4] In experiments in which extracted teeth were brushed mechanically with water alone for the equivalent of thirty years' normal brushing, the teeth showed no macroscopic signs of wear with either a hard bristle or a medium nylon brush. When, however, a popular brand of dentifrice was used grooves appeared on the teeth after the equivalent of a year's brushing; there was no difference in depth between the grooves produced by nylon and those from bristle. The results of such an experiment in vitro cannot perhaps be applied clinically without reservation; but it seems fairly safe to assume that, while there is little to choose between bristle and nylon, the composition of dentifrice should be further investigated. Wade suggests that patients with gingival recession should be told to use plain white toilet soap rather than a proprietary dentifrice which may be abrasive. It has been suggested that nylon brushes may cause gingival recession, but there is no definite clinical evidence of this. In fact, patients with the troublesome condition of sensitive dentine at the cervical margin are often relieved of their pain by reasonably hard brushing. The reason is obscure, but it may be that keratinisation is induced by the friction of the brush.

Obviously, if a brush is to be used on the gums and teeth, it must be used intelligently: it is worse than useless to attack the teeth as if one were getting down to a dirty floor with a scrubbing brush—nor, for that matter, is the habit of a patient who used a well known brand of scouring powder to be recommended. For

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[6] *Ibid*, 1916, i, 820.

[1] See Miller, S. C. Text Book of Periodontia. London, 1950.
[2] See Asgis, A. J. *Dent. Dig.* 1929, 35, 307.
[3] Wade, A. B. *Brit. dent. J.* 1953, 94, 204.
[4] Wade, A. B. *Ibid* (in the press).

NORMAL AND ABNORMAL DESCENT OF TESTIS

John Hunter's observations on migration of the testis and in the fœtus were numerous. He was of the opinion that respiration played no part in the descent of the testis, since the testis was usually in the scrotum before respiration began. Nor could descent of the testis be influenced by the cremaster muscle, since no such function was found in hedgehog or other quadrupeds. Hunter also thought that the effects of posture, abdominal pressure, and the pressure of respiration should be considered when the testis did not descend in fœtal life.

In 1841 Curling dissected out the inguinal canal and, drawing up the gubernaculum, traced three processes: (1) the external process, which was the broadest and connected to Poupart's ligament; (2) the middle portion, a long band of muscle-fibres which escape from the external inguinal ring to pass down into the bottom of the scrotum, there blending with the dartos muscle; and (3) the internal band, which passes inwards to become attached to the os pubis and the sheath of the rectus muscle (Curling 1856). He noted that the middle band of fibres soon become indistinct and waste away, although remnants are seen throughout life. These may be found during operations on the testis or after death: on pulling the testis from the scrotum, the lower part of the testis is firmly anchored to the bottom of the scrotum by a dense fibrous band. This band forms the middle band of fibres of the gubernaculum. Curling was of the opinion that the pull of the gubernaculum was the sole cause of the descent of the testis.

In 1887 Lockwood published his Hunterian lectures on the development and transition of the testis—normal and abnormal. After many dissections and much anatomical research he originated the theory of multiple gubernaculum tails. The attachments of these tails he enumerated in the order in which they seem to develop:

(1) The abdominal tail went to the aponeurosis of the external oblique muscle near the anterior superior iliac spine.

(2) The pubic tail went to the root of the penis. The saphenous tail made its way down into the medial side of the femoral triangle.

(4) The perineal tail passed down into the perineum and became attached to the ischial spine.

(5) The scrotal tail passed down into the bottom of the scrotum, where it blended with the dartos muscle.

Lockwood thought that the scrotal tail was the most highly developed, and therefore drew the testis down into the scrotum. If this tail were ill developed or absent, the testis might be drawn into an ectopic position by the other tails, and thus come to lie in the perineum. McGregor (1929) in his dissections was unable to find any of Lockwood's divisions of the gubernaculum, and Sonneland (1924) denied the existence of any evidence of tails either anatomical or embryological.

McGregor (1929) described the "third inguinal ring." His research was stimulated by the work of Burdick and Coley (1926), who attributed ectopia of the testis to passage of the testis under Scarpa's fascia. McGregor undertook new dissections of the region and concluded that ectopia of the testis was due to the development or lack of development of the various fascial planes, which created congenital fascial ridges, pockets, and anomalies, forming the third inguinal ring. This ring could easily be felt clinically and was the gateway from the inguinal canal to the scrotum.

Various workers felt that, although the anatomical arrangements described might explain why the testis became ectopic, they did not explain the underlying cause of the movement in the first instance. Sebileau and Descomps (1916) and Klein (1906) therefore studied the problem from the viewpoint of phylogenic and ontogenic development. In the camel and the otter the testes remain inguinal, whereas in the whale, the elephant, the rhinoceros, and other pachyderms they remain inside the abdomen; in swine, wild boars, civet cats, and other carnivores the testes are perineal; and in the kangaroo they are pubopenile. These workers did not find any animals in which the testes were interstitial or femoral.

From these studies it is clear that most of the ectopic misplacements of the testis in man have a counterpart in the lower animals. Up to now, in spite of all the research on this subject, nobody has yet been able to state categorically the mechanism causing descent of the testes. There seem to be two processes influencing its descent:

(1) The formation of the gubernaculum very early in fœtal life—even before the development of the abdominal musculature—creates a pathway for the testis to follow through the forming inguinal canal into the scrotum. Whether or not the gubernaculum actively contracts and pulls the testis down into the scrotum remains to be proved.

(2) There seems to be some evidence that hormones play a part in descent of the testes.

CLINICAL PICTURE OF PERINEAL TESTIS

The patient always presents with a swelling in the perineum. In every case this lies behind the root of the scrotum and in front of the anus, and is lateral to the median raphe of the scrotum. The skin over the scrotum appears perfectly normal, and the swelling can be slipped around in any direction. The scrotum is always asymmetrical; the side containing a testis appears normal, whereas on the side of the perineal testis the scrotum is rudimentary.

CASE-RECORDS

Case 1.—A boy, aged 3 years, was seen at the Belgrave Hospital for Children, on May 6, 1923, complaining of pain in the perineum. A perineal testis was found, and the right side of the scrotum was empty.

Operation.—Through an inguinal incision the ectopic testis was delivered from the perineum and transferred to the right side of the scrotum. The testis was made to descend to the bottom of the scrotum through a passage made for it with the finger, the spermatic cord being sufficiently long to allow this. The wound was closed without drainage. Recovery was uneventful.

Follow-up.—The child was seen again in 1924, when the testis appeared normal in every respect and was equal in size to the left testis.

Case 2.—A boy, aged 20 months, was admitted to the Belgrave Hospital on Jan. 16, 1930, because of a small swelling in the left side of the perineum. The left side of the scrotum was empty. The swelling was as big as a small marble and freely movable upwards.

Operation.—An inguinal incision was made and the spermatic cord isolated at the external abdominal ring. By gentle traction the ectopic testis was delivered and passed into the left side of the scrotum. The wound was closed without drainage, and recovery was uneventful.

Follow-up.—When the boy was seen five years later, the testis appeared normal.

Case 3.—A boy, aged 1 month, was brought to the Belgrave Hospital on Jan. 17, 1952, because of a swelling in the right side of the perineum. The right side of the scrotum was empty. The swelling, which was about the size of a small marble, was freely movable upwards.

Operation.—A small right inguinal incision was made, and the testis was delivered into the wound from the perineum by gentle traction on the cord. A small hydrocele was found and incised. The testis was drawn into the right side of the scrotum, to which it was fixed with stitches. The wound was closed without drainage. Recovery was uneventful, and the testis appeared completely normal a month after the operation.

SUMMARY

Three cases of perineal testis are described. The anatomical development of the testis and gubernaculum children especially, there is much to be said in favour of eating a raw apple after meals, and, until the child is old enough to manage a brush properly, the teeth can be kept free of food debris by lint or cotton-wool wrapped round the finger.

PRIMITIVE POISONS

PRIMITIVE races put their poisons to three uses: they apply them to weapons for use in the chase and in war, they use them with intent to kill or annoy those whom they dislike, and they find them particularly suited to judicial ordeal, for trial and execution are simultaneous. The investigation of these poisons is complicated by the fact that few are simple preparations: numerous other ingredients, sometimes as many as twenty, are added for purposes of magic, or to obtain the ideal consistence for anointing weapons and to ensure rapid absorption. Many of these additions are virtually inactive pharmacologically, although potent poisons are sometimes mixed, as when brucine, opium, or arsenic are added to the already deadly sap of the Upas tree.[1]

In ancient Europe the poisons of choice were probably hemlock, the active principle of which, conine, has nicotine-like properties, or *Datura stramonium*, which was used to inspire the pythoness of the Delphian oracle. As arrow poisons, aconite, hellebore, and yew were used; the active principles are aconitine, protoveratrine, and taxine, which slay by cardiac and medullary depression. Various concoctions of viper venom or putrefied human blood were favoured here and there.[2] In Africa very many plants have been used as sources of poison, the chief being those containing strophanthin-like glycosides and strychnine or brucine. In some places today fowls or dogs have taken the place of human litigants and so the trial by ordeal has lost some of its drama.[2 3] Less widely used as weapon poisons are sources of eserine, croton (producing hæmolysis, nephritis, and respiratory depression), the sap of various Euphorbias (severe local inflammation with tissue necrosis), cobra venom (hæmolysis, curariform paralysis, and central depression), and various other snake venoms and extracts of poisonous larvæ, centipedes, and decomposing flesh, human and animal. Incidentally, cobra venom has in recent times been the subject of an unsuccessful clinical trial as an analgesic.[4]

Sometimes in Dahomey the true judicial ordeal is falsified when poison is given to one party only, whose guilt has been previously decided by the witch doctor, who may have been influenced by gifts made before the ceremony. In these circumstances, "tout à coup, l'un des deux plaideurs meurt en quelques instants, frappé en apparence par la colere d'un dieu vengeur et, en réalité, par une énorme dose de boundou" (strychnine).[3]

In Madagascar arrow poisons have never been used, but judicial ordeal was popular, and a strophanthin-like poison from *Tanghinia venenifera*, the "ordeal tree," was widely used. It is recorded that in one ordeal 6000 people died. In North-east Asia and Alaska arrows are poisoned by being left imbedded in a corpse, and extracts of various plants of the anemone family are used. These have general effects similar to aconitine and a local irritant action like cantharidin. In East and Central Asia weapons are poisoned with aconite, croton, various cadaveric extracts, and crushed spiders. In Indo-China the principal poisons are strophanthin-like, and are obtained from various species of strophanthus and from "the celebrated deadly Upas tree," *Antiaris toxicaria*,[1] the active principle of which is antiarin. Each tree has its owner who alone may exploit it.[5] It grows also in Malaya, Java, Sumatra, Borneo and elsewhere.[1 2] An arrow poison in use in Borneo today has recently been examined[6] and found to have properties similar to antiarin, although its botanical origin is uncertain. Ordeal poisons are not used in Asia but for criminal purposes there are hyoscyamus and abrin. In Malaya and in the islands to the south and east strophanthin-like and convulsant poisons (strychnine and picrotoxin) are popular. Derris, the common garden insecticide, is used on weapons and for poisoning fish; it is relatively nonpoisonous to man,[1] but it causes vomiting, convulsions, and death by respiratory depression in animals.[7]

In the New Hebrides bacteriological warfare was developed: arrows were smeared with material infected with tetanus bacilli and vibrios, the latter, if fresh, causing death in 12–15 hours. Severe sepsis and gas gangrene due to accidental contamination of the arrows are, of course, common in all parts of the world. Various other poisons, similar to those used in Malaya, are also available in the Pacific Islands. The greater part of North America is without useful weapon poisons, but crushed snakes, putrefied deer liver, menstrual blood and rattlesnake venom were used here and there, chiefly by the Indians in the south-west. Central America has no effective weapon poisons, but South America has the best known of all arrow poisons, curare, and animal putrefactive products and venoms are also used. Inorganic poisons are little used by primitive peoples except for criminal purposes. Arsenic is probably the most wide spread and has been used on the Malay kris, as well as in food.

POOR MAN'S TISSUE CULTURE

FEW pathologists engaged in the routine diagnosis of morbid conditions are familiar with the microscopical appearances of living cells. The techniques of fixation and staining are well established, and especially convenient in these days when much work has to be delegated to technicians. Furthermore the apparatus for the newer techniques is seldom available outside research centres. Pulvertaft and Jayne,[8] however, have described a technique for examining cells in exudates which is suitable for routine use and calls for no special apparatus beyond a phase-contrast *microscope* and suitable illumination.

After two hours' incubation on serum agar the cells, spherical at first, begin to move and show their several characteristics. All are capable of throwing out pseudopods and may show motion of some kind for as long as fourteen days. Polymorphs, lymphocytes, and endothelial cells can be distinguished, and often malignant tissue can be clearly differentiated. The cells of malignant tissue are often arranged in three-dimensional masses and even form acini—a feature never found in non-malignant exudates. A few of the cells scraped from malignant tumours may survive and even divide by mitosis, but Pulvertaft and Jayne do not consider that malignancy can be established by studying individual cells. This technique of cell culture on serum agar is particularly well suited to the investigation of exudates for diagnostic purposes, but it has other applications. Since cells remain alive and motile for days, they may be submitted to pharmacological and other tests, or the effects of radiation may be studied. In addition to exudates, scrapings from malignant tumours and their metastases can yield suitable material for study.

This kind of work is clearly in its infancy, but now would seem the moment for enterprising pathologists to test its value in diagnosis.

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and the various theories postulated on the descent and abnormal positions of the testis are discussed.

I wish to thank Sir Cecil Wakeley for permission to publish his case-histories, and Dr. Frank Stansfield for much kind advice and help in preparing this paper.

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POSITIVE-PRESSURE HOOD AND SPLIT FRONT FOR THE BOTH RESPIRATOR

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CONSIDERABLE distress is experienced by many patients on their removal from the "iron lung," or cabinet respirator, for nursing purposes; and, though a skilful operator can provide efficient ventilation for the occasion with a mask and positive pressure, the procedure is uncomfortable for the patient and can only be used for short periods.

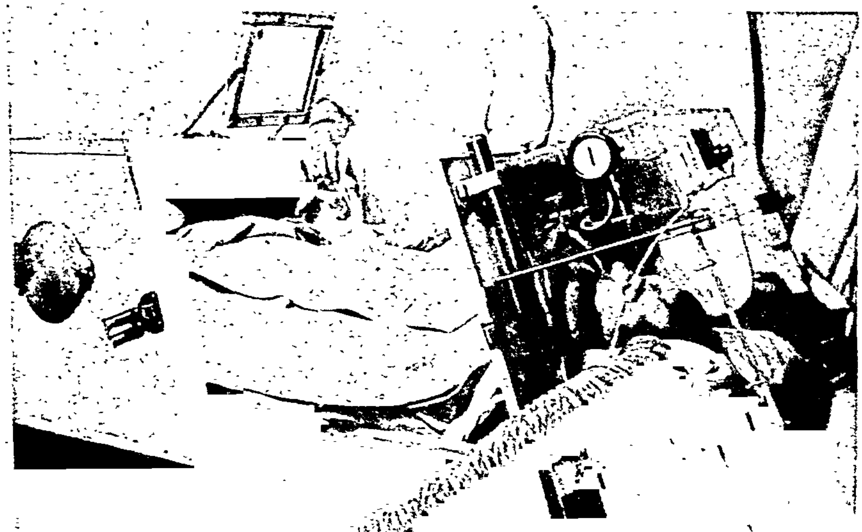

Fig. 1—Positive-pressure hood in action, with cabinet respirator opened. Note flap-valve to right of patient's head.

In our efforts to discover a more satisfactory form of ventilation we have relied on the resources of the hospital workshops and have been limited to the use of materials of ordinary availability.

The pressure-hood described here has been used for four months with excellent results. The principle of the apparatus is not new, but the hood has been of such obvious benefit to patient and nurses that we feel that some account of the appliance should be given now before the start of the poliomyelitis season. It provides comfortable respiration by positive-pressure inflation of the lungs, and enables a patient to be removed from the cabinet respirator for an indefinite period; in practice we have used the hood for two hours at a time.

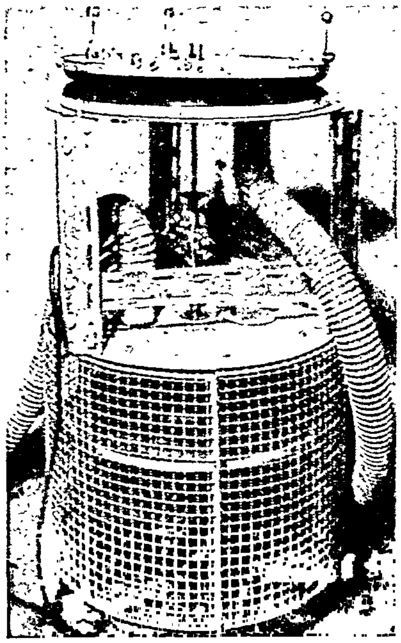

Fig. 2—Two Both bellows linked together to develop positive hood pressures and negative cabinet pressures in synchrony.

THE HOOD

The hood (fig. 1) is an open box-shaped structure made from $^3/_8$-in. 'Perspex' sheeting. In use the open side of the box is applied to the head-piece of the Both respirator to enclose the patient's head, and the air-pressure in the hood is then raised and lowered by connecting it to a Both bellows.

The over-all dimensions of the two irregular quadrangles which form the sides of the hood are 21·5 × 14·5 × 21·75 × 12·75 in., and the width of the hood is 17·75 in. The sheets of material are held together with screws and perspex cement.

In the side of the hood to the right of the patient is a circular opening, 4·5 in. in diameter, covered by a rubber flap, which admits air to the hood during the suction phase of the bellows and prevents air from escaping during the pressure phase. On the same side, in the lower right-hand corner of the hood, is a metal tube 6 in. long and 0·5 in. in diameter through which a rubber tube may be passed to convey oxygen to a nasal catheter or a mask

On the left side of the box are fittings for attaching a pressure gauge and the air-hose of a Both bellows.

The two clamps which hold the hood in position are made from steel rods 0·25 in. in diameter. Each rod is bent

Special Articles

JUNIOR MEDICAL STAFFING IN HOSPITALS

FIVE YEARS OF FAMINE

T W Hurst, F H A, A C I S, GROUP SECRETARY
C B Linfoot, F H A, A C I S, DEPUTY SECRETARY
T K Woodhouse, ADMINISTRATIVE ASSISTANT
WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE

Difficulties in providing hospitals with junior medical staff were already serious before the National Health Service was established It was hoped that, with the new Act, the situation would improve, but after nearly five years the problem seems to be as far from solution as ever

EXTENT OF SHORTAGE

Some measure of the great increase in the number of posts for junior medical staff may be obtained by taking figures for a non teaching group of hospitals in an industrial area Junior medical staff (i e , equivalent grades below senior registrar) taken over in July, 1948, at voluntary and municipal hospitals in that group numbered 10 The latest establishment figure for similar grades is 30 A fair proportion of these 30 posts remain unfilled, and perusal of the advertisement columns of the medical journals shows that many other hospital management committees are repeatedly advertising posts of this type with no apparent success We understand that a committee recently spent over £100 in advertising one post which did not attract a single applicant

As the necessary pre-war statistics do not exist, it is impossible to make an exact comparison between the position in pre nationalisation days and today Prof W H Wynn,[1] however, has quoted figures showing that, in 1950 there were 5824 junior medical posts, of which 1622 were in teaching hospitals A rough estimate puts the number of junior medical posts in non-teaching hospitals before nationalisation at about 1500

CAUSES OF SHORTAGE

Perhaps the most obvious cause of the present shortage was the sudden transition to a system which provided "free" medical, hospital, and health services for all, with consequent increased demands on these services

Formerly the smaller non-teaching hospitals were mostly staffed by a nucleus of residents, supplemented by leading medical practitioners of the area, who served as honorary physicians and surgeons In this way, general practitioners contributed their share to the hospital services, but this arrangement has now ceased in all but a few small general-practitioner hospitals for which special provision is made in the new service

With the appointment of separate hospital consultants and subordinate medical staffs, contracts of service have been related to more reasonable working hours than were customary in the medical profession in past years No longer is the doctor expected to work the long hours which previously gave him little opportunity for relaxation and study Like other sections of the employed population, he is entitled to a reasonable amount of leisure time

A further important factor is the expansion of the hospital service A survey of British Health Services[2] shows that in 1936 there were 2795 hospitals with a total of 410,829 beds In 1950, total beds in hospitals of all classes were 504,321—an increase of 93,492

The shortage of hospital staff may also be aggravated by

1. (1) A desire on the part of general practitioners to reduce their working hours to a reasonable level
2. (2) A scarcity of general practitioners in certain areas, which makes it difficult for them to give the necessary attention and treatment to their patients and leads them to refer patients to hospital whom they would otherwise have treated themselves

On the other hand, an increase of the proportion of doctors in general practice (as envisaged in the Working Party's recommendations) might not, on balance, help the hospitals, for it would reduce the number of doctors available for the hospital service Again, the public now tends to demand attention at consultant level, thus preventing the general practitioner from carrying out his normal duties

Continuing advances in medical science are resulting in more elaborate forms of treatment and creating new branches of medicine which require separate staff, and this development contributes towards present day shortages Since nationalisation, lack of funds has obliged hospital authorities to retain small hospital units which in many instances are not economic in providing the increased services required of them Much time must be wasted by medical staffs travelling between hospitals of this type—time which would be spent more profitably if larger hospital units were established

There must be many other possible reasons for the present difficulties in providing medical staff for the hospitals We need mention only the following contributory causes

(a) Insufficient recruitment to the medical profession.

In England and Wales 2104 posts at 456 hospitals have been approved as preregistration house officer posts under the Medical Act, 1950 In 1951 there were 1531 registrations with the General Medical Council, which suggests a 25% deficiency between supply and demand

(b) Employment of doctors on non clinical duties—e g administrative medical staff employed by Ministries regional hospital boards local authority health services, marine services, and industry

(c) Call up of doctors for military service

The Under Secretary of State for War stated recently that there were 1550 doctors in the Army, apart from the other Services

(d) Reduction in supply of doctors from other countries (e g , refugees)

POSSIBLE REMEDIES

It seems certain that doctors will not go back to the earlier unsatisfactory conditions of long working hours, nor should they be expected to do so Similarly, it is unreasonable to expect a hospital doctor to participate in various different kinds of specialist work—any more than we ask a plumber to do the work of a joiner It becomes necessary, then, to inquire

(a) Can the number of patients now attending hospitals be reduced ? Or do the existing numbers represent a more or less permanent demand upon the hospital service ?

(b) Have the hospital services developed to such a stage that the country cannot afford further expansion ? The advances of medical science make it impossible for such services to remain static

Any reduction in the demand on the hospital service is likely to be achieved only by placing more work on the shoulders of general practitioners The burden borne by practitioners might in turn have to be lightened by discouraging patients from making unreasonable demands upon the services which are now "free" to all In time it may be possible to reduce numbers by instructing the public more intensively in preventive medicine and by

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[1] *Lancet* 1952 ii, 1225

[2] P E P (Political and Economy Planning) London, 1937

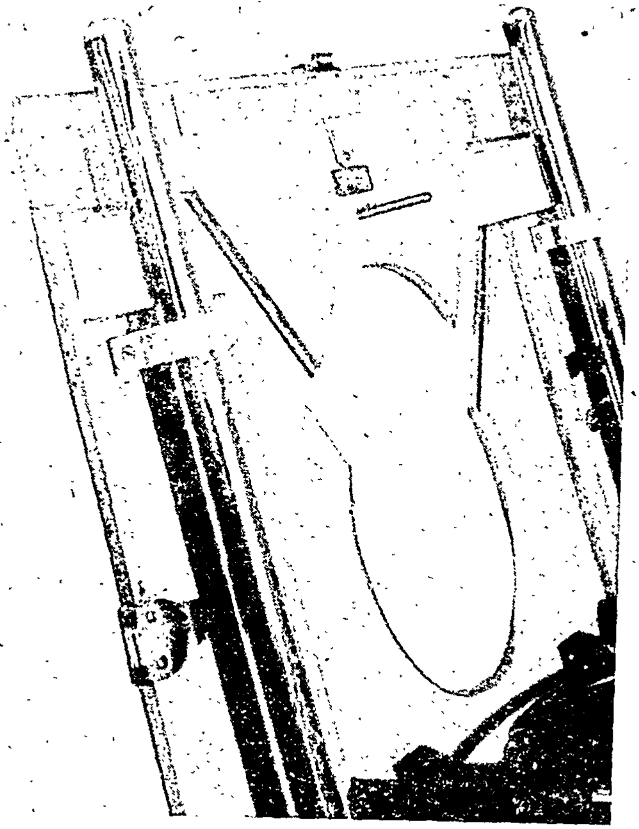

Fig. 3—Split front open.

to a right-angle about 1 in. from one end, and the bent-down ends fit into sockets secured to the respirator head-piece. The rods can be removed when the hood is not in use. Their free ends pass through slotted lugs, bolted to the back of the hood, and are threaded to carry wing nuts which can be tightened against the lugs. The lower edge of the hood rests on a wooden batten screwed to the head-piece of the respirator below its head-rest. The batten forms a shelf which takes most of the weight and helps to keep the hood in position.

The union between hood and respirator is made airtight by applying strips of adhesive ‘ Sorbo ’ rubber to the respirator head-piece along its lines of contact with the hood.

Our patient spent alternate periods of two hours in the hood and cabinet respirator, and an interesting point to us was his decided preference for hood ventilation when he was not feeling too well. It was our impression that the positive-pressure technique provided better oxygenation and produced a type of chest movement different from that produced by the cabinet respirator, the upper lobes of the lungs appearing to fill first with the positive-pressure method.

Whether the hood affords the patient any protection against droplet infection is not known, but it seems reasonable to suppose that it may do so.

The size and transparency of the hood, and the air-flow over the face, from the bellows during the pressure phase and from the atmosphere during the suction phase, were other features of the apparatus appreciated by the patient.

VENTILATION

The pressures used ranged from 0·5 cm. H_2O below atmospheric pressure to 12·0–20·0 cm. H_2O above atmospheric pressure. Pressure effects on the ears were not noticed below a pressure of 20·0 cm. H_2O, but higher pressures can produce earache. There was no complaint of flatulence due to swallowing air, despite the fact that drinks were taken freely, through a long feeding-tube, while the hood was in use.

Occasionally we combined hood and cabinet ventilation, providing a positive pressure in the hood and negative pressure in the cabinet simultaneously. Th patient's comment on this form of respiration was tha it made breathing “ too easy ” and abolished his natura urge to inspire. This method produces satisfactor *ventilation* with mean pressures close to the atmospheri level.

Fig. 2 shows two bellows linked together to develo positive hood pressures and negative cabinet pressure in sychrony. With the double bellows both hood an cabinet are always ready for use and the change-ove from one form of ventilation to the other is simplified. We suggest that this apparatus affords facilities fo studying some of the possible ways of applying negative and positive pressure to the chest; we agree with Ritchie Russell (1952) that these have not been fully explored.

COMMUNICATION

A disadvantage of the hood is that the patient in the hood cannot hear or speak to his nurse. Since our patient was in the hood for two or more hours at a time, we fitted a small microphone and speaker inside it and overcame the difficulty in that way. This device also enabled him to enjoy radio and television programmes, the screen for the latter being reflected in a mirror mounted on the cabinet.

CONTRA-INDICATIONS

The hood must not be used in unsuitable cases, because there is a danger that vomitus or secretions collecting in the pharynx may be forced into the airway before they can be removed. In such an emergency the nurse can reach the patient's pharynx by inserting her hand through the flap-valve opening. In doing this her arm will of course hold open the flap and interrupt inflation.

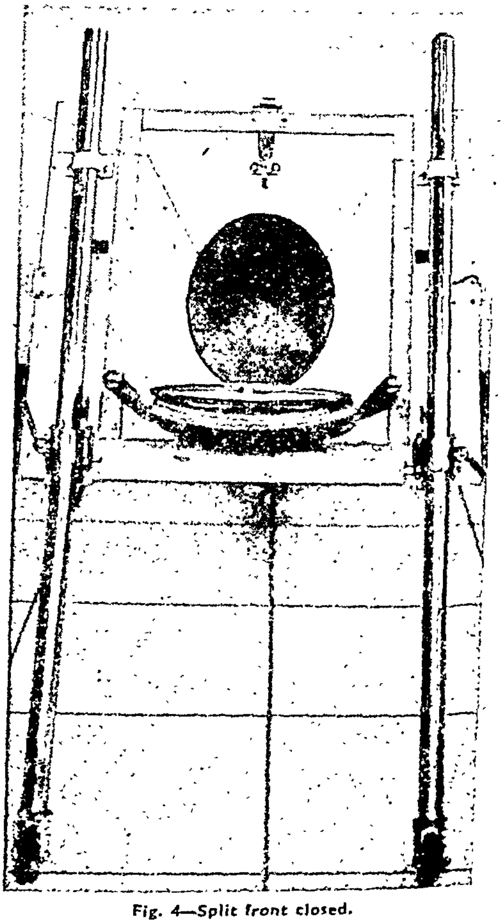

Fig. 4—Split front closed.

so greatly improving methods of treatment that patients will require less hospital care But if for the present we are to regard the demand for hospital treatment as unalterable, we must consider what further economies in medical man-power can be made The following possibilities suggest themselves

1 Train non medical technical staff to carry out preliminary investigations under medical instructions and to arrange for routine test investigations of new patients—e g , electrocardiograms, test meals, barium meals
2 Erect health centres as quickly as possible By saving the time of general practitioners, this may enable them to give some help in hospitals Alternatively, adopt some other means of economising in the use of general practitioners
3 Enlarge the medical schools and encourage more students to train as doctors
4 Require doctors to work in hospital for a period longer than the year prescribed under the Medical Act, 1950, and restrict the entry of doctors to non clinical posts which seem to have lesser claims on the medical profession
5 Encourage students or qualified doctors from abroad to take up medical work in this country
6 Create more full time consultant posts to replace some of the part time consultant appointments This would enable more work by consultant staffs to be done in the hospitals
7 Redistribute specialised beds in existing hospitals so as to avoid unnecessary travelling between hospitals in the various groups

When money is to be had for the purpose, the building of larger hospital units would result in a saving of medical man-power

If it proves possible to re educate the public in the use of the health services, some assistance with hospital work should be obtainable from doctors now employed in general practice Already many hospitals are using practitioners as part-time clinical assistants, and this arrangement might be extended, especially in connection with duties in casualty departments where the greatest difficulty is experienced

Another way of overcoming the staffing difficulties at a hospital where accident and acute cases are admitted might be to introduce a senior resident officer (of, say, junior consultant status) who would be appointed for several years and would be in line for promotion to consultant He should be given facilities for his family to reside with him at the hospital

Married women doctors not already engaged in practice might be encouraged to undertake part-time duties at hospitals, and retired doctors might also be prepared to do part-time work

Another possible method of overcoming the shortage in non-teaching hospitals might be to pay junior medical staff at a lower rate in teaching hospitals than in non-teaching hospitals On the other hand it might be possible to arrange for the transfer of junior medical staff from the teaching hospitals to the non-teaching hospitals for a period of service

CONCLUSION

In looking at recruitment to the medical profession attention must be paid to all the medical services concerned, not only the hospital service, and this is a matter which seems to call for discussions at high level between Government representatives, hospital authorities, local health authorities, executive councils, universities, the General Medical Council, and the representative medical organisations So that these discussions may achieve a useful result at the earliest possible date we suggest that the bodies mentioned should appoint representatives to attend a conference, with the Minister of Health in the chair, to discuss what should be done We recognise, of course, that before such a conference was held it would be necessary to obtain statistics showing the number of medical posts in hospital, general practice and so on, the number of qualified doctors, and the output of doctors from the universities It would also be desirable to have information about the man-power necessary for professions other than medicine, for industry, for the Armed Forces, and for other needs, and of the number of people available to do the work

SCOTLAND'S FIRST HEALTH CENTRE

THE first health centre in Scotland, opened by Mr James Stuart, the Secretary of State, on May 15, is an adventure in combined planning and administration and, as with similar adventures that are already under way in England,[1] its progress will be keenly watched

This centre, at Sighthill, a growing new suburb on the south west fringe of Edinburgh, was planned by the Department of Health for Scotland with the cooperation of Edinburgh Corporation and the good will of the local medical committee It contains suites for six general practitioners along with a pharmacy, a laboratory, and space for an X ray department, four dental surgeries, accommodation for infant-welfare and school health service clinics, and a gymnasium and a physiotherapist's room The building is also to be the headquarters of the health visitors and district nurses working in the area At present it serves a population of 10,000–12,000

DESIGN AND FUNCTION

Architects are a frustrated professional group, for since 1939 they have had little chance to show their paces The housing programme that has gone forward since the end of the war has provided scant opportunity for initiative, and only occasionally, as in the Festival of Britain, have the public been enabled to see how the profession's views have been shaping during its enforced quietude At Sighthill the architects of the Department of Health [2] have had the first chance in years of stepping out, it is little wonder that they show themselves mettlesome For a building of this sort, the centre is exceptional in that the architectural team has, subject to the general requirements, had a free rein both in designing the building and in choosing the furnishings The mixed array of coachmen can now congratulate themselves on their forbearance

Initially the Department had to choose between a small and relatively inexpensive centre, which might prove inadequate, and a more elaborate one that might turn out to be over large for the demands on it The choice fell on the second of these options both the number and the size of the rooms is large (the floor area totals some 35,000 square feet), and the cost, with equipment, is about £160,000

General Description

The building (fig 1) is in the form of a hollow square of one storey, except for one side where a second storey houses the dental surgeries and staff rooms It is built of concrete brick (clay is scarce in Scotland) with a prefabricated roof of copper on fibre The wings could be extended, and internal flexibility is assured by a 4 ft 9 in module The partition walls are of formed slag concrete blocks, these have no weight bearing responsibilities and can thus be pulled down at will (The idea

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[1] See Taylor, S *Lancet* 1952 i 253 (Harlow) Wofinden, R C Parry R H *Ibid* p 1297 (Bristol), *Ibid* ii 772 (Woodberry Down) *Ibid* p 911 (Nottingham)

[2] The architects were ROBERT GARDNER MEDWIN (chief architect) ROBERT MORTON (deputy chief architect for special buildings) JOHN OGILVIE and GEORGE LAWRENCE (senior architects responsible for development of design and supervision) ERIC HALL (assistant architect), and R. J WALKER D A MACGILLIVRAY, and R F A LAIDIE (assistants)

The hood can be removed from the respirator in a few seconds.

Four months after his introduction to the hood the patient had recovered sufficiently to be transferred to a cuirass respirator, but subsequently he developed a secondary infection from which he died. At necropsy his lungs showed no abnormal changes attributable to intermittent positive-pressure breathing.

SPLIT FRONT

A divided head-piece or "split front" (figs. 3 and 4) is a great advantage in cabinet respirators from the point of view both of patient and staff; such a divided head-piece can be used with or without the hood. Smith (1953) has described an excellent split front; the only advantage we claim for our head-piece is that it can be made for a few shillings in any hospital workshop. The existing front of the cabinet is removed, and a new split one is substituted. Both divisions are made from stout plywood. The sides of the detachable upper section move in metal runners extending upwards from the sides of the lower section to which they are fixed. The meeting edges of the upper and lower sections are tongued and grooved so that they interlock when they are brought together.

This split front is still a sloping front, and it remains difficult to nurse a patient in the prone position. We are testing a further simple modification which we hope will overcome this difficulty.

SUMMARY

A positive-pressure hood for use with the cabinet type of respirator is described.

This hood is a much more convenient method of ventilating patients than the positive-pressure mask. It was designed to ventilate the patient during nursing procedures, but we *found that it could be used for much* longer periods.

Ventilation with either alternative or combined positive and negative pressure can be provided easily, and we suggest that these methods should be further investigated.

A simple method of splitting the front of the Both respirator is described.

We are most grateful to the staff of the Fazakerley Group of Hospitals maintenance departments for their enthusiastic coöperation in this work and for their technical skill.

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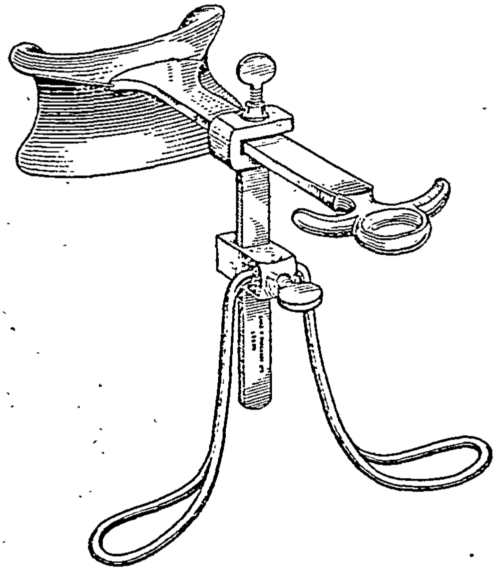
New Inventions

IMPROVED PELVIC STAND FOR DOYEN'S RETRACTOR

THIS stand is designed for placing between the patient's thighs and holds a Doyen's retractor firmly in place when exposure is needed for pelvic and bladder operations. This support does away with the cumbersome chain and weights previously employed and has several advantages over a similar type used in Birmingham. The illustrated design is smaller than the Birmingham pattern, is more easily sterilised, and has the advantage that the height of the jaws can be adjusted before insertion between the thighs, thus avoiding possible contamination from the skin in operations on fat women.



The stand is usually wrapped in a sterile towel before being placed between the thighs, to protect the vulva from any chance of bruising.

The original stands were kindly made for me by Messrs. Rolls Royce and I am indebted to Miss C. Jenner for the illustration. The instrument is now manufactured by Messrs. Chas. Thackray, of Leeds.

Crewe and South Cheshire Hospitals

DEREK FREETH
M.D. Lond., M.R.C.O.G.

Reviews of Books

The Birmingham Hospitals Centre

STANLEY BARNES, M.D. Birm., F.R.C.P., LL.D., chairman of the executive board of the hospitals centre. Birmingham: Stanford & Mann. 1952. Pp. 144. 15*s*.

THIS is the story of the building of the centre now the pride of Birmingham and the envy of medical professors in this and other countries. Beginning with the origin of the scheme Professor Barnes describes the troubles met and overcome, the amalgamation of the General and the Queen's Hospitals, and the formation of a limited company to organise the finance, control the expenditure, and supervise the building. He tells of the completion of the great modern hospital now called "the Queen Elizabeth," of the Nuffield Nurses' Home, and of the Medical School, and of their baptism of fire in the second world war.

Among many generous donors and helpers three men stand pre-eminent in ability, devotion, and unwearying effort—the late Sir Charles Grant Robertson, then vice-chancellor of the university, Sir Harry Vincent, and Professor Barnes himself. It is regrettable that the scheme for a big hospital centre has in the last few years been in part spoilt. Land presented to the city for the purpose of hospital development has been used for the erection of some two hundred houses. Much of the detail makes fascinating reading and could have been expanded without loss of interest—the care taken to eliminate noise, the designing of a unit of 60 beds, the relative merits of a many-storeyed building in contrast to one built on the pavilion system. The book is a wonderful tribute to a great scheme triumphantly carried through and would have been a classic on the subject of hospital construction if more details had been given.

Human Blood Coagulation and its Disorders

ROSEMARY BIGGS, PH.D., M.D., graduate assistant, department of pathology; R. G. MACFARLANE, M.A., M.D., clinical pathologist, Radcliffe Infirmary, Oxford. Oxford: Blackwell Scientific Publications. 1953. Pp. 406. 32*s*. 6*d*.

A FULL-LENGTH monograph on this subject is timely. Dr. Biggs and Dr. Macfarlane justly point out that the subject and its complications can no longer be regarded with tolerant detachment by the ordinary doctor. "Blood coagulation research," they say, "has led to the discovery of a new vitamin, the recognition and treatment of a whole range of newly defined hæmorrhagic diatheses; it has raised problems in genetics and eugenics, introduced with all their attendant problems anticoagulant drugs for the treatment of thrombosis, and has been concerned with many subsidiary develop-

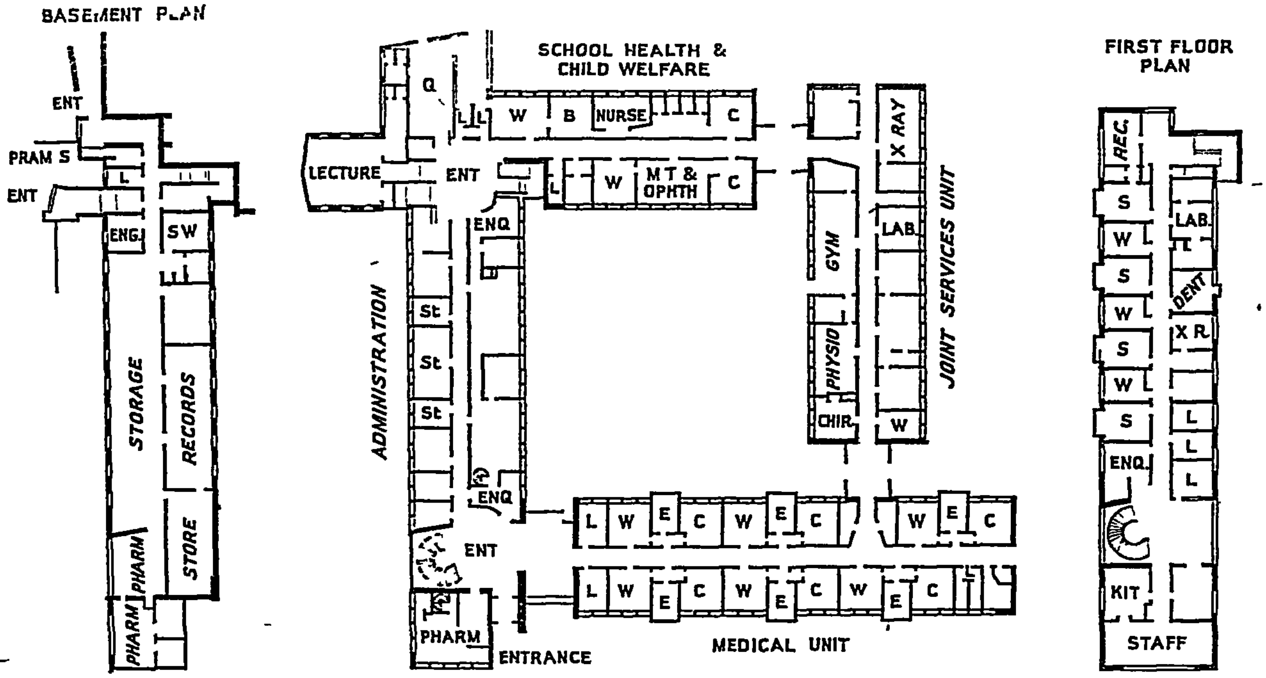

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Fig 1—Plan of building

B Baby weighing room C consulting room E examination room L lavatory M T, minor treatment. Q playroom S surgery St study or lecture room W waiting room S W switch room

of putting up rather more temporary partitions was mooted but abandoned, mainly because of the need for noiselessness.) The ceilings—of insulation board topped with a quilt of glass wool—are reckoned to afford thermal and sound insulation. Heating is provided electrically from conduits embedded in the floors; the electricity is turned off at peak hours, at which times the rooms draw warmth from the heat stored in the fabric of the building.

The architects have relied on light, bold use of colour, and diversity, with a careful choice of furnishings, to give an air of richness and avert the chill institutional atmosphere. The many colours on the walls range through and sometimes, it seems, beyond the breadth of the rainbow; but the chocolate hue once revered by hospitals and public-houses is nowhere to be found. Throughout, the colours (except in the corridors, each of which is painted differently) are not restful: they are challenging, and occasionally the challenge may have overreached its mark, anyhow for those facing it every day—one doctor's room, for instance, has a greenish mustard carpet which draws the eyes by its repulsiveness. As to diversity, the walls of the main entrance hall are, in different sections, of stone, of painted plaster, and rough-cast; adjacent rooms rarely have the same colour motif; and in some rooms one wall differs from its three neighbours.

The Hall

The visitor approaching the main entrance (fig 2), at the junction of the administrative and general-practitioner wings, gains a sense of spaciousness. The surrounding gardens are unfenced; and to the left of the door is a large covered verandah with open fields beyond. Inside the door is a large stone-flagged hall, of which the commanding feature is a "suspended" staircase, winding up without visible means of support except for a spine of reinforced concrete.

This staircase has a strikingly light and gay air, which is heightened by the huge window behind it, stretching from floor to roof. To the left of this staircase, beside the entrance door, is the dispensary; and on the other side is the corridor of the administrative wing. To the right of this, facing the entrance, is an inviting-looking inquiry bureau with its large window framed in unpainted West African hardwood. (West African hardwoods recur in variety throughout the building.)

The visitor, turning to the right to enter the general-practitioners' wing, passes two further large windows. That on the right, or outer, side is double, with a wide interval between the two layers where plants are growing

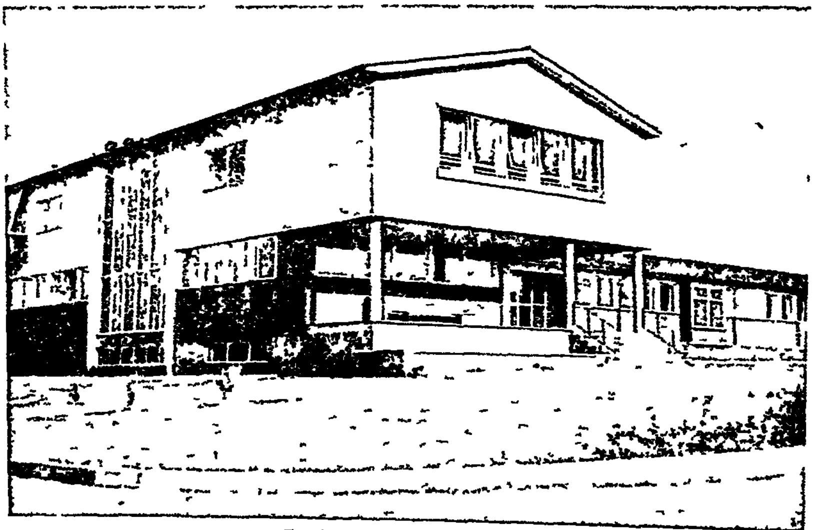

Fig 2—The main entrance

ments, such as synthetic resins and water repellent surfaces." But existing published work on this subject is bewildering: "The number of aliases, false clues, conflicting statements and fallacious deductions to be found there would arouse the envy of the most prolific writer of detective novels." The object of the authors is "to reduce this profusion to the smallest possible residue of useful and sober facts; to sort out the different names which really belong to the same thing, the different things which have the same name, the things which probably do exist from the things which probably do not, and to present what is known about the probable ways in which the things which remain react together to produce a clot," and it takes some 400 pages to present this residuum. Nevertheless we have nowhere seen it better or more clearly done. The book is divided into two parts: the first deals with the physiology of blood-clotting and some allied problems, the second with the disorders of blood coagulation. Both sections are divided into chapters at the end of which are most useful outline summaries. The first of three valuable appendices presents a scheme for differential diagnosis of coagulation defects, the starting-point being the determination of the "thromboplastin time" (old style prothrombin-time); the second gives properly detailed information about the preparation of reagents, and the third full descriptions of the techniques employed.

This book presents all schools fairly, glosses over no gaps, and gives the most readable and balanced account of the subject available today.

Les vomissements du nourrisson

EMILIO ROVIRALTA, head of the service of pædiatric surgery, Barcelona. Paris: Flammarion. 1952. Pp. 236. Fr. 1800.

THIS monograph does not, as its title might suggest, deal comprehensively with all the causes of vomiting in infancy, but only with those likely to be encountered by the pædiatric surgeon. The author places much value on radiography in the differential diagnosis of the various conditions, and the book is well illustrated with representative radiographs. Pyloric stenosis naturally receives a good deal of space, and the author has observed a striking coincidence of pyloric stenosis with partial intrathoracic stomach, to which he gives the name "syndrome phréno-pylorique." He favours medical treatment for hiatus herniæ, with œsophageal dilatation if stenosis is severe. Among other conditions described are volvulus of the stomach, œsophageal atresia, malrotations, and other congenital malformations of the gastro-intestinal tract. Most of the book is devoted to diagnosis, and it will be useful to physicians as well as surgeons who have to deal with babies.

National Health Service

A Guide for Practitioners. Editor: MAX SORSBY, L.M.S.S.A., vice-chairman, Local Medical Committee, London. Edinburgh: E. & S. Livingstone. 1953. Pp. 262. 12*s.* 6*d.*

EVEN after five years, many doctors in the N.H.S. have only a hazy idea of the administrative side, regarding it as a necessary evil, to be placated rather than understood. This book leaves little excuse for such an attitude. Those creatures of myth, the statutory bodies, here come to life and are seen to be composed of a great many public-spirited men and women, both inside and outside the profession, who devote much time and trouble to the thankless task of administering the service. Not all will agree, however, with Dr. Sorsby's somewhat gloomy picture of the decline of the status of the general practitioner, and he might have added a reminder that general practice is still very largely what the practitioner makes it. An account of the General Medical Services Committee and the British Medical Association is followed by a section on the Special Services, which, as Sir Allen Daley notes in his foreword, reminds doctors of how services needed by their patients, but which they cannot provide themselves, can be obtained. Dr. Sorsby lists some remediable deficiencies and argues forcibly for relieving the general practitioner from the responsibility for getting acute cases into hospital. Such an extensive organisation as ours should surely be able to shoulder this important part of the service, leaving the family doctor freer to do his proper work.

Dr. Horace Joules, looking forward, suggests decentralisation, with integration of all health and social welfare organisations in all-purpose local health authorities, each handling a population of about a quarter of a million. Students, he says, should be taught along lines which will fit them more closely for their future work. He believes that a salaried service will develop, and argues that a list of 3500 will preclude most doctors from giving more than the minimum diagnostic and therapeutic services. Both these points are debatable.

Human Parasites and Parasitic Diseases

K. D. CHATTERJEE, M.D. Calcutta, visiting physician R. G. Kar Medical College, Belgachia, Calcutta. 1952. Obtainable from Das Gupta and Co., 54, College Street, Calcutta, 12. Pp. 766. £6.

THE human parasites of the title are the protozoa and worms which are responsible for disease in man, and a few, like *Endolimax nana*, which are not, but which are important for differential diagnosis. The author describes their structure and biology fully, and the clinical features of the diseases they cause, including treatment, in some detail. He does not seriously discuss prevention and control, except drug prophylaxis, and the sections on transmission by arthropods are not always as comprehensive as one would wish.

Two other features are obvious to the reader. One is that the author's first love is for the protozoa, which are treated and discussed more fully and effectively than the worms; they get 469 pages and the worms 284. The other is that parasites not found in India are not so well done as those which the author obviously knows at first hand. The accounts of the trypanosomes, the schistosomes, and *Onchocerca volvulus*, for instance, fall far short of the excellent studies on the amœbæ, leishmaniæ, and malaria parasites. With these reservations, however, the book is very good. It is not the terse, dogmatic textbook so appealing to the undergraduate, but rather the comprehensive treatise, the reference book, in which one may find accounts of the theories and movements of research, and descriptions of experiments. The long lists of references enhance the value of this book to research-workers. The writing is lucid and the subjects are set out and discussed in a clear and orderly manner. The illustrations vary; the photographs are in general excellent, but some of the coloured drawings (for instance that of *Glossina palpalis*) are less successful. The production and printing are superb.

This is a major work which parasitologists will need and should have. For the next edition Dr. Chatterjee might with advantage ask the collaboration of authors who have met the non-Indian conditions at first hand.

Society and the Homosexual

GORDON WESTWOOD. London: *Gollancz.* 1952. Pp. 191. 9*s.* 6*d.*

THE general tenor of this book is reminiscent of Havelock Ellis: cool, descriptive, unprofessional, socially responsible. The author is well read in the clinical and legal literature of the subject, and has had advice and guidance from Dr. Edward Glover. He makes a sustained plea for more sympathy from the public and more leniency from the law. Most impartial readers will agree with the author that, as things are, a prison sentence is much more likely to do harm than good to homosexual men.

Materia Medica, Pharmacology and Therapeutics (29th ed. London: J. & A. Churchill. 1952. Pp. 512. 20*s.*).—Dr. A. H. Douthwaite took over this popular veteran from the original author, Sir William Hale-White, in 1931; and he has again smartened up his charge. For example, news of the antibiotics, anti-histamines, A.C.T.H., cortisone, and the methonium compounds has been deftly introduced as part of the revision. Some (they will not be students) may mourn the almost complete elimination of pharmacognosy; for the emphasis is now on pharmacology and therapeutics, with a nice tribute to Sir William and a less bustling age in the retention of *Materia Medica* in the title. The regularity with which a new edition has been called for through the years demonstrates the trust of generations.

Fig 3—A consulting room

That on the left reveals the inside of the square with two transplanted silver birches taking root and grass seeds tentatively sprouting The only furniture in the hall is a couple of cheerfully (and differently) coloured metal garden chairs

General practitioners' Wing

The corridor lined by doors leading into the general practitioners' suites is, like the others, notably silent This is due partly to the flooring of rubber squares, and partly to the substance of the walls and ceiling, and in the doctors' rooms double walls make the silence doubly silent On the right of the entrance to each suite is a capacious waiting-room (14 ft square), in front is an examination room (8 ft by 12 ft), and to the left is the consulting room (14 ft square, without fittings)

The waiting room has a large central table and, at present, 20 chairs—though it could take twice this number These chairs, of which the building contains 230, are comfortable, light, convenient, and, as chairs now go, cheaply come by They are made of unpainted 5 ply wood with a laminated back support which gives spring, they are readily stacked, and they cost £2 9s 6*d* each

The examination-room contains a couch and a wash-hand basin and board The consulting-room (fig 3) has a large desk and a wash hand basin and board

Each of these rooms, it may be noted, is differently floored, decorated, and furnished The doctor's room has a parquet floor of split hardwood, partly concealed by a thick carpet, and, in keeping with the present vogue the decoration of one wall differs impressively from that of the three others In this room, too, white-painted venetian blinds of malleable aluminium take the place of curtains

'Combined-services" Wing

Continuing anti clockwise round the square, the next wing is taken up by "combined services" This wing contains a sterilising room, to serve the whole centre, flanked by two dressing rooms It also includes a laboratory, at present used only as a side room, accommodation (but not at present equipment) for an X ray department, and a room (still unoccupied) for a chiropodist There is, too, an excellent gymnasium, with changing rooms attached, intended for use mainly by children with slight physical defects, and another room that will be equipped by the physiotherapist, who has lately been appointed

Child-welfare and School health Clinics

The third side of the square—opposite that occupied by the general practitioners—is devoted to child welfare and school-health service clinics Here the absence at present of an antenatal clinic may seem strange, but in Edinburgh such clinics are usually operated by the hospital service This wing, though connected with the others, can be approached by a separate entrance with, nearby, a covered perambulator park

Near this entrance is a bright children's playroom, with a scaled down lavatory and wash-room attached The floor is tiled with rubber in three colours—blue, yellow, and red—in check formation Most of one side is occupied by a large window, beyond which is a wired in verandah Of the other sides, two are cheerfully painted (one in grey, the other in scarlet), while the large wall facing the window is covered with flower patterned paper—a surprising, and perhaps well judged, deviation from the *Hey-Diddle Diddle* theme that might have been thought inevitable The ceiling is yellow

Another feature of this wing is a kitchen, which can be used for demonstration or for nourishment

The Fourth Quarter

To look at, the administrative wing, which leads back to the main entrance is as fascinating as any other administrative department But it does contain a lecture room and two studies, which are likely to prove useful in connection with the centre's welfare activities and also any teaching of medical undergraduates or postgraduates

Up the Stairs

The four dental surgeries, on the first floor above the administrative wing, have been constructed after much study, including a "mock up" of one surgery Facing north, each surgery has a bay which is wholly filled by a sloping window Two of the surgeries are given over to priority work under the local authority, one is for general dental services, and the fourth is destined for major operations The dentists have their own X ray room and a sitting room

The rest of this floor is taken up by two staff rooms (one for the medical staff) with a kitchen attached

DISCUSSION

This centre, like the few that have already been opened in Britain, is surrounded by question marks The building is not palatial—though the architects delude the visitor into thinking that it is—but it is large and has cost a lot of money, and no one would pretend that we are likely to see many like it taking shape up and down the country

Instead of centres having such a noble start, should they have the sort of start that can be followed up? But then again, how soon can a start of any sort be developed? The construction of health centres calls not only for much money but also for the cooperation of several interested parties, and some such parties are notably uninterested And what of the consumer's reaction? Can we plan for the future on the basis of a few exceptional efforts? May not these efforts recoil on the heads of their planners by attracting patients from far as well as near, thus disturbing a city's health services and dismaying workers in neighbouring areas who are doing their best with less elaborate resources?

What of laboratories and X ray departments? Are they wanted, are they to be run by technicians, and, if so, the urine, but, as a group, those with the ulcer beyond the lesser curvature and those with a duodenal ulcer excreted significantly increased amounts.

Of men with an antroduodenal ulcer all those with a history less than five years excreted a normal amount of urinary pepsinogen, whereas those with a history longer than five years excreted an amount which increased progressively with the length of history, up to about three times the normal figures.

The test is of little value in routine gastroduodenal diagnosis.

My grateful thanks are due to Dr. F. Avery Jones, who suggested this investigation and has been a source of advice and encouragement throughout. I should also like to thank Dr. G. Discombe for laboratory facilities and advice on technical matters, and Dr. R. Doll and Mr. A. Heady for suggesting the statistical methods used and for their critical reading of drafts.

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MUMPS ORCHITIS WITHOUT PAROTITIS IN INFANTS

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THE commonest cause of an acute swelling in an infant's scrotum is an indirect inguinal hernia, which may be very difficult to reduce. From these herniæ can be separated the cases where it is possible to "get above the swelling," and these fall into two groups: those due to torsion of the testicle or of the testicular appendix; and those of unknown cause. In these there is swelling of the testicle itself, with or without involvement of the epididymis, and with œdema of the scrotal skin. I report here one such case which was shown by serological tests to be almost certainly mumps orchitis, and suggests that this virus may be responsible in many other similar cases.

Although Hippocrates knew of an epidemic swelling near the ears sometimes associated with orchitis, and Hamilton (1790) gave the classical description of mumps, it is not until quite recently that we have understood that this is a generalised infection. It was known that orchitis occurred without parotitis in young adults during epidemics of mumps, and it was suspected that meningo-encephalitis might have a similar ætiology. Kane and Enders (1945), using serological tests, showed that the central nervous system was involved in mumps even when there was no parotitis. Henle et al. (1948) have shown that man can develop antibody to the mumps virus and excrete the virus from the salivary glands without any clinical evidence of mumps. Before this it was considered that mumps was an epidemic disease of the salivary glands that occasionally affected the gonads also.

The present conception is that mumps is due to a specific virus, which may be neurotropic (Philibert 1932) and circulates in the blood after multiplication, presumably in the salivary glands. During the viræmic phase the virus may become localised in several of the glands, of which the testicle is the commonest.

If infection of the central nervous system is always present it gives symptoms in only about 10% of cases, although a higher percentage show a cellular reaction in the cerebrospinal fluid (Candel 1944). However, the signs of meningitis may be the only indication of the disease, and the diagnosis can only be made with certainty by demonstrating rising antibody titres. The same is true for orchitis. After puberty orchitis is known to be common with mumps, varying from 16 to 64% with different epidemics at least half of the cases being only slight. Only one case of mumps orchitis in infancy has been published (Steiner 1896), and the diagnosis was based on circumstantial evidence, the infant having no parotitis. No reports have been published of any attempts to show by serological evidence that any infants have had an orchitis caused by the mumps virus.

Henle et al. (1947) have shown that, in mumps, two antibodies develop—a soluble antibody (S) and a virus antibody (V). The S titre rises quickly and starts to fall after three or four weeks, whereas the V titre rises and falls more slowly and remains high for a longer time. Traces may persist for months, if not longer. If complement-fixation tests are done on the patient's serum, it is possible, by tracing the rising and falling titres, to prove the identity of the infecting agent. With single tests a high S titre is good evidence of a recent infection. In infants there might possibly be both S and V antibody in various amounts due to passive transfer across the placenta; but this is only likely where the mother has had a recent attack of mumps. On this basis it should be possible to diagnose both meningo-encephalitis and orchitis in infancy if they are due to the mumps virus. Perhaps this virus causes symptoms in the central nervous system and the testis more readily than in the salivary glands in infants.

CASE-RECORDS

Case 1.—A boy, aged 7 months, was brought to the casualty department of this hospital on April 15, 1952, with a swelling of the right side of his scrotum. His mother said she thought he had been unwell for about a week, because he had had disturbed sleep and "kept lifting his bottom as though it hurts." She also thought that he had been feverish, and her doctor had confirmed this two nights ago. However, the infant had not vomited, fed well, and had normal micturition and bowel actions. On the morning before he was brought to hospital he developed a swelling of the right side of the scrotum, which became red.

On examination he was well nourished and rather flushed (rectal temperature 102·6°F), with a swollen reddened right side of the scrotum, which felt œdematous. The right testicle could be distinguished from the epididymis and was three or four times the normal size; it seemed tender and was firm to palpation. The cord was thickened, soft, and boggy, but contained no nodules. There was some enlargement of the inguinal glands, more marked on the right than the left. There was no enlargement of the salivary glands and no change in Stensen's duct.

Treatment and progress.—Mumps orchitis was suspected, even though the mother denied any contact or that there was any mumps in the neighbourhood. Sulphadimidine was prescribed as a precautionary measure, and the infant was given chloral and sent home. Two days later, when he was seen again in the outpatients department, the orchitis was subsiding. Two weeks later the orchitis had completely settled, but his mother volunteered that his older brother had developed parotitis, which had been diagnosed as mumps on April 20—i.e., five days after the patient had developed his scrotal swelling. Further, she had discovered that several of the neighbouring children also had mumps.

Complement-fixation tests.—To adduce further evidence for the diagnosis of mumps, this infant and his brother were referred to Dr. J. A. Dudgeon, who tested the sera for mumps antibodies. Blood was taken from both boys on May 13, about four weeks after the onset, and complement-fixation tests were made according to the method of Henle et al (1947) The following titres were found

	Mumps V	*Mumps S*
Patient	1 80	1 40
Brother	1 160	1 80
Control (negative)	Nil at 1 10	

These findings strongly suggest that both the patient and his brother were infected with the mumps virus about *four weeks before the blood was taken* At this time the infant had orchitis without parotitis

Case 2 —A boy, aged 6 months, was admitted to the Jenny Lind Hospital, Norwich, on April 11, 1951, with a tender swelling of the left side of his scrotum The swelling had developed during the twenty four hours before admission, and there appeared to be little systemic disturbance There was no vomiting, and the infant fed well

On examination he was well nourished, weighed 21 lb (birth weight 8 lb 7 oz), and had slight pyrexia (temperature 99 8°F), a clean tongue, no enlargement of the salivary glands, and no redness of Stensen's duct The left side of his scrotum was swollen, with the skin thickened and reddened The left testicle and epididymis were enlarged to about three times the normal size but could not be clearly distinguished from each other The cord was swollen but soft and contained no nodules It was possible to get above the swelling but there were palpable inguinal glands, chiefly on the left side It was decided to explore the scrotal contents to exclude a torsion of the testicle

At operation the same evening the scrotum was incised and the thickening of the skin appeared to be due to œdema The tunica vaginalis was thickened and, on being opened, let a little clear fluid escape, revealing a swollen firm testicle two or three times the normal size and bluish white except for a few punctate hæmorrhages The testicle was anterior to the epididymis, and the mesorchium was very short The cord was thickened with œdema but not twisted The tunica albuginea was not split The scrotal incision was closed, with a small rubber drain down to the tunica

Postoperatively the boy's temperature was 101 8°F next morning but fell to normal in the next twenty four hours The swelling rapidly subsided, and the infant was discharged seven days later

Follow up —Three weeks after discharge the infant was again examined and the testicle felt quite normal, but just *over a year later it was only half the size of the one on the right* side

DISCUSSION

When case 2 was treated, I suggested the diagnosis of mumps orchitis, but this was considered untenable because mumps orchitis was reputed not to occur in infancy and to be extremely rare before puberty In the light of the subsequent case 1, and because the findings at operation were so like those described by Smith (1912), Gall (1947), and Charny and Meranze (1948) in adult cases of mumps orchitis, I maintain that my suggestion was correct, and that this infant did have mumps orchitis

In the last four years, since the beginning of 1948, seven infants aged less than 1 year have been seen at Great Ormond Street with acute painful swelling in the scrotum, excluding cases of hernia Three of these proved to be cases of torsion, but the remaining four, including case 1, were diagnosed as non specific epididymo orchitis or partial torsion One of them was operated on, and the findings were very like those in case 2 Possibly all four of these cases were really mumps orchitis, if this is so, *mumps orchitis is commoner than torsion in this small series*

Treatment

The treatment of mumps orchitis remains controversial but in the more severe cases in adults drainage of the hydrocele by opening the tunica vaginalis relieves the symptoms and brings the temperature down by crisis (Nixon and Lewis 1946) Wesselhoeft and Vose (1942) maintain that it is necessary to incise the tunica albuginea as well to prevent the pressure atrophy of the contents However, the pathological studies of Charny and Meranze (1948) refute the usefulness of this procedure, they state that the material which they examined indicates that the testicular damage is not due to pressure atrophy and the testicular œdema is not severe They maintain that the seminiferous tubules are invaded in a patchy, but not usually complete, way with inflammatory cells, and the tubules so affected atrophy while the others survive This is not a complete confirmation of the findings of Gall (1947) or of the report of Wolbach cited by Smith (1912) Both these workers, while agreeing about the infiltration with inflammatory cells, consider that there is also a good deal of œdematous reaction within the testicle Several of the operation notes of reported cases of mumps orchitis mention the fact that, when the tunica albuginea is incised, the contents do not tend to be extruded Further study of this question seems to be required, because the advocates of opening the tunica albuginea maintain that testicular atrophy can be prevented if this is done soon enough, and the clinical benefit of merely opening the tunica vaginalis is well substantiated The problem is not easy to resolve, because testicular atrophy by no means always follows mumps orchitis, and, when there is some atrophy, spermatogenesis is usually diminished rather than abolished Sterility is rare, even after untreated bilateral orchitis, and the endocrine function of the testes seems to be unaffected The impotence which has been reported is almost certainly psychological

If my contention that the mumps virus is a common cause of orchitis in infancy is proved to be correct, and more cases are diagnosed as such, this diagnosis should only be made with the utmost caution Though it is relatively simple to differentiate between this condition and a hernia, even when the latter is irreducible and causing acute symptoms, it is not at all easy to differentiate between mumps orchitis and torsion In case 1 torsion was excluded because of the history of a week's lassitude, the pyrexia, and the palpation of a swollen testicle separate from the epididymis and mobile in the scrotum None of these points of differentiation was present in case 2 *If there is any doubt, the scrotal* contents should be explored at once, and, if the findings suggest orchitis, no further treatment is necessary, unless it be to incise the tunica albuginea, when a biopsy specimen could be taken If there is torsion, this can be dealt with Serological tests can be undertaken afterwards in the orchitis cases to establish the ætiology, but operation should not be postponed while their results are awaited

SUMMARY

The present concept of mumps and the usefulness of serological tests in diagnosis are discussed

A case of mumps orchitis without parotitis in an infant, where the diagnosis was supported by a complement fixation test, is reported, and a further similar case, which was operated on but in which no serological tests were made, is added

It is suggested that orchitis in infancy may often be due to mumps

All doubtful acute scrotal swellings should be explored by operation

I wish to thank the surgical staff of the Hospital for Sick Children, Great Ormond Street, *for permission to use their* records, Mr A B Birt, F R C S, for permission to publish case 2, and Mr *Denis* Browne, F R C S, *for much* helpful advice

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who is to supervise the work ? Indeed, is it economic to have an X-ray department for, say, 20,000 people ?

These questions are not new: what is new is the occasion, by practice, to grope towards some of the answers. Most of the questions concern the general practitioner; and unfortunately to some of them no final answer is possible until the rôle—and the will—of the practitioner in this new age is seen more clearly. This, of course, is no reason for not pressing on with health centres; for these may themselves help to determine the practitioner's rôle and will. The immediate need is for experience with centres large and small, elaborately and simply equipped; and it is to be hoped that the opportunity at Sighthill will be fully seized by equipping the X-ray department, and by trying different forms of operation and control both here and in the laboratory.

As to economy, at Sighthill the playroom, the gymnasium, and one or more of the staff rooms are perhaps dispensable. Elsewhere in the building—and especially in the general-practitioners' suites—advantage will no doubt be taken of the flexible design to experiment with smaller rooms, in order to establish the sizes that are most economical of space without being inconvenient or oppressive. Perhaps, too, experience may show that practitioners and patients will accept less rigidly secluded waiting-rooms.

With regard to construction materials, the copper roof is a little flourish that will not always be repeatable; and similarly hardwood may be less prominent in later centres. But, all in all, the designers have made good use of ordinary materials, abjuring the exotic.

Meanwhile, plans are well advanced for the second Scottish centre, which is to be built at Stranraer, near the hospital. It is to be rather smaller than that at Sighthill; but this will not stop the Health Department's architects from feeling sedately elated at the prospect of once more escaping from the fantasy of the drawing-board into the actuality of bricks and mortar—and colour.

SENIOR REGISTRARS

THE Minister of Health and the Joint Committee for Consultants and Specialists have been discussing the position of those senior registrars in England and Wales whose appointments will soon be ending in accordance with the arrangements made in 1951 for reducing the number of senior-registrar posts to bring it more into line with the estimated number of vacancies for consultants and senior hospital medical officers in the various specialties. The Joint Committee have represented to the Minister that to avoid undue hardship a longer time should be allowed for this adjustment to be brought about, so that in suitable cases these senior registrars and former senior registrars may have longer to seek higher hospital appointments or other medical posts outside the hospital service. The Minister has come to the conclusion that transition to the senior-registrar complement envisaged by the plan of 1951 may be smoothed in that way without detriment to the hospital service.

Accordingly the Minister has authorised hospital boards to retain senior-registrar posts in excess of those covered by the plan of 1951, for a period not extending beyond the end of 1955 at the latest, where this will avoid extra staff having to be employed in other grades and, fully suitable candidates are forthcoming for the retained posts.

As the engagements of the present holders come to an end the posts which are to be retained will be advertised. Applications will be entertained from the present holders, from other senior registrars whose appointments will end in the near future, and, in certain circumstances, from former senior registrars. The term of these posts will be one year, but boards will be free to allow a second year where other employment has not been obtained by the end of the first year.

Though the holders of these posts will continue to be free to compete for higher hospital appointments, they will do so in competition with other candidates, and their retention as senior registrars will not give them any special claim or constitute any guarantee that they will be successful in the competition.

In addition, there will still, of course, be nothing to prevent a retiring senior registrar from applying for, and being appointed to, a post within the training establishment. If, however, he is reappointed to the same post, the term of his reappointment will be limited to two years.

The Joint Committee have expressed their agreement with these arrangements.

MINISTRY'S OBSERVATIONS

The Ministry of Health, in a letter to hospital boards, states:

"Where it is decided to retain a post it should be advertised at the appropriate time as a post for one year, with a possible extension to two years (but not beyond 31st December, 1955) if the holder has not obtained other employment in the meantime. The present holder will be free to compete for it and applications should also be entertained from any other persons in their fourth or subsequent years as senior registrars in the specialty and those who though not now holding posts as senior registrars have occupied such posts for three or more years and have vacated them since memorandum RHB(50)106/BG(50)96 was issued on 6th November, 1950. The applications should go to the Appointments Committee for consideration and recommendations. It is most important that there should be a genuine competition which gives equal opportunity to the present holder of the post and to others similarly situated.

"Where a transitional post becomes vacant before 1st January, 1955, it may be advertised again but transitional posts becoming vacant on or after that date should be abolished and other arrangements made for the work hitherto performed by the holders.

"In some regions where the reduced establishment of senior registrars has already been reached, it may be that in the case of a few of the posts which have been abolished difficulties have been caused in the staffing of the hospitals and to the men in posts similar to those which this scheme is designed to relieve. In such circumstances the Minister would see no objection to the revival of a post temporarily as a transitional post, but this should be exceptional. . . .

"In their own interests it should be made clear to successful applicants that their selection for transitional posts must not be taken as conferring on them any special claim to higher hospital posts or constituting any guarantee of their being successful in due course in the competition for these posts. . . .

"It is essential that this transitional arrangement whould not interfere with the four years training plan and that the number of posts within this plan should not be reduced on account of the retention of the transitional posts. The Minister regards it as of the greatest importance that the opportunities of younger men who wish to start training in the senior registrar grade should not be prejudiced by the new arrangements.

"There can, of course, be no objection to a senior registrar who has completed training in one specialty transferring to another specialty and completing a further four years in this second post; such interchange may be of great benefit to the specialty. There is also nothing to prevent a fourth year senior registrar from applying for the same or another post in the same specialty which falls within the training plan, but it is essential that his greater experience should not determine his appointment rather than that of a potentially better future consultant and in any case no senior registrar should be reappointed to the same post for more than an additional two years. The criterion for selection should always be that the applicant likely to make the best consultant at the end of his four years training should be chosen."

One or two schemes had been set going whereby patients could be discharged from hospital properly and rather more quickly than before At Cambridge, with the coöperation of general practitioners and the district nursing service, some surgical patients with clean operations were discharged from hospital within four or five days He agreed with Lord Moran that the teaching of nurses should be done at the bedside We seemed at present in danger of getting too many nurses trained to too high a standard They were in fact going to be not very good doctors rather than very good nurses The nurse so trained looked for an administrative job, no other would give an increased salary

Lord Haden-Guest regarded dilution of the nursing profession as a defeatist policy We must do something which was more productive of efficiency It was true that there was a great deal of difference between ordinary nursing and nursing in a mental hospital, but the use of the word "dilution" was unfortunate, because there was already too much dilution in the nursing profession It was better to have carefully trained people rather than those who had just picked up knowledge as they went along He saw no immediate solution in prospect, and the Nuffield report did not in fact offer one What it offered was a survey of the facts, and he would like to know what action the Government were prepared to take to remedy the situation revealed in the report

Lord Woolton, Chancellor of the Duchy of Lancaster, replying for the Government, said that the discussion might lead one to think that the situation was worse than it actually was The nursing force in this country had increased by two and a half times in the last 50 years The demand had increased even more, but that also was a sign of progress, more care was being taken of the sick Nursing staff was recruited not so much by stereotyped regulations as by showing people who might enter the nursing profession that it was held in high esteem The Nuffield report offered a wealth of new information, and the Minister of Health had at once summoned his advisory committee to consider what action should be taken Lord Woolton was not so depressed as some of the speakers by the fact that 74% of the basic work in hospitals was done by student nurses A great deal of that work did not require high professional skill, but it did require a great deal of personal kindness In talks with nurses he had been horrified to find that promotion went in the line of administration It was a great pity if highly trained nurses were being called upon to do clerical work which involved an entirely different sort of capacity and different attitude of mind It seemed to him from this report that they ought to see what reorganisation could be obtained both in the direction of the personnel employed in administration and also in the fuller use of orderlies

In the last four years the number of full-time trained nurses in England and Wales had gone up from 40,000 to 47,000 and student nurses had gone up from 42,000 to 50,500, there had been a drop from 12 000 to 11,500 in assistant nurses, and other nursing staff had risen from 16,000 to 25,500 making a total of 135,000 full-time nurses compared with 110 000 in 1948 In 1948 the shortage of beds due to the shortage of nurses was 57 000 Last year the figure was 28,500 When the Minister of Health urged the hospital authorities to cut staff he stipulated that this must not be done by throwing domestic work on to the nurses The reason for the restriction of the engagement of nurses was that the Minister felt that the problem was becoming to a considerable extent one of distribution of nurses Some places were considerably better off than others, though still short and in order that the nurses might be employed to the best advantage the Minister brought in the restriction order

Therapeutic Substances (Prevention of Misuse) Bill

Mr Iain Macleod the Minister of Health, in moving the second reading of this two-clause Bill[1] in the House of Commons on May 13, explained that the Penicillin Act, 1947, had been found to be too narrow because it applied only to antibiotics Clause 1 of the Bill was, he admitted, extremely wide, and on principle he did not like to ask for such wide powers But he thought it right to do so because we were in an age of immense advances in chemotherapy and we did not know what sort of substances would be discovered He was therefore asking for powers to make regulations similar to those made under the 1947 Act in respect of any substance which appeared to the Minister of Health capable of causing danger to the health of the community

Isoniazid, the drug which had given rise to this clause, was a simple chemical substance it was cheap to make and it could be bought over a chemist's counter At the moment the Pharmaceutical Society had suggested to their members that it should only be supplied on a doctor's prescription But Mr Macleod felt that this arrangement did not discharge his duty to the public and that it was more satisfactory that he should be enabled to make regulations for isoniazid similar to those that could be made for antibiotics

According to the Bill, before making a regulation he would have to consult the Medical Research Council and he was prepared to give an assurance that he would also consult the manufacturers concerned This was the general practice under the Penicillin Act and he would be prepared to continue these consultations provided it was clearly understood that the final decision must be taken only on medical grounds

The second clause, popularly known as the penicillin for pigs clause was, Mr Macleod admitted, to use the Prime Minister's accidental coinage, a pigmeal solution to a new problem It had been found that the addition of a minute quantity of antibiotics to feeding stuffs had a remarkable effect in encouraging the growth and fattening of pigs The Medical Research Council had assured him that this addition would have no adverse effect upon human beings who ate the meat thus produced He would guard against the possibility of creating by this wider use of antibiotics a sort of black market in penicillin by ensuring that the antibiotics were used in such a way that they could not be extracted and used for medication At the moment he would only make regulations applying to penicillin, because this was the only substance of this kind of which we had sufficient supplies But it was possible that later aureomycin and terramycin would also be used for this purpose

Mr Macleod admitted that he had several times boasted that he had not introduced any legislation, in extenuation he pleaded that this was only a little Bill, which wisely extended an Act which had been found to be too narrow and which brought forward a new and most interesting use for antibiotics which might have a most important effect on our food-supplies

QUESTION TIME

Hospital Nursing Staffs

Mr R W Sorensen asked the Minister if the distribution of nursing staff among hospitals had improved as a result of the reviews of hospital staffs made at his request by hospital authorities —Mr Iain Macleod replied It is too early to assess the results of the reviews of hospital staffs, but I hope that they will make a useful contribution to the improvement in the distribution of nursing staff which I am seeking to achieve by this and other means

Mr Sorensen In the meantime is anything being done to secure a more equitable distribution of the nurses available since some of the hospitals are virtually understaffed and others grossly overstaffed ?—Mr Macleod That was one of the thoughts in my mind when I issued the circular which has received so much criticism, but other progress is going on all the time The line that seems most promising at the moment is the seconding of nurses, which is being done increasingly over the country, particularly to sanatoria

Mr A Blenkinsop Will the Minister at the same time make sure that there is no suggestion of compulsory secondment, in view of the attitude which I am sure the nursing associations would take on the matter ?

Hospital Circulars and Regulations

Mr S Hastings asked the Minister if he would issue a booklet with index giving a summary of the regulations issued by his department to hospitals since the appointed day which were still in operation —Mr Macleod replied I assume the hon

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[1] See *Lancet* Feb 7 1953 p 280

In England Now

A Running Commentary by Peripatetic Correspondents

It is of course impossible to get inside the mind of a tubercle bacillus, to appreciate its hopes, joys, conflicts, and despairs ; but we can safely assume that, in common with all other living creatures, it is deeply conscious (*a*) of having a value, and (*b*) of being incomplete. Otherwise why should it go on going on as it does ?

Its behaviour is certainly changing. Either it has learned by experience (which, experience teaches us, is extremely unlikely), or else its world-environment, to which it has to adjust, has been altering in character. Not so many human generations ago (but millions of T.B. generations ago) it used to make its home in young human beings, where its standards of living were so prodigal that it ran through the available resources in a matter of months, bankrupting its host who then, as you might say, died of galloping consumption. Thus large families of bacilli would perish miserably and be buried in a common grave—all except the few who, going while the going was good, achieved extremely hazardous airborne emigration to virgin territories. They were hectic times. It was a short life, but, we can only hope, a gay one.

Airborne emigration (or deportation) still helps to solve problems of overpopulation and famine, but nowadays the immigrant seems to behave more circumspectly. Many are content to join the closed community of a primary focus. Kept on short commons, in cramped quarters, they live under a monastic discipline ; but they survive. Some fine old families must have been eking out an existence on the same small holding for more than half a century. There can be no promiscuous population-increase and no overcrowding. The B.C.G. in particular seems innately schooled to respect its billets and does not go " chopping down doors and staircases for firewood," and longevity is its reward for this consideration.

But " for aye to be in shady cloister mew'd " is not every bacillus's cup of broth. Given half a chance, bolder spirits will break loose and abuse hospitality. There is this difference, however : their host has met their sort before and has become (to coin a phrase) somewhat allergic towards them. The would-be marauders are hampered at every turn by Defence of the Realm Regulations. Life is altogether much harder for them. All legislation, they will learn, is devised to prolong life, not to make it easier or more enjoyable.

The introduction of antibiotics is doing much to ensure the survival of the few : those privileged classes who are snugly ensconced in their family seats. Vagrants, even if they do not perish, are rendered impotent to found dynasties and eventually must die of old age without issue. And now there is a worse threat which the race will have to meet. A.C.T.H. would appear to burn down the fortresses and turn the inhabitants loose, in the byways, where they fall an easy prey to the antibiotics. But, as their leader might remark " We have faced fearsome odds in the past and have survived. The magnitude of the threat will not dismay us. We will hold our ground and show our true colours in every clime—even where baths of acid may blanch the weaklings. Our ancient cultures must not be allowed to perish."

* * *

The missionaries of the 19th century are often criticised for having insisted that their naked converts in tropical countries must be clothed. The missionaries are accused not only of having disrupted local customs, but also of introducing unhygienic habits among those who are unable to wash their garments as often as is desirable in a hot climate, of having thus encouraged body parasites and the diseases they carry, and of having spread malnutrition by preventing the synthesis of vitamin D from the action of the sun on the uncovered skin. Nowadays missionaries are better informed, and few of them think that, unless an African or a Polynesian is forced against his or her will into some garment at least as unrevealing as an Edwardian bathing dress, salvation is impossible.

But times have changed, as debates in the Nigerian house of representatives in Lagos show. Several Nigerian politicians have urged that legislation should be introduced to make nudity illegal. They argue partly on the grounds of decency and modesty ; but it is clear that the main reason for their proposal is political. In countries which are striving for self-government, the word " primitive " is considered insulting, and people who go around without clothes are looked upon as primitive. To make things worse, visiting journalists and anthropologists even take photographs of these naked villagers, and when these appear in magazines abroad it is alleged that they damage the prestige of the whole Nigerian people. In the debates it was left to government officials to point out that to insist that, for instance, the pagan tribes on the plateau in Nigeria wear clothes is to ignore the customs and traditions of the people, for in some areas wearing clothes is still considered a sign of loose living. These European officials then found themselves attacked for attempting to keep the country in a state of servitude.

* * *

It sometimes seems to me that what is really holding up the great chlorophyll controversy is our lack of a unit of scent ; and here I believe I can help. After some thought, I have rejected the olf and the pong, and I now finally come out in favour of the smel. One smel shall be the effect produced at standard temperature and pressure, and at one metre distance from the nose, of—what ? A red, red rose ? A piece of musk ? One milligramme of methyl mercaptan ? Perhaps a kipper could be kept at the National Physical Laboratory under exactly the right conditions, and we could standardise from there, the technique to be known as the Beezer Test. The most delicate redolence would come in millismels ; a microsmel for a fragrance ; at the other end of the scale we would have the kilosmels and macrosmels produced by farmyards, glue factories, and sulphuric-acid works.

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How fitting that the giant slab of glass and concrete which houses the U.N. secretariat should dominate the East River. New York is the gateway through which successive waves of immigration have flowed into America, each leaving a backwater in the city. Italians, Germans, and Jews have their own colonies, and Chinatown is a fantastic little oriental pond among the skyscrapers. Now the floodtide of Puerto Rican immigrants pours into the East Side unchecked by McCarran since they are American citizens ; there they are packed 8 or 10 to a room and the local cinemas show films in Spanish. My barber is a German who scarcely speaks English, the janitor is Austrian, and the elevator operator Italian. Yiddish newspapers are sold at the nearest street-corner and a babel of foreign tongues and broken English surrounds the Irish traffic cop on Broadway. In this cosmopolitan cauldron of first-generation Americans, the only " foreign " accent is a British one.

Ward rounds are linguistic exercises. There is the South American coronary who speaks a little French, and the Pole who describes his hæmatemesis with gestures and a few words of German ; and today an S.B.E. from East Germany lay under a huge placard bearing the painfully inscribed cri de cœur, " I HURT ALL OVER."

* * *

The dog is a poodle, somewhat careless in his dress and casual in ablutions, but nevertheless of an apparent innocence that attracts everyone. He belongs to my neighbour, but a few days ago was in my garden, as is his custom, and honoured us (in our absence) by entering the house. There he found a box of thyroid tablets within his reach. They were active tablets, made by a well-known firm and of the strength of gr. 1½. This he could not have known, for he at once consumed gr. 147. Today he is in the garden again and I have the honour to record the important clinical observation that thyroid gland has no obvious or statistically significant effect upon voice production in the poodle. But there is a look in his eye which I have not noted before. I suspect some lowering of the innocence threshold.

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Now that judges are prepared to decide for us not only which papers we ought to read but also which to believe, may we look forward to a decision—from the House of Lords of course—in the case of Walshe *v.* Fulton : in *re* the Motor Cortex ?

Member has in mind circulars issued to hospital authorities Some consolidation on particular subjects has already been effected, and this will be extended as circumstances permit A useful index to all circulars is prepared annually by the Birmingham Regional Hospital Board and is widely circulated

Tuberculosis Among Immigrants

Mr **SAMUEL STOREY** asked the Minister what proportion of the notifications of tuberculosis referred to persons who had recently entered the country from Eire —Mr **MACLEOD** replied The present returns from medical officers of health make no distinction as to nationality

Mr **STOREY** In view of the fact that the incidence of tuberculosis is 50% higher in Eire than it is in this country, and also that in some parts of the country a large proportion of infections are amongst persons who have recently come from Eire, does the Minister not think it a good thing to insist upon radiographical screening and a certificate of fitness before allowing people to come from Eire to seek employment in this country ?—Mr **MACLEOD** There are a number of other people and Ministries involved in this The hon member is quite right that a certain amount of difficulty has been caused by people coming from Eire, and I will see whether we ought to get more information on this subject and whether steps should be taken at the ports and airports

Mass Radiography

Dr **BARNETT STROSS** asked the Minister how many mass-radiography units were in use in England and Wales, what was the approximate number of cases X rayed per week or month, and how far the number of units in use was to be increased in the near future —Mr **MACLEOD** replied 63 units are now in use Last December the 62 units then in use made 190,386 examinations 5 additional units have recently been allocated and arrangements are in hand to bring them into operation

Bone-conduction Hearing-aids

Replying to a question, Mr **MACLEOD** stated that up to April 18, 958 patients in England and Wales had been supplied with bone conduction hearing aids

Fibre-glass and Industrial Injury

In answer to a question Sir **WALTER MONCKTON**, the Minister of Labour, stated that the Factory Department had maintained a close watch on the manufacture and handling of fibre glass in factories, but there was no evidence to show that it was injurious to the lungs, although it might give rise to a mild skin irritation which soon disappeared Samples of materials consisting of fibre glass and resins which were now being used in the aeroplane industry were being investigated microscopically by the chemical branch of the Factory Department to determine the size and nature of the dust given off when components made from these materials were machined

Vivisection Licences

Mr **PETER FREEMAN** asked the Home Secretary how many certificates were issued last year to perform experiments on living animals under the Cruelty to Animals Act, 1876, in how many cases no experiments were performed, and whether he would consider curtailing the issue of such unnecessary certificates —Sir **DAVID MAXWELL FYFE** replied In 1952 I granted 678 licences, valid for five years During that year 1335 licensees performed no experiments under the Act Every year the revocation of licences which have not been used during their currency is reviewed

Mr **FREEMAN** Many of these 1335 have never performed a single experiment since they first received a certificate, and will the Minister not consider curtailing the number of certificates issued in this way ?

Sir **DAVID MAXWELL FYFE** We keep a check on current years to find the licensees who have not performed an experiment When we have discovered this we work back to see whether they have up to that time not performed an experiment for, say, four or five years If they have not we prune the list

Use of Agene in Flour

Lord **HANKEY** asked Her Majesty's Government for lists of countries in Europe and North America in which the use of agene in flour for human consumption was permitted and of those countries in which agene was prohibited

Lord **CARRINGTON**, the joint parliamentary secretary to the Ministry of Agriculture and Fisheries, replied The treatment of flour for human consumption with nitrogen trichloride (agene) is permitted in the United Kingdom, Eire, Holland, Germany, Norway, Denmark, Italy, Sweden, and Finland It is prohibited in Canada, the United States, France, Belgium, Spain, Portugal, Switzerland, Turkey, and Greece

Medical Posts in the Civil Service

Dr A D D **BROUGHTON** asked the Secretary to the Treasury in which medical journals he now advertised the vacancies for appointment of registered medical practitioners in the Civil Service —Mr J A **BOYD CARPENTER** replied None, Sir Since no recruitment is taking place, vacancies are not at present being advertised at all

Dr **BROUGHTON** Can the Financial Secretary state in terms which are more easy to understand why there have been no advertisements of civil servant medical officer posts in the medical journals recently ? Is it possible that the Financial Secretary is in disgrace with the medical profession, and that the British Medical Association has imposed a ban upon the publication of advertisements of this sort ? If that is so, would he inform the House what the trouble is about ?

Mr **BOYD CARPENTER** Those issues, particularly the one relating to myself, are of an intriguing character, but they are wholly different from the point raised in the question The hon. gentleman asked in which medical journals vacancies are advertised, and the answer that I have already given him is " None "

Synthetic Detergents Inquiry

Mr **HAROLD MACMILLAN**, Minister of Housing and Local Government, in a written reply said that after consulting the Secretary of State for Scotland and the Minister of Health he had appointed a committee with the following terms of reference

> " to examine and report on the effects of the increasing use of synthetic detergents and to make any recommendations that seem desirable with particular reference to the functioning of the public health services "

The chairman of the committee is Sir Harry Jephcott, F R I C, and the 14 members include the following doctors

Dr N R Beattie, principal medical officer Ministry of Health (attached to Ministry of Housing and Local Government) Dr J C Cruickshank, professor of bacteriology as applied to hygiene London School of Hygiene and Tropical Medicine, Lieut -Colonel E F W Mackenzie director of water examination, Metropolitan Water Board

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Public Health

Smallpox

No new cases were reported from Yorkshire in the week ended at noon on May 19, but the Baildon miner who was admitted to hospital with smallpox on May [illegible], died on May 13 The total number of confirmed cases in the outbreak is 30, including 8 deaths The last patient who might have spread the disease was taken to hospital on May 5 Although the period of surveillance of known contacts has almost expired special vigilance must be maintained for a longer period because the source of infection of 4 patients who fell ill several weeks ago has not been traced

Diphtheria Immunisation in Antrim

In his report for 1951, Dr P V Pritchard, medical officer of health for county Antrim, says that not enough children are being immunised against diphtheria to maintain a safe level of protection in the county Figures for 1951 indicate that less than 30% of the children are being immunised Dr Pritchard points out that the facilities for immunisation in the county are not as extensive as elsewhere, for the county health committee's instructions are that immunisation should be carried out solely by general practitioners except in a small minority of cases dealt with by medical officers of the public-health department at long established clinics The committee lately reconsidered the matter, but decided to continue the present system and not to extend immunisation in clinics Some Antrim doctors claim that a satisfactory number of children are being immunised and that the figures are unreliable because returns are incomplete But Dr Pritchard says that an inquiry into the quantity of diphtheria prophylactic supplied to doctors in the county has failed to support this claim In his view the only solution is to offer the public the alternatives of immunisation by the family doctor or at a health committee clinic

Letters to the Editor

THE PROBLEM OF PEPTIC ULCERATION

SIR,—Michael Smyth cannot goad me into a quarrel. I have too high a regard for him. His enthusiasm and his "fine careless rapture" are a joy to all who have the privilege of his friendship. I think, however, that he begs the question when he says: "If it were possible to cure a patient's duodenal ulcer, and leave him with the whole stomach, this should be done: better a whole stomach than an austerity remnant with its dumping syndrome and all that."

It is not possible. Gastrojejunostomy leaves, not a whole stomach, but a stomach with a hole—a very different matter. Having secreted a ferment in response to a meal, the stomach now finds when it gets to work that there is no meal left, and nothing to digest but itself. Gastrojejunostomy does not cure ulcer, but merely shifts the seat of attack somewhere else. A review of the records of New Lodge Clinic would give Mr. Smyth the low-down on some of his friends.

With regard to "austerity stomachs," the whole point of my article, if it had any, was to debunk and discourage the "austerity stomach" with its dumping syndrome and all that. A good gastrectomy does not dump. It does not develop another ulcer. Why therefore do a bad one that is likely to go wrong merely because it is easier to undo when it does go wrong?

Let us get rid of this eponymity in gastric surgery. Most of it is wrong anyway. All gastrectomies are modifications of the Billroth I or the Billroth II, and who modified them is anybody's guess. Who was Hofmeister? Who was Polya? Neither Michael Smyth nor I were operating when gastric surgery was being designed, but Richard Lewisohn of New York, the man who introduced blood-transfusion to surgery, was. Lewisohn was first assistant to Czerny, the inventor of the Lembert suture, and knew all the men whose names are now history. He writes[1]:

> "The reader may be surprised to hear that about thirty years before Hofmeister and Polya the principles of both methods were described, the first by von Eselsberg in 1889, the second by Kronlein in 1887."

The so-called Hofmeister technique, as reference to any textbook of the time will show, was merely a transverse gastrectomy with a reduced opening—an unsatisfactory job. The wide application of proximal jejunum to lesser curve was introduced by Lake and Finsterer. Finsterer's plan of attaching transverse colon to stomach has been abandoned in the modern operation because it distorts the proximal jejunum, and because the leak it was designed to forestall does not happen.

London, W.1. HENEAGE OGILVIE.

JUNIOR HOSPITAL STAFF

SIR,—I have been privileged to read the paper by Hurst, Linfoot, and Woodhouse before publication.[2] I think they state the present difficult position very well, but I must disagree with several of their conclusions.

1. I do not think there is an absolute shortage of doctors, only a maldistribution. If all the established hospital posts were filled (which is plainly not possible) we should I think find that many were redundant. Most teaching hospitals have more residents and registrars than the work warrants. Their posts are training posts. But must all this training be done at the teaching hospitals? Throughout the country there must also be a considerable number of experienced doctors, mostly ex-registrars, whom luck or inclination has not led into general practice.

2. To do laboratory or radiological investigations *before* the patient has been examined would in my view lead to a great waste of these facilities, which are already under great pressure.

3. General practitioners in their part-time rôle as clinical assistants can be of very great help in all the outpatient departments. But, economically speaking, they can be of little use in those positions where a continuous emergency service is required. They can never replace the resident surgical officer, the medical registrar, the obstetric registrar, the resident anæsthetist, the casualty officer, and the orthopædic registrar. In any of these positions at least six clinical assistants would be required to replace one resident, and even then there could be no satisfactory continuity in treatment and policy.

The provincial hospitals actually find it most difficult to find good doctors to fill these particular jobs. Good house-physicians, house-surgeons, and obstetric house-officers are not so scarce, because this type of resident job helps the prospective general practitioner.

Much has been written in the press recently about the unenviable job of the casualty officer. Further successful (or even unsuccessful) litigation against junior casualty officers will lead to extinction of the species.

The reasons why good registrars are difficult to come by in the peripheral hospitals are also widely recognised. A registrar post even in the best non-teaching hospital very rarely leads to senior-registrar and so to consultant status.

I would like to bring forward two suggestions which if found acceptable would do a great deal to improve the medical services given by the provincial hospitals:

1. The post of registrar should be abolished at all teaching hospitals. No senior-registrar jobs need be held outside teaching hospitals. The direct effect would be that the ambitious senior house-officer at the teaching hospital would be forced to spend at least two years as a registrar at a peripheral hospital before he could apply for a senior-registrar post at the teaching hospital. In this way the peripheral hospitals would get better registrars than many can get at present. These doctors themselves instead of often being largely supernumerary would get a very full practical training which would be completed academically after the return to the centre.

2. A new category of S.H.M.O. casualty officer should be created to take charge of the casualty room in every hospital in which the volume of work could carry such an appointment. The primary duty of this doctor would be to see each casualty patient at least once. If the patient is seen by a junior doctor in the evening then he *must* be referred to see the senior casualty officer next morning.

I believe there are sufficient experienced ex-registrars willing to take such posts, as they require experience and maturity of judgment but no higher qualifications.

Royal Albert Edward Infirmary,
Wigan. F. R. ZADIK.

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[1] J. Mt Sinai Hosp. 1947, 14, 470.

[2] This paper appears on p. 1037.

TRICHOMONAS VAGINITIS

SIR,—Whatever may be the source of the infection in trichomonas vaginitis, it is certainly not the bowel. Refutations of the bowel hypothesis are to be found in the standard works on the subject, and a mass of evidence has been built up against it through the years.

Stabler, Feo, and Rakoff[1] inoculated cultures of the intestinal trichomonad, *T. hominis*, intravaginally. 50 patients were inoculated, 151 inoculations being made in all. Not only were these workers unable to produce vaginitis, but they also demonstrated that the protozoa could not even be recovered after a short interval. Subsequent vaginal inoculations with *T. vaginalis* produced a typical infection in 8 out of 10 of these patients.

An investigation carried out by American workers into the relative incidence of *T. vaginalis* in the vagina and *T. hominis* in the bowel in 200 women showed that, whereas 23% harboured *T. vaginalis*, in only 1% could *T. hominis* be demonstrated. This is surely not the result one would expect if the disease was "in most cases self-communicated" as Miss Landau (May 16) suggests.

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[1] Stabler, R. M., Feo, L. G., Rakoff, A. E. *Amer. J. Hyg.* 1941, (C) 34, 114.

Medicine and the Law

The State-aided Plaintiff

A CORRESPONDENT has taken exception to a few sentences in our leading article of May 2, where, in speculating on the causes of the undoubted increase in claims against medical practitioners and hospitals we mentioned the influence of the Legal Aid and Advice Act, 1949. The State aided plaintiff, we suggested, has his free run; 'State aided litigation tends to be fought to a finish without compromise'; the ordinary deterrents of having to pay his own costs and the costs of a successful defendant do not apply. Our correspondent's unfortunate experience contradicted this view. Though a State aided plaintiff, he found himself obliged to compromise his claim for a sum less than his disbursements. The Act and its attendant regulations, he found, imposed upon him a liability for payments to the Legal Aid Fund which came near to a threat that he might be made bankrupt even when he had succeeded in a claim brought on solid grounds.

His case indeed was hard; we may hope it was exceptional. He was claiming damages for professional negligence on the part of his family solicitors who had ignored a specific direction. When they denied liability, he put the matter into the hands of a second firm. He understood himself to be entitled to legal aid; the firm thought otherwise but, after reference to the Law Society, he was found to be qualified. The defendant solicitors offered to settle on the basis of some three-fifths of his claim. He was persuaded to accept this offer whereupon the defendants paid into court a very much smaller sum and the action went on. He was naturally indisposed to accept this smaller sum thus paid in; but his own solicitors warned him that, if the verdict he might obtain should not exceed that sum, he would be personally responsible for all the costs accruing after the date of payment into court.

Though this is not the place in which to set out, or even to summarise, the Act and regulations, it is certainly true that the new Legal Aid system is a flexible scheme which rightly seeks to satisfy the needs of the citizen and yet to protect the Exchequer and the taxpayer. In effect the State aided litigant makes what contribution he can to the Legal Aid Fund. If the assisted person wins, his position as regards costs is much the same as if he had received no legal aid; his unassisted opponent has apparently to pay full "party and party" costs—not merely 85% of them. The Fund has a first charge on any property, wherever situated recovered by or preserved for the assisted plaintiff. If the assisted person loses, his liability for the sum awarded is the same as that of an unassisted person who has lost. As regards costs, however, the Act limits his liability to "the amount (if any) which is a reasonable one for him to pay, having regard to all the circumstances, including the means of all the parties and their conduct in connection with the dispute." His house, his furniture, and the tools of his trade must be left out of account in assessing the amount of costs that he must pay. Under the regulations the court may order him to pay "such amount, if any, as the court thinks reasonable, having regard to all the circumstances." Much will depend on the interpretation given by the courts to that flexible word "reasonable." Meanwhile, in the phrase of the author of the leading textbook on the subject (himself an active participant in the framing of the new procedure), the privileges given by the provisions of the Act "may well provide an assisted person with a bargaining weapon of the 'Heads I win and tails you lose' variety against an unassisted opponent." That opinion, despite the converse experience of our correspondent, goes far to justify the general tenor of our previous statement.

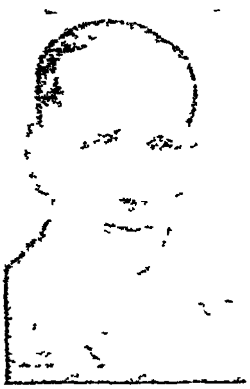
Obituary

KENNETH NORMAN ABBOTT HERDMAN

M A, M D Edin., D.A

Dr Herdman consultant anæsthetist to Leith Hospital who died on May 7 had approached his specialty by way of general practice. After graduating at the University of Edinburgh as M.A. in 1924 and as M B four years later, he held house-appointments at Leith Hospital a clinical tutorship at the Edinburgh Royal Infirmary, and a clinical assistantship at the Eye, Ear, and Throat Infirmary.

As a Territorial he was called up from his busy practice in Edinburgh at the beginning of the late war. He became a specialist anæsthetist at No 23 General Hospital in the Middle East then he went as anæsthetist to one of the units in the Eighth Army, the 15th (Mobile) Casualty Clearing Station. With No 15 he took part in the memorable advance from the Battle of Alamein along the North African coast to the end of the campaign at Cape Bon.



James Bacon & Son

Returning to civilian life he gave up general practice to concentrate entirely on anæsthesia and J. A. R, on behalf of his fellow-surgeons, writes

'Kenneth Herdman was one of those invaluable and all too rare doctors who specialise after a long experience in general practice. His experience in general medicine, and his gifts as a well-qualified and expert physician allied to his own sound judgment, gave him the power of accurately assessing patients' general conditions before, during and after operation. This was a great boon to his surgical colleagues, who sought his advice freely in the handling of their cases. They knew that his experience combined with superlative technical excellence, made him absolutely safe and reliable for their own work and also when need arose for themselves and their relatives.

"Tall gallant and debonair Kenneth Herdman never spared himself, and never complained, though his health had been precarious for some time. Ever considerate of others, it was characteristic of him that he was invariably punctual at all his engagements. This punctuality, with his unassuming cheerful efficiency, was particularly appreciated by the operating-theatre staffs with whom he worked. He was an outstanding man and he set us all a noble example of courage, unselfishness, and skill."

Dr Herdman leaves a widow and two sons.

CHRISTOPHER JOSEPH McSWEENEY

M.A. Dubl., M.D N U I, F R.C.P I, D.P H.

Dr McSweeney, medical superintendent of the Cork Street, Fever Hospital died on April 17 at the age of 54. A man of energy, ability, and character he was about to enter the most important stage of his life's work.

He was born at Cork and educated in that city at the Christian Brothers' College and at University College, from which he graduated as M.B with first-class honours in 1921. After holding an extern assistantship at The Rotunda Hospital, Dublin, he took the D.P.H., and in 1925 he was appointed assistant M.O H. for Cardiff where two years later he was promoted to be deputy M.O H. He also lectured on infectious diseases at the Welsh National School of Medicine.

In 1930 McSweeney took his M.D degree; in 1933 he became M.R.C.P I, and in the following year he returned to Dublin to take charge of Cork Street Fever Hospital. He brought with him a reputation for medical administration and during the years, through many vicissitudes he persisted in his purpose of providing new buildings for the hospital. The task was lately completed, and he moved his residence to the new hospitals only a few days before his death.

No-one working with these protozoa in the laboratory can fail to be impressed by the many wide differences they exhibit. *T. hominis* has entirely different growth requirements from *T. vaginalis*, and fails to grow in media which support a profuse growth of *T. vaginalis*.

Uncritical acceptance of the view that the infection originates in the bowel can only obscure the true facts and postpone fuller investigation of the actual means of transmission of this troublesome infection.

Liverpool. M. G. McENTEGART.

DIAGNOSIS OF ACUTE MENINGITIS IN INFANCY

SIR,—Dr. Haworth, in his article of May 9, rightly calls attention to the frequent absence of the "classical signs" of meningitis in infancy and to the necessity for early lumbar puncture. Recent emphasis in your leading article of April 11 on the hazards of lumbar puncture should not deter us from the use of this valuable diagnostic aid. The wide range of antibiotic and chemotherapeutic agents now available should further reduce the mortality. But how often is the hospital clinician needlessly handicapped by the indiscriminate use of these drugs which, in many cases, only result in disguising the clinical signs and making the identification of the causal organism difficult or impossible? In these difficult cases a full history from the general practitioner is always helpful, but what is probably more important is a detailed account of the treatment given prior to admission.

W. P. SWEETNAM
Halifax General Hospital. Consultant Pædiatrician.

DIET AND IMMUNITY

SIR,—Your leading article of May 9 ends with a statement for which there is surely little evidence. This statement reads:

> "... we can learn from the Scottish blackface ewes and their lambs that ... the most effective interval between injections of the antigen [A.P.T.] is two months, ... and that routine immunisation with A.P.T. should not be applied to infants during the first few months of life."

In one of the papers under review [1] it was shown that, with the particular dosage used in ewes, an interval of nine weeks between injections was definitely better than an interval of four weeks; but no other interval was tried. The optimum interval depends on the size of the dose and perhaps on the species of animal, and it is probable that an interval of three months can be regarded as best in the immunisation of young babies with A.P.T.[2] It was also shown [1] that a rough correlation existed between the total passive maternally conferred diphtheria antitoxin of lambs, and their response to the first and to the second injection of A.P.T. given in a course of active immunisation. Considerable if not total interference with the primary response was caused by the presence of sufficient antitoxin to neutralise half the A.P.T.

Evidence had previously, however, been published [2] showing that babies can be successfully immunised by two doses, each 0·5 ml. of A.P.T., if the titre of maternally conferred antitoxin is below 0·04 unit per ml. at the time of the first injection.

In recent unpublished work carried out at these laboratories and in collaboration with Dr. N. R. Butler of University College Hospital, we have been investigating the efficiency of three prophylactics in the immunisation of babies. All consisted of purified toxoid, partially or totally adsorbed on mineral carriers. Of 167 babies receiving the first injection at the age of about 1 week and the second injection either at 6 or 14 weeks, 161 (96·3%) had active antitoxin titres above the Schick level when measured at the age of 9 or 12 months. Of 115 babies receiving injections at the ages of 6 and 14 weeks, all but 1 had titres above the Schick level when 9 or 12 months old. This population was a random sample, 6·4% of whom had cord-blood titres of 1·0 unit per ml. or more, compared with 7·1% in 3000 samples of cord-blood tested here during the last few years.

From the evidence available, it would appear that a very high proportion of babies born at the present time can be satisfactorily immunised against diphtheria during the first few months of life, so long as a precipitated or adsorbed prophylactic is used. Attention has, however, been drawn to the fact that a large proportion of failures might follow the use of plain fluid purified toxoid, if the first of three injections were given at or before the age of 10 days.[3]

Wellcome Research Laboratories,
Beckenham, Kent. MOLLIE BARR.

INVOLVEMENT OF AUTONOMIC NERVE-FIBRES IN DIABETIC NEUROPATHY

SIR,—As Dr. Allwood and Mr. Burry (April 18) point out, it is not necessary to have a rate of heat loss as great as 240 kg. cal./hr./m^2 if only gross changes in blood-flow are to be estimated by means of skin-temperature measurements. It is sufficient if the extremity of a nude subject is placed in a cold box or if the extremity of the warmly dressed subject is exposed in a cold room.[4] Even under these conditions, however, the estimation of blood-flow changes in the feet by skin-temperature measurements may be especially difficult. In my own experience 25% of normal subjects show only a twofold increase in foot blood-flow (measured plethysmographically) in response to prolonged heating of the forearms and hands in water-baths at 45°C, and this increase may be too small to detect by means of skin-temperature measurement.

Pickering and Hess [5] found that it was sometimes difficult to produce vasodilatation in the feet, and they described one normal subject in whom they completely failed to produce vasodilatation (estimated by skin-temperature measurement). Because of this, failure to produce a marked increase in the skin-temperature of the feet, in response to warming the body elsewhere, has to be regarded with circumspection before it is interpreted as being due to autonomic involvement.

Even if one assumes that the skin-temperature measurements of patients with diabetic neuropathy are a reasonable reflection of the limb blood-flow, failure to produce vasodilatation in response to warming cannot be interpreted as being due to disease of the autonomic nervous system unless certain other possibilities are excluded. For example, occlusive vascular disease may be responsible for this effect, and the fact that 'Priscol' (tolazoline) may produce vasodilatation in patients suffering from diabetic neuropathy is not adequate evidence of the absence of vascular disease. It is quite conceivable that priscol may dilate a diseased artery although physiological stimuli will not. Disuse of the limbs with a consequent decrease in their metabolic activity and increase in their venous pressure may also affect the vasomotor reactions. Lewis and Pickering [6] have shown that the relative disuse of one limb even for half an hour will produce differences in the skin-temperature of the limbs which persist after warming the body. Similar differences are produced if the initial temperature of one limb is lower than that of the other.

It is for these and similar reasons that I suggested that Dr. Martin's conclusions (March 21) should be examined with caution.

Physiology Department,
St. Mary's Hospital Medical School,
London, W.2. A. McPHERSON.

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1. Barr, M., Glenny, A. T., Howie, J. W. *J. Path. Bact.* 1953, 65, 155.
2. Barr, M., Glenny, A. T., Randall, K. J. *Lancet*, 1950, i, 6.
3. Barr, M., Glenny, A., T. Hignett, S., Randall, K. J., Thomson, A. *Ibid*, 1952, ii, 803.
4. Fetcher, E. S., Hall, J. F., Shaub, H. G. U.S. Air Force Memorandum. March, 1949.
5. Pickering, G. W., Hess, W. *Clin. Sci.* 1933, 1, 213.
6. Lewis, T., Pickering, G. W. *Heart*, 1931, 16, 33.

Meanwhile he was responsible for much of the teaching of his specialty He was lecturer in infectious diseases and deputy professor of preventive medicine at Trinity College, and consultant in fevers for the National Children's Hospital, Dublin He was examiner in fevers for the D P H, for the Dublin medical schools and to the nursing councils of Northern Ireland and Eire In 1936 he was elected fellow of the Royal College of Physicians of Ireland, and from 1937 to 1939 he served the college as censor

"Christopher McSweeney," writes J D, "had four main characteristics which were the foundation of his success He was an excellent teacher, clear and logical in his exposition and impressive in his manner with students and postgraduates He was an excellent clinician, with an encyclopædic knowledge of medicine and with a balanced and clear judgment He was a successful writer with a scholarly approach his book *A Clinical Approach to Fevers* was published two days before his death Lastly, he was a delightful person to know combining strong opinions with an easy tolerance of the views of others He was pleasant company and will long be remembered in Dublin for his wit His death at the beginning of the work of his great new hospital, and at the transition period during the reorganisation of the Irish health services, will be felt seriously in Dublin"

Dr McSweeney married in 1923 Miss Evelyn Harvey Donegan and they had one son

Dr L M ROSE

M J writes "Given only a few years more, Toby Rose would assuredly have made a place of note for himself in his chosen specialty Under a mask of casualness, which was sometimes apt to deceive his elders, he was a critical and most observant physician, who judged his own performance by rigorously perfectionist canons But he had other qualities which made him more than just a good clinician in a simply mechanical sense He was a man of taste, with fastidious and eclectic enthusiasms The natural temper of his mind was unhurried and traditionalist in outlook, and gave him a flavour somehow faintly uncontemporary His liking for old-fashioned forms was no dull conservatism but sprang partly from appraisal of their value as a discipline, and partly from appreciation that tradition at its best contains, for the subtle, a distinctive element of fun It was from this that his particular love of Oxford and for the Royal Navy—otherwise sufficiently dissimilar institutions—stemmed

"He was a gay companion and a good conversationalist who could easily make the small happenings of everyday life take on a vivid and amusing air He was a really brilliant mimic, and when he assumed the persona of his victim became instantly gifted with the power to parody his thought as well as the mannerisms of his speech It was characteristic that, throughout the months in which his last illness was making steady inroads upon his health, he said practically no word of it to anyone except in terms so vague and light as to rouse no suspicion of its gravity He was a brave man, and it is proper that we should mourn him"

Appointments

FARLEY, D L B, M B Lond, F R C S surgical registrar, The Hospital for Sick Children Great Ormond Street London

MARCUS RAPHAEL, M D Lpool, F R C S whole time asst. consultant general surgeon, hospitals in the central Wirral area

PLEASANT, D V, M B Brist. appointed factory doctor, N Bristol, Gloucester

[illegible] M B Lond F R C S hon ear nose and throat of St John and St Elizabeth London

M R C P house physician The Hospital for eat Ormond Street, London

Welsh Regional Hospital Board

BUCKLEY, DORA, M R C S, D T D asst. M O in thoracic medicine (S H M O), Cymla Chest Hospital Neath

EDMUNDS P K D M R C S D M R D consultant radiologist

F R C S asst. traumatic surgeon H M C

mb D.A consultant anæsthetist, wddach H M C

Notes and News

WORLD HEALTH ASSEMBLY

THE sixth World Health Assembly, which opened in Geneva on May 5,[1] continued its discussions last week After he had been sworn in as the new director general of the World Health Organisation Dr M G Candau addressed the assembly The name of his predecessor, Dr Brock Chisholm had, he said, become identified during the last few years with the basic ideals of the organisation infinite respect for the dignity of man, wherever and under whatever conditions he lived clear and serene vision of the forces which would decide his fate, and unbroken determination to devote every day's energy and work towards the creation of a peaceful world in which the material, spiritual and cultural progress achieved by each nation would benefit all Dr Candau knew that he would justify the trust that had been placed in him if he was able to follow the path laid down by Dr Chisholm

At the first meeting of the committee on administration, finance, and legal matters, Mr M P Siegel, assistant director general, said that, as far as its regular budget was concerned, the organisation was in a wholesome financial position During 1952, 95% of the contributions due for that year from active member states had been collected But a serious situation had arisen, in the financing of the expanded programme of technical assistance for 1953[2] The total estimated cost of the year's programme had been set at $9,455,000, but the amount earmarked for W H O by the United Nations Technical Assistance Board was only $5,078,000 Wherever possible, therefore, new activities planned for the technical assistance programme had been postponed, and the utmost economy had been achieved in carrying on with existing schemes Generous help had been given by UNICEF, and certain projects had been transferred to the regular W H O programme As a result of these and other measures, it had not proved necessary to draw on the working capital fund to meet this serious difficulty

The committee on programme and budget adopted a resolution, to be placed before the assembly, which hoped that "longer term arrangements for financing future programmes will be made," and that in future the technical assistance programme would be planned in priority categories to allow for possible reductions in income

The assembly unanimously agreed to a request for membership from Nepal, which becomes the 80th member state of W H O The assembly also voted, by 43 to 6, with 13 abstentions, to welcome the return of the republic of China to active participation in the organisation, and to accept a lower assessment until her financial position had improved

THE DISABLED IN THE WORKSHOP

THE story of the Michael Works is one of splendid and undeserved failure Mr John Arthur, who founded this factory for severely disabled men in 1945, and was its manager, has now written an account[3] of the work done during its three years of independent life, the lessons learnt, and the results for the disabled men he befriended Of some 80 men who entered the works, no fewer than 40 were able to return to open industry

Mr Arthur's aim was to prove that men so severely handicapped as to be considered unemployable could often do as good a day's work as the able bodied, more—that they could maintain themselves economically, and need owe nothing to charity or public funds The Michael Works experiment demonstrated this beyond cavil When it was handed over to Remploy in 1949 the balance sheet showed that in each year of its operation it had paid its way It lost its independence only because it had too little capital to tide over the difficulties occasioned by the fluctuating purchase tax of 1948 Much had been learnt, however, not only about goods and markets but about disabled men and their response to opportunities for steady work

The second part of the book discusses the different kinds of disabilities these men were able to overcome—crippling rheumatism, cerebral palsy, deafness, amputations, epilepsy and tuberculosis Through the book runs Mr Arthur's sympathy and common sense, and his inspiration

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[1] See *Lancet*, May 16 1953, p 986

[2] *Ibid*, Jan 31, p 249

[3] Through Movement to Life London Chapman & Hall 19[illegible] Pp 93 7*s* 6*d*

HOSPITAL COSTING

SIR,—Dr. Avery Jones (May 16) expresses surprise at my two examples of hospital extravagances of bed-linen and farms and gardens. As regards bed-linen he says that there are important fallacies, for the reason that on stocktaking ward deficiencies are taken into account but not any excesses. This is news to me, as indeed is his statement that if a complete stocktaking of the entire hospital is taken on a single day these apparent discrepancies largely melt away. This is certainly not my experience. Apart from the point that there should be no excesses in wards, which itself indicates extravagant issuing, if Dr. Avery Jones will turn to p. 19 of the Health Service Accounts for 1951–52 he will see the words "including stock taking" and one assumes that this refers to a complete stocktaking, and not merely to wards. He says further, that "it does appear that the stocktaking system in hospitals needs overhauling." This presupposes that a stocktaking system already exists. Does it?

I agree with Dr. Avery Jones as far as gardens are concerned. They are essential amenities. But the gardens (and farms) referred to in the Auditor-General's report are not "amenity" gardens, which are included under the heading "Maintenance of Buildings, Plant, *and Grounds*," but gardens which exist for the sole purpose of providing produce which would otherwise be purchased. Farms are trading departments whether run by a hospital or a commercial concern, and the principle of business should therefore be observed. My point is that if the farms cannot be run without loss then hospitals should abandon them and purchase their supplies in the open market. They will find this method far cheaper. If Dr. Avery Jones wants a fallacy he will find it in the statement often heard, but never justified, that supplies from hospital gardens are better than those bought in the open market. "Amateur farmers" are a source of considerable extravagance to hospitals.

I welcome his point about bed occupancy. There is no doubt that much may be done to secure economies in this direction; but I question his statement that it is "perfectly feasible to achieve a 93% occupancy." It would be interesting to have the views of others on this point; I fear I have already taken up too much of your space.

ADMINISTRATOR.

SIR,—May I put in a plea for an old-fashioned method of securing economy which is in danger of being forgotten altogether? Having selected at each level of administration officials who are capable of exercising some judgment, is it not possible to allow them to do so? In other words, can we not get back to some measure of personal responsibility? One is a little sickened by the cowardice of the present system, in which an offender is seldom personally blamed but punishment by directive is visited on all for the defect of one.

If costing could trace wastefulness back to its source, it would show up the responsibility of the individual, but it is doubtful if such a degree of efficiency can be obtained. Costing is more likely to lose itself in a bog of false comparisons. It tends, too, to push up the standard of spending constantly, because those whose expenditure is about the average feel a comfortable complacence which encourages them to spend a little more, while those at the bottom of the scale feel a positive duty to catch up. In the modern hospital world the only real crime of administration is to fail to get your share from the hat.

If units of administration on every level were really allowed to handle their money, if an official knew that the success or failure of his budget was solely the concern of his committee and himself, "don't care" and "try it on" would disappear from the service. At present it is asking much of the most conscientious administrator not to fall back on them.

HOSPITAL SECRETARY.

SIR,—Writing about hospital costing last week, Dr. Avery Jones referred to the need for special study into the subject of bed occupancy and mentioned the possibility that this might be undertaken by an independent body. This subject, expanded slightly into the term "making the best use of the available beds," was the first special study chosen by the King's Fund Hospital Administrative Staff College; and work has been going on for more than a year. A number of experiments have been conducted during that time in hospitals of many different kinds, and it is hoped that a report will be issued by the early autumn.

King Edward's Hospital Fund for London,
Hospital Administrative Staff College,
2, Palace Court, London, W.2.

P. H. CONSTABLE
Principal.

ASCORBIC ACID AND GLUCOSE-1-PHOSPHATE IN RHEUMATOID ARTHRITIS

SIR,—The excellent paper by Dr. Lovell and his colleagues (May 16) was of especial interest to us, for we have also been investigating the action of glucose-1-phosphate in rheumatoid arthritis. In a pilot experiment, single doses of 25 mg., 50 mg., or 100 mg. were given intravenously to some 20 patients with rheumatoid arthritis. The clinical impression was that in some cases there was a transient improvement. A "double blind" experiment is now being made with photographic assessment[1] to see if the clinical impression can be confirmed.

It is clear from Dr. Lovell's paper that in the 4 cases investigated glucose-1-phosphate did not have an effect comparable with that of cortisone and that it is unlikely to prove useful as a treatment for rheumatoid arthritis. Our experiment is being continued for it is of some theoretical importance to see if there is any evidence that glucose-1-phosphate has a beneficial effect in some cases even though it be transient. We have already discussed[1] in some detail the difficulties in assessing the transient effects on rheumatoid arthritis of irregularly acting drugs and how the effects of rapidly metabolised substances may be missed.

The discussion by Dr. Lovell and his colleagues was very stimulating. They suggest that the means by which cortisone diminishes the tuberculin reaction may be different in the guineapig and in man. We would point out that, if the hypothesis of Long et al.[2] explaining the desensitising action of cortisone is true for the guineapig, then there is some evidence to suggest a species difference between the guineapig and man with respect to cortisone and ascorbic-acid metabolism.

Long et al. have suggested that cortisone desensitises by facilitating the oxidation of ascorbic acid to dehydroascorbic acid and that there is a shift of the equilibrium, ascorbic acid $\rightleftharpoons$ dehydroascorbic acid, to the right. But in man Stewart et al.[3] have shown that the ascorbic acid in the blood is partly in the dehydro form (20%) and that the effect of cortisone is that the dehydroascorbic acid vanishes without altering the total amount of ascorbic acid, which is then present only in the reduced form. This corresponds to a shift of the equilibrium to the left in man—the opposite of that proposed by the Long hypothesis in the guineapig. If there is a shift of the equilibrium to the right, a rise in electrode-potential (oxidation-reduction potential) would be expected; but we have shown[4] that in man cortisone causes a fall in the electrode potential of the subcutaneous tissues, corresponding to a shift of the equilibrium to the left—again the opposite of the supposed change in the guineapig.

We have also found in man and the rabbit that the intravenous injection of ascorbic acid produces a considerable

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1. Loxton, G. E., Le Vay, D. *Lancet*, 1952, i, 1280.
2. Long, D. A., Miles, A. A. *Ibid*, 1950, i, 492; Long, D. A., Miles, A. A., Perry, W. L. M. *Ibid*, 1951, i, 1085, *Ibid*, ii, 902.
3. Stewart, C. P. Horn, D., Robson, J. S. *Biochem. J.* 1953, 53, 254.
4. Loxton. G. E., Le Vay, D. *Nature, Lond.* 1953, 171, 524.

EXPERT COMMITTEE ON INFLUENZA

THE World Health Organisation recently set up an expert committee on influenza whose first session was held in Geneva in September, 1952 The report of this meeting is now published[1] The committee discussed a number of theoretical and practical aspects of the study, prevention, and treatment of influenza, and it has made recommendations on diagnostic procedures, collection and distribution of epidemiological information, and control measures Stress is laid on vaccination as the best method at present available for preventing influenza, but vaccination is still, in the committee s opinion, in the experimental stage, requiring further study and improvement Control measures against possible influenza pandemics and the many difficulties which might arise in this event are discussed This is a subject where there is room for more detailed recommendations on the control measures which are possible if a pandemic should arise in the near future and on research into alternative emergency methods Appendices describe technical details of laboratory diagnosis.

RESEARCH AND MENTAL HEALTH

LAST February the National Association for Mental Health held a stimulating conference on 'the practical application of research and experiment to the mental health field' At the time we were able to report some of the papers and discussions[2] Now—with commendable speed—the full proceedings of the conference have been published, and may be had from the association.[3] They read extremely well and will be useful for reference

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University of Cambridge

On May 9 the following degrees were conferred

M.A—B W Davy
M.D—* Gordon Osborne, J W B Forshaw P B Kunkler
M Chir—J P. Stephens

* By proxy

Those who will receive honorary degrees on July 13 will include Mr H R Dew, Bosch professor of surgery and dean of the faculty of medicine of Sydney University on whom the degree of SC D is to be conferred.

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on May 16, with Mr Arthur Gemmell, the president, in the chair, the following were elected to the council

As representatives of the fellows—A M. Claye Leeds J F Cunningham Dublin V J F Lack, London, D McK Hart, Glasgow J A Stallworthy Oxford

As representatives of the members—A L Deacon Birmingham, A S Duncan, Edinburgh.

The following were admitted to the fellowship

H. H Fouracre Barns J W D Buttery H C Callagher A B Concanon S E Craig Gladys V S Cunningham J N I Emblin L W Gall D S Greig Uma Pati Gupta T N Hart A M Hartnell William Hawksworth O V Jones C W A Kimbell W M Lemmon J T Louw D J MacRae Mary H Maveur S D Meares Shivaprasanna Misra Coralie W Rendle Short, Kathleen M. Robinson, Dorothy M Satur L J te Groen R A Tennent, E W L Thompson H K Waller J A. Waterman, B H Watson S A. Way J L Wright

The following were admitted to the membership

C H Borsman D M Brodie Patrick Bruce Lockhart K G Cockburn S B Cooper Janette G Cowie H J G de Villiers H G Dixon Margaret M Downes E M Edwards A H Foate G S Foster A. E Fyfe G H Garfield J M Gate Louis Goldman, N G Gourlay, Michael Grant R W Grayburn David Hay G C S Hunter Valentine M. Husband Sarah I Jacob R A Kenihan Kamala Khadenga H H Kirk B V Kyle J C McCawley John Macpherson J S McVeigh Jean Murray Jones T J M. Myles Ll M Norburn E M O Dwyer Selvam Panchalingam Evelyn Peters R. M. McK Pratt M J M Solomons W K. Sutton, T A. Thompson, R. S Wurm

Faculty of Ophthalmologists

The following have been elected officers for 1953–54

President Mr J H Doggart immediate past president Mr O M Duthie vice presidents Mr R C Davenport and Dr John Marshall hon. secretary, Mr E F King, hon. treasurer Mr E G Mackie

University of Sheffield

Dr P G Walker has been appointed a part-time honorary lecturer in biochemistry

Royal College of Surgeons of England

At a meeting of the council on May 14, with Sir Cecil Wakeley, the president, in the chair, Mr E Stanley Lee was admitted to the court of examiners, and Mr R V Cooke was re elected a member of the court Mr C Le Q Darcel and Dr L M. Franks were appointed as Imperial Cancer Research Fund lecturers

The Gilbert Blane medal for 1953 was awarded to Surgeon Captain J G Holmes (Alverstoke) for his work in the promotion of naval medical science and naval medical hygiene The Begley prize was awarded to R Danbury (Royal Free)

Prof F Davies (Sheffield) and Mr J Dobson (Wigan) were admitted to the fellowship having been elected as members of the college of twenty years standing A diploma of fellowship was granted to K D Shastri (Bombay)

Diplomas of membership and postgraduate diplomas were granted to those named in our report of the comitia of the Royal College of Physicians of London (*Lancet*, May 9, 1953, p 956)

The *Faculty of Anæsthetists* will hold the first examination for their fellowship in November Applications for examinerships are invited in our advertisement columns

Scottish Society of Anæsthetists

The following have been elected officers for 1953–54

President Dr W M Shearer Vice president Dr I M C Dewar Hon secretary Dr A G Miller, other members of the executive council Dr T J C MacDonald Dr H W C Griffiths Dr A Tindal Dr M Muir, Dr R Milne Dr M C MacQueen, and Dr R. G Grieve

The prize which the society is offering annually for the best paper submitted by a registrar was awarded to Dr F S Preston.

Papal Honour

The Pope has created Sir Daniel Davies a knight commander of the Order of St Sylvester in recognition of his services to the Roman Catholic Church and in particular to Cardinal Griffin and to priests and other patients at the Hospital of St John and St Elizabeth, London

International Congress of Hippocratic Medicine

This congress will be held at Evian from Sept 3 to 6 under the presidency of Professor Laignel Lavastine Further particulars may be had from Monsieur Paul Maubert Direction Cachat, Evian, Haute Savoie, France

Committee on N H S Costs

The committee which the Minister of Health has appointed to inquire into the cost of the National Health Service is now prepared to receive written evidence from persons and organisations Memoranda of evidence should be sent as soon as possible either direct to the secretary of the committee, Mr E Halliday Ministry of Health, Savile Row, W 1, or in Scotland via Mr R P Fraser, Department of Health for Scotland, St Andrew s House, Edinburgh, 1

Committee of Inquiry on the Rehabilitation of Disabled Persons

Any person or organisation who wishes to give evidence to this committee which has been set up by the Minister of Labour and National Service, the Minister of Health, and the Secretary of State for Scotland, under the chairmanship of Lord Piercy, should send to the joint secretaries of the committee Ministry of Labour and National Service, 32, St James's Square London, S W 1, a memorandum of the views they wish to put forward

N A P.T Canadian Exchange Scholarships

The Canadian exchange scholarships offered by the National Association for the Prevention of Tuberculosis have been awarded this year to Dr Bertram Mann, consultant chest physician at the Royal Halifax Infirmary, Yorkshire, who will leave England for three months in Canada early in September, and to Dr J J Laurier, assistant medical director of the Sacred Heart Hospital, Montreal, who has already arrived in England fall in the electrode potential of the subcutaneous tissues. This finding lends support to the suggestion that some ascorbic acid is normally present in the tissues in the dehydro form, for if it was all in the reduced form no change would be expected, the electrode potential depending on the proportion of the reduced to the oxidised forms and not on the absolute amount. Of course the situation is not as simple as this; for there are no doubt numerous other oxidation-reduction systems influencing the electrode potential, some of which may not react with the electrode.

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[1] *World Hlth Org techn Rep Ser* 1953 64 Obtainable from H.M. Stationery Office, P O Box 569, London, S E 1 1s 6*d*.

[2] *Lancet* Feb 14, 1953 p 340

[3] N.A.M H 39 Queen Anne Street London W 1 Pp 133 6s 6*d*. Reports of the sessions on mental deficiency mental illness and child care may be had separately at 2s 7½*d* postage paid.

It would be worthwhile repeating the experiments of Stewart et al. and the electrode experiments in the guineapig, for this might reveal a species difference between the guineapig and man and at the same time afford an additional test, from a different aspect, of the Long hypothesis and perhaps help investigators to avoid some as yet undiscerned and unintentional confounding.

Dr. Frank Fletcher, of Benger's Ltd., kindly gave us the glucose-1-phosphate.

Brook Hospital,
London, S.E.18.

GEOFFREY E. LOXTON
DAVID LE VAY.

TOXIC EFFECTS OF PHENYLBUTAZONE

SIR,—The common toxic sequelæ of phenylbutazone ('Butazolidin') therapy—gastric disturbance and occasionally hæmorrhage, dermatitis, and swollen feet due to salt retention—are as a rule not serious, and seldom occur unless the dosage is large. Patients with rheumatoid arthritis who do not show rapid benefit from 400 to 600 mg. (2 or 3 tablets) of phenylbutazone per day are probably better without it. Agranulocytosis, however, is a different problem because it can so easily be lethal. Here also it was hoped that there would be no danger with small dosage, except when the patient was sensitised by intermittent medication.[1] The case reported here shows that continuous administration of phenylbutazone in small dosage, even for a short time, may cause agranulocytosis, and that routine white-cell counts are useless. Even when symptoms of toxicity are noted and phenylbutazone is withheld, neither the total white-cell count nor the percentage of granular cells may give any indication of danger; the number of cells may decrease steadily after the phenylbutazone has been withdrawn.

In the present case there was an aplasia of all the marrow elements, reflected later in the decrease of hæmoglobin. The value of treatment with adrenocorticotropic hormone (A.C.T.H.) in such a case is still undecided, but antibiotic therapy and blood-transfusion were obviously essential. It therefore seems that the only precautions that can be taken against the dangers of phenylbutazone aplasia are to avoid intermittent dosage, especially with gaps of 10–20 days which may encourage sensitisation, and to warn the patient that any fever, malaise, or sore mouth or throat must be reported at once, when antibiotic therapy should immediately be started and the white-cell count watched. The clinical value of phenylbutazone in certain cases is such that with these precautions its use is justified, but its haphazard use is most dangerous.

A married woman, aged 46, with five months' history of rheumatoid arthritis, was admitted to hospital on Feb. 2, 1953, with involvement chiefly of the hands and wrists. The erythrocyte-sedimentation rate (E.S.R.) was 82 mm. in one hour (Westergren) and Hb 60% (8·9 g. per 100 ml.). Treatment in the first instance consisted of rest, physiotherapy, and intravenous iron from Feb. 11 to March 2, a total of 1·53 g. being given.

Phenylbutazone therapy was started on Feb. 16, and the patient took 1 tablet (200 mg.) orally twice daily, with good clinical response within a few days. After taking this dose for ten days she developed a patchy erythematous rash on the arms and chest, without other symptoms. On Feb. 26 the dosage was reduced to 1 tablet daily and 'Antistin' was given. On Feb. 27, the white-cell count was 13,200 per c.mm. (polymorphs 80%). The rash cleared after five days.

Five days later, on March 7, she complained of vomiting and diarrhœa, and next day the rash reappeared and the temperature rose rapidly to 103°F. The phenylbutazone was discontinued on March 9, but pyrexia and rash persisted, the latter becoming more extensive and papular. The mouth was dry and a little sore, but not ulcerated, and there was no sore throat. On March 12 the white-cell count was still normal—7500 per c.mm. (polymorphs 75%). On March 13, four days after the phenylbutazone had been stopped, the first signs of developing agranulocytosis appeared in the peripheral circulation. The clinical symptoms gradually improved, and from March 15 the patient was apparently well and symptomless. For eight days, from March 17 to 25, there were no polymorphs in the peripheral blood, and the white-cell count was 850–1900 per c.mm. During the same period the Hb decreased from 83% (12·3 g. per 100 ml.) to 58% (8·6 g. per 100 ml.). Examination of the sternal marrow on March 18 showed:

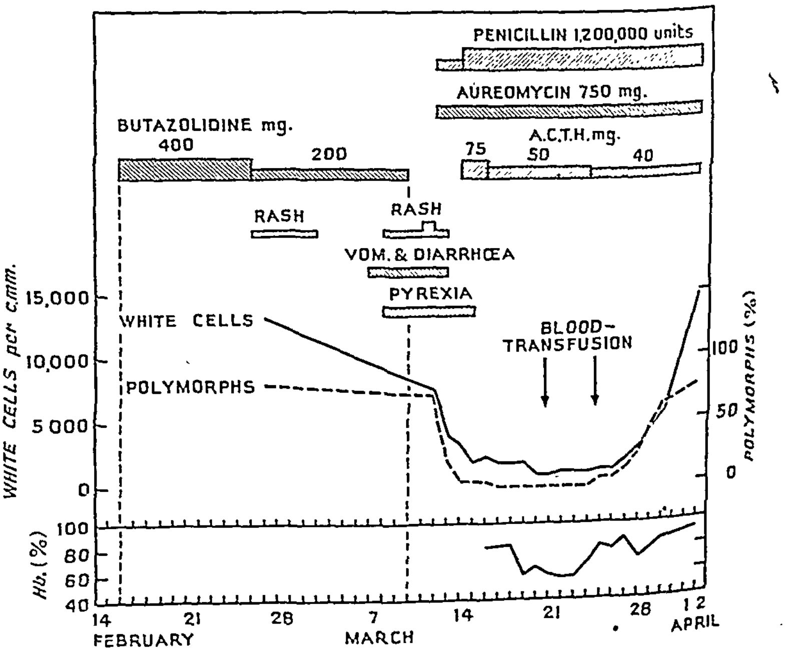
Polymorphs	0	Basophils	0
Metamyelocytes ..	0	Basomyelocytes ..	0
Myelocytes	16 %	Lymphocytes	20%
Myeloblasts	44 %	Monocytes	0
Eosinophils	10 %	Normoblasts	1·5%
Eosin-myelocytes ..	0	Hæmocytoblasts ..	9·5%

Peroxidase-positive 26 %; Peroxidase-negative 74 %
Megakaryocytes increased but no mature platelets budding off.

The findings indicated a toxic arrest of development of red cells and neutrophils.

From March 12 the patient was given procaine penicillin 600,000 units and aureomycin 750 mg. daily. Two days later therapy with A.C.T.H. 75 mg. daily was started. This dosage was reduced to 50 mg. after two days, and to 40 mg. after a further eight days. Two blood-transfusions, each of 2 pints, were given on the fourth and eighth days of agranulocytosis. On March 25, a day after the second transfusion, a white-cell count showed polymorphs 6% in the peripheral blood and the Hb increased to 83% (12·3 g. per 100 ml.). Thence onwards the numbers of white cells, including polymorphs, continued to increase, and on April 2 the white-cell count was 14,800 per c.mm. (polymorphs 78%) with Hb 94%.

The patient's rheumatoid condition did not deteriorate either on reduction of the dose of phenylbutazone or when it was discontinued. She had no rheumatic symptoms from the time the temperature and general



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1. *Brit. med. J.* 1952, ii, 1427.

West London Hospital Medical School

Sir Clement Price Thomas will deliver the Alex Simpson Smith lecture at 11, Chandos Street, W 1, on Thursday, June 11, at 4 30 P M He will speak on Benign Tumours of the Lung

Indian Medical Service Dinner Club

The annual dinner of the club will be held at the Connaught Rooms, Great Queen Street, London, W C 2, on Friday, June 26, at 7 30 P M Tickets may be had *from the hon secretary* of the club, Medical Board Room Commonwealth Relations Office, Matthew Parker Street, S W 1

University College, London

Madame S Filitti Wurmser of the University of Paris will deliver two lectures at the college, Gower Street, W C 1, on Tuesday and Wednesday, June 9 and 10, at 5 P M She is to speak on the Physical Chemistry of an Immunological Reaction The first lecture is entitled Étude quantitative de l'isohémagglutination humaine, and the second Les isoagglutinines anti B de divers génotypes

United Hospitals Festival Choir

This choir, which is made up of members of the medical, nursing, administrative, and technical staffs, and students from over 60 hospitals in the Greater London area, is giving a performance of the *Messiah* in the Royal Festival Hall on Wednesday, June 24, at 7 45 P M They will be accompanied by the London Symphony Orchestra The proceeds of the concert will be given to the British Commonwealth and Empire Nurses War Memorial Fund Tickets may be had from the Royal Festival Hall box office

Chelsea Clinical Society

At the annual dinner on May 12 the toast of The Society was proposed by Archimandrite James Virvos, provost of the Greek Cathedral, who remarked that everyone wants to be on good terms with doctors but prays never to be treated by them The medical men of modern times had much in common, he said, with those of remote antiquity, and in those days Homer was already describing the doctor as a man worth many others Hippocrates employed the science of comparative observation and used the method of deduction which protected him from speculation, and his work and teaching showed an integrity that justified his title as the Father of Medicine The modern medical society was a link with the ancient Greece, the cradle of medicine Responding, Mr Eric Steeler, the president, spoke of the miracle of Athenian civilisation, developing within the short space of four hundred years, and of the way that in modern times Greece had kept open the gateway of freedom Turning to the society's affairs he was able to report an instructive year, which had included a notable discussion on juvenile delinquency a memorable address by Sir William MacArthur, and a cheerful evening when Mr Gilbert Harding revealed new sides of his personality Mr D N Matthews then dealt faithfully and wittily with The Guests at what he called ' this our annual gastro enterological meeting " Recalling that the gods destroyed Asclepios with a thunderbolt because they jealously thought him too good a physician, he saw no reason to suppose that the lack of thunderbolts today was due to any lack of watchfulness on the part of the celestial authorities Sir Ernest Gowers, in reply, spoke of old days in his father's house, when he used to watch the sheep and cattle being driven up Queen Anne Street on their way to Smithfield In his early youth he had learnt that the medical profession were the elite of the world and all the rest were *merely patients* One of the characteristics of the profession was that its members did not like entrusting their affairs to laymen, but in the end they always won—because, of course, they were always right In adding his thanks on behalf of the guests, Sir Cecil Wakeley, P R C S, did not put forward the same claim

Mr Steeler as outgoing president then bestowed his badge of office upon his successor Dr J N Loring

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Dr J R. Macintyre has been appointed a nominated member of the executive council of the island of St Helena

Mr *David N* Matthews is spending a week at Düsseldorf, lecturing and performing demonstration operations at the West German Plastic Centre Dr J D Ebsworth is accompanying *him to give* the anæsthetics

Diary of the Week

MAY 24 TO 30

Monday, 25th

UNIVERSITY OF ST ANDREWS
5 P.M (Medical School Small's Wynd Dundee) Dr Irving Wright (president of the American Heart Association Peripheral Vascular Disease

Tuesday, 26th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C.2
3 45 P M *Prof Geoffrey Hadfield* Hormones and Hum Breast Cancer (Imperial Cancer Research Fund lectur

WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospit Medical School, W 2
5 P M Prof C L Oakley Site of Production of Antibodie (Almroth Wright lecture)

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Stree W C 2
5 30 P.M Dr D I Williams Erythrodermias

INSTITUTE OF [illegible] OLOGY
4 30 P M [illegible] Women Dovehouse Stree S W [illegible] Non-specific Infections i the Male and Female

Wednesday, 27th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 1
2 P.M Brigadier J S K Boyd, F R S Phage typing in Epidemio logical Investigation

INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Clefts, Vesicles, and Bullæ

EUGENICS SOCIETY
5 30 P M (Burlington House Piccadilly, W 1) Prof Dugal Baird Miss E M. Scott, M A Intelligence and Child bearing

Thursday, 28th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Prof R V Christie Chronic Bronchitis and its Complica tions

ROYAL *SOCIETY OF MEDICINE 1, Wimpole Street* W 1
4 P M *Section of Urology* Mr Terence Millin, Mr J C Anderson Dr L M Franks Radical Treatment of Carcinoma of *Prostate*

INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children Great Ormond Street, W C 1
5 P M Prof S van Creveld (Amsterdam) Clinical Significance of New Clotting Factors

INSTITUTE OF DERMATOLOGY
5 30 P M Dr I W Whimster Developmental Anomalie Hyperplasias and Tumours of Neuro ectodermal Deriva tives in the Skin

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield Morris Orthopædi Hospital Oxford
8 30 P M Dr A X Cavadias Vasculature of Bone and Healing of Fractures

UNIVERSITY *OF* ST ANDREWS
5 P M *Prof Z M Bacq (Liége)* Chemical Protection against *Ionizing Radiation—Therapy of Radiation* Sickness

Friday, 29th

POSTGRADU [illegible] DON
2 P M Pr [illegible] ding Peptic Ulcer
4 P.M Dr [illegible] Amenorrhœa
ST MARY'S [illegible] addington, W 2
5 P M Dr [illegible] *Cruickshank* Puerperal Infection

INSTITUTE OF DERMATOLOGY
5 30 P M Dr G B Dowling, Dr P D Samman *Dr J L M* Wigley Clinical demonstration

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road W C 1
3 30 P M Mr William McKenzie Indications for Tonsillectomy

Births, Marriages, and Deaths

BIRTHS

BLACHFORD —On May 12, in Birmingham to Sally (*née* Taylor) wife of R D Blachford M D —a daughter

MARRIAGES

TURNER—DENCE —On Saturday May 9 at Tunbridge Well Winston M L Turner M D, M R C P to *Helen M* Dence M R C S L R C P

DEATHS

SPEIRS —On May 11 at Furze Bank, Diss Norfolk, Hugh Meredith Speirs, M D Edin , aged 75 illness settled, and on April 2 the E.S.R. was 4 mm. in one hour (Westergren). The course of the illness and its treatment are shown in the accompanying figure.

Our thanks are due to Dr. H. J. Gibson for repeated white-cell counts.

Rheumatism Research Unit,
Royal National Hospital for
Rheumatic Diseases, Bath.

G. D. KERSLEY
L. MANDEL.

SIR,—In view of the recent correspondence about toxic and sometimes fatal effects of phenylbutazone the following report of two cases developing agranulocytosis may be of general interest.

CASE 1.—Mrs. A, aged 26, had had rheumatoid arthritis of hands, feet, and knees, with attacks and remissions, for over three years; and ulcerative colitis with attacks and remissions for three years. Almost invariably the two conditions alternated—a period of active colitis bringing relief of arthritic signs and symptoms, and a remission in the colitis being spoilt by activity in the arthritis.

In August, 1952, for the first time both conditions were active together, and her condition was very unhappy. By October the colitis was under control, but the arthritis was very disabling. Orthopædic help—manipulation and plaster splints for the ankles—was needed.

Perhaps inadvisedly (on account of the intestinal lesion) treatment with phenylbutazone was started on Oct. 21 (1 g. intramuscularly daily for ten days, followed by 1·2 g. by mouth daily for eighteen days).

There was improvement both in pain and swelling after the first few injections, and the improvement was maintained. But just before the month was up she felt rather low and a bit nauseated, and she became jaundiced with an enlarged tender liver. The phenylbutazone was stopped, but during the next week she had an ulcerative stomatitis and was found to have a total polymorph-count of 28 per c.mm. Penicillin and pyridoxine were started, and fortunately recovery from the agranulocytosis was rapid; within one week she had 4000 polymorphs per c.mm. The jaundice persisted for two to three weeks, but cleared entirely, and the liver returned to normal size. The patient is now in good form, though still using walking plasters.

CASE 2.—Miss B, aged 43, had suffered from rheumatoid arthritis for ten years, and during this time had received courses of physiotherapy, two courses of gold injections, and autogenous vaccine therapy at other clinics. In June, 1952, her arthritis flared up following a urinary-tract infection which was controlled by chemotherapy. After a short remission, there was further swelling of the wrists and one ankle, and the erythrocyte-sedimentation rate rose to 65 mm. in the 1st hour. She was anxious to try phenylbutazone, and as her initial white-cell count appeared within normal limits (Hb 72%; white cells 5250 per c.mm., polymorphs 56%), we decided to begin treatment with 0·2 g. t.d.s. (together with oral iron and vitamin supplements) on Oct. 27.

She had immediate relief from pain, although there was no demonstrable reduction in joint swelling or other signs. An attempt to reduce the dose produced an increase in her pain, and the dose was therefore again increased to 0·6 g. daily at the end of November.

In December she developed an upper respiratory tract infection with a low pyrexia of 99° to 100°F. Phenylbutazone was stopped and she was treated with penicillin, followed by chloramphenicol, without effect. In view of this failure to respond, she was admitted to hospital, where her blood was found to contain only 400 white cells per c.mm. (lymphocytes 98%). Her general condition was otherwise surprisingly good; in spite of massive doses of penicillin (later combined with aureomycin, pentnucleotide, and pyridoxine) she did not respond to treatment; her white-cell count fell to 200 per c.mm. (all lymphocytes) and pyrexia continued. A transfusion of fresh blood failed to help, and she died five days after admission from terminal bronchopneumonia, resulting from agranulocytosis.

At necropsy the sternal marrow appeared pink and healthy, and showed evidence of a return to normal activity. Although the spleen was slightly enlarged, it seemed unlikely that this was, in fact, a rheumatoid hypersplenism, since earlier white-cell counts had always been within normal limits, and quite unlike the picture accompanying Felty's syndrome.

Reviewing the first case, it seems that perhaps the presence of ulcerative colitis should have excluded the use of phenylbutazone; the daily dose of the drug and the length of treatment were greater than those now generally employed. This comment also applies to the second case, but an attempt to reduce the dosage and length of treatment was strongly resisted by the patient.

We have since obtained good results in other cases with smaller doses—e.g., 0·2 g. t.d.s., reducing within a few days to 0·2 g. b.d., followed by a further reduction as soon as possible.

In our opinion only uncomplicated cases should be treated as outpatients, and a white-cell count should be carried out initially and repeated at intervals of three days for the first week or two. Thereafter, and even during the preliminary stages, the responsibility for reporting every minor symptom such as a sore throat, skin rash, icterus, or febrile reaction should be placed firmly upon the patient. To do this, the patient must be guaranteed immediate access to the clinician in charge (or his representative) by means of a printed note which mentions the common toxic symptoms, and advises the patient to report to hospital on any suspicion that he or she may be the victim of an unfavourable reaction; a similar procedure is adopted with patients on thiouracil, troxidone, and other potential marrow toxins.

Patients who have any obvious complication—e.g., gastro-intestinal, hepatic, or endocrine dysfunction, or abnormal hæmopoiesis—which would make them unusually sensitive to the drug should certainly never be treated as outpatients, if at all.

General Hospital,
Nottingham.

J. D. PROCTER
R. GWYN EVANS.

THE TRAINING OF NURSES

SIR,—The General Nursing Council's desire to close the Fevers Register has produced great concern among those engaged in the management of infectious diseases, whether as hospital physicians or public-health administrators. It might be concluded that this is simply due to the formidable problem which staffing of their hospitals will present. But to some of us this is not the only, or indeed the main, cause for concern. It in large measure arises from the belief that the whole direction and emphasis of nurse training is proceeding without regard to the needs of the community.

Up till the emergence of that strong and fearless character, Florence Nightingale, nursing as we know it was non-existent. The value of her reforms lay not least in the persuading of the medical profession of the benefits to be obtained from an efficient and honourable nursing service. And, during the latter part of the 19th and first part of the 20th century, the training of nurses was felt as a concern (in the old Quaker sense) by even the most senior medical men, who took a large part in the teaching and administrative affairs of nurses. During the last twenty years the nursing profession has very properly increasingly organised itself; but one unfortunate result both of the great improvement in the quality of the nurse and of the development of the nursing profession by its own seniors has been the lessened interest of the medical profession, perhaps particularly in its junior ranks. I believe that it is true to say that the proportion of hospital doctors who feel a personal sense of participation in the training of nurses is now much smaller than it was twenty or thirty years ago.

It is natural that a profession should display a desire for the continued improvement of its stature; but there are good reasons for suggesting that the development of the nursing profession must be circumscribed by the needs of the community. The kind of nurse the community trains should be the kind of nurse that the community requires. No matter how desirable a certain reform may seem, its adoption must always defer to this overriding question: "Will it result in producing the kind of nurse who will best serve the community?"

The great medical and surgical advances of the last twenty years have demanded a high level of nursing

MITRAL STENOSIS

DIAGNOSIS AND TREATMENT

ANDREW LOGAN
M B St And, F R C S, F R C S.E
LECTURER IN THORACIC SURGERY, UNIVERSITY OF EDINBURGH, THORACIC SURGEON, SOUTH EAST SCOTLAND REGION

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(Concluded from p 1018)

Medical Treatment

Not all patients with mitral stenosis require treatment, and, when the diagnosis is made, the most important question to be decided is whether anything need be done about it In the absence of symptoms, treatment with drugs and restrictions other than advice against the pursuit of an unsuitable occupation are rarely necessary When there is undue dyspnœa on exertion or a severe symptom such as paroxysmal dyspnœa or hæmoptysis, it is best to avoid the amount of exertion that brings it on Though in patients with a progressive disability cardiac failure may be postponed by suitable restrictions, it is almost equally important, by not imposing excessive restrictions, to avoid the unnecessary invalidism and unhappiness which these patients often experience, and to prevent cardiac neurosis Advice may be needed regarding pregnancy because the increased load on the circulation may prove too great a burden for a diseased heart

When auricular fibrillation develops, as it usually does in patients who have progressive disability, digitalis will be required to control the heart-rate Before signs of cardiac failure are manifest, digitalis does nothing to relieve dyspnœa and its administration is not only valueless but also harmful Apart from its action on the heart it is a vasoconstrictor In some patients it appears to precipitate the onset of auricular fibrillation It is of no value in the management of sinus tachycardia unless there is cardiac failure Since it is known to be a "heart drug," the patient may gain an exaggerated impression of the gravity of her illness It is true that, when cardiac failure is imminent, it may be difficult to discern when the borderline has been reached, and then a short therapeutic trial of the drug is justified After the onset of cardiac failure full digitalisation must usually be continued for the rest of the patient's life, unless failure has been precipitated by some transient factor such as an acute respiratory infection If digitalis is not sufficient to control the failure, injections of mercurial diuretics and restriction of sodium intake may be needed

Intercurrent acute infections should be promptly treated Respiratory infections are common in patients with mitral stenosis, and may be responsible not only for part of the dyspnœa but also for the onset of cardiac failure The importance of not mistaking pulmonary congestion and œdema for acute bronchitis has already been emphasised

Watch should be kept for subacute bacterial endocarditis, and this diagnosis should be considered in any obscure fever lasting for more than a few days

Recurrence of rheumatic fever is most common in the first year after the initial attack, and something may be done to prevent this, particularly in young people, by the daily administration of sulphonamide or penicillin

ACUTE PULMONARY ŒDEMA

The patient should be reassured, made comfortable with pillows in the upright sitting posture, and given an injection of morphine (preferably intravenously) gr $^1/_6$–$^1/_4$ (10–15 mg) If possible, oxygen should be administered Unlike attacks of left ventricular failure, acute pulmonary œdema does not respond to digitalis If there is bronchospasm, aminophylline 0 25–0 5 g may be given by slow intravenous injection Should these measures not suffice, pressure cuffs should be applied to the thighs as far proximal as possible with the object of temporarily diminishing the venous return to the right auricle Intertracheal suction may be needed to remove excessive secretion, but this must be done with the patient upright On no account must she be laid flat

Classification

We have found it unprofitable to classify cases of mitral stenosis according to their severity, for there is no good way of weighing one contributory factor against another Limitation of physical activity is the basis of the following classification recommended by the American Heart Association

Class I —Without limitation of physical activity Ordinary physical activity causes no discomfort

Class II —Slight to moderate limitation of physical activity Ordinary physical activity causes discomfort

Class III —Moderate to great limitation of physical activity Less than ordinary physical activity causes discomfort

Class IV —Unable to carry on any physical activity without discomfort

But this is not a satisfactory gauge of severity in patients with rheumatic heart disease Those who are relatively little disabled by dyspnœa on exertion may be subject to dangerous attacks of pulmonary œdema They vary widely in their standards and in their tolerance of discomfort, and in some of them superimposed anxiety or neurosis is difficult to assess The degree and duration of each valvular defect and of myocardial damage, and the presence or absence of auricular fibrillation, all modify cardiac function Some factors balance each other for a time Pulmonary arteriolar resistance protects the lungs from pulmonary œdema but puts a severe strain on the right ventricle and leads to its eventual failure

Indications for Surgical Treatment

Operation should be considered in every case in which the diagnosis of mitral stenosis is made In many the possibility can be readily dismissed, in others the decision can be reached only after full investigation, while in others again the indications may be clear The ideal cases for valvulotomy are those with a severe valvular lesion and little damage to the myocardium The hearts of these patients are not large, though the characteristic pattern of mitral stenosis is apparent on radiography (fig 3)

Operation has not been advised in patients who have no symptoms whatever Indeed few patients with mild disability have yet undergone operation But it is in the latter group that the operation may eventually prove most useful, because it may prevent severe symptoms from developing On the other hand it is possible that if an operation is performed too early it may have to be repeated at a later date Time alone can show whether this is so

Most difficulties arise in advising those patients who have had prolonged severe disability—the "chronic mitrals" They have abandoned hope of spontaneous improvement, and understand only too well that treatment with rest and drugs is palliative, and that ever-increasing discomfort lies before them Some patients with very large hearts have been accepted for operation because it was thought that the state of the myocardium might allow improvement if obstruction was relieved It is in this group that operation carries the greatest risk

Paroxysmal dyspnœa, pulmonary œdema, and recurrent hæmoptysis are strong indications for valvulotomy Embolism is more debatable technique; but it would be dangerous to conclude from this that *all* those who wish to qualify for the designation "nurse" must of necessity reach this high standard. There is still, and there always will be, a real need for the "bedside" nurse who is highly trained in the practical duties of nursing. The requirements of the community make it necessary, I believe, to contemplate two spheres of nursing. All who enter the profession must qualify by undergoing a basic course of training; those who aspire, by reason of special interests or aptitudes, to the highest ranks would require to undertake further training. It might be argued that this principle has already been conceded by the recent introduction of the grade of assistant nurse. But the term "assistant nurse," as at present used to describe those who have taken something similar to a basic nursing course, is an erroneous one and its implication of inferiority is unfortunate.

It should be possible, as you suggested some years ago,[1] to define a "basic nursing course" which would constitute the warrant for the designation State-qualified Nurse (S.Q.N.). Such persons should be able to be trained in *any* hospital which comes up to a certain preordained and strictly exercised standard. The duration of such training should, I think, be one year, followed by a further year working as a nurse in an approved hospital. The best material which passed through this basic course would be attracted to specialise in general, surgical, medical, infectious-disease, mental, and children's specialties, and it would be from those who have taken such special courses that the ward sisters, theatre sisters, &c., would come. These State-qualified nurses would constitute the body of the hospital nursing strength, working as nurses under the more highly trained sisters. The nurse-in-training could then be regarded more correctly as a student and as only a part-time worker in the ward routine.

The controversy over the Fevers Register has brought more sharply into focus the serious hazard to which a health service may be exposed if attention is directed solely to the training of more highly qualified nurses. Anyone who examines the content of the student nurse's curriculum must reach the conclusion that there is a danger that the modern general nurse is being transformed into a kind of unsatisfactory medical student, unbalanced by possession of a pseudoscientific mental equipment, while the real needs of the service and the public are neglected.

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THOMAS ANDERSON.

INTRA-ARTERIAL TRANSFUSIONS

SIR,—I am prompted to write to you by Professor Schaeffer's letter (May 9) describing an apparatus to prevent air-embolism in intra-arterial transfusion. It may be of interest to your readers to know that an essentially similar piece of apparatus was described in your columns[2] in 1941, and has been available from Medical and Industrial Equipment Ltd., 12, New Cavendish Street, London, W.1, for some nine years.

Newcastle upon Tyne, 2.
A. MACKENZIE.

SIR,—In the intra-arterial transfusion outfit described by Professor Schaeffer, the essential part of the instrument is the glass float inside the drip chamber, which prevents air embolus. This drip chamber and its glass float were first described by Macintosh and Pask[2] in the *Lancet* in 1941, and again illustrated by myself in 1945.[3] It has become widely known in this country, if not the world, since that time under the name of the Oxford Safety Dripper.

Department of Anæsthetics,
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W. W. MUSHIN.

Parliament

THE N.H.S. INQUIRY

Debate in the Commons

SPEAKING on a token vote on the Health Estimates on May 18, Mr. ANEURIN BEVAN said that, though it was reasonable for an inquiry to be held into the National Health Service, he could not understand why the Minister had not used the Central Health Services Council, which had been appointed to advise him not only of any changes which might be necessary but of any defects which might be thrown up in experience of the administration of the service. Why had the Minister then set up an independent committee? Could it be to obtain an alibi to cut the service? The terms of reference suggested that the committee were to advise the Minister how the funds made available by the Exchequer were to be apportioned. In Mr. Bevan's view *priorities of expenditure inside the* service were social priorities and were a matter of political opinion and judgment.

The expenditure in the two parts of the N.H.S. where the patient initiated expenditure—i.e., the dental and ophthalmic services—had begun to fall once the initial backlog of neglect was worked off. On the pharmaceutical side the picture was slightly different. Here the initiative in expenditure lay mainly with the doctor, not the patient. On that side expenditure was still rising despite the shilling charge. It was surely a reflection on the medical profession that last year we spent £400,000 on 'Dexedrine' when the equivalent in the official formulary would have cost about £158,000. But for this *we should not penalise the patient but investigate* the profits of the big drug houses and stiffen more severely the discipline over the general practitioner.

Though Mr. Bevan agreed that there were questions of priority to be settled both inside and outside the service, he did not see that the Guillebaud Committee was the body to do it. It might be that the Central Health Services Council were too deeply involved in the administration of the N.H.S. to take an objective view. But the House of Commons was an opinion-making body and it was nonsense to ask an outside committee "What do you think our opinion should be about this?" That was why he stuck to his words that it was cowardice to set up a committee. If the Government wanted to cut the health service, why did they not say so instead of calling a committee into existence and hoping to hide behind it.

THE MINISTER'S SPEECH

Mr. IAIN MACLEOD, Minister of Health, said that the appointment of the committee had been greeted with almost universal approval in the press. Two questions to be decided were: Was there anything to inquire into? and, if so, who should undertake the inquiry? On some matters within the area of dispute he wanted advice, though he agreed that the decisions could be taken only by the House of Commons. Giving examples of the matters on which he wanted advice, Mr. Macleod said it was one view that the central accounting system of this country was never designed for the burden that the health service had put upon it in the management of several thousand hospitals. There would be great economies if the hospitals could plan three or five years ahead. If the block grant was to be effective they must be reasonably certain of stable prices for some years ahead. Ambulances were a hospital service in Scotland and a local-authority service in England: which system was the better? Had local authorities found their right rôle in the health service?

Mr. Macleod felt that, after five years, there was an unanswerable case for some investigation. He desired an independent view from independent-minded people not tied either to the professions or to political parties. Expenditure in the health-service field could not be controlled unless man-power was controlled, because salaries and wages accounted for two-thirds of the cost of hospitals, and hospitals accounted for nearly two-thirds of the cost of the scheme. They must try to relate the numbers employed to the service obtained and he hoped that as an outcome of the inquiry more staff might be available for the hospitals and sanatoria which were at present in the greatest need.

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1. *Lancet*, 1945, i, 664.
2. Macintosh, R. R., Pask, E. A. *Lancet*, 1941, ii, 10.
3. Mushin, W. W. *Ibid*, 1945, i, 611.

In general it may be said that operation is advisable whenever there is considerable or progressive disability, and none of the contra-indications referred to below is present

Contra-indications

AGE

The youngest patient operated on in this series was sixteen years of age The principal indications in her case were attacks of pulmonary œdema and recurrent hæmoptysis Now, eighteen months later, she declares that she has no disability

In youth there is a greater risk of further attacks of rheumatic fever, and therefore of increase or recurrence of mitral stenosis, than in later years, but this risk would not justify the denial of valvulotomy to a child whose life was endangered by the mechanical effects of mitral stenosis Except when the disability is severe or rapidly increasing, and clearly the result of obstruction at the mitral valve, it is probably better to delay operation until about the age of twenty

14 patients were over fifty, the oldest being fifty-nine We have found the behaviour of the heart at operation less good in patients over fifty

SEVERITY

Too Mild

Mitral stenosis without symptoms or a history of rheumatic fever is often diagnosed at some routine examination such as that for National Service or life assurance The physical signs of valvular disease may be obvious and pathognomonic, but there is little or no evidence of cardiac enlargement and none of cardiac insufficiency In many of these patients the condition will be judged too mild for valvulotomy, and it may remain benign throughout a life of normal span These patients should, however, be kept under observation for evidence of progression Only in this way can be selected the ideal time for valvulotomy as a prophylactic measure in mitral stenosis

Progression is best judged by the patient's own account of the symptoms To wait for an increase in objective signs will usually be to wait too long

When there is doubt as to the degree of severity in this group, additional help may be obtained from cardiac catheterisation A normal or slightly raised pulmonary arterial pressure at rest, with little rise on exertion, probably confirms that the obstruction is slight Calculation of blood flow is necessary for precision In the few patients in whom the resting mean pulmonary arterial pressure has been in the upper range of normal or slightly above (15–20 mm Hg), and the rise of pressure on exertion has been small (10 mm Hg), a significant, although not a severe, degree of stenosis has been found at operation

Too Severe

There is no need to describe in detail the manifestations of advanced rheumatic mitral disease In many patients the condition has progressed too far for operation to be of value Gross enlargement of the heart, recurrent or intractable cardiac failure, and cardiac cirrhosis of the liver are evidence of such severity These patients have not only mitral obstruction but also so much damage to the myocardium that, although the mechanical obstacle to an adequate cardiac output is relieved and some benefit must accrue, this may not be commensurate with the risk involved They must nevertheless be considered carefully, because they have no prospect of improvement without operation

ASSOCIATED VALVULAR LESIONS

Mitral Incompetence

Predominant mitral incompetence will contra-indicate valvulotomy until it is possible to introduce an adequate supplementary mitral cusp We have not observed the diminution of regurgitation by valvulotomy alone Possibly, when significant stenosis is also present, the total disability may be reduced by valvulotomy and consequent relief of obstruction, even if the degree of regurgitation remains unchanged The importance of a regurgitant stream felt immediately after valvulotomy is variable

The diagnosis of predominant mitral incompetence accompanying mitral stenosis may be very difficult The various points which are of importance have been discussed previously (Logan and Turner 1952b), but may be summarised as follows

In the absence of aortic valvular disease (whose significance must be assessed on peripheral rather than cardiac signs) and of systemic hypertension, any evidence (clinical, radiological, or electrocardiographic) of hypertrophy or enlargement of the left ventricle suggests that there is significant mitral incompetence A loud harsh mitral systolic murmur supports the diagnosis but may be misleading Systolic expansion of the left atrium observed at fluoroscopy is an unreliable sign The pulmonary capillary-venous tracing obtained at cardiac catheterisation may give supporting evidence but is often of no value A clear first heart sound and "opening snap" rarely accompany predominant incompetence

We believe the clinical examination is more important than accessory methods in this admittedly difficult differential diagnosis No method should be neglected, and attention to all the evidence should enable errors to be avoided

Aortic Incompetence

The diagnosis of aortic incompetence is made by hearing the characteristic long, blowing, high pitched early diastolic murmur which begins immediately after the second heart sound, is best heard along the left sternal edge, and is often audible at the apex and to the right of the upper sternum The significance of this murmur cannot be judged from its intensity or duration but depends on the peripheral signs of aortic regurgitation—a collapsing arterial pulse, an increase in the pulse pressure, and abnormal pulsation in the aorta seen on X-ray examination In the absence of significant mitral incompetence or systemic hypertension left ventricular enlargement or hypertrophy can be attributed to aortic incompetence Enlargement of the left ventricle can be observed radiologically long before there is electrocardiographic evidence of hypertrophy

Of this series of 100 patients subjected to valvulotomy, 30 had signs of aortic incompetence We have operated on only 2 patients with aortic incompetence complicating mitral stenosis in whom there was electrocardiographic evidence of left ventricular hypertrophy, and both did well 6 of the 30 have had radiological signs compatible with left ventricular enlargement, but reference has already been made to the difficulty of differentiating this from right sided enlargement

Palpation of the cardiac impulse at the apex is a good guide to left ventricular hypertrophy The heave may be unmistakable when there is still no radiographic enlargement In aortic incompetence enlargement of the left ventricle may become obvious in the postero anterior view earlier than in the left anterior oblique view

We have regarded severe aortic incompetence as a contra indication to operation for associated mitral stenosis Mild aortic incompetence has been ignored Difficult cases lie between these two extremes When tight mitral stenosis and considerable aortic incompetence occur together, as they often do, there is no a priori reason for withholding valvulotomy In uncomplicated aortic incompetence a surprisingly great degree of regurgitation may be found without symptoms The left ventricle may not fail for many years Associated mitral stenosis may be difficult to assess, but, unless aortic

The Government viewed the present cost of the pharmaceutical services, as did their predecessors, with the greatest concern. It was the only part of the health service which was not under financial control at present. Prescriptions were now running at the rate of 241 million a year in Great Britain, and the average cost of a prescription had climbed from 38*d*. in 1949–50 to 40·5*d*., 47*d*., and 50·7*d*., and he had made an estimate of 52*d*. for each prescription for this year. The rise was due to a general increase in ingredient costs, although that was flattening out, to the increasing use of new, valuable, and expensive drugs, and to the important increase in the proportion of proprietaries. The increase of 3½*d*. last year in each prescription was mainly due to large quantities being supplied. Before the health service was introduced the proportion of proprietaries was 6%: it was now 25%, which accounted for about half the drug bill, and the whole of the amount he had to pay out, taking into account the hospitals, was about £60 million.

In a month or so, when the final arrangements were made for the two schedules laid down by Sir Henry Cohen's committee, which referred to drugs not of proved therapeutic value, doctors were to be asked not to prescribe them. But the biggest problem was that 4000 proprietaries came in the categories which the Cohen committee advised were not superior to standard preparations but which they thought ought to be prescribable, subject to satisfactory price arrangements being made. The problem, which was not a new one, was what was to be done in this matter. There was a genuine case for many of these firms, but the trouble was that there were firms who were merely wrapping up standard preparations in pretty packages and forcing them on the notice of doctors by salesmanship. The Government had decided to start a number of investigations into the cost of manufacture of certain of these proprietaries, which seemed at first sight to be specially expensive. He hoped this would yield substantial savings. In due course he would circulate to doctors the names of those preparations concerning which satisfactory agreements on prices had not been reached. This action should not be taken to be the end of the story, and he did not rule out more drastic measures if this should fail.

Discussing the charges, Mr. Macleod related that the 1*s*. charge in the first month caused a drop of 14% in the number of prescriptions, but by September the deterrent effect was ¼%. The dental charges for adults had led to a slight fall in conservative treatment, while the number of children's courses for the last quarter of 1952 was 170,000 as against 350,000 in 1950, and they comprised 22% of the courses under the N.H.S. in 1952 as against 9% in 1950. The number of school dentists had risen from 812 in January, 1951, to 998 in January, 1953.

For the first time since 1946, he continued, there was now a genuine measure of priority for the priority classes. The main problem was how to meet the thrusting needs of the hospital service. Last year the hospitals underspent by £14 million owing partly to the Government's requests to them not to overspend and partly to the fact that the Government for so many months held the cost of living virtually stable. In this year's estimates £15¼ million extra had been provided for the hospitals, and, adding certain other sums to this total, he was providing £20 million over the out-turn for the last year for that purpose. No-one could say that there had not been coöperation with the Chancellor of the Exchequer in finding the money. With this £20 million he could maintain the service, bring into full use developments which had been finished recently, and provide for modest future development.

Mr. Macleod admitted that if the Chancellor offered him more money he would not look to free dentures and free medicines but to the mental health of the country. But he agreed that the policy of successive charges would in time destroy the service. He did not know if we were at end of charges, but at least we had called a halt. What we wanted to achieve was a system by which the service had an interest in economy which was as natural and rewarding as was its interest in medical efficiency. That was the essence of the problem which the Guillebaud Committee was trying to solve.

FURTHER DEBATE

Mr. **Arthur Blenkinsop** suggested that in the Minister's view there were two sections of the community—one which might reasonably be expected to pay charges and the other which might be expected to receive the benefits. The richer section of the community might use the social services, but they paid more in rates and taxes than the benefits they derived. Thus the social services were the responsibility of the rich in so far as these were willing and able to make some extra provision out of their resources to provide benefits for the poor. To Mr. Blenkinsop it seemed that this paternal approach was bedevilling the service. It took no account of the interdependence of all sections of the community. By imposing charges we were asking that the whole provision of our social services should be directed to one section of the community, who were assumed to be unable to pay for the benefits they received. Yet, in Mr. Blenkinsop's opinion, it had been open to the Government to withdraw the charges, instead of making extra revenue available to those who were already well off. Mr. Blenkinsop deplored the maintenance of the financial ceiling for the health service. The Minister had said with pride that the hospital authorities had saved large sums from their estimates last year, but many knew that these savings had been made at the cost of the proper running of the service.

Mr. **Frederick Messer** accepted the need for an investigation into the organisation of the N.H.S., but asked that the emphasis should be on efficiency rather than economy. In a comprehensive service unification was important, and Mr. Messer pointed out that each of the 14 hospital regions cut through the staff of the local health authorities. We should, he held, investigate the possibility of a rearrangement of the regional-board structure so that the periphery was coterminous with the local authorities—not of course a single local authority, because obviously a regional board must be larger than any single local health authority. He regretted that the service was divided into three sections, and he was anxious that more attention should be given to the preventive side. Would the Minister consider whether the executive councils could not become part of the local health authorities? Not only would this save administrative costs but it would bring the general prctitioner into a closer relationship with the preventive service.

Dr. **Santo Jeger** believed that on the whole people would spend on their health what they needed. In America about 4½% of the national income was spent on health, but 90% of it was spent privately and only about 10% publicly. In this country we spent about 4% of our national income on health; but about 90% of it was spent publicly, and only 10% privately.

Colonel **Malcolm Stoddart-Scott** also felt that the organisation of the executive councils was unsatisfactory. He believed there were too many. Some councils administered their areas at a cost of 10*d*. per head of the population, others at 2*s*. 10*d*. He believed that by cutting the number of councils we could save at least £500,000 a year. He also recommended that the powers of the regional hospital boards should be swept away. On the whole they acted only as post-offices between the hospital management committees and the Minister. They also increased the difference between the standards of the teaching hospitals and the other hospitals. He would like to see the H.M.C.s rise in standard to that of the governors of teaching hospitals and to have increased powers and direct access to the Minister. The regional offices of the Ministry could, he suggested, be strengthened to deal with over-all planning, and he thought that the teaching hospitals should be brought under the Ministry's regional over-all planning.

Mr. **H. A. Marquand** pointed out that the proportion of our national income which was being spent on the N.H.S. was dropping, because the Government had stuck to the £400 million ceiling even though circumstances had changed and the Chancellor had twice been able to reduce taxation. Yet, Mr. Marquand held, there were cogent reasons for raising the ceiling. If we had the steel, for instance, it was false economy to deprive hospitals of fuel-saving appliances. The increase in our population, regurgitation is severe, the symptoms are probably due to mitral stenosis Pulmonary hypertension from aortic regurgitation does not develop until left ventricular failure is manifest, and therefore cardiac catheterisation may be of value in the assessment

When there is difficulty in differentiating an Austin Flint murmur from the mid-diastolic murmur of mitral stenosis, we have found that the presence of an opening snap is conclusive evidence of mitral stenosis

Aortic Stenosis

Aortic stenosis has to be of considerable degree before effects on the circulation are evident The left ventricle hypertrophies but dilates little, and this is reflected in the quality of the apical impulse, in the contour (and, later, the volume) of the left ventricle, and in the electrocardiogram The pulse rate is slow to rise, and the pulse is small and sustained (plateau type) The blood-pressure is low if stenosis is severe, and the pulse-pressure is reduced These features may be modified by the aortic incompetence which often accompanies the stenosis The aortic second sound is often weak or absent The familiar basal systolic murmur and thrill signify sclerosis of the aortic valve but not necessarily stenosis, which must be diagnosed on other grounds

GROSS CARDIAC ENLARGEMENT

It is impossible to lay down absolute standards of size beyond which it is unwise to operate Left atrial enlargement is not related to the degree of stenosis, it is the size of the right ventricle which matters most

Cardiac enlargement in patients with mitral stenosis is related to the effects of rheumatic myocarditis rather than to the valvular defect The benefit which will accrue from relieving the strain on damaged muscle by diminishing mechanical obstruction is obvious, but there must be a stage of cardiac damage, indicated by gross enlargement, beyond which significant benefit cannot be expected and the risk of operation is too great. In short, the degree of cardiac enlargement is only one of the factors which must be taken into consideration in assessing the desirability of operation

ACTIVE CARDIAC DISEASE

Subacute bacterial endocarditis is an obvious contra-indication to operation Except when the mechanical obstruction at the mitral valve is an immediate threat to life, it would seem more reasonable to wait for six months after successful treatment before undertaking valvulotomy, if only to diminish the risk of dislodging emboli Only 2 patients in this series had had such an infection in neither of them was there any untoward incident during or after operation

In the presence of valvular heart disease clinical signs of active rheumatic carditis may be impossible to assess Electrocardiography is not a reliable guide unless there are significant changes in serial records, and is of no value if there is auricular fibrillation Nobody would advise operation for anyone with obvious signs of rheumatic activity in the form of pericarditis, swollen joints, anæmia, or a high erythrocyte sedimentation rate, but there are patients with vague joint pains or a moderately raised erythrocyte sedimentation rate in whom the decision is difficult We have operated on such patients without evidence of postoperative recrudescence There have been others without symptoms of activity before operation who have apparently developed mild rheumatic fever during convalescence There is no evidence that operation necessarily aggravates the rheumatic process, and delay in patients with tight stenosis may carry the greater risk

Preoperative Treatment

Before any deliberate thoracotomy, patients are instructed in breathing exercises by a physiotherapist so that they may be efficient after operation in the expectoration of bronchial mucus and the promotion of full re-expansion of the lungs

Cardiac failure is corrected if possible, but occasionally the operation has had to be done while there were still signs of congestive cardiac failure 3 patients with intractable cardiac failure have been considerably improved by *ligation of the inferior vena cava*; after which, if improvement continues, it may be possible to treat the valvular defect Benefit may accrue mechanically from increasing the vascular bed in the lower half of the body, and the diminution in venous return may improve the cardiac output by lowering the right auricular filling pressure and hence lead to improvement in renal blood-flow

Digitalis is given to patients with auricular fibrillation, and quinidine is given prophylactically to all patients with sinus rhythm

Operation

The main steps of the operation performed in most cases were as follows

Under cyclopropane anæsthesia, with the patient lying on the right side, a standard left thoracotomy was made through either the fifth interspace (in patients under thirty years of age) or the bed of the resected fifth rib (in patients over thirty) The pericardium was opened from apex to base of the heart 1 cm anterior to the phrenic nerve and parallel to it The left auricle was incised to allow digital exploration of the atrium and the mitral valve The anterior and posterior commissures of the valve were divided by pressure with the index finger The auricular and pericardial incisions were repaired, a low intercostal drain was introduced into the pleural space, and the chest was closed During the operation blood was replaced by transfusion according to the weight of blood lost

In 41 cases the lung felt abnormally heavy and solid, and in 34 there was a clear pleural effusion of 20–30 ml The heaviness of the lung bore no constant relation to the size of the mitral orifice or to the preoperative assessment of pulmonary congestion, and was not prognostic of difficulty during convalescence In 80 cases a wedge of tissue was removed, for microscopy, from the anterior segment of the lung—a site chosen in preference to the lingula, which is more often involved in primary pulmonary disease

In most cases there was 10–20 ml of clear pericardial liquid, but in 20 cases the quantity was between 30 and 300 ml In 6 cases the pericardium was completely adherent to the epicardium by dense avascular adhesions

In almost all the cases a diastolic thrill was felt on the surface of the heart immediately to the left of the interventricular branch of the left coronary artery, diminishing in intensity towards the apex of the left ventricle In some the thrill could also be felt on the inferior surface of the left ventricle near the interventricular artery A systolic thrill below the left lower pulmonary vein, maximal on the auricular side of the coronary sulcus but also present on its ventricular side, was felt in 14 cases out of 22 in which mitral regurgitation was found at cardiotomy A similar thrill was felt in 4 cases out of 9 in which mild regurgitation was produced by valvulotomy In 3 cases a systolic or systolic and diastolic thrill was felt at the origin of the aorta, and in these aortic valvular disease had been diagnosed before operation

The occasional disappearance of a systolic or a diastolic left ventricular thrill after valvulotomy was believed to be caused rather by the less forceful action of the heart than by the correction of incompetence or by the relief of obstruction

In the earlier days of mitral surgery the fragility of the distended left atrium was an argument against the use of the atrial approach to the valve It is now known, however, that the atrial wall holds sutures well, even against high pressures The auricle is normally broad enough to accommodate the index finger, and, when that with its higher proportion of aged and young people, was another reason for spending more on the N.H.S. Again, much of our hospital equipment was obsolescent, and finally the needs of the new towns and housing estates must be considered. He hoped that the Minister would ask the Guillebaud Committee to consider how the service could be run more economically by providing better capital equipment, and whether it might not be sensible to present the capital account of the health service separately from the current account. Mr. Marquand said that the Trades Union Congress, before appointing a representative to the Guillebaud Committee, had questioned the terms of reference, as they had thought the words "to avoid a rising charge" implied that the committee must keep within a ceiling. The T.U.C. had been given a "clarification," and the Chancellor of the Exchequer had given an assurance that the committee had been given no ceiling. Mr. Marquand asked for a definite assurance that the committee would be free to recommend changes which would involve increased expenditure.

GOVERNMENT REPLY AND DIVISION

Commander T. D. GALBRAITH, Under-Secretary of State, Scottish Office, replying to the debate, said the Guillebaud Committee would be able to study the merits of whole-time and part-time service, but it would not deal with rates of pay. He was sure that the committee would arrange sittings in Scotland and hear Scottish evidence.

Mr. BEVAN moved to reduce the token vote for the National Health Service for the current year by £5. The motion was negatived by 293 votes to 268: Government majority 25.

Hospital Nursing Services

In the House of Lords on May 12, Lord CROOK said that he noted with concern that today there were employed in the hospitals 47,000 fully trained nurses and some 8000 part-time nurses as against 52,000 trained nurses and another 48,000 in training in 1948. Present employment could not meet the needs of the present situation, much less the potential growth of the health service. He had chosen this moment to raise the subject, he explained, because the report of the Nuffield Provincial Trust made it plain that the most skilled nurses were not being used in the most skilful jobs. The report made it clear that proper use was not being made of ward orderlies, though 25,000 members of that grade were now employed. Almost three-quarters of the time spent on nursing duties in the wards was contributed by student nurses, and only 16% of the time spent on nursing duties was given by trained nurses. The staff nurse had only a small amount of time to devote to actual nursing. The time spent in training the student nurses was negligible, ranging from eleven hours a week to seven minutes. One of the deterrents to the recruitment of nurses had been domestic work, and Lord Crook was glad that the amount of domestic work performed by student nurses was today much lower. Instead, the worrying thing was the nature of the nursing duties allocated to them. Everyone was accustomed to student nurses taking pulses and temperatures, but the report showed that, apart from doing dressings, student nurses now gave injections, were responsible for checking drugs, and carried out urine tests. Indeed, 72% of the total time spent on the dressings of patients was contributed by student nurses. Yet the theory of wound dressing was, in the main, shown to be picked up rather than taught. Much of the waste of man-power, Lord Crook continued, was due to the poor design of buildings and the shortage of good equipment. There should be some system of priorities to make certain that money was spent on equipment that would ease the man-power problem. The report revealed shortages of elementary hospital equipment which ought not to exist in a State health service, and the Central Health Services Council had said that they saw no reason why financial stringency should prevent the provision of, for instance, adequate facilities for the sterilisation of bedpans.

The number of under-staffed hospital beds in April this year was 28,502, and the present shortage of nurses was estimated to be 10,420. In the last four and a half years the improvement had been very slow, and Lord Crook hoped that the House would be given an assurance about the 5% reduction in staffs which he understood the Ministry had told hospital management committees to make. If the cut was applied to domestic staff, domestic work would again fall on the student nurses who would flow out of the hospitals even faster than they were doing so now.

Lord MORAN said that since three-quarters of the patients in hospitals were nursed by student nurses, it was important that these students should have the benefit of instruction and supervision by trained nurses. The scarcity of nurses was not a passing factor. As the wastage of student nurses in training was 50%, no great increase in the number of trained nurses could be looked for in the future. We must concentrate on making the best use of those we had. For instance, he asked, were there any activities of the nurse which could be done by somebody who was not a nurse? He wondered whether some nursing procedures were not apt to degenerate into rituals. Was it necessary to take the pulse, respiration, and temperature of a patient up to the moment he walked out as a convalescent? One hour of the sister's nine-hour day was devoted to clerical work and nearly all of it could be done by a secretary. Yet when an enterprising provincial hospital instituted the secretarial system they were told to desist on the grounds of economy. Another hour was given up to going round with doctors. In the male ward surely much of that was unnecessary. At the risk of offending many of his own profession, Lord Moran suggested that no doctor should go round a ward before 10 A.M. or between noon and 2 P.M., or after 5 P.M. There must be more coöperation with nurses if they were to economise their time.

The question whether any of the nurse's activities could be done by a nurse who was not necessarily a trained nurse was, he admitted, more controversial. The theme of the job analysis described in the Nuffield report was that the trained nurse had been taken away from the bedside and that she ought to be brought back to the patient. He agreed that the nurse must learn the art of accurate and discriminating observation at the bedside. Only the repetition of apparently menial duties allowed the nurse to get to know her patient. On the other hand it was said that all, or most, of these bedside duties could be done by a person not as skilled as a trained nurse, and at a time of great scarcity of trained nurses it logically followed that less skilled persons should be provided for the work. Nobody had ever introduced dilution into a trade or profession without profound controversy, but, he pointed out, dilution had taken place among almoners; among dentists it was being considered; and the doctor had already been diluted. After all, the nurse was dilution. She was now doing jobs which the doctor did years ago. It was inevitable that there should be dilution in the nursing profession. Those who spoke for the nursing and medical professions were generally attached to teaching hospitals, yet half the hospital beds in this country were in mental hospitals. Surely the case for dilution of the nursing profession was overwhelming. If the diluting agent could be the assistant nurse everyone would be happy, but there did not appear to [illegible] of getting [illegible]ly. anything like enough of them. [illegible] He felt that orderlies trained for a year would be most useful, at any rate in hospitals where acute cases were not treated.

We could not leave aside redistribution when considering the best use of the trained nurse. In sanatoria, in mental hospitals, and in institutions for the chronic sick and elderly, there was probably a gross shortage of trained nurses. But if a nurse was to be sent to these institutions, Lord Moran believed that she must go voluntarily—there could be no direction of labour. He also felt that, at a time when nurses were so scarce, it was surely wise to be very prudent before further depleting the hospitals where acute illness was nursed.

Lord AMULREE agreed that some form of dilution was the only way round our difficulties. One of the ways in which dilution could be introduced without serious harm was by making different arrangements, so that nurses could care for more people than they did now.

is so, exploration of the mitral valve through an incision in the auricle presents no difficulty—the incision being controlled with a purse-string suture or light clamp. In a man aged fifty-three valvulotomy for mitral stenosis was intended, but the auricle proved to be a mere muscular nodule without a lumen. Valvulotomy was therefore not done, and the patient died six months later from acute pulmonary œdema. In 3 similar cases seen later it was found convenient to open the atrial wall in a line from the tip of the auricle to the front of the left upper pulmonary vein. By gentle traction on the auricle and vein the atrial wall in that line can be raised to form a ridge below which a light curved clamp can be applied. In 4 other cases, in which the upper pulmonary vein was capacious, an incision confined to the anterior wall of the vein was used, the vein being controlled at its pulmonary end with a double loop of silk and at its atrial end with a clamp. This venous incision gains advantage from the facts that, when the atrium contains clot, the part related to the pulmonary venous orifice is likeliest to be free from clot, and that, when the atrial wall is sclerosed or calcified, the vein does not share in this rigidity.

From observations during pulmonary resection it is clear that an atrial incision near the termination of the two left pulmonary veins would be simple to control, but the occasion to use this approach has not arisen.

In some cases the auricle, though not atrophic, has a lumen not quite wide enough for the index finger, and exploration through an auricular incision will cause an atrial tear which may be difficult to control either because of its relation to the left coronary artery or merely because it is not readily accessible. It is better to make an adequate incision in a line of easy control than to risk an accidental tear in an incorrect position.

To permit histological examination of the heart muscle the tip of the auricle was cut off before closure of the auricular incision. This series of specimens is still being studied. The finding of Aschoff nodes and other evidence of rheumatic infection does not correspond closely to the clinical evidence of active rheumatic carditis.

The incision, whether in auricle, atrium, or vein, was closed with a continuous 00 silk suture.

BEHAVIOUR OF HEART AT VALVULOTOMY

Extrasystoles occurred in almost all the cases during the earlier manipulations of the heart. In this series intravenous 1% procaine 0.5–4.5 g was given in all the cases, but extrasystoles were quite as common as in the series treated in another hospital in which procaine was not given. Neither procaine nor amethocaine was applied to the pericardium or epicardium or injected into the myocardium, but care was taken to preserve the surface of the heart from unnecessary damage, and especially from drying. Extrasystoles were not produced by touching any of the accessible parts of the interior of the heart. While the finger lay in the stenosed valve, the ventricular action rapidly diminished in force and rate but in most cases quickly returned almost to its earlier state on withdrawal of the finger. In some the beat continued to be slow and weak or even to deteriorate after completion of valvulotomy, and in these the intravenous injection of 'Methedrine' 5–20 mg was usually followed by an increase, first in the vigour, and later in the rate, of the beat.

The reason for progressive slowing of the heart is unknown. Anoxia does not appear to be the cause. It is not clearly related to cyclopropane anæsthesia. In a few cases the deterioration progressed until the heart stopped. Its action, except in 1 case in which the ventricle began to fibrillate, returned after cardiac massage.

Ventricular fibrillation was observed in 3 cases, 1 of them fatal, in this series and in 1 case in the series in which intravenous procaine was not given.

Sudden improvement of the heart's action after valvulotomy is rarely to be expected, probably because enough blood passes easily through the stenosed orifice for basal requirements. The benefit from valvulotomy can be appreciated only when greater demands are made on the circulation.

EXPLORATION OF ATRIUM

The absence of palpable movement of the atrial blood was a striking feature in most cases. The uncovered finger was not used, and the sensitivity of the gloved finger to the flow of blood is not comparable with its sensitivity to minute hard bodies. With the finger close to the orifice of a pulmonary vein through which a quarter of the whole circulation is flowing no current is appreciated. There is no sensation of turbulence above the mitral valve. In nearly all the cases the medial (anterior) cusp bulged with a sharp impulse into the atrium at each ventricular systole. In the exceptions the whole cusp was apparently rendered rigid by disease.

In 26 of the 100 cases of predominant stenosis regurgitation of blood from the ventricle was felt before valvulotomy. In none of these was regurgitation abolished by valvulotomy. It was thought that in some it had been reduced, but the impairment of the heart's action which sometimes occurs during valvulotomy may have been responsible for diminution of the leak. In addition the enlarged orifice alters the character of the flow, and comparison of a broad soft current with a narrow hard jet is inaccurate. In 7 cases there was slight regurgitation after valvulotomy when none had been felt before. The lightest touch on the anterior cusp either before or after valvulotomy, if the cusp was mobile, led to the regurgitation of blood into the atrium.

Three grades of size of the mitral orifice were recorded. In group 1 the valve would admit no more than the tip of the index finger. By comparison with post-mortem specimens this was judged to be in most cases about 1 × 0.5 cm. Group 2 ranged from admission of the extreme tip to admission of the whole terminal phalanx. In group 3 the second phalanx or more was admitted. In the combined series of 130 cases there were 17 in group 3, the orifice loosely admitting the first knuckle of the index finger. They are referred to here only to illustrate points in diagnosis. At present we do not know precisely what degree of stenosis and what degree of regurgitation are of dynamic significance. Variables such as auricular fibrillation, myocardial damage, mobility of the cusps, atrial size, pulmonary hypertension and pulmonary vascular resistance may always prevent precision. We consider that a broad regurgitant jet through a valve which admits the proximal interphalangeal joint of the index finger signifies predominant mitral incompetence, and in our experience no reduction in the regurgitation can be expected after division of the commissures. A faint regurgitant jet through a tightly stenosed valve is not of dynamic significance. When the mitral orifice just admits the terminal phalanx of the index finger, the degree of stenosis is significant, and there may or may not be also significant regurgitation. In cases with regurgitation through an orifice admitting the terminal phalanx no appreciable reduction of regurgitation has been achieved by valvulotomy, although the patients have been improved.

EMBOLISM

Embolism is the greatest immediate danger associated with valvulotomy. It must be weighed against the possibility of embolism without operation, and of progressive ill health from unrelieved mitral stenosis. The finding of clot in the auricle or atrium is unpredictable. It is more common in those who have auricular fibrillation or have had previous embolic incidents than in those with normal rhythm and without previous embolism. If

A MODIFIED SCHLESINGER TEST FOR UROBILIN IN URINE

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The testing of urine for urobilinogen and urobilin is of special importance in the early diagnosis of hepatitis, in following the course of the disease, and, by its final disappearance, in denoting complete recovery. The significance of the test is emphasised in a comprehensive review of liver-function tests by Gray (1950).

Ehrlich's test for urobilinogen must be made on freshly voided urine because urobilinogen is readily oxidised to urobilin on exposure to air. As immediate testing of urine is not always practicable, the test for urobilin thus has an obvious advantage. Schlesinger's test as usually performed, however, is relatively insensitive to small increases in urobilin. A modified procedure, which has been in use in this laboratory during the past two years, has proved very much more sensitive in detecting any increase in urobilin.

Principle.—The modification consists essentially in extracting the zinc-urobilin complex with chloroform and examining the chloroform solution in filtered ultraviolet light for a characteristic golden-yellow fluorescence. The best technique was decided by preliminary experiments as a result of which the following points were noted:

(1) Filtration before extraction with chloroform removes up to 40% of the fluorescence and must therefore be avoided.

(2) Addition of acid or alkali to the urine is unnecessary and undesirable. The zinc-urobilin is especially sensitive to acid.

(3) The use of iodine as oxidant in converting urobilinogen to urobilin is unsatisfactory because excess of iodine interferes with the production and extraction of the complex. This difficulty is avoided by the use of ammonium persulphate.

(4) Extraction with chloroform by gentle shaking for about 10 sec. removes 90–100% of the zinc-urobilin without any complicating emulsion.

(5) The test may be made on any convenient volume of urine (as little as 2 ml. if desired) by using proportional volumes of the other reagents.

Method.—To 5 ml. of urine in a small separator add a few crystals of ammonium persulphate and shake to dissolve. Add 5 ml. of saturated alcoholic zinc acetate and mix. Add 10 ml. of chloroform, shake gently, allow to separate, and run off the chloroform layer into a test-tube. Add a few drops of absolute alcohol to clarify, mix and examine in filtered ultraviolet light.

Interpretation.—The observation of a golden-yellow fluorescence is a positive indication of the presence of urobilin. A gross or moderate increase in urobilin is unmistakable, but greater certainty in detecting slight increases can be obtained by dividing the chloroform into equal parts, adding a crystal of trichloracetic acid to one to destroy any zinc-urobilin complex present, and comparing the fluorescence of the two portions side by side, when any definite yellow fluorescence in the untreated portion becomes easily discernible. A white or blue fluorescence is regarded as negative. Normal urine yields a bluish-white fluorescence which may occasionally have a slight yellow tinge, but a distinct yellow fluorescence may always be regarded as indicating increased excretion of urobilin. The test may be applied to fresh urine or to urine which is several days old with equally reliable results.

If a fluorimeter is available, the test may be made roughly quantitative by measuring the fluorescence with a primary Wood's screen and a secondary yellow or orange screen, before and after addition of a crystal of trichloracetic acid, the latter reading providing the blank, and comparing with a standard sodium-fluorescein solution (0·1% diluted 1 to 1000 or 1 to 2000).

The qualitative effect of bilirubin is to impart a yellowish colour to the chloroform solution but shows no fluorescence. Quantitatively, bilirubin interferes with the fluorimeter reading by absorbing the ultraviolet light used for activating the fluorescence. This effect can be largely overcome by diluting the chloroform solution stepwise until successive readings show a linear relation between reading and dilution.

REFERENCE

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CORTISONE AND LIVER FUNCTION

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Since the amount of fibrous tissue deposited in the liver of rats given carbon tetrachloride is reduced if cortisone is administered simultaneously (Aterman 1950, 1952, Cavallero et al. 1951), it is of interest to discover whether this neutralising effect is associated with a corresponding change in the function of the liver. Drill and Ivy (1944), who studied various liver-function tests in dogs receiving carbon tetrachloride, regarded the 'Bromsulphalein' retention test as one of the most sensitive indices of liver damage. After the adaptation of this test to small animals, and the demonstration of its suitability for assessing the degree of liver damage in the experimental fibrosis of carbon-tetrachloride poisoning in rats (Ahmad and Frazer 1952), it was chosen for a study of the effect of cortisone on the liver function of such rats.

METHOD

23 male albino rats of an inbred strain used in this laboratory, weighing 150–206 g. (average 177 g.) and fed on the stock laboratory rat cake diet ad lib., were given twenty-one subcutaneous injections of 0·2 ml. of carbon tetrachloride in seven and a half weeks at intervals of two or three days. After the seventeenth injection food, but not water, was withdrawn for sixteen hours, and next morning the bromsulphalein test was made by the method of Ahmad and Frazer (1952). Next day treatment with cortisone was started in a group of 12 rats, the remainder being kept as controls. Cortisone acetate ('Cortone' Merck) was given intramuscularly in two divided doses, the daily dose being 12·5 mg. on the first and last day, and 10 mg. and 8·75 mg. alternately for the rest of the experiment, with a day's interval in which no cortisone was given. Each rat therefore received 90 mg. of cortisone in ten days. Throughout this period the injections of carbon tetrachloride were continued in both groups. After the twenty-first injection, which coincided with the last day of the treatment with cortisone, all the rats were again starved for sixteen hours, and next day the bromsulphalein test was repeated. The rats were then killed, pieces of their livers were fixed in 5% formol-saline solution, and 7μ sections of liver were stained with hæmatoxylin and eosin and with the Mallory-Azan stain.

Another group of 5 male rats, weighing 200–240 g. (average 215 g.), was given cortisone alone in the same dosage as the previous group. Since the bromsulphalein retention of normal rats had been found to be fairly constant (Ahmad and Frazer 1952), the first test, before the start of the treatment with cortisone, was omitted, and the bromsulphalein retention was determined in this group only at the end of the experiment.

It should be emphasised that, in the calculation of the amount of bromsulphalein to be given, the considerable loss of weight caused by cortisone was taken into account The standard dose of bromsulphalein in each case was 25 mg per kg of body-weight

RESULTS

Table I shows the results of the experiment Judged by the amount of bromsulphalein retention at the time of the first test, the carbon tetrachloride had produced different degrees of liver damage This variation in susceptibility is a well-known feature of *carbon-tetrachloride* poisoning in rats But, whereas the continuation of the injections of carbon tetrachloride in the controls led to only minor changes of liver function during the ten days' interval between the first and the second *bromsulphalein tests, the simultaneous administration* of cortisone to the other group produced a striking deterioration in the elimination of bromsulphalein *in practically* every rat Improvement was shown by only 1 rat The degree of deterioration did not seem to be related to the loss of weight sustained In contrast to this group, however, the control rats, receiving cortisone only, showed no conspicuous change in the rate of elimination of bromsulphalein (table II)

TABLE I—EFFECT OF CORTISONE ON BROMSULPHALEIN EXCRETION OF RATS TREATED WITH CARBON TETRACHLORIDE

Carbon tetrachloride with cortisone						Carbon tetrachloride only					
First test (before treatment with cortisone)			Second test (after treatment with cortisone)			First test			Second test (10 days later)		
Rat no	Body weight (g)	B S P retention (%)	Body weight (g)	Loss of weight (g)	B S P retention (%)	Rat no	Body weight (g)	B S P retention (%)	Body weight (g)	Gain or loss of weight (g)	B S P retention (%)
1	196	23 40	144	52	84 44	3	230	3 82	247	+17	8 08
2	228	41 91	192	32	23 82	7	264	5 10	261	−3	8 08
4	232	7 65	194	38	40 85	14	268	4 46	283	+15	5 10
5	246	45 31	193	53	98 80	23	266	4 46	265	−1	4 96
6	208	11 91	156	52	71·49						
12	230	15 74									
15	246	7 02	195	51	88 93						
18	224	8 29	187	37	59 57						
21	218	27 44	178	40	48 93						
24	192	59 57									

Standard dose of bromsulphalein 25 mg per kg of body weight intravenously
10 mg per 100 ml of serum = 100 % retention
Normal value = 2 91 % ±0 052

The histological examination of the liver sections tended to bear out these results Since cortisone lessens the amount of fibrous tissue in early fibrosis, it is not surprising that in all but one animal (table I, no 5), the fibrosis was mild or absent The main interest attaches to the changes in the liver cells The cytological effects of the subcutaneous administration of small doses of carbon tetrachloride have been described by several workers (Cameron and Karunaratne 1936, Brunschwig et al 1945, Glynn and Himsworth 1946, Himsworth 1947) They consist, briefly, of fatty vacuolation eosinophilic staining of the cytoplasm with or withou pyknosis of the nucleus, and a peculiar "ballooning" o "hydropic degeneration" of some of the liver cells A characteristic feature of this picture is the zonal, pre dominantly centrilobular, distribution of these cellula changes Although the extent of the lesions may vary, a a rule there is, in the absence of advanced fibros sufficient intact parenchyma left, particularly in th periportal region, *to explain the degree of bromsulphalei* clearance found in this group (fig 1)

TABLE II—EFFECT OF CORTISONE ON BROMSULPHALEIN EXCRETION IN NORMAL RATS

Second test* (after treatment with cortisone)			
Rat no	Body weight (g)	Loss of weight (g)	B S P retention (%)
25	160	40	2 12
26	162	44	2 12
27	165	44	1 91
28	186	54	1 91
29	160	54	2 12

*Normal value = 2 91 % ±0 52

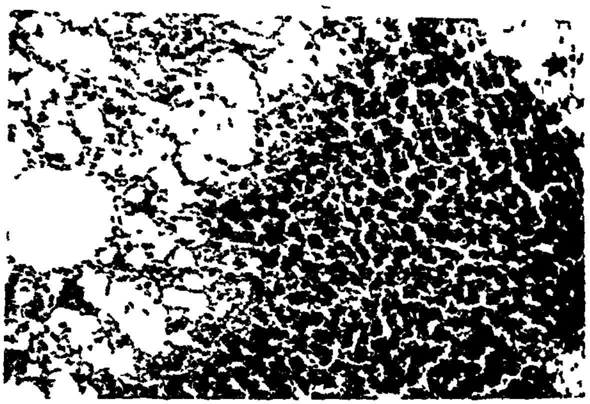

Fig 1—Rat no 23 (twenty-one injections of carbon tetrachloride) characteristic localisation of "ballooning" round central hepatic vein Note amount of histologically intact liver parenchyma. (5% formol saline solution Hæmatoxylin and eosin × 100)

The histological picture is changed in the rats receivin both carbon tetrachloride and cortisone The charac teristic zonal distribution of the cellular degenerativ changes is obliterated to various degrees, instead, th impression of a mosaic (figs 2 and 3) is gained, see particularly well in sections stained with Mallory Azan *The* dominant *feature now is an apparently haphazard* distribution of cells which vary greatly in their staining reactions and present more vacuolation as well as various transition forms to the "balloon like" cells The number of the latter is possibly also increased, whereas the number of histologically intact cells is distinctly reduced The whole picture now is one of rather severe damage Within broad limits it was possible to correlate the impairment of liver function with the histological picture Rat no 2 (table I), for instance, showed the least histological damage, whereas rat no 5 (table I), with severe functional impairment, *not only showed* the most

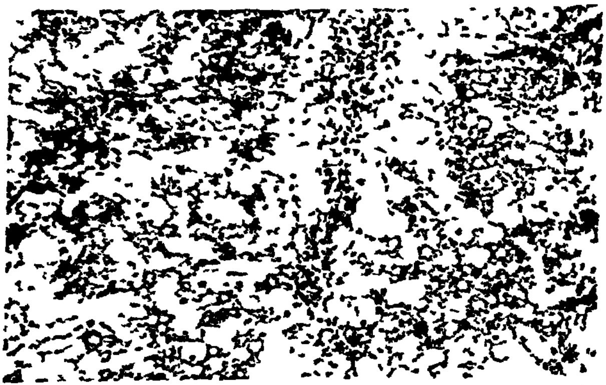

Fig 2—Rat no 5 (twenty-one injections of carbon tetrachloride, cortisone 90 mg in ten days) mosaic of cells with more vacuoles and unequal staining reaction (5% formol saline solution Hæmatoxylin and eosin × 100)

clot is found, the chance of its dislodgment is considerable, but, in view of the alternative dangers, is not so great as to force the abandonment of valvulotomy in a patient already judged to require it. In the first 44 of this series clot was found in 4 and embolism occurred in all. In 1 it was a fatal cerebral embolism. From that time precautions have been taken against embolism, first in patients with auricular fibrillation or known to have suffered embolism, and later in all cases. In the 66 cases, since precautions have been taken, clot has been found in 15 and embolism has occurred in 2. In addition, 1 patient developed embolism two months later, and another, with a past history of embolism, ten days after operation.

During all manipulations of the auricle and atrium, until it is reasonably certain that no clot remains in them, both common carotid arteries are compressed in the neck. It has not been considered necessary to expose the arteries of the neck provided that they are palpated with certainty and compressed. Before the auricle is clamped or sutured, an incision is made near its tip, and 3–5 oz. of blood is allowed to gush out so that loose clot may be carried with it. If the flow is not free, or fragments of clot are seen in the escaped blood, this lavage is repeated. If clot is felt within the atrium, lavage is repeated after exploration of the atrium and before valvulotomy. By this means all loose clot is removed before the valvular orifice is enlarged. This is the essential part of the procedure, and its success remains surprising.

The numbers are too small to show whether carotid compression is of value. The value of this manœuvre is uncertain, because in this series no patient whose carotid arteries were compressed during operation developed systemic embolism in any branch of the aorta beyond the carotids. We have some reason to suspect that the procedure may be dangerous because of the risk of cerebral anoxia; and, until the experience of other observers using a similar technique is known, we have decided to give it up.

Besides apparently loose clot, which has varied in quantity from minute fragments in the auricle to a mass filling a large part of the atrium and requiring ring forceps for its removal, two other types of clot have been observed:

(1) A layer of tough, largely organised, and widely attached clot lying on the wall of either auricle or atrium; (2) An organised clot attached by a pedicle to the auricular or atrial wall and with unorganised clot on its surface.

If a wide plaque of clot is found it is disturbed as little as possible. Part of it may need to be separated from the atrial wall to allow access to the valve, or the finger may be passed through the layer of clot. There appears to be little danger from this kind of clot, provided that its removal is not attempted. The second type, apart from small polyps in the auricle, has been seen on only one occasion:

A pedicled sphere, 3 cm. in diameter, was felt within the atrium. The attempt to remove it through the auricle was unsuccessful. It felt like a tumour, but the fragments removed consisted of organised clot. The main mass was left in the atrium, and no ill effect has arisen from it in the fifteen months since operation. The danger that it may enlarge and cause symptoms in virtue of its position or by the detachment of fragments is great enough to have justified a more sustained attempt at its removal before valvulotomy. The pedicle was on the posterior atrial wall within easy reach of the exploring finger. A 3 cm. incision on the posterior atrial wall close to the pedicle and large enough for delivery of the mass could probably have been safely closed.

In the series of 100, clot was found in 20 cases. In 1 case the rhythm was normal and in 18 that of auricular fibrillation. In 9 there was a history of systemic embolism. In 6 induration of the atrial wall was appreciated before the auricle was opened.

VALVULOTOMY

Valvulotomy was in all cases performed by digital pressure on the commissures. In some cases instrumental division of the commissures would have improved the orifice, but a knife was not successfully used. In the earlier part of the series efforts at division of the commissures were readily given up when the orifice would loosely accommodate the first knuckle of the index finger, and complete division of a commissure, which was later recognised as having occurred in a few cases, was accidental. It is possible that in no case in the series was the posterior commissure completely divided, but in most of the later cases the anterior commissure was completely divided. Until the finger has passed through the orifice and can feel the cusps from the ventricular side, the fact that the orifice is at the ventricular end of a funnel is not readily appreciated. The orifice from above feels like a hole in a diaphragm, and the commissures curve away from the posterior cusp anteriorly and posteriorly. The site of the commissures becomes clear by their division. Complete division of the anterior commissure has an unmistakable termination, but to achieve it without the help of a knife both persistence and a fair amount of force may be required.

In some cases the cusps felt almost normal and were held together by adhesions so fragile that valvulotomy was accomplished almost during the estimation of the size of the valve gap; yet in these cases with only slight valvular damage the symptoms of stenosis were severe. Two main obstacles to satisfactory valvulotomy were diffuse rubbery toughness of the commissures, for which a knife was probably necessary but not used, and massive sclerosis at the commissures, by which the valve ring, ventricular wall, and cusps were fused in one tough lump, whose division, even if it had been possible, held no prospect of benefit. Resilient sclerosis was encountered on 8 occasions, and massive sclerosis at the commissures on 5. In a few cases a mass of fused chordæ tendineæ was felt below the divided mitral commissures, and since it appeared to contribute to the stenosis its division was attempted. Whereas it required no special skill to divide the commissures in the correct line, the site of division of this mass of chordæ was erratic, and in 1 case its division was followed by rupture of chordæ and some degree of valvular incompetence.

Calcification of the cusps was recorded in 27 cases, in which rough calcified nodules, apparently uncovered by endothelium, were felt on the surface of the cusps. In 7 cases the calcification was extensive; the margins of the valvular orifice seemed to be entirely calcareous, and after valvulotomy calcareous spicules were felt crossing the space resulting from division of the commissures. Calcification did not usually prove an obstacle to division of the commissures, but in 1 case, in which calcification was mainly in the anterior commissure, the line of division of the commissure passed medial to the calcified area, and valvulotomy was followed by some regurgitation.

Deaths from Operation

The risk carried by the operation cannot be assessed on the statistical analysis of a series of cases. The risk for an otherwise healthy adult, under forty years of age, with uncomplicated mitral stenosis must be very slight. Apart from 1 instance of incompatible blood-transfusion no such patient has died in this series. The risk must increase with age, severity of cardiac failure, size of heart, auricular fibrillation, past history of embolic incidents, and concomitant disease in the lungs or elsewhere.

In this series 7 patients died as a direct result of the operation:

(1) A woman of 52, with a severe disability, long-standing auricular fibrillation, and a history of cerebral embolism, died of cerebral embolism which followed displacement of clot from the left atrium by the exploring finger. This death took place

TABLE I

School	No on school register	No of consents obtained	No completing 9 diagnostic swabs	No completing all tests
A	126	116 (92%)	84 (67%)	51 (40%)
B infants	176	139 (79%)	104 (59%)	50 (28%)
B juniors	249	195 (78%)	135 (54%)	73 (29%)
Total	551	450 (82%)	323 (59%)	174 (32%)

The figures in parentheses are percentages of children on the school register

Various workers have reported that diphenan will rid children of oxyurids, and it has been claimed to be non-toxic and tasteless, and to have the advantage of being a vermicide as opposed to a vermifuge (Brann 1922, Disque 1921, Kuitunen-Ekbaum and James 1950, Kjerrulf 1921 Koslowsky 1920, Kretschmer 1920, Schuckhardt 1920, Schule 1920, Selter 1921)

METHODS

Sampling

In the present series all the parents of children attending two county schools, each serving semi-urban districts, were invited to submit their children for examination, and treatment if necessary There were relatively few refusals or "no replies"

In only one or two isolated cases was a child withdrawn by a parent during the survey The school absentee-rate in each school approximated throughout to normal school experience, and it is therefore suggested that the percentage of consents obtained is probably a more valid measure of the sample examined than is the percentage of children who completed all the tests

The planned course, in its entirety, consisted of nine successive daily diagnostic swabs, followed, when any of these were positive, by 10 days' treatment and a further nine post-treatment swabs This necessity for an unbroken attendance for 30 school days was a stringent requirement, nevertheless we have included in this report only those children who satisfied it (table I)

Diagnostic Criteria

The 'Cellophane'-tape technique described by Graham (1941) and Watson and Mac Keith (1946) was used throughout Impressions were taken by applying the cellophane with a wooden applicator to the skin in the anal region The strip of cellophane was then immediately stuck on an ordinary microscope slide The slides were examined unstained under a low-power objective, when the ova were easily seen

No fixed time was laid down for the examination of a slide before classifying it as negative, but on the average 20 slides an hour were examined Some of these hardly required more than a glance owing to the large numbers of ova present No attempt was made to count the ova, but each slide was arbitrarily classified into one of three groups according to the relative number of ova present in the fields examined (No subsequent use was made of this classification)

It is known that the proportion of children found infested increases with the number of impressions taken, up to about 13 (R Mac Keith, personal communication)

The disorganisation of school life occasioned by this survey and the extra work placed on the laboratory were considerable, so we decided on a diagnostic standard of nine daily impressions as being the maximum expedient in the circumstances Even so some 7000 slides were examined

TABLE II—ANALYSIS OF TREATMENT

School	Age (yr)	Dosage (g t.d.s)	Treatment (days)	Manufacturers recommended dosage
A	5–10 –	0 5	10	For children aged 1½–10 yr 0 25 g t.d.s for 7 days followed by repeat course after 7-day interval
B infants	3– 7	0 75	10	
B juniors	6 +–10 –	1 0	10	

Treatment

Diphenan tablets were given thrice daily at the school under supervision for 10 successive days No untoward symptoms were reported, and the children took the tablets willingly Details are given in table II

The circumstances of the survey made it impossible for a second controlled course of treatment to be given as recommended by the manufacturers

Diphenan is said to act by causing extreme muscular contraction of the worm with death within a few moments of contact If diphenan were as effective as has been claimed, both adult and gravid worms would be destroyed, and therefore post-treatment examination should give negative results, at least for a time

RESULTS

The results are tabulated in table III, which shows that of the 174 "positive" children 20% were "cured," 44% were improved in the sense that they gave fewer positive swabs after treatment than before, 18% were worse, and 18% gave the same number of positives before and after treatment

It will be seen that complete cures, judged by the absence of positive post-treatment swabs, were few, most of these 35 children had been lightly infested, 31 of them having given one, two, or three positive swabs out of the nine taken for diagnosis

TABLE III—ANALYSIS OF RESULTS

School	No of children completing course	No giving all negative swabs after treatment	No giving fewer positive swabs after treatment	No giving same no of positives after treatment	No giving increased no of positives after treatment
A	51	6	26	12	7
B infants	50	6	20	13	11
B juniors	73	23	31	6	13
Total	174	35 (20%)	77 (44%)	31 (18%)	31 (18%)

Only in the juniors of school B was treatment given to children who had given nine diagnostic negatives, and of these 15 children only 6 remained negative Of the remainder 6 gave one positive, 2 gave two, and 1 gave three positive post-treatment swabs The results were also analysed for each year of age, but the findings were not significantly different from those given above for the group as a whole

Although the crude figures (table III) indicate that 64% were cured or improved, detailed study of the results of the pre treatment and post-treatment examinations showed that the shift in the direction of improvement was relatively slight, and this could be explained by the tendency towards extra cleanliness during the survey, irrespective of the treatment

The results are even more disappointing when it is realised that the dosage given was at all times considerably in excess of that recommended

Oxyuric infestation is undoubtedly widespread, at least among school children (Jones et al. 1939, Mac Keith and Watson 1948, Coutelen 1950) and our findings suggest an incidence of about 80% The degree of infestation varies in each child from time to time, and seldom are there symptoms indubitably attributable to this parasite

There are many inherent difficulties in investigating the effect of any given treatment in a condition with such characteristics, and, though the present work may leave much to be desired as regards scientific precision, we offer it as an objective assessment of a widely used remedy early in our experience before we adopted routine precautions against systemic embolism.

(2) A man of 42, with severe pulmonary hypertension died as a result of a technical error. Blood which had been prepared for another patient was transfused and proved highly incompatible. After three days' anuria the patient died from tubular necrosis of the kidneys.

(3) A woman of 42, with auricular fibrillation, severe chronic congestive failure, and cardiac cirrhosis of the liver was accepted for valvulotomy because of her otherwise hopeless outlook. She had been bedridden for three years. The valvulotomy was satisfactory, although the cusps were heavily calcified. Her subsequent cardiac condition gave no cause for concern, but two days later she suddenly had an epileptic fit and died. Necropsy did not reveal a satisfactory cause.

(4) A woman of 57, with a severe progressive disability, auricular fibrillation, and high pulmonary hypertension was accepted in spite of her age because there was no other obvious contra-indication to operation. During the thoracotomy the heart-rate became steadily slower, and cardiac massage was given. Simultaneously it was observed that ventricular fibrillation had begun. Massage was continued for half an hour, and various drugs were given but without avail.

(5) A man of 34, with a severe disability, congestive cardiac failure, right ventricular filling pressure 22 mm. Hg, a large heart, electrocardiographic signs of considerable right ventricular hypertrophy, and pulmonary hypertension (mean pressure 75 mm. Hg). The valve was calcified, but the anterior commissures were satisfactorily divided. Two days later the patient suddenly collapsed and died. Necropsy revealed in the left atrium a mass of adherent clot which completely obstructed the mitral orifice. It is believed that this formed shortly before death.

(6) A woman of 38, with intractable cardiac failure, auricular fibrillation, and gross enlargement of the heart, mainly from aneurysmal dilatation of the left atrium, was operated on in the hope that she might obtain sufficient relief to leave her bed and to lead a somewhat more active existence. At operation the anterior commissure of a not very tightly stenosed valve was completely divided. During the closure of the auricle the heart's action stopped, but it was restored by cardiac massage and with methedrine. During the following night her condition deteriorated and the heart again stopped.

(7) A woman of 50, with considerable progressive disability and auricular fibrillation, gave a history of recent systemic embolism. At operation the left atrium was found to contain much clot, loosely pedicled in the auricle. Repeated gushes of blood were required, to wash it out. On coming round from anæsthesia the patient was confused, but there were no localising signs of cerebral embolism. On the fifth postoperative day she suddenly lost consciousness, and she never fully recovered. She developed mesenteric embolism on the tenth day and died forty-eight hours later.

It will be evident that these deaths occurred in patients with severe heart-disease in whom the prognosis without operation was poor. Each gladly accepted the risks of operation because there was a reasonable chance of improvement. Refusal to accept patients in this group would be to deny the chance of a new lease of life to many.

Postoperative Results

Our first patient was a woman of 28 who for some years had been unable to earn her living and was largely confined to the house.

She could walk slowly on the level but was unable to climb stairs. She slept propped up in bed and was subject to attacks of dyspnœa and recurrent hæmoptysis. She had a low fever believed to be related to intense pulmonary congestion and probable patchy infarction. She had signs of mitral stenosis and aortic incompetence. The mean pressure in the pulmonary artery was almost as high as that in the aorta, and electrocardiography confirmed the presence of severe right ventricular hypertrophy (fig. 4a).

At operation tight mitral stenosis was found, and both commissures were partly divided. The orifice, which would not admit the extreme tip of the index finger, was made large enough to accommodate the first knuckle. Convalescence was uninterrupted.

During the next year she trained as a shorthand typist, returned to amateur dramatics, and went for a holiday climbing hills. At Christmas she took an active part in the chorus of a pantomime on the public stage. In the next year she obtained a full-time secretarial post, took charge of a troop of Girl Guides, and was annoyed because she was not accepted for service in the Navy. She ended the year again acting in pantomime, and in addition running the Christmas show at a large factory. She is not aware of undue dyspnœa on exertion and has had no further hæmoptysis. The electrocardiographic signs of ventricular hypertrophy have disappeared (fig. 4b).

Although not all the results are comparable with the first, most of the patients in this series of 100 cases subjected to valvulotomy for predominant mitral stenosis have been much improved. The results of surgical treatment in those with predominant mitral incompetence have been reported separately (Logan and Turner 1952b).

It must be remembered that valvulotomy is not curative. Changes in cusps, chordæ tendineæ, and cardiac muscle persist. The period of follow-up in this series is necessarily short. The best results have been, as might be expected, in those with tight stenosis, normal rhythm, little enlargement of the heart, and no cardiac failure except that associated with paroxysmal dyspnœa. Most of the patients with recurrent hæmoptysis also fared well.

No patient previously subject to attacks of paroxysmal dyspnœa or hæmoptysis (except that due to pulmonary tuberculosis) has had a recurrence.

Those with severe pulmonary hypertension often have secondary changes in the pulmonary arterioles and considerable right ventricular hypertrophy. These changes are at least in part reversible, and striking improvement sometimes takes place.

In 2 cases pulmonary infarction had been so extensive that there was a delay of several months before valvulotomy could be considered even from the point of view of anæsthesia. Both made good postoperative progress.

Age does not preclude improvement even after many years' disablement. Auricular fibrillation presumably indicates myocardial as opposed to valvular damage, and tends to develop in the older patients. Those with auricular fibrillation are usually disabled by dyspnœa on exertion, tiredness, and weakness rather than by paroxysmal dyspnœa and recurrent hæmoptysis; but improvement is often considerable, although the arrhythmia persists and only the mechanical obstruction has been changed.

A patient, aged 42, spontaneously reverted to sinus rhythm three months after valvulotomy, but about six months later fibrillation returned without her being aware of it, and has persisted.

Generally speaking, when the heart is large its muscle is considerably damaged, and great benefit cannot be expected; but, when there is also stenosis and this is reduced by operation, there may be gratifying improvement.

Most patients who are underweight gain about a stone (6 kg.) within a few months of the operation and sometimes within a few weeks.

As already mentioned, some are obviously too ill for operation to be considered; and in others operation is precluded by important complications. But our experience suggests that most patients with predominant mitral stenosis can be safely subjected to valvulotomy in confident expectation of improvement.

Only 7 patients in this series have been followed up for more than two years; 27 have been followed up for one to two years, 26 for six months to a year, and 33 for less than six months. This therefore is necessarily a preliminary report. In 66 out of 74 patients who underwent operation more than three months ago the results could be classified as good or very good. Most patients claim to be very much improved, but it is difficult to classify a result as good if a large heart remains the same size and auricular fibrillation continues—although change in

SUMMARY

An attempt has been made to assess the efficacy of *p*-benzyl-phenyl-carbamate (diphenan) as a vermicide

In 174 school children, aged 3–10 years, in whom infestation with threadworms was demonstrated, diphenan was given far in excess of the normal dosage for ten days

Subsequent examination showed few cures and these mostly in lightly infested children The condition of many was unchanged and that of some worse after treatment

No toxic reactions were encountered

This work would have been quite impossible without the coöperation of the parents and the willing assistance of the school teachers and the school nurse, Miss D Vickers, on whom this work placed a very real burden We also thank Dr C H Jellard and Dr J J Mackintosh and Mr C W Sivell for many hours of tedious work, and gratefully acknowledge the financial assistance and permission to use school facilities given to us by the Norfolk Education Committee and by Dr T Ruddock West, the school medical officer

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OBSERVATIONS ON THREE CASES OF ACUTE PORPHYRIA

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The following clinical and biochemical observations on patients with acute porphyria in three generations of one family appear to throw some light on the causal effects of porphobilinogen and uroporphyrin

Case 1 —A man, aged 27, had suffered for many years from periodic attacks of hoarseness of voice, paralysis of the arms with wristdrop, and acute abdominal pain accompanied by obstinate constipation He was seen by one of us (F R F), and a diagnosis of acute porphyria was made on clinical grounds and later confirmed by biochemical investigation He was admitted to Manchester Royal Infirmary on March 9, 1942

Progress—For the first three weeks his condition improved considerably, and there was some return of dorsiflexion of the wrists On March 30, however, another attack developed, with intense abdominal pain and vomiting, increasing hoarseness, restlessness, and muscular weakness Nine days later his legs became weak and his voice almost inaudible, and he developed a bilateral facial paresis, but no weakness of tongue or palate Next day he began to have a muttering delirium and occasional muscular spasms which spread from his arms and fingers to his face There was bilateral ptosis, but the pupils reacted to light, and ocular movements seemed full and equal It was impossible to test sensation Pulse and respiration increased in rate though there was no pyrexia during the attack He died on April 11 of respiratory failure

Histology—Dr E Pollak made a comprehensive neurohistological examination and found three processes localised to different parts of the nervous system (1) a very chronic segmented degeneration of myelin sheaths of all peripheral nerves examined (Mason et al 1933), (2) an acute destruction of anterior-horn cells and certain cranial and sympathetic nuclei in the form of a vacuolar degeneration, and (3) a toxic encephalopathic process in the medulla affecting the substantia reticularis

Biochemical Findings (Kench 1943)—48 mg of uroporphyrin III was excreted per litre of urine, mainly as zinc complex Neither uroporphyrin I nor protoporphyrin was detected Urinary coproporphyrin was 163 µg per litre before the attack and 128, 43, and 148 µg per litre during the attack, consisting of approximately equal quantities of isomers I and III Stools contained 0 13 mg of coproporphyrin per 100 g of fresh material during a remission, and 1 81 mg per 100 g during the final attack No uroporphyrin was detected at any time There was an intense positive porphobilinogen reaction in the urine, but the concentration was not measured The liver contained 13 5 mg of coproporphyrin III and 50 µg of protoporphyrin No ether soluble porphyrins were detected fluorimetrically in blood or cerebrospinal fluid, and traces only were found in the spleen

Urine specimens from twelve other members of the patient's family were examined for porphobilinogen and uroporphyrin Except the patient's mother (case 2) all these persons were normal both clinically and biochemically There was no history of consanguineous marriages in the family

Case 2 —The mother, aged 64, had first noticed that her urine was abnormal shortly before the birth of her eldest child (case 1) twenty seven years earlier Her urine was reddish-brown when it was passed but darkened on standing Since that time her urine had been continuously dark, but in spite of this she had never had any of the usual symptoms of porphyria Her only complaint had been of regular attacks of severe prostrating headache and vomiting, which began about the time of onset of the porphyria and resembled migraine (Waldenström 1937)

Biochemical Findings—Studies made in 1943 (Kench 1944) showed uroporphyrin III to be the only porphyrin which could be isolated from the urine, and it was present in concentrations up to 2 mg per litre After experimental *d* glucosamine and liver therapy, however, the excretion of uroporphyrin was greatly increased for twenty eight days, with a maximal value of 27 mg of uroporphyrin per litre Urinary porphobilinogen also showed a peak value at that time, accompanied by an unprecedented attack of headache, vomiting, sleeplessness, and severe constipation of three weeks' duration

Investigation of the urine in November, 1952, has shown the excretion of uroporphyrin and porphobilinogen to be virtually unchanged from values observed in 1943, the porphobilinogen concentration (mean of 7 specimens) being 1 4 Vahlquist units per ml of urine (Vahlquist 1939)

Case 3 —The son of case 1 has been examined at intervals during the last ten years for biochemical or clinical evidence of acute porphyria Now aged 14, he remains in good health, with no clinical signs or symptoms of the disease, but, whereas his urine was quite normal two years ago, it now contains 0 63 Vahlquist units of porphobilinogen per ml The presence of porphobilinogen is characteristic of acute porphyria (Hammond and Welcker 1948) No uroporphyrin could be measured in the urine by the spectrophotometric procedure of Sveinsson et al (1949), either before or after the urine was heated at 100°C at pH 5 2 for thirty minutes (Grieg et al 1950)

These three cases show a grading in clinical severity associated with differences in excretion of porphobilinogen and uroporphyrin as follows

		Biochemical observations	
	Clinical manifestations	*Uroporphyrin*	*Porphobilinogen*
Case 1	+++	+++	+++
Case 2	+	+	+++
Case 3	–	–	+

Porphobilinogen is probably not the causal factor of the characteristic neurological changes in acute porphyria (Rimington 1952), but porphobilinogen and these features is not to be expected. No patient who survived has been made worse.

It will be seen from table II that many results are classed as good, although only partial division of one or both commissures was achieved at operation. An incomplete valvulotomy reducing tight stenosis to moderate stenosis is compatible with great improvement. It is not yet known whether regression will take place, because of either residual stenosis or re-fusion of the cusps.

Apart from the 7 deaths from operation and 1 subsequent death, which are discussed separately, the results were poor in 2 cases:

(1) A woman of 28 had a very large heart and tight stenosis with extensive calcification of the cusps. It had been appreciated that myocardial damage must be severe, but we had hoped that by decreasing the mechanical obstruction material benefit might follow. Although she stood the operation well, the functional result two years later is disappointing although it may be that her life has been prolonged.

(2) A woman of 27 was considerably improved for six months after operation, after which her condition gradually regressed. She was so impressed by the initial result that she volunteered to undergo another operation if the same effect could be achieved. She was observed for a further twelve months, and it became apparent that she was approaching her preoperative state. Accordingly cardiac catheterisation was repeated, and it was found that her pulmonary hypertension (45 mm. Hg at rest) was the same as before operation and rose promptly on exercise. Both mitral commissures had been partially divided, and it seemed either that the cusps had again become adherent or that pulmonary arteriolar resistance was unchanged and a dominant factor in her pulmonary hypertension. Unfortunately at the first investigation her pulmonary capillary venous pressure had not been recorded, but on the second occasion the pulmonary-artery/capillary-venous gradient amounted to 20 mm. Hg, indicating a moderate degree of resistance in the pulmonary arterioles. Since she was young and her symptoms were disabling, a second thoracotomy was done. The extent of recurrent fusion of the cusps was negligible, but it was possible to complete the division of the anterior commissure and increase the division of the posterior. She was again improved, but the second operation took place only three months ago.

The result in 6 patients has been classified as fair: 1 developed a hemiplegia five months later, 2 had very large hearts, 2 are unintelligent, and we doubt that they are as much improved as they maintain, because they did not have much pulmonary hypertension or very tight stenosis, and the valvulotomy was incomplete. In 1 who did not have very tight stenosis but had quite extensive division of the commissures the reason for lack of greater improvement is obscure.

LATER DEATHS

One patient died after returning home*:

A woman of 59 (case 41), with recurring paroxysmal auricular fibrillation which precipitated severe pulmonary œdema, experienced a further attack, with a ventricular rate of 200, a month after returning home. She recovered after intravenous digoxin but ten days later developed hemiplegia from cerebral embolism. Necropsy showed that clot had formed along the line of the auricular incision. Whether this happened during the attack of paroxysmal tachycardia or in the immediate postoperative period was impossible to say. Postoperative convalescence had been smooth, apart from transient symptomless auricular fibrillation.

Assessment of Improvement

Assessment of improvement must be largely subjective, but in most patients the change following valvulotomy leaves the clinician in no doubt that pulmonary congestion has been relieved and the ability of the heart to raise its output on exertion has been increased. Improvement is easiest to assess in those who were previously most disabled. Some patients are convinced that from being grossly disabled they have become normal again.

Dyspnœa is a good guide to deterioration or improvement in patients with mitral stenosis, and reduction of dyspnœa on exertion is the most commonly appreciated effect of valvulotomy. Those who were obliged to sleep propped up in bed may find after operation that they can lie flat without discomfort. Because of the wide variation in the frequency of the attacks prolonged postoperative observation is required before it can be concluded that paroxysmal dyspnœa and hæmoptysis have ceased.

Cough, sputum, and repeated attacks of "bronchitis" are common manifestations of pulmonary congestion and œdema in patients with mitral stenosis, and several patients have remarked on improvement in this respect after valvulotomy.

Vital capacity.—Breathing exercises under the guidance of a physiotherapist were given before and after operation so that a reliable measure of vital capacity might be recorded. There is often some restriction of left diaphragmatic movement after thoracotomy, and it is best to wait three months before attempting to assess improvement by measurement of the vital capacity. In this series the vital capacity has proved a poor guide to the severity of mitral stenosis or to postoperative improvement. The value of more detailed tests of pulmonary function is now being investigated.

Nutrition.—Most patients have gained considerable weight after operation, some of them 7–14 lb. before leaving hospital three or four weeks after operation.

Ability to do more.—Most patients notice an increased feeling of well-being and do things which they were previously unable to do because of lassitude and weakness. A return to household duties and social activities is not the least of the benefits of successful valvulotomy.

Cardiac size.—In most cases there has been no change in the size of the heart other than that resulting from resection of part of the left auricle, but in a few an appreciable reduction has taken place. Preoperative films may show variation in cardiac size according to the position of the diaphragm and the phase of the cardiac cycle in which the exposure was made. This fact makes all but considerable changes in size impossible to estimate.

Electrocardiography.—Regression of signs of right ventricular hypertrophy has been observed in 4 cases. These were all in patients with tight mitral stenosis and severe pulmonary hypertension in whom a wide valvulotomy was achieved.

Psychology.—The psychological effects of the operation have been favourable in every case, but in those relatively little disabled this makes the assessment of organic improvement more difficult.

Pulmonary hypertension and cardiac output.—The measurement of intracardiac pressures and of the cardiac output at rest and on exertion and the calculation of pulmonary resistance are the only objective assessments likely to be of real value. These tests have not so far been repeated after operation in this series. It would be necessary to wait at least a year for improvement to become stabilised. The relationship between accentuation of the pulmonary second sound and pulmonary hypertension is not constant, but intensity is useful as a rough guide and has slowly diminished in most cases.

CHANGE IN CLINICAL SIGNS

The change in clinical signs produced by valvulotomy cannot be predicted from the findings at operation or from the extent of the valvulotomy. In some cases a diminution in signs has resulted, but in most there is little change. Since the sclerotic changes are not affected by the operation, it is perhaps not surprising that the diastolic murmur persists; but we had expected that the uroporphyrin together were related in these three patients to the severity of clinical manifestations Under optimal conditions in vitro the yields of uroporphyrin from highly purified porphobilinogen have not exceeded 40% (Westall 1952), hence the sum of porphobilinogen and uroporphyrin may be a more reliable index of the biochemical disturbance which obtains

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* A second death (case 57), unrelated to the valvulotomy ten months previously, has recently occurred.

It will be of interest to observe if and when clinical manifestations appear in case 3, and whether these will be associated with measurable quantities of urinary uroporphyrin

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PERIPHERAL NEUROPATHY DUE TO ISONIAZID

REPORT OF TWO CASES

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One of the advantages of isoniazid in comparison with *p* aminosalicylic acid (P A S) in the chemotherapy of tuberculosis is the diminished incidence of toxicity No significant intolerance of isoniazid has been observed so far in the present M R C chemotherapy trial, although some cases have shown toxic responses to P A S (Medical Research Council 1952, 1953)

The preliminary reports on isoniazid mentioned hyper-reflexia, transient extensor plantar responses, hesitancy of micturition, vertigo, evanescent proteinuria, and occasional severe eosinophilia as manifestations of toxicity In the past year further toxic reactions have been reported, blood dyscrasias and nervous complications being the most important

Agranulocytosis has been described by Ferguson (1952) and by Varadi and Kelleher (1953) Various nervous complications include acute pellagra (McConnell and Cheetham 1952), confusional psychosis (Hunter 1952, Leitner 1952, Zabad 1953), hyperæsthesia (Pegum 1952), polyneuritis, motor weakness, and schizophrenia (Heilmeyer et al 1952), and peripheral neuropathy (Selikoff et al 1953, Counihan et al 1953)

CASE-RECORDS

Case 1 —A man, aged 23, had periodic bronchitis and asthma since the age of 12 Valvular heart disease, presumably rheumatic, had been diagnosed at 14 Two siblings died of tuberculosis

After the diagnosis of pulmonary tuberculosis in November, 1951, he spent six months in a sanatorium, and was under chest clinic supervision in October, 1952, when further extension of his disease was detected Daily domiciliary treatment was instituted with P A S 18 g and isoniazid 300 mg (5 mg per kg of body weight) After six weeks' chemotherapy he complained of hypersensitivity of hands and feet, with considerable sweating of palms and soles Muscle power gradually weakened in wrists and fingers, and dyspnœa became troublesome P A S therapy was discontinued, but, the symptoms persisting, the isoniazid therapy was also discontinued, and he was given thiamine tablets (vitamin B_1) 18 mg daily During the period of chemotherapy the patient's domestic conditions were extremely unsatisfactory, and his diet was probably deficient in first-class protein, and he received no vitamin supplements Four weeks after cessation of chemotherapy he was admitted to hospital

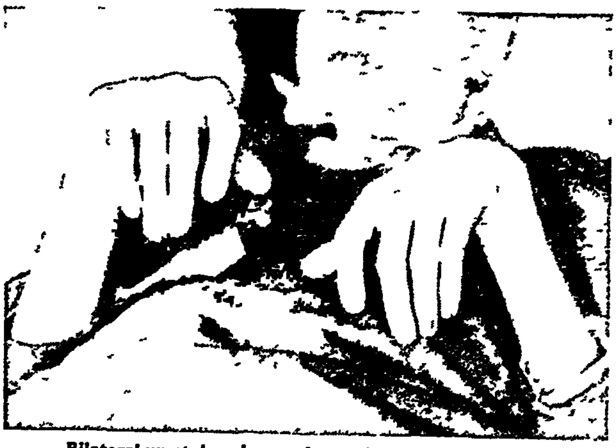
On admission his general condition was very poor, and he had persistent moderate pyrexia, pulse rate 124, and blood pressure 105/75 mm Hg A harsh systolic murmur was audible over the whole of the precordium, with apical triple rhythm Signs of congestive failure were present, with jugular engorgement and sacral œdema The liver was moderately enlarged, and ascites was detected Electrocardiography showed right ventricular preponderance and sinus tachycardia Moist sounds were audible over the whole of the chest, and radiography of the chest revealed chronic bilateral tuberculosis with considerable cavitation The heart was also shown to be enlarged Wasting of the forearms and of the small muscles of the hands was pronounced, with bilateral wrist drop Ankle dorsiflexion was also weak, and the peripheral tendon reflexes could not be elicited Passive joint movement and muscle pressure were unduly painful There was no significant loss of joint sense, but patchy cutaneous hypæsthesia was present on the front of the shins and dorsum of the feet The soles of the feet looked rather red and raw Although the patient's manner was petulant, his responses were rational and he showed no cerebral impairment

A blood count and examination of the urine were normal Sputum was smear positive for acid fast bacilli

Treatment was started with intramuscular thiamine 200 mg, which on two occasions failed to evoke a diuresis Mersalyl (2 ml) also failed to have a significant effect The patient's general condition deteriorated somewhat, the œdema increasing, with little improvement in the peripheral limb changes Mental confusion was noticed once or twice, and thickening and exfoliation of the skin on the back of the hands were thought by the staff to be due to excoriation produced by bandages holding the wrist splints These features of classical pellagra became obvious, and therapy with intramuscular nicotinamide 100 mg and mersalyl was followed by rapid clinical improvement Chemotherapy was restarted with streptomycin and P A S, the vitamin B complex being continued orally

Progress —A month after admission the signs of congestive failure had improved, the blood pressure was 120/90 mm Hg, and the pulse rate was 80 Triple rhythm, with a generalised systolic murmur, persisted There was no impairment of cutaneous sensibility, and the motor weakness had improved considerably, apart from a persisting weakness of the left wrist extensors There was some residual wasting of the peripheral muscles, and both knee and ankle reflexes were absent The chest film showed a decrease in the heart size, and the hyperkeratosis on the dorsum of the hands gradually improved

Case 2 —A girl, aged 18, had had bilateral extensive tuberculosis for three years Streptomycin and P A S were given in 1949 for six weeks with little improvement In 1952 isoniazid alone was administered for three months at home in a daily dosage of 450 mg (12 mg per kg of body weight) Again there was no significant change in either the chest film or her general condition, and a further three month course of isoniazid alone was given four months later



Bilateral wrist-drop in case 1, on admission to hospital first heart sound and the opening snap would be modified. Presumably vibration of the leaflets rather than the *actual closure or opening of the valve* is responsible for these signs. We have not noted the disappearance of a systolic murmur after valvulotomy, but in some cases a systolic murmur has been produced although unaccompanied by dynamic evidence of mitral incompetence.

Dangers in Delay

A correct decision on whether to perform valvulotomy requires a more precise assessment of mitral disease than was customary, or helpful, before surgery became possible. Without such an assessment patients may be kept under observation until the best time for operation has passed; and occasionally deterioration is rapid. At the present time, too, when many patients with mitral disease await admission to hospital for investigation or operation, there are unavoidable delays, during which lives are lost. The principal dangers are from acute pulmonary œdema, congestive cardiac failure precipitated by acute respiratory infection, pulmonary embolism or infarction, and systemic embolism. It might be thought that to patients subject to these dangers the risk from operation would be great, but in our experience this is not evident and the results of operation are often gratifying.

Since valvulotomy has only recently been established most patients in this series were operated on too late—not too late for considerable or material benefit to *accrue but too late for them to gain the fullest advantage.*

In each case, granted the opportunity, there must have been an optimal time, and the responsibility of physicians in the future is to select it. This will not always be easy; but in our view the error is likely to be on the side of operating too late rather than too soon. Once any considerable stenosis has developed, the passage of time will usually lead to progressive damage to the heart in the form of muscular dilatation and hypertrophy; damage to the pulmonary vessels in the form of arteriolosclerosis and atheroma; and damage to the lungs and liver in the form of chronic passive congestion. It bears repetition that progression of symptoms, at any stage, means that operation should be considered.

Summary

Of 200 patients with mitral valvular disease subjected to operation, 130 came from one *medical unit, and of* these the first 100 with predominant stenosis are reviewed.

Cases of all grades of severity, except those without symptoms and those with very large hearts and uncontrollable cardiac failure, were included. In the absence of contra-indications operation should be considered for every patient with mitral stenosis in whom symptoms are progressive.

The ages of the patients ranged from sixteen to fifty-nine, 14 being over fifty. 83 were female.

The more important symptoms and signs of predominant mitral stenosis are described and compared with those in 17 cases of predominant mitral incompetence. The value of the various signs in judging the advisability of surgical treatment is discussed.

In distinguishing predominant stenosis from predominant incompetence emphasis is laid on the qualities of the first heart sound and opening snap. The qualities of an apical systolic murmur and systolic expansion of the atrium are of relatively little value. Mistakes can usually be avoided by paying attention to all the relevant factors.

Radiography is indispensable. Electrocardiography sometimes gives useful confirmatory evidence. Cardiac catheterisation may be valuable in *difficult cases.*

The patients with the highest pulmonary arterial pressures tend to have a high pulmonary arteriolar resistance, tight mitral stenosis, normal rhythm, right ventricular hypertrophy, recurrent hæmoptysis, and breathless attacks but not pulmonary œdema; they seldom have auricular fibrillation. A *relatively* low pulmonary arterial pressure may be due to severe myocardial damage.

40% of the patients had established or paroxysmal auricular fibrillation. Auricular fibrillation is a disadvantage but not a contra-indication to operation. 19% who had sinus rhythm before operation developed auricular fibrillation in the immediate postoperative period. The restoration of sinus rhythm with quinidine is discussed.

Pregnancy often aggravates the symptoms and signs of mitral stenosis. Valvulotomy is sometimes an alternative to the *termination of pregnancy. The results in* 3 such cases are reported.

The outstanding unpredictable risk of the operation is embolism; but cardiotomy may be an effective method of evacuating clot from the left auricle and atrium without the production of systemic embolism.

In the present series 7 patients died as a result of the operation. The causes of death were embolism (2 cases), ventricular fibrillation, transfusion reaction, cardiac arrest, probable hepatic failure, and probable intracardiac thrombosis. 5 of these patients were severely ill before operation. 1 patient died later.

Of 74 *patients followed up for* more than three months the results are good in 66, fair in 6, and poor in 2. In 1 of the patients with a poor result a second operation has achieved better division of the commissures.

In patients with intractable œdema ligation of the inferior vena cava may prove to be a useful prevalvulotomy procedure.

It is emphasised that valvulotomy is not curative, and changes in cusps, chordæ, and cardiac muscle persist.

Team-work is necessary in the investigation and treatment of these patients and the recording of their cases. We acknowledge with gratitude the help of the staff of the cardiac unit in the Western General Hospital, the staff of the thoracic unit in the Eastern General Hospital, and the radiological staffs of both hospitals.

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DIABETES AND PERIPHERAL ARTERIAL DISEASE

A CLINICAL STUDY

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As it has long been known that arterial disease is a common complication of diabetes mellitus, I was surprised to find only 6 cases of diabetes in 100 cases of intermittent claudication due to obliterative arterial di

The object of the present study wa whether there was any difference betwe occurring in diabetics and in no investigate the prevalence and type disease in a group of diabetics.

METHO

100 unselected diabetics, a the diabetic clinic of the ined. A short clinical points noted included claudication or of rest was also made conc and angina pect recorded and the absence of the

Towards the end of the second course the patient began to complain of paræsthesiæ, "hot feelings," in the hands and feet Stiffness and numbness of the legs, with occasional shooting pains, became more pronounced Her appetite had been poor during this course of chemotherapy, improving when the isoniazid was stopped Two weeks after the cessation of isoniazid therapy there were signs of peripheral neuropathy Neither ankle reflex could be elicited, patchy areas of anæsthesia were present over the front of the legs and the dorsum of the feet, and muscle pressure was very painful Appreciation of movement and position was absent in the toes, but no significant objective change, motor or sensory, was detected in the arms

Her symptoms improved gradually, and three weeks later the signs of neuropathy were noticeably less In view of her poor general condition, gross disease, and emaciation no further chemotherapy was proposed, no vitamin supplements were given, and treatment was symptomatic

DISCUSSION

Pegum (1952), drawing attention to "burning feet" in a patient receiving 150 mg daily of isoniazid for one week only, suggested that this condition was caused by competitive inhibition of nicotinic acid by the isoniazid McConnell and Cheetham (1952) emphasised this possibility when they described a case of acute pellagra following two weeks' chemotherapy in a patient who received isoniazid 8 mg per kg body-weight Zabad's (1953) case of confusional psychosis following isoniazid therapy responded dramatically to nicotinamide administration, and probably Hunter's (1952) case was also due to conditioned nicotinamide deficiency

Dementia, dermatitis, and diarrhœa are characteristic of complete pellagra, but milder degrees of pellagra may be recognised, with pigmentation, neuritis, and ataxia (Morris 1949) Appreciation of passive movements of the toes may be lost, and muscle tenderness and superficial anæsthesia may appear (Brain 1947) Napier (1952), however, believes that probably an associated deficiency of vitamin B_1 is the cause of the neuritic signs of pellagra

The association of peripheral neuropathy with congestive cardiac failure in case 1 suggested thiamine deficiency The absence of response to vitamin B_1 and the evidence later obtained that the patient had received thiamine 18 mg daily for three weeks before admission ruled out this possibility Further, his disease progressed for a few days in hospital until overt signs of pellagra appeared The subsequent dramatic response to nicotinamide suggests that the neuropathy was directly due to a deficiency of this vitamin and possibly of other members of the vitamin-B_2 complex We also feel justified in assuming that the onset of cardiac failure at the same time as the neuropathy was related to such a deficiency, and that this was precipitated in a previously damaged heart Mersalyl alone had little influence on the œdema until nicotinamide was concurrently administered Electrocardiographic changes, such as alteration of the ST segment, occur in pellagra, and Rachmilewitz and Braun (1945) report that these disappear when nicotinic acid alone is given Weiss and Wilkins (1937) have described a case similar to ours, with dermatitis of pellagra, peripheral neuropathy, and œdema

Peripheral neuropathy alone, however, may not explain the disproportionate motor weakness in case 1 compared with the relative paucity of objective sensory changes Other members of the vitamin-B_2 complex may be involved in producing pellagra Pyridoxine (vitamin B_6) is a pyridine derivative similar to nicotinamide and isoniazid, the latter may block its action by competitive inhibition It has been shown by Hammouda and Nagi (1948) that pyridoxine deficiency may produce muscular weakness

SUMMARY

Two cases of peripheral neuropathy following isoniazid therapy are described

It is suggested that this recognised complication of isoniazid therapy is due to a deficiency of nicotinamide and possibly of other members of the vitamin-B_2 complex

We wish to thank Dr O F Thomas and Dr W D Gray for their encouragement, Dr W J Chisnall and Dr W G Merrick, who as general practitioners first saw the patients, for their help, and Mr J Wall for the photograph

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NEPHROTOXIC EFFECTS OF DRUGS USED IN TREATMENT OF PETIT MAL*

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DURING a clinical trial of 'Milontin' (N-methyl a phenyl-succinimide) evidence of renal damage, consisting of microscopic hæmaturia and granular casts, was discovered in half the children treated (Millichap 1952) In seven patients this side effect was slight and transient, but in three, receiving large doses of milontin, it was more severe The dose was reduced in one case, and in two the drug was withdrawn Sequelæ developed in none, and subsequent specimens of urine, examined a week or two later, were normal These findings, since confirmed by Dr G A Thompson and others (personal communications), were associated in three patients with increased frequency of micturition

Hitherto, with troxidone ('Tridione') and aloxidone ('Malidone') these microscopic urinary abnormalities have not been reported Their potential sequelæ, however, have been published as five cases of the nephrotic

TABLE I—NEPHROTOXIC EFFECTS OF TROXIDONE IN 8 OF 12 CHILDREN TREATED

Case no	Age (yr)	Sex	Proteinuria	Microscopic hæmaturia	Granular casts	Time of onset (wk)	No of abnormal weekly specimens
1	13¾	M	+ +	+ +	–	5	3
2	11¾	M	–	+	–	8	1
3	11½	M	–	+	+ +	6	3
4	10¾	M	–	–	–	6	2
5	10½	M	–	–	–	7	1
6	10	M	–	+ +	+	2	4
7	9	M	–	–	+	6	1
8	8½	M	–	+	–	8	1

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* Part of a communication (by J G M) to the International League against Epilepsy in February, 1953, and to the British Pædiatric Association

nutritional state of the skin and toe-nails noted. Finally an exercise test was made, the pulsations being recorded from each foot before and after ninety seconds' vigorous dorsiplantar flexion of the foot at the rate of one per second. This is sufficient exercise to test the patency of the arteries of the thigh and leg (McDonald and Semple 1952).

Criteria for diagnosis of arterial disease of legs.—Patients with unequivocal symptoms and signs presented no difficulty. A history of typical intermittent claudication or of gangrene was regarded as evidence of arterial disease. Where these manifestations were absent the decision was more difficult. Disappearance or gross diminution of the pulsations from the foot after exercise (inverse reaction) was accepted as indicating the presence of arterial obstruction, because this response to exercise has always, in our experience, been associated with arterial obstruction (McDonald and Semple 1952). Ejrup (1948), in his extensive studies, considered that an inverse reaction was invariably associated with arterial obstruction except in cases of coarctation of the aorta or of gross anæmia. Patients in whom one or more of the peripheral pulses were absent and who also showed an inverse reaction after exercise were therefore accepted as having obliterative arterial disease, as were those in whom all pulses were present but who showed an unequivocal inverse reaction. Patients with a normal response to exercise but with absent pedal pulses presented more difficulty. Absent pulses were noted in 13% of normal young men by Silverman (1946); one or both dorsalis pedis pulses were most commonly missing. Similar findings have been reported by other workers (Morrison 1933), and a personal survey of 80 surgical patients, aged more than 40, in this hospital was in close agreement. In this work, therefore, those who were found to have either one absent pulse at the foot or both dorsalis pedis pulses absent were not considered to have arterial disease. Patients in whom both posterior tibial pulses were absent were accepted as having obliterative arterial disease, and in the majority there was collateral evidence of this (rest pain, absence of recordable pulsations at the feet, or angina pectoris).

TABLE I—COMPARISON OF DIABETICS WITH AND WITHOUT ARTERIAL DISEASE OF LEGS

—	Patients without arterial disease (*58 cases*)		Patients with arterial disease (*42 cases*)	
	No.	Remarks	No.	Remarks
Sex :				
Male ..	27		21	
Female ..	31 (*53%*)		21 (*50%*)	
Age (yr.) :				
50–59 ..	25 (*43%*)	Mean 61·6 yr. Range 50–79 yr.	10 (*24%*)	Mean 65·6 yr. Range 50–79 yr.
60–69 ..	25 (*43%*)		16 (*38%*)	
70–79 ..	8 (*14%*)		16 (*38%*)	
Duration of diabetes :				
1 yr. or less ..	21 (*36%*)	Mean 5·4 yr. Range $^1/_{12}$–35 yr.	18 (*44%*)	Mean 5·7 yr. Range $^1/_{12}$–45 yr.
1–5 yr. ..	16 (*28%*)		12 (*28%*)	
6–10 yr. ..	10 (*17%*)		1 (*2%*)	
More than 10 yr.	11 (*19%*		11 (*26%*)	
On insulin ..	28 (*47%*)		20 (*48%*)	
Coronary-artery disease	1 (*2%*)		7 (*16%*)	
Hypertension :				
Blood-pressure 150+/100+ mm. Hg	10 (*17%*)		9 (*21%*)	
170+/100 or less mm. Hg	13 (*25%*)		10 (*24%*)	

A study was also made of 52 successive cases of gangrene admitted into the medical and surgical units of the Middlesex Hospital. The relevant case-records were available for examination, and a proportion of these patients were seen personally. Femoral arteriograms were made in half of these patients.

TABLE II—NUMBER OF PATIENTS WITH AND WITHOUT OBLITERATIVE ARTERIAL DISEASE IN EACH DECADE

Age-group (yr.)	Total	With arterial disease	Without arterial disease
50–59	35	10 (*28%*)	25 (*72%*)
60–69	40	15 (*37%*)	25 (*63%*)
70–79	25	17 (*68%*)	8 (*32%*)

$\chi^2 = 9{\cdot}883,\ n = 2,\ P < 0{\cdot}01.$

RESULTS OF SURVEY OF DIABETICS

Age and Sex

The mean age was 63·3 years, with a range of 50–79 years. 52 (52%) of the patients were women, and the age-distribution of the sexes was similar.

Prevalence of Arterial Disease

58 patients (58%) had no symptoms or signs of arterial disease of the legs. Details of these cases are shown in table I.

42 patients showed evidence of arterial disease of the legs. Symptoms of arterial disease were present in 10 patients, of whom 4 had intermittent claudication, 3 had past or present gangrene, and 3 had intermittent claudication and gangrene. The remaining 32 patients had no symptoms specifically attributable to arterial disease; the rest pain, numbness, and paræsthesiæ experienced by some of them could have been caused by diabetic neuropathy. Of these 32 patients 12 had absent pulses and an abnormal response to exercise, 13 showed normal pulses and an abnormal response to exercise, and in 7 both posterior tibial pulses were absent although no inverse reaction could be demonstrated. In some of the last-named no pulsations were recordable from the foot at rest, and an exercise test was therefore impossible. Details of these patients are shown in table I.

It will be seen from table I that the two groups are similar in most respects. The sex-distribution, the number taking insulin, and the proportion with hypertension (either systolic or diastolic) are the same. There are, however, significantly more patients with coronary heart-disease among those with arterial disease of the legs, and there are more with arterial disease in the eighth decade of life. The effect of age is shown clearly in table II, where it will be seen that the proportion with arterial disease increases each decade, and that there is a particularly sharp increase in the eighth decade. In table III is shown the duration of the diabetes in the different groups. It is apparent from this table that the occurrence of arterial disease is independent of the duration of clinical diabetes mellitus.

RESULTS OF SURVEY OF GANGRENE

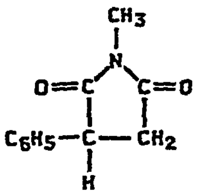
Of these 52 patients 25 were diabetic and 27 non-diabetic. Although glucose-tolerance tests were not

TABLE III—DURATION OF DIABETES IN DIFFERENT AGES, WITH AND WITHOUT ARTERIAL DISEASE

Age-group (yr.)	Total	Mean duration of diabetes (yr.)	
		With arterial disease	Without arterial disease
50–59	35	2·8 (Range $^1/_{12}$–20)	5 (Range $^1/_{12}$–24)
60–69	40	8·5 (Range $^1/_{12}$–45)	4·9 (Range $^1/_{12}$–35)
70–79	25	6·0 (Range $^1/_{12}$–19)	8·0 (Range $^6/_{12}$–20)

syndrome resulting from troxidone therapy (Barnett et al 1948, Briggs and Emery 1949, White 1949, Nabarro and Rosenheim 1952, Kelley and Panos 1952)

Since, as shown below, the structural formulæ of troxidone and aloxidone are closely related to milontin it seemed reasonable to postulate that their effects on the kidneys might be similar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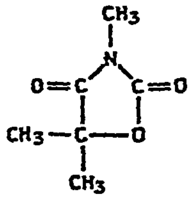
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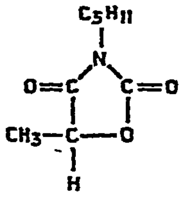
('Tridione')


ALOXIDONE
('Malidone')

OXAZOLIDINEDIONES

INVESTIGATION

At the Fountain Hospital two groups of children with epilepsy were treated, one with troxidone and another with aloxidone, 0 3 g five times a day

The dose of troxidone used in this trial was the average dose used by Lennox (1945), i e, 1 5 g daily, it was smaller than the average dose of milontin producing urinary changes

Since transient albuminuria and casts are known to follow major epileptic seizures (Novick 1920), two patients in whom these occurred were excluded from the test The urine was examined microscopically on one or more occasions before treatment and weekly thereafter

The premedication specimens and those from five control children were normal.

In group 1 troxidone was given to twelve boys, aged 8–14 years Table I shows that in eight of them signs of glomerulo-tubular damage were discovered within 8 weeks of the start of treatment Red cells and granular casts were present in the urine of two patients 7 weeks after the withdrawal of troxidone In the remainder the urine had returned to normal.

TABLE II—NEPHROTOXIC EFFECTS OF ALOXIDONE IN 4 OF 8 CHILDREN TREATED

Case no	Age (yr)	Sex	Proteinuria	Microscopic hæmaturia	Granular casts	Time of onset (wk)	No of abnormal weekly specimens
1	$12^1/_2$	F	—	—	—	4	2
2	12	F	—	—	—	4	4
3	11	M	—	—	+	2	4
4	10	F	—	+	++	1	1

Group 2 consisted of eight children, aged 9–12 years, treated with aloxidone for 8 weeks In four abnormal urinary constituents were discovered Table II shows the degree of this nephrotoxic effect and the time and frequency of its occurrence in each case.

In most instances an excess of red cells or of granular casts was present while a test for protein in the urine was negative

One red cell in every high-power microscopical field was considered an abnormal number In denoting microscopic hæmaturia + was used to indicate 1–5 red cells per high-power field, and ++ 5-15 red cells The control premedication specimens of urine contained either none or very few red cells

SUMMARY AND CONCLUSION

Of twelve children treated with troxidone, eight showed microscopic urinary abnormalities Similar evidence of renal damage, hitherto unreported, was discovered in four out of eight children treated with aloxidone

To avert the more serious sequelæ of these nephrotoxic effects, regular microscopy of the urine seems desirable whenever the drug is given to children and whenever it is given in moderate or large doses

That discrimination is necessary in the use of these compounds is illustrated by two cases in which signs of renal damage persisted after withdrawal of troxidone

We wish to thank Dr Charles F Harris for his encouragement, Dr H. F B Brewer for laboratory facilities at St Bartholomew's Hospital, Dr Robert Hodgkinson for help in the preparation of this paper, Miss B Kirk for technical assistance, and the ward sisters of the Fountain Hospital for their coöperation

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Preliminary Communication

THE EFFECT OF GLUTAMIC ACID ON THE COMA OF HEPATIC FAILURE

DESPITE much recent research the underlying biochemical disturbances in hepatic coma remain obscure In an earlier communication[1] the rôle of disordered amino-acid metabolism in the pathogenesis of this syndrome was emphasised, particularly with reference to glutamic-acid metabolism in the brain and the possible presence of methionine sulphoxide, a glutamic-acid antimetabolite, in the plasma and cerebrospinal fluid of certain cases of hepatic coma Glutamic acid $(COOH\ CH_2\ CH_2CH\ NH_2COOH)$ is the only amino-acid oxidised by the brain[2]; it is deaminated to α-ketoglutaric acid, which enters the Krebs cycle and therefore associates glutamic acid with carbohydrate metabolism It binds ammonia to form glutamine, which is then metabolised without liberating ammonia Waelsch[3] believed that the equilibrium between glutamic acid and glutamine in the brain might act as one of the metabolic buffers of the tricarboxylic acid cycle and also ensure an adequate supply of α-ketoglutarate However, according to Weil-Malherbe[4] the primary rôle of glutamic acid in cerebral metabolism is based on the three enzymic reactions deamination, transamination, and amidation, which are all part of an integrated system for the removal of intracellular ammonia Glutamic acid is also essential for the synthesis of acetylcholine[4] and for cation transport in the brain,[5] kidney,[6] and probably in other tissues

In view of the important rôle of glutamic acid in both cerebral and hepatic metabolism and its action in

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[1] Walshe J M. *Quart J Med* 1951 20 421
[2] Quastel J H Wheatley A. H M. *Biochem J* 1932 26 725 Krebs H A. *Ibid* 1935, 29, 1620, 1951, Weil Malherbe H *Ibid* 1936 30 665
[3] Waelsch H *Lancet* 1949 ii 1
[4] Weil-Malherbe, H *Physiol Rev* 1950 30 549
[5] Terner C., Eggleston, L V, Krebs H A. *Biochem. J* 1950, 47 139
[6] Stern, J M., Eggleston L V Hems R. Krebs, H A. *Ibid* 1949, 44, 410

TABLE IV—STATE OF POPLITEAL AND FEMORAL ARTERIES IN PATIENTS WITH DIABETIC AND NON-DIABETIC GANGRENE

—	Patients with femoral or popliteal arteries obstructed	Patients with femoral and popliteal arteries clear	Total
Diabetic gangrene ..	1	7	8
Non-diabetic gangrene..	16	2	18

$\chi^2 = 11{\cdot}1$, $n = 1$, $P < 0{\cdot}01$.

done in the non-diabetics to exclude diabetes, it was considered that the great majority of undiagnosed diabetics with an area of gangrene would show glycosuria on examination of the urine.

Age and Sex

Of the 25 diabetics 15 (60%) were women, whereas of the 27 non-diabetics only 3 (11%) were women. The difference between these is highly significant. The age-distribution was similar; the range in the diabetics was 54–80 years, with a mean of 67 years, and in the non-diabetics 40–85 years, with a mean of 62·7 years.

Prevalence of Intermittent Claudication

Of the 25 diabetics 6 (25%) gave a history of intermittent claudication, and 4 of these had claudication from six months to thirteen years before the onset of gangrene. Of the 27 non-diabetics 20 gave a history of intermittent claudication; 18 of these had intermittent claudication from a month to seven years before the onset of gangrene. The difference between the prevalence of intermittent claudication in the two groups is 49% ±12 (standard error) and is highly significant.

Results of Femoral Arteriography

Of the 25 diabetics 8 were investigated by this method and 10 limbs were arteriographed. The femoral and popliteal arteries were seen to be normal in 9 (90%) of these 10 limbs. In the non-diabetics arteriograms were done in 18 patients and 21 legs were so examined. The femoral and popliteal arteries were normal in only 2 (10%) of these 21 limbs, and in 2 others there was gross narrowing almost completely obstructing the femoral or popliteal arteries at some level. These details are shown in table IV. It will be seen that there is a significant difference between the two groups as regards the popliteal and femoral arteries.

The vessels obstructed in the diabetics were the anterior and posterior tibial and the peroneal arteries, although arteriographic information on these more distal vessels is less precise than in the thigh. Detailed arteriographic findings are given in tables V and VI.

In summary, arterial disease in diabetics presents first with gangrene, but in a few as intermittent claudication. The femoral and popliteal arteries are commonly not obstructed. In the great majority of non-diabetics intermittent claudication precedes gangrene, and there is usually complete obstruction of the femoral or of the popliteal arteries. In diabetics obstruction of the more distal vessels of the leg is common.

DISCUSSION

Prevalence of Arterial Disease in Diabetics

This has been the subject of many papers since Seegen (1870) first reported the common association of disease of the coronary arteries with diabetes mellitus, and since Heitz (1924) noted the association of coronary heart-disease, intermittent claudication, and diabetes.

In table VII are summarised observations made by several investigators in the past twenty-five years. From this table it will be seen that the reported prevalence of arterial disease of the legs varied widely from 50% (Pearl and Kandel 1939) to 3% (Dry and Hines 1941). Lack of standard criteria for the recognition of arterial disease explains many of these discrepancies. Rabinowitch et al. (1934), who were most insistent on the need for such criteria, accepted radiographic vascular calcification as synonymous with arterial disease, as did Jackson et al. (1949). Strictly speaking this is true, but it has been pointed out by Lansbury and Brown (1934) that such calcification does not mean arterial narrowing. Pearl and Kandel (1939), who found that more than half their diabetics had symptoms of arterial disease, accepted "mild pains" and "cramps" as indicating such a change. Naide (1945) regarded the occurrence of pain, coldness, numbness, tingling, and cramps as signifying arterial disease. These symptoms, however, result from diabetic neuropathy without arterial disease. Herzstein and Weinroth (1945) used oscillography to determine the presence of arterial disease; the absence of two pulses or the occurrence of claudication was also considered significant.

TABLE V—SITES OF ARTERIAL OBSTRUCTION SHOWN ARTERIOGRAPHICALLY IN 8 DIABETICS

Case no.	Age (yr.)	Sex	Side	Femoral arteriograms
1	54	M	Left	Left femoral and popliteal arteries normal
2	58	M	Left	Complete obstruction of whole length of left femoral artery
4	61	F	Left	Obstruction of posterior tibial and peroneal arteries; femoral and popliteal normal
			Right	Obstruction of anterior and posterior tibial arteries; femoral and popliteal normal
5	60	F	Left	Posterior tibial artery obstructed; other tibials narrowed; femoral and popliteal normal
			Right	Posterior tibial and peroneal arteries obstructed; femoral and popliteal normal
13	78	M	Right	Tibial arteries obstructed; femoral and popliteal normal
16	58	M	Right	Femoral and popliteal arteries normal
19	66	F	Right	Femoral and popliteal arteries well filled and slightly irregular; anterior and posterior tibial arteries obstructed
22	79	M	Right	Femoral and popliteal arteries clear; anterior and posterior tibial arteries obstructed above ankle

There appeared to be general agreement among these workers that the severity of the diabetes bore little relation to the occurrence of arterial disease (Rabinowitch et al. 1934, Pearl and Kandel 1939, Dry and Hines 1941, Herzstein and Weinroth 1945). The same conclusion was reached by Root and Sharkey (1936) in an analysis of the findings at 175 necropsies on diabetics and by Bell (1952) in 1559 necropsies. Mandelberg and Sheinfield (1946), investigating 128 amputated legs, reported a similar finding. The present results agree with these reports.

Opinion has been less unanimous on the relation of the duration of the diabetes to the prevalence of arterial disease. Some believe that there is a direct relation between the two (Millard and Root 1948, Herzstein and Weinroth 1945). This was denied by Pearl and Kandel (1939). The present results suggest that advancing years rather than the duration of the diabetes is the more important factor. It is worth noting in this connection Colwell's (1942) theory, from a study of insulin-requirement curves, that diabetes mellitus begins at birth and has passed through at least half its course by the time it is first observed clinically. In the present survey it was not unusual to find well-marked arterial disease of diabetic type in patients with a month's history of clinical diabetes. Dolger (1950) suggests that vascular removing excess ammonia, which may be one of the toxic factors producing hepatic coma, it was decided to try the effect of large doses of the amino acid intravenously in hepatic coma Glutamic acid was prepared for intravenous use, as the sodium salt, by the method of Mayer-Gross and Walker[7] To date it has been used in five episodes of coma in three patients with subacute or chronic liver damage It has not yet been possible to try this therapy in any patient with acute virus necrosis of the liver

CASE-RECORDS

Case 1—A man, aged 45, with long standing cirrhosis of the liver associated with ulcerative colitis, had hepatosplenomegaly, ascites, and œsophageal varices Laboratory tests showed strongly positive serum flocculation reactions, a low serum albumin level and a slightly raised serum bilirubin level He was admitted to hospital in February, 1952, after a "flare up" of his colitis There was little change in his condition until the morning of March 9, 1952, when he was found to be in deep coma There was a strong fetor hepatis and the plantar responses were doubtfully extensor Intravenous glucose therapy was started together with B vitamins Next day coma was deeper, the patient was hiccuping almost continuously, his plantar responses were definitely extensor, and he had a transient ankle clonus By that evening his condition appeared to be deteriorating, and it was decided to give intravenous glutamic acid, 23 g of the sodium salt was given at 6 P M The immediate effect was flushing, salivation, and increased depth of respiration Some four hours later the patient regained consciousness, next day he was mentally normal, and he has remained so to the time of writing fourteen months later

Case 2—A man, aged 51, was admitted to hospital after a hæmorrhage from large œsophageal varices As the laboratory tests suggested that liver damage was slight, he was considered a suitable case for surgery, and on March 25, 1952, a side to side portacaval shunt was constructed Four days after operation he became confused and was found to have increased tendon-jerks and bilateral ankle clonus, there was a strong fetor hepatis Next day, March 30, a high protein milk drip by intragastric tube was started By April 2 he was in deep coma and, besides his other abnormal reflex signs, he had developed bilateral extensor responses Fluid balance was maintained with intravenous glucose and electrolyte solutions, and on this day 23 g of sodium glutamate was added to the intravenous drip This led to a lessening in the depth of coma, and he became noisy and restless On April 4 a further 23 g of glutamate was given, and during the day he regained consciousness, although his abnormal reflex signs persisted for a further twenty four hours He progressed well until April 22, when he became mentally confused, and examination again revealed a prolonged ankle clonus Next day he was in light coma, 10 g of glutamic acid was given by gastric drip, and by the following morning his mental state was almost normal Oral glutamic acid was given until April 28, when it was discontinued On the morning of April 29 he was confused and noisy, and all the abnormal neurological signs noted earlier had returned Intravenous glucose was again started, but by evening he was in light coma, 23 g of sodium glutamate was therefore added to the drip, and next morning he was sufficiently improved to coöperate and to take food by mouth, treatment with oral glutamic acid was started again, and he was given 10 g daily for three weeks before the dose was reduced over the subsequent two weeks No further episode of coma occurred until he died at home in coma some eight months later

Case 3—A married woman, aged 61, was admitted to hospital for investigation with a history of recurrent attacks of jaundice over the previous twenty months, these had been associated with loss of weight and a gradual deterioration in her health Laboratory tests showed strongly positive serum flocculation reactions, a low serum albumin level and a high serum globulin level A firm liver was palpable just below the right costal margin, and there was a large spider nævus on the left shoulder On April 11, 1953, three weeks after admission to hospital, she became confused and did not recognise her relations She remained able to take milk and glucose by mouth, and B vitamins were given intramuscularly By April 14 there was much fluid retention and oliguria, for which she was treated with the ion exchange resin 'Katonium' (in the usual 75% ammonium form), she was also given oral glutamic acid 20 g daily Urine flow was re established by April 17, but coma was deeper, and there were extensor plantar responses and ankle clonus Treatment with intravenous glucose and electrolytes was started, and all other therapy was stopped Next day, the eighth day in coma, her condition was deteriorating, and in the evening 23 g of sodium glutamate was added to the intravenous drip During the night the coma became lighter, and by the following morning she was just able to recognise her relations and to answer simple questions That afternoon a further 23 g of glutamate was given, and by 8 P M she was fully conscious and demanding food Treatment with oral glutamic acid was started, but she became confused and aggressive about thirty six hours after emerging from coma, the dosage of the glutamic acid was therefore raised to 30 g daily, which coincided with a change to a normal mental state, and her tendon jerks and plantar responses returned to normal At the time of writing (May 19) this improvement has been maintained

DISCUSSION

The failure of oral glutamic acid to terminate the episode of coma in case 3 may well have been due to the simultaneous administration of the ion-exchange resin katonium in the 75% ammonium form Possibly this neutralised the ammonia-binding power of the glutamic acid before it could influence cerebral metabolism It has certainly been shown that ammonium ion exchange resins and ammonium chloride can produce a syndrome closely mimicking hepatic coma in patients with cirrhosis of the liver[8] Apart from this one failure glutamic acid appeared to exert a beneficial effect in five episodes of coma, on four occasions after intravenous use and once on oral administration, on one occasion also the withdrawal of glutamic-acid therapy appeared to precipitate coma This evidence strongly supports the thesis that glutamic acid influences favourably the coma that may develop in patients with subacute and chronic liver disease Whether it will have any effect on the course of acute virus necrosis of the liver remains to be seen, but in this condition it cannot act as more than a supportive therapy until such time as the virus invasion can be dealt with by the natural defence mechanisms The exact means whereby glutamic acid exerts its effect in restoring consciousness to patients in hepatic coma is not clear, it is not even certain if this action is on cerebral or hepatic metabolism, although it seems more likely that the beneficial effect is on the brain rather than the liver The most probable explanation is that glutamic acid acts by its ammonia-binding power, but its action on the Krebs cycle may also be important in view of the findings of Amatuzio and Nesbitt,[9] that the blood-pyruvate level is considerably raised in hepatic coma, and the work of Seligson et al,[10] who have found that in blood pyruvate and blood-α-ketoglutarate levels are raised in patients with liver injury Whatever the mechanism of its action, intravenous glutamic acid appears worthy of further trial in the treatment of hepatic coma In this connection the following method of administration has proved satisfactory 20 g of glutamic acid is neutralised with sodium hydroxide to give 23 g of sodium glutamate in 80 ml of water[7], this solution is added to 500 ml of 5% glucose and given intravenously over three or four hours Too rapid administration leads to salivation, flushing, and vomiting and should therefore be avoided

Not more than 23 g of sodium glutamate has been given intravenously on any one day, because this contains 130 m eq of sodium and, if used in larger doses, might lead to undesirable retention of water For oral use damage in diabetics and the insulin insufficiency stem independently from common ætiological factors.

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[7] Mayer Gross, W Walker, J W *Ibid* p 92

[8] Gabuzda, G J jun, Phillips G B Davidson, C S *New Engl J Med* 1952 246, 124 Phillips G B Schwartz, R Gabuzda G J jun Davidson C S *Ibid* 247, 239

[9] Amatuzio D S Nesbitt S *J clin Invest* 1950 29, 1486

[10] Seligson D, McCormick, G J, Sborov, V *Ibid*, 1952, 31, 661

Although the numbers in this series were small, it seems clear from the present study that increasing age is the most important factor in the development of arterial disease in diabetics, and that after the age of 70 more than two-thirds of diabetics will show arterial changes in the legs. This effect of advancing years has been noted by Pearl and Kandel (1939) and Herzstein and Weinroth (1945), but the latter also emphasise the importance of duration of the diabetes.

Prevalence of Diabetes in Peripheral Arterial Disease and its Effect on such Disease

A high prevalence of diabetes mellitus has been a prominent feature of many reports of cases of arteriosclerotic disease of the legs. In table VIII are shown figures found by different investigators.

From table VIII it will be seen that in the previously published series there was a higher prevalence of diabetes mellitus than was found by me. Lindbom (1950) recorded the lowest prevalence, and Boyd (1950), reporting more than 1000 cases of arterial disease of the legs, did not give figures for diabetes but merely referred to it as a factor to be considered in treatment. It is perhaps significant that both Lindbom and Boyd, in common with me, were reporting cases presenting with intermittent claudication, whereas this was not the case in the earlier reports, which included patients presenting with gangrene as the only manifestation of arterial disease. This is reflected in the higher prevalence of gangrene in most of these reports compared with my series, in which only 6 cases (6%) gave evidence of past or present gangrene when first seen, and 2 of these were diabetic. From a consideration of these facts it seemed possible that they were interrelated, and that the higher prevalence of gangrene recorded in other series might reflect the higher prevalence of diabetes mellitus, and that the lower prevalence of diabetes and gangrene in my series and in that of Lindbom (1950) might be explained by the selection of cases with intermittent claudication. The higher prevalence of gangrene in diabetics has been recognised (Allen et al. 1946) and was reported but not commented on by Rabinowitch et al. (1934).

The study reported here confirms this impression and suggests that arteriosclerotic disease of the legs in diabetics presents more often with gangrene, whereas in non-diabetics intermittent claudication commonly precedes such an event. Intermittent claudication affecting the calf is in most instances due to obstruction of the femoral or of the popliteal arteries; it may be deduced from this that in diabetic arteriosclerotic disease of the legs the femoral and popliteal arteries are relatively

TABLE VI—SITES OF ARTERIAL OBSTRUCTION SHOWN ARTERIOGRAPHICALLY IN 18 NON-DIABETICS

Case no.	Age (yr.)	Sex	Side	Femoral arteriogram
1	68	M	Right	Popliteal artery obstructed
			Left	Femoral artery obstructed upper third
2	48	M	Right	Femoral artery almost obstructed; tibial arteries obstructed
			Left	Femoral artery almost obstructed; tibial arteries obstructed
4	68	M	Right	Femoral artery obstructed lower third
			Left	Femoral artery obstructed upper and middle thirds
5	40	M	Left	Femoral artery obstructed
6	85	M	Left	Lower femoral and popliteal arteries obstructed
7	64	F	Left	Upper femoral artery obstructed
8	76	F	Left	Middle and lower femoral artery obstructed
9	72	M	Left	Lower femoral and popliteal arteries obstructed
10	54	M	Right	Femoral artery obstructed over entire length
14	70	M	Right	Femoral artery obstructed over entire length below profunda
15	70	M	Left	Femoral artery obstructed in lower third
16	67	M	Right	Femoral artery obstructed over entire length below profunda
17	70	M	Right	Femoral artery obstructed over entire length below profunda; anterior and posterior tibial arteries also obstructed
18	63	M	Left	Femoral artery obstructed over entire length below profunda
19	43	M	Left	Femoral and popliteal arteries normal; posterior tibial and dorsalis pedis arteries occluded
20	68	M	Right	Femoral and popliteal arteries normal; tibial arteries irregular
22	44	M	Right	Femoral artery obstructed from origin of the profunda femoris to Hunter's canal
23	66	M	Right	Femoral artery obstructed from origin of the profunda femoris to adductor opening

TABLE VII—INCIDENCE OF ARTERIAL DISEASE IN DIABETICS IN PUBLISHED REPORTS

Reference	No. of diabetics	Findings and comments
Eliason and Wright (1926)	..	20–25% of diabetics die of gangrene
Rabinowitch et al. (1934)	458 aged 50 yr. or more	44·7% showed evidence of vascular disease of legs
Rabinowitch et al. (1934)	1500 of all ages	8% with gangrene, 0·25% with intermittent claudication
Pearl and Kandel (1939)	100 (87 aged 40 yr. or more)	50% + had symptoms of vascular disease; most showed abnormalities of peripheral pulses; no relation to severity or duration of diabetes
Dry and Hines (1941)	7073	3% with symptoms and signs of arterial disease of legs; no relation to severity of diabetes
Naide (1945) ..	89 of 10-yr. standing	3% with severe symptoms of vascular disease + necrotic areas; 10% with mild (unspecified) symptoms and lesions; 23·5% with absent peripheral pulses only
Herzstein and Weinroth (1945)	249	42% with vascular disease in age-group 51–60 yr.; 63% with vascular disease in age-group 60 +; no relation to severity, but commoner in diabetics of over 5-yr. duration
Jackson et al. (1949)	75 young diabetics of 10-yr. standing	16% with vascular calcification
Reuting (1950)	50 followed since 1924	38% dead (8% of coronary disease). Of 31% alive 88% with vascular calcification in legs
Present series..	100 aged 50 yr. or more	10% with intermittent claudication or with gangrene; 32% with signs of arterial disease; 7% with clinical evidence of coronary artery disease

TABLE VIII—PREVALENCE OF DIABETES MELLITUS AND GANGRENE IN ARTERIOSCLEROTIC DISEASE OF LEGS IN PUBLISHED REPORTS

Reference	No. of cases	Prevalence of diabetes	Prevalence of gangrene
Brown (1933)	365	33%	More than 20%
Bernheim and London (1937)	99	14%	9%
Hines (1938)	280	20·3%	54%
Lindbom (1950)	74	12%	Not stated
Present series	100	6%	6%

0 5 g tablets of the free amino-acid have been used and appear to be well tolerated by these patients when given in divided doses to a total of 20 g daily

SUMMARY

The effect of glutamic acid on the coma of hepatic failure has been investigated

Five episodes of coma in three patients with subacute or chronic liver injury were treated with glutamic acid

On each occasion a return of consciousness closely followed the administration of glutamic acid, which therefore appears worthy of further trial in the treatment of hepatic coma

I wish to thank Dr J D Nabarro, Prof R S Pilcher, Prof M L Rosenheim, and Dr Cedric Shaw for permission to use glutamic acid therapy on their patients

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M A M B Camb , M R C P

Medical Societies

ATLANTIC CITY MEETINGS

OVER three thousand doctors met for the annual meetings of the American Federation for Clinical Research, the American Society for Clinical Investigation, and the Association of American Physicians, which were held at Atlantic City, New Jersey, from May 3 to 6 Altogether over four hundred papers were accepted for these meetings, but only eighty were read in the time available "Purely clinical" papers were in a minority, the trend being more and more towards laboratory and fundamental research In line with this, approximately 15% of all papers submitted referred to the use of radioactive-tracer techniques The tide of papers describing the pharmacology of A C T H and cortisone seems to be ebbing

Hæmatology

ABSENCE OF GAMMA GLOBULIN

C A. JANEWAY (Boston) said that in children with deficient reaction to infection, *similar to that in nephrosis, electophoresis* of the plasma had shown complete absence of the gamma globulin fraction A total of 14 such cases had been discovered, and this disorder might be more common than was initially supposed All the patients were boys with a history of multiple suppuration Arthritis and bronchiectasis were common features, and one child had had recurrent attacks of mumps In another, however, primary vaccination took normally, and revaccination showed that an immune reaction had developed The disease was probably due to a sex linked recessive gene, manifest in the male, and was apparently associated with a primary failure of gamma globulin synthesis It could be cured by weekly intramuscular injections of gamma globulin, with penicillin chemoprophylaxis, penicillin alone was ineffective

AUTO IMMUNE HÆMOLYTIC DISEASE

L E YOUNG and G MILLER (Rochester, New York) said that in auto immune hæmolytic disease the presence of sensitised red cells was apparently diagnostic, and could be detected by an anti globulin serum (the Coombs test) This, however, was not the whole story since the crises and remissions of the anæmia could vary independently of the number of sensitised red cells

L E -CELL PHENOMENON

In other papers the L E cell phenomenon came in for a good deal of attention This or very similar changes in the leucocytes could be simulated by adding a rabbit anti human granulocyte serum to a suspension of normal human leucocytes FINCH and his associates at Boston had noted clumping, vacuolisation, and rosette formation of the damaged cells, which, if they were phagocytosed by other cells, could produce a picture indistinguishable from that seen in disseminated lupus erythematosus Other reports confirmed this work

C E BUTTERWORTH (Birmingham, Alabama) had found that desoxyribonuclease, added to normal human leucocytes, might do the same thing He cautioned against the belief that the finding of L E cells was necessarily diagnostic, since he had found this change occasionally in normal leucocytes incubated without enzyme

CARRERA and associates at New Orleans had tested L E serum with leucocytes from other species, and found a wide species difference in the ability to form L E cells One particular specimen of L E serum, which gave negative results with human leucocytes, was strongly positive with those from the horse

PLATELET GROUPS

M STEFANINI and G PLITMAN (Boston) had separated 250 normal plasmas into platelet free and platelet rich fractions, and by multiple testing had found that with certain combinations platelet agglutination would occur Four platelet groups, analogous to, but distinct from, the four blood groups, were proposed, with the following distribution in the white population of North America group 1 (9%) group 2 (3%), group 3 (equals 1 + 2) (4%), and group 4 (0) (84%) Factors such as these might operate in certain cases of thrombocytopenia which exhibit progressively less response to repeated transfusions of platelets

ACTION OF THROMBIN

S SHERRY and W TROLL (Cincinnati) had confirmed that thrombin acted as a proteolytic enzyme, and had found that a synthetic substrate—tosyl arginine methyl ester (T A M E)—was split by thrombin in a characteristic fashion, and to an extent closely dependent on the amount of thrombin present Furthermore, when T A M E was added to thrombin fibrinogen systems, clotting did not proceed until all the T A M E had been split Thrombin could be accurately assayed by its T A M E splitting activity.

ANOXIC POLYCYTHÆMIA

F STOHLMAN and J C ROSE (Washington, D C) reported on a patient with cyanosis of the lower half of his body secondary to a reversal of flow in a patent ductus arteriosus The sternal marrow, which was well oxygenated, was hyperplastic, whilst the iliac marrow, which was poorly oxygenated, was hypoplastic The patient's blood showed polycythæmia This was interpreted as evidence of a humoral mechanism in anoxic polycythæmia and against the theory that direct action of anoxia on the bone marrow was the stimulus for red cell production

Immunology

GAMMA GLOBULIN IN POLIOMYELITIS

W M HAMMOND (Pittsburgh) discussed the use of purified gamma globulin in the prevention of poliomyelitis The widespread availability of this material, and the publicity that it had received, made it imperative to remember its limitations Its use against poliomyelitis was analogous to its use in the prevention of measles, with the added disadvantage that primary cases were less easy to detect, since they were commonly aparalytic Mass passive immunisation with this agent had been advocated, but he thought that this was a wasteful and useless procedure In a trial conducted under the most favourable circumstances, during the phase of rising incidence in a severe epidemic, with its use limited to the most susceptible age group, it was shown that only one in about four hundred injections actually prevented an infection He advocated reserving this material for the prophylactic immunisation of (1) contacts of paralytic cases, and (2) contacts of those who, during an epidemic, developed an undiagnosed febrile illness which might be non-paralytic poliomyelitis

RED CELLS AND INFECTION

R A NELSON (Bethesda) described an immunological phenomenon whereby normal red cells appeared to be an integral part of a reaction to invading organisms If virulent *Treponema pallidum* was added to a suspension of normal red cells in serum from a case of syphilis (antiserum) the organisms adhered to the red cells and could be centrifuged with them out of suspension If the same experiment were repeated with white cells the treponemata remained in suspension With both red and white cells, the treponemata were removed from suspension and were phagocytosed

Endocrinology

TRIIODOTHYRONINE

Several studies were reported which confirmed the work of Gross and Pitt-Rivers in England on the metabolic activity unaffected, and that the brunt of the lesion falls on the more distal vessels. This belief is strengthened by the arteriographic studies of cases of diabetic gangrene reported here. Further evidence is afforded by the finding, in 42 diabetics aged more than 50 with evidence of arterial disease of the legs, that the popliteal pulse was absent in only 6 patients, whereas 70% of 100 patients presenting with intermittent claudication had this pulse missing.

Since Buerger's (1915) dictum that gangrene in diabetics is arteriosclerotic it has been assumed by most, and stated by many, that there is no difference between arteriosclerotic disease of the legs in diabetics and in non-diabetics (Lisa et al. 1942, Wilder 1940, Samuels 1950, Pratt 1949, Allen et al. 1946). On the other hand, Warren (1938), in his extensive pathological studies of diabetes mellitus, considered that the arterial lesion in diabetic legs was distinctive, and that the vessels involved were mainly the smaller muscular arteries. This was confirmed by Bohan (1949). Lewis (1946) stated: "in diabetes, and sometimes apart from it, gangrene of a toe may result from thrombosis of the digital vessels, the pulses of the foot remaining intact"; and Learmonth (1950) referred to the digital thromboses of diabetes. Root (1952) noted that, although sclerosis of the large arteries may develop, the characteristic diabetic vascular lesion is in the smaller blood-vessels. Recognition of this may be a factor, with the antibiotics and improved surgical technique, in the increasing tendency towards the more conservative treatment of diabetic gangrene (Regan et al. 1949, McKittrick et al. 1949, Grunberg et al. 1951), compared with the high amputation recommended by earlier workers (Eliason and Wright 1926).

SUMMARY

100 diabetics, aged more than 50, were examined for the presence of obliterative arterial disease of the legs.

Signs of arterial disease were found in 42%, although only 10% had symptoms attributable solely to impaired circulation.

The occurrence of arterial disease was related to increasing age but not to the severity or to the duration of the diabetes.

A sixth of those with arterial disease of the legs had clinical coronary arterial disease.

Of 52 consecutive cases of gangrene almost half were in diabetics.

Arterial disease in diabetics presented more often with gangrene than with intermittent claudication, and the usual site of obstruction was in the more distal vessels of the leg and foot, the femoral and popliteal arteries being clear; in both these respects the reverse held true in non-diabetic arterial disease.

I wish to thank Prof. A. Kekwick for his interest and help at all times, Mr. P. B. Ascroft for giving me access to his cases of gangrene, Dr. David Sutton for the femoral arteriograms, and Dr. John Friend for his help in arranging for me to see the diabetics. Part of this work was included in a thesis accepted for the degree of M.D. of the University of Aberdeen in 1952.

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SOME FACTORS AFFECTING UROPEPSINOGEN EXCRETION IN MAN

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BOTH urine and blood-plasma contain pepsinogen, a pro-enzyme which by acidification is converted into a proteolytic enzyme probably identical with gastric pepsin. There is evidence, reviewed by Bucher (1947), that pepsinogen reaches the urine in the following way. It is manufactured by the parietal cells of the gastric mucosa, where it can be demonstrated by Motteram's (1951) staining method. Part is secreted into the lumen of the stomach, where it is converted into pepsin by the action of hydrochloric acid, and another fraction is taken up by the blood-stream, whence it is excreted in the urine as uropepsinogen.

In the present investigation a simplified method of estimation (Fawcett 1951) based on those of Anson and Mirsky (1932), Bucher (1947), and Mirsky et al. (1948) has been used, and some factors of clinical interest have been studied. We can confirm the findings of Janowitz et al. (1950) and agree that this estimation sometimes helps in the diagnosis of duodenal ulcer from other lesions causing similar symptoms. It is also an index of adrenocortical activity, as Spiro et al. (1950) have shown.

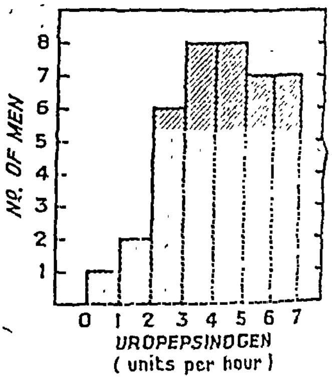

Fig. 1—Distribution of excretion of uropepsinogen (average 4·5 units per hour) in 39 normal males.

METHOD

Urine is collected for twenty-four hours or during a measured overnight period, and the volume of urine

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removing excess ammonia, which may be one of the toxic factors producing hepatic coma, it was decided to try the effect of large doses of the amino-acid intravenously in hepatic coma Glutamic acid was prepared for intravenous use, as the sodium salt, by the method of Mayer-Gross and Walker [7] To date it has been used in five episodes of coma in three patients with subacute or chronic liver damage It has not yet been possible to try this therapy in any patient with acute virus necrosis of the liver

CASE-RECORDS

Case 1 —A man, aged 45, with long standing cirrhosis of the liver associated with ulcerative colitis, had hepatosplenomegaly, ascites, and œsophageal varices Laboratory tests showed strongly positive serum flocculation reactions, a low serum albumin level and a slightly raised serum bilirubin level He was admitted to hospital in February, 1952, after a "flare up" of his colitis There was little change in his condition until the morning of March 9, 1952, when he was found to be in deep coma There was a strong fetor hepatis and the plantar responses were doubtfully extensor Intravenous glucose therapy was started together with B vitamins Next day coma was deeper, the patient was hiccuping almost continuously, his plantar responses were definitely extensor, and he had a transient ankle clonus By that evening his condition appeared to be deteriorating, and it was decided to give intravenous glutamic acid, 23 g of the sodium salt was given at 6 P M. The immediate effect was flushing, salivation, and increased depth of respiration Some four hours later the patient regained consciousness, next day he was mentally normal, and he has remained so to the time of writing fourteen months later

Case 2 —A man, aged 51, was admitted to hospital after a hæmorrhage from large œsophageal varices As the laboratory tests suggested that liver damage was slight, he was considered a suitable case for surgery, and on March 25, 1952, a side to side portacaval shunt was constructed Four days after operation he became confused and was found to have increased tendon-jerks and bilateral ankle clonus, there was a strong fetor hepatis Next day, March 30, a high-protein milk drip by intragastric tube was started By April 2 he was in deep coma and, besides his other abnormal reflex signs, he had developed bilateral extensor responses Fluid balance was maintained with intravenous glucose and electrolyte solutions, and on this day 23 g of sodium glutamate was added to the intravenous drip This led to a lessening in the depth of coma, and he became noisy and restless On April 4 a further 23 g of glutamate was given, and during the day he regained consciousness, although his abnormal reflex signs persisted for a further twenty-four hours He progressed well until April 22, when he became mentally confused, and examination again revealed a prolonged ankle clonus Next day he was in light coma, 10 g of glutamic acid was given by gastric drip, and by the following morning his mental state was almost normal Oral glutamic acid was given until April 28, when it was discontinued On the morning of April 29 he was confused and noisy, and all the abnormal neurological signs noted earlier had returned Intravenous glucose was again started, but by evening he was in light coma, 23 g of sodium glutamate was therefore added to the drip, and next morning he was sufficiently improved to coöperate and to take food by mouth, treatment with oral glutamic acid was started again, and he was given 10 g daily for three weeks before the dose was reduced over the subsequent two weeks No further episode of coma occurred until he died at home in coma some eight months later

Case 3 —A married woman, aged 61, was admitted to hospital for investigation with a history of recurrent attacks of jaundice over the previous twenty months, these had been associated with loss of weight and a gradual deterioration in her health Laboratory tests showed strongly positive serum flocculation reactions, a low serum albumin level and a high serum globulin level A firm liver was palpable just below the right costal margin, and there was a large spider nævus on the left shoulder On April 11, 1953, three weeks after admission to hospital, she became confused and did not recognise her relations She remained able to take milk and glucose by mouth, and B vitamins were given intramuscularly By April 14 there was much fluid retention and oliguria, for which she was treated with the ion exchange resin '*Katonium*' (*in the usual 75% ammonium form*), she was also given oral glutamic acid 20 g daily Urine flow was re established by April 17, but coma was deeper, and there were extensor plantar responses and ankle clonus Treatment with intravenous glucose and electrolytes was started, and all other therapy was stopped Next day, the eighth day in coma, her condition was deteriorating, and in the evening 23 g of sodium glutamate was added to the intravenous drip During the night the coma became lighter, and by the following morning she was just able to recognise her relations and to answer simple questions That afternoon a further 23 g of glutamate was given, and by 8 P M she was fully conscious and demanding food Treatment with oral glutamic acid was started, but she became confused and aggressive about thirty six hours after emerging from coma, the dosage of the glutamic acid was therefore raised to 30 g daily, which coincided with a change to a normal mental state, and her tendon jerks and plantar responses returned to normal At the time of writing (May 19) this improvement has been maintained

DISCUSSION

The failure of oral glutamic acid to terminate the episode of coma in case 3 may well have been due to the simultaneous administration of the ion-exchange resin katonium in the 75% ammonium form Possibly this neutralised the ammonia-binding power of the glutamic acid before it could influence cerebral metabolism It has certainly been shown that ammonium ion-exchange resins and ammonium chloride can produce a syndrome closely mimicking hepatic coma in patients with cirrhosis of the liver [8] Apart from this one failure glutamic acid appeared to exert a beneficial effect in five episodes of coma, on four occasions after intravenous use and once on oral administration, on one occasion also the withdrawal of glutamic acid therapy appeared to precipitate coma This evidence strongly supports the thesis that glutamic acid influences favourably the coma that may develop in patients with subacute and chronic liver disease Whether it will have any effect on the course of acute virus necrosis of the liver remains to be seen, but in this condition it cannot act as more than a supportive therapy until such time as the virus invasion can be dealt with by the natural defence mechanisms The exact means whereby glutamic acid exerts its effect in restoring consciousness to patients in hepatic coma is not clear, it is not even certain if this action is on cerebral or hepatic metabolism, although it seems more likely that the beneficial effect is on the brain rather than the liver The most probable explanation is that glutamic acid acts by its ammonia-binding power, but its action on the Krebs cycle may also be important in view of the findings of Amatuzio and Nesbitt,[9] that the blood-pyruvate level is considerably raised in hepatic coma, and the work of Seligson et al,[10] who have found that in blood-pyruvate and blood α-ketoglutarate levels are raised in patients with liver injury Whatever the mechanism of its action, intravenous glutamic acid appears worthy of further trial in the treatment of hepatic coma In this connection the following method of administration has proved satisfactory 20 g of glutamic acid is neutralised with sodium hydroxide to give 23 g of sodium glutamate in 80 ml of water [7], this solution is added to 500 ml of 5% glucose and given intravenously over three or four hours Too rapid administration leads to salivation, flushing, and vomiting and should therefore be avoided

Not more than 23 g of sodium glutamate has been given intravenously on any one day, because this contains 130 m eq of sodium and, if used in larger doses, might lead to undesirable retention of water For oral use voided per hour is calculated. Results are substantially the same whichever period of collection is used. Urine uropepsinogen is stable under toluene for four days at 20°C and for fifteen days at 0°–4°C.

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[7] Mayer Gross, W, Walker, J W *Ibid* p 92

[8] Gabuzda, G J jun Phillips G B Davidson C S *New Engl J Med* 1952, 246, 124 Phillips G B Schwartz, R., Gabuzda G J jun Davidson, C S *Ibid* 247, 239

[9] Amatuzio D S Nesbitt S *J clin Invest* 1950 29, 1486

[10] Seligson, D McCormick, G J Sborov V *Ibid*, 1952, 31, 661

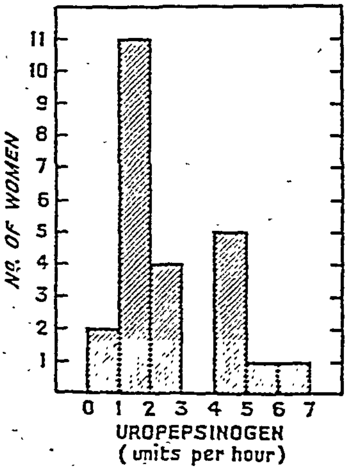

Fig. 2—Distribution of excretion of uropepsinogen (average 2·8 units per hour) in 24 normal females.

Each assay is performed in duplicate to ensure reliable results. Urine is incubated with a human hæmoglobin substrate for thirty minutes at 37°C. At pH 1·5–1·8 the possible effect of cathepsins is eliminated because the proteolytic activity of urine is stable at this pH, whereas cathepsins are not. Excess hæmoglobin is precipitated by trichloracetic acid, and the degree of proteolysis is measured by the Folin and Ciocalteau procedure. A blank determination, in which the enzyme is inactivated, accounts for chromogenic substances present in urine and substrate.

The difference between the extinction coefficients of "test" and "blank," interpreted on a calibration curve prepared from standard tyrosine solutions, is a measure of the proteolysis due to uropepsinogen activity.

Our unit of uropepsinogen is the same as that of Mirsky et al. (1948), who define it as "that quantity which, during a 10 minute incubation of the standard assay, releases 1 mg. of 'tyrosine-like' substance."

TABLE I—EXCRETION OF UROPEPSINOGEN BY PATIENTS WITH DUODENAL ULCER

Sex	No.	Mean excretion of uropepsinogen (units per hr.)
Men	62	8·7
Women	12	5·1
Total	74	8·1

Correcting for dilution and for the thirty-minute incubation period, in our assay 1 unit/100 ml. of urine ≡ 0·0015 mg. of tyrosine.

Results are expressed as the number of units excreted per hour.

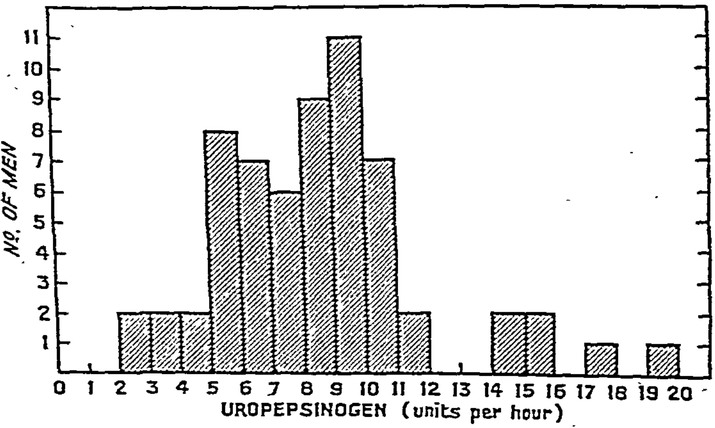

Fig. 3—Distribution of excretion of uropepsinogen (average 8·7 units per hour) in 62 males with duodenal ulcer.

RESULTS

Controls.—63 hospital patients with no clinical evidence of peptic ulcer excreted an average of 3·9 units of uropepsinogen per hour. In the 39 men the average was 4·5, and in the 24 women it was 2·8. Figs. 1 and 2 show the distribution among these patients. Comparison of 10-year age-groups showed no significant variation.

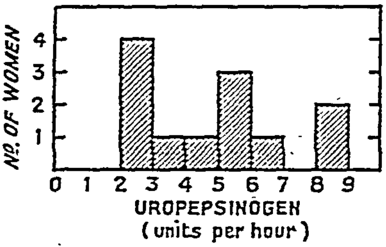

Fig. 4—Distribution of excretion of uropepsinogen (average 5·1 units per hour) in 12 females with duodenal ulcer.

Duodenal ulcer.—In 74 patients the diagnosis of duodenal ulcer was confirmed either at operation or by strong clinical and radiological evidence, and by the finding of a high gastric acidity. While the mean rate of excretion of uropepsinogen for all these patients was 8·1 units per hour, the rate for the 62 men was 8·7, and the rate for the 12 women was 5·1 (table I). The distribution of excretion-rates in men and women with duodenal ulcer is shown in figs. 3 and 4.

Gastric ulcer.—Of 21 patients with gastric ulcer, 18 excreted uropepsinogen at the normal rate. There were 11 men and 10 women in this group, but no sex distinction could be drawn within it. The other 3 of these patients excreted more than the normal amount (fig. 5).

Gastric carcinoma.—16 patients showed excretion-rates similar to the normal, though there were more low readings than in any of the other groups (fig. 6).

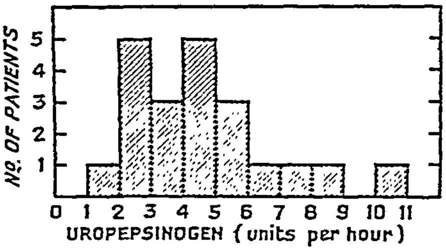

Fig. 5—Distribution of excretion of uropepsinogen (average 4·9 units per hour) in 21 patients with gastric ulcer.

Effect of operation.—The early response to a gastric operation was measured in 6 patients with duodenal ulcer and was as follows:

Mean preoperative excretion 8·0 units per hour.
Mean greatest postoperative excretion 20·0 units per hour.
Mean final excretion 5·5 units per hour.

In these patients the maximum rate of output was always reached in thirty-six to seventy-two hours. 4 cholecystectomy patients were used as controls, and the immediate effect on the mean excretion-rate was a rise of uropepsinogen from 2 units per hour to 4.

The end-effect of various gastric operations on uropepsinogen excretion is set out in table II. Gastric resection reduces the excretion-rate, but even after total gastrectomy 6 patients still produced moderate amounts of uropepsinogen. In none did it disappear from the urine, even several months after operation. Vagotomy produced no significant alteration in peptic activity shown by uropepsinogen estimation.

Effects of either cortisone or adrenocorticotropic hormone.—5 patients without clinical evidence of peptic ulcer, to whom this treatment was being given for reasons other than this study, responded with a twofold to threefold increase in uropepsinogen excretion (table III).

0 5 g tablets of the free amino-acid have been used and appear to be well tolerated by these patients when given in divided doses to a total of 20 g daily

SUMMARY

The effect of glutamic acid on the coma of hepatic failure has been investigated

Five episodes of coma in three patients with subacute or chronic liver injury were treated with glutamic acid

On each occasion a return of consciousness closely followed the administration of glutamic acid, which therefore appears worthy of further trial in the treatment of hepatic coma

I wish to thank Dr J D Nabarro, Prof R S Pilcher, Prof M L Rosenheim, and Dr Cedric Shaw for permission to use glutamic acid therapy on their patients

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M A, M B Camb, M R C P

Medical Societies

ATLANTIC CITY MEETINGS

OVER three thousand doctors met for the annual meetings of the American Federation for Clinical Research, the American Society for Clinical Investigation, and the Association of American Physicians, which were held at Atlantic City, New Jersey, from May 3 to 6 Altogether over four hundred papers were accepted for these meetings, but only eighty were read in the time available "Purely clinical" papers were in a minority, the trend being more and more towards laboratory and fundamental research In line with this, approximately 15% of all papers submitted referred to the use of radioactive-tracer techniques The tide of papers describing the pharmacology of A C T H and cortisone seems to be ebbing

Hæmatology

ABSENCE OF GAMMA GLOBULIN

C A. JANEWAY (Boston) said that in children with deficient reaction to infection, similar to that in nephrosis, electophoresis of the plasma had shown complete absence of the gamma globulin fraction A total of 14 such cases had been discovered, and this disorder might be more common than was initially supposed All the patients were boys with a history of multiple suppuration Arthritis and bronchiectasis were common features, and one child had had recurrent attacks of mumps In another, however, primary vaccination took normally, and revaccination showed that an immune reaction had developed The disease was probably due to a sex-linked recessive gene, manifest in the male, and was apparently associated with a primary failure of gamma globulin synthesis It could be cured by weekly intramuscular injections of gamma globulin, with penicillin chemoprophylaxis, penicillin alone was ineffective

AUTO IMMUNE HÆMOLYTIC DISEASE

L E YOUNG and **G MILLER** (Rochester, New York) said that in auto-immune hæmolytic disease the presence of sensitised red cells was apparently diagnostic, and could be detected by an anti globulin serum (the Coombs test) This, however, was not the whole story since the crises and remissions of the anæmia could vary independently of the number of sensitised red cells

L E -CELL PHENOMENON

In other papers the L E -cell phenomenon came in for a good deal of attention. This or very similar changes in the leucocytes could be simulated by adding a rabbit anti human granulocyte serum to a suspension of normal human leucocytes **FINCH** and his associates at Boston had noted clumping vacuolisation, and rosette formation of the damaged cells, which, if they were phagocytosed by other cells could produce a picture indistinguishable from that seen in disseminated lupus erythematosus Other reports confirmed this work

C E BUTTERWORTH (Birmingham, Alabama) had found that desoxyribonuclease, added to normal human leucocytes, might do the same thing He cautioned against the belief that the finding of L E cells was necessarily diagnostic, since he had found this change occasionally in normal leucocytes incubated without enzyme

CARRERA and associates at New Orleans had tested L E serum with leucocytes from other species, and found a wide species difference in the ability to form L E cells One particular specimen of L E serum, which gave negative results with human leucocytes was strongly positive with those from the horse

PLATELET-GROUPS

M STEFANINI and **G PLITMAN** (Boston) had separated 250 normal plasmas into platelet free and platelet-rich fractions, and by multiple testing had found that with certain combinations platelet agglutination would occur Four platelet groups, analogous to, but distinct from, the four blood groups, were proposed, with the following distribution in the white population of North America group 1 (9%), group 2 (3%), group 3 (equals 1 + 2) (4%), and group 4 (0) (84%) Factors such as these might operate in certain cases of thrombocytopenia which exhibit progressively less response to repeated transfusions of platelets

ACTION OF THROMBIN

S SHERRY and **W TROLL** (Cincinnati) had confirmed that thrombin acted as a proteolytic enzyme, and had found that a synthetic substrate—tosyl arginine methyl ester (T A M E)—was split by thrombin in a characteristic fashion, and to an extent closely dependent on the amount of thrombin present Furthermore, when T A M E was added to thrombin fibrinogen systems, clotting did not proceed until all the T A M E had been split Thrombin could be accurately assayed by its T A M E splitting activity.

ANOXIC POLYCYTHÆMIA

F STOHLMAN and **J C ROSE** (Washington, D C) reported on a patient with cyanosis of the lower half of his body secondary to a reversal of flow in a patent ductus arteriosus The sternal marrow, which was well oxygenated, was hyperplastic, whilst the iliac marrow, which was poorly oxygenated, was hypoplastic The patient's blood showed polycythæmia This was interpreted as evidence of a humoral mechanism in anoxic polycythæmia and against the theory that direct action of anoxia on the bone marrow was the stimulus for red cell production

Immunology

GAMMA GLOBULIN IN POLIOMYELITIS

W M HAMMOND (Pittsburgh) discussed the use of purified gamma globulin in the prevention of poliomyelitis The widespread availability of this material, and the publicity that it had received, made it imperative to remember its limitations Its use against poliomyelitis was analogous to its use in the prevention of measles, with the added disadvantage that primary cases were less easy to detect, since they were commonly aparalytic Mass passive immunisation with this agent had been advocated, but he thought that this was a wasteful and useless procedure In a trial conducted under the most favourable circumstances, during the phase of rising incidence in a severe epidemic, with its use limited to the most susceptible age group, it was shown that only one in about four hundred injections actually prevented an infection He advocated reserving this material for the prophylactic immunisation of (1) contacts of paralytic cases, and (2) contacts of those who, during an epidemic, developed an undiagnosed febrile illness which might be non paralytic poliomyelitis

RED CELLS AND INFECTION

R A NELSON (Bethesda) described an immunological phenomenon whereby normal red cells appeared to be an integral part of a reaction to invading organisms If virulent *Treponema pallidum* was added to a suspension of normal red cells in serum from a case of syphilis (antiserum) the organisms adhered to the red cells and could be centrifuged with them out of suspension If the same experiment were repeated with white cells the treponemata remained in suspension With both red and white cells, the treponemata were removed from suspension and were phagocytosed

Endocrinology

TRIIODOTHYRONINE

Several studies were reported which confirmed the work of Gross and Pitt-Rivers in England on the metabolic activity

TABLE II—EFFECT OF GASTRIC OPERATION ON EXCRETION OF UROPEPSINOGEN

Operation	No. of cases	Mean excretion of uropepsinogen (units per hr.)	
		Before operation	After operation
Partial gastrectomy ..	16	6·0	4·0
Vagotomy	8	9·0	10·0
Total gastrectomy	6	4·5	2·0

Pernicious anæmia.—In the only available inpatient with this disease the urine showed no peptic activity.

DISCUSSION

Diagnostic Value

Most methods used in the diagnosis of gastroduodenal disease are subject to limitation in accuracy or cannot be used in seriously ill patients. We have found this test useful when the usual investigations could not be done or had failed to help. For example, the problem of a patient with gastro-intestinal hæmorrhage of unknown origin may be solved by finding increased excretion of uropepsinogen. Duodenal ulcer, rather than œsophageal varices, is likely to be responsible. In pyloric stenosis of possibly malignant origin a duodenal ulcer may likewise be detected as the cause. Only 1 of 16 patients with gastric carcinoma had an increased excretion of uropepsinogen (fig. 6). On the contrary, there is a tendency towards a low excretion-rate in these patients which, though it is hardly of diagnostic value, may be of interest as a possible effect of the low-protein diet commonly taken by them. Bucher (1947) found that this effect is produced by such a diet in women.

TABLE III—EFFECTS OF GIVING EITHER A.C.T.H. OR CORTISONE TO FIVE PATIENTS WITHOUT CLINICAL EVIDENCE OF PEPTIC ULCER

Drug	Mean excretion of uropepsinogen (units per hr.)	
	Resting level	Acting level
A.C.T.H.	3·0	8·5
Cortisone	1·0	3·0
,, ...	3·0	9·0
,, ...	4·0	10·0
,, ...	9·5	14·0

Effect of Surgery

Since pepsin is a sine qua non in the causation of gastroduodenal ulcer, it is useful to inquire what factors affect its production. Factors which reduce the amount of pepsin may well be favourable to the healing of ulcers. We find that such a reduction follows gastric resection but not vagotomy and gastro-enterostomy. The level which remains after total gastric resection suggests that some of the uropepsinogen may be related to extragastric sources. It is noteworthy that the gastro-intestinal defect of pernicious anæmia is associated with a total disappearance of uropepsinogen (Farnsworth et al. 1946).

We believe that the immediate postoperative response may be due to handling of the stomach at operation, and a similar view has been taken by Hirschowitz (1950). A further factor may be the stimulus provided by adrenocortical activity which follows surgical operations. Our findings, like those of Spiro et al. (1950), are that there is increased uropepsinogen elimination in patients given adrenocorticotropic hormone (A.C.T.H.). They observed this effect within twenty-four hours of giving A.C.T.H. to normal patients, but in those with an already increased rate of excretion the rise was delayed. If A.C.T.H. alone was responsible, the change might not be expected in the early urine collections after operations for duodenal ulcer. In fact, the highest readings we have obtained were those from urine excreted on the second postoperative night in patients with duodenal ulcer. Since nothing comparable was seen in similar studies on the 4 cholecystectomy patients, the early uropepsinogen flux may be due to a direct gastric mechanism. The manipulation which usually accompanies operations on the stomach may be responsible, for in patients with duodenal ulcer the stomach is already manufacturing more than the normal amount of uropepsinogen.

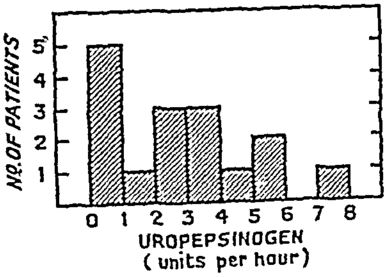

Fig. 6—Distribution of excretion of uropepsinogen (average 3·1 units per hour) in 16 patients with gastric carcinoma.

SUMMARY

A simplified method for estimating uropepsinogen is described.

The excretion of uropepsinogen has been estimated in 180 hospital patients.

Active duodenal ulcer is associated with an increased rate of excretion. This helps to distinguish (1) a duodenal ulcer from other causes of hæmatemesis, (2) a duodenal ulcer from a gastric ulcer or carcinoma, and (3) a duodenal ulcer from other sources of dyspepsia, such as the appendix.

There is a sex difference in the duodenal-ulcer patients corresponding to that seen in normal persons.

The response to various surgical operations has been studied.

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TREATMENT OF OXYURIASIS WITH DIPHENAN

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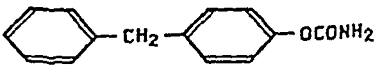
DURING a study of oxyuriasis in children at school A we gained the impression that diphenan was a less effective remedy than previous reports had led us to suppose. We accordingly extended our investigation to school B, and we now present our findings at these two schools.

Chemically diphenan is *p*-benzyl-phenyl-carbamate:



There are various proprietary preparations of the drug and most of the early studies were made in Germany with one of these, 'Butolan.' Diphenan is an official preparation appearing both in the *British Pharmacopœia* and the *British Pharmaceutical Codex.*

of triiodothyronine in myxœdema It now seems clear that this compound, not *l* thyroxine, is the hormone naturally active at tissue level Its effects are about five times stronger and are also more rapid in onset than those of *l* thyroxine, but they do not persist as long S P Asper and his associates at Baltimore had found that a myxœdematous patient could be cured by the new hormone with little or no increase in the titre of serum protein bound iodine R W Rawson et al (New York) confirmed this They had found that I¹³¹-labelled triiodothyronine disappeared from the circulation *much more rapidly than similarly labelled thyroxine*

FRUCTOSE FOR DIABETES

Several speakers attested to the advantages of giving fructose in the treatment of diabetic ketosis This sugar can participate in the glycolysis cycle without conversion to glucose or the participation of insulin J H Darragh et al (New Haven), for example, had noted that the intravenous fructose tolerance of patients at the height of diabetic ketosis was normal shortly after the institution of treatment with insulin and saline Glucose given under the same circumstances resulted in a prolonged rise in the serum concentration of this sugar A solution containing 2 5% fructose and 0 45% saline was given intravenously to six patients, and it seemed that there was a more rapid correction of the ketosis and of the dehydration than had previously been possible.

LOCALISATION OF INSULIN

R H Williams (Seattle) had injected insulin labelled with I¹³¹ and shown that this hormone localises particularly in the liver and the kidney Within the kidney it occurred almost entirely in the cells of the proximal convoluted tubules Such kidney localisation could be inhibited, in part, by the simultaneous administration of glucose or by growth hormone This method was a useful marker as to where the insulin appeared to be going, but must be checked by bio assay to verify that what was traced actually was insulin

ACTION OF GROWTH HORMONE

E Shorr et al (New York) reported on the metabolic effects of crystalline growth hormone given to two pituitary dwarfs Nitrogen, phosphorus, and calcium retention were produced, along with a rise in the glomerular filtration rate and a reversible insulin resistant diabetes Both patients resumed the growth rate normal for their age The effect was somewhat variable and tended to decrease the longer the hormone was given In one case there was a paradoxical resumption of its effect on withdrawal

STEROIDS

L Hellman et al (New York), by simultaneously administering differentially labelled acetate, cholesterol, and testosterone, had traced the main pathways for synthesis of the steroid compounds in a patient with a complete biliary fistula (thus obviating reabsorption from the gut) They showed that steroids of biological interest—biliary cholesterol, plasma cholesterol, cholic acid, testosterone, and other steroid hormones—could be derived both from dietary cholesterol and from acetate, and that these compounds seemed to have a common pathway for most of their synthesis Administered testosterone was converted into its urinary metabolites without the intervention of an enterohepatic recirculation The steroid nucleus, once formed, did not seem to be completely ruptured in its metabolism, since no labelled carbon dioxide could be detected in the expired air

F H Tyler et al (Salt Lake City), measuring blood levels of 17 hydroxy corticosteroids had found that certain stresses, such as the injection of adrenaline or of insulin, which produced eosinopenia *might have no effect on the amount of* the circulating adrenal corticoids However, after surgical operations, or other "life threatening" stress there might be a considerable rise in blood levels of these hormones, much in excess of what could be produced by maximal stimulation of the adrenals with intravenous A C T H

G W Thorn (Boston) had confirmed these results by assay of the urinary metabolites of compounds E and F He also noted the dissociation between the output of adrenal steroids and eosinopenia In one experiment in which the subject rebreathed into a Douglas bag with CO_2 absorber to the point of anoxia and unconsciousness, there might be a considerable increase in the output of *steroids* without significant eosinophil fall Thus it seemed that steroids other than those of *adrenal origin* contribute to the rise in the blood levels seen as a response to stress and possibly changes in the utilisation of these hormones might be a factor explaining the dissociation seen between eosinopenia and steroid output

C P Rhoads (New York), reporting the work of the late Konrad Dobriner, noted that abnormal steroid found only occasionally in patients with adrenal disease and never in normal subjects (even after A C T H stimulation) was frequently present in the urine of patients with rheumatoid arthritis and in such patients its amount could be increased by giving A C T H It was suggested that the presence of this abnormal steroid—17-hydroxy pregnenolone—was evidence for the existence of a primary adrenal defect in rheumatoid arthritis

TEST OF THYROID FUNCTION

R P Levy et al (Cleveland) described a thyroid function test involving a single-injection of thyrotropic hormone, measuring the results in terms of the serum protein bound iodine, and the I¹³¹ uptake The advantage of this test was that it measured thyroid reserve as well as current function

Cardiovascular Studies

CARDIAC OUTPUT

I Starr (Philadelphia) gave an interesting demonstration of his preparation simulating cardiac function at necropsy The cadaver heart was perfused in situ with blood from a large syringe actuated by a piston whose stroke and velocity could be accurately controlled. Simultaneous ballistocardiographic records were obtained The method was applied in many subjects and a large body of data built up, giving the cardiac output in relation to many variables such as body-build, pulse rate, and blood pressure By applying the method of multiple regression to the data, a *most interesting relationship* was established—the cardiac output in man could be calculated with excellent reproducibility from a formula derived from three simple clinical observations the diastolic blood pressure, the pulse pressure, and the body surface area The degree of accuracy probably compared quite favourably with more complicated catheter techniques

VALVULOTOMY IN PREGNANCY

C F Burwell (Boston) cautioned against the too ready use of mitral valvulotomy during pregnancy This operation was not a satisfactory alternative to termination when cardiac failure threatened to supervene during pregnancy in a patient with mitral stenosis, since benefit was not always *forthcoming and might be delayed for several weeks* Moreover the danger of congestive failure increased up to the end of the second trimester, after which time it gradually declined Mitral section should be done before pregnancy if possible, so as to improve the prognosis for pregnancy, or, if the patient was already pregnant, every effort should be made to get her through pregnancy without operation If operation had to be done *termination was the operation of choice,* and mitral section should be reserved for those bad risk cases where termination was not acceptable In any case mitral section should not be done in the last two months of pregnancy

ORTHOSTATIC PULSUS ALTERNANS

W M Daily and R F Sheffield (McKinney, Texas) described orthostatic pulsus alternans in three *patients* with organic heart disease Alternation was present only in the erect or semi erect position, and could be abolished by any measure which increased the return of blood to the heart, such as lying horizontally, immersion in water, infusions of blood or noradrenaline, or moderate exercise It could be provoked by measures which reduced the return of blood to *the heart, such as standing up, venesection, or the application* of venous occlusive tourniquets to the limbs It seemed that in this condition weakened heart muscle did not contract maximally except under conditions of increased initial stretch such as were provided by increased return of blood to the heart or the incomplete emptying of a previously weak beat

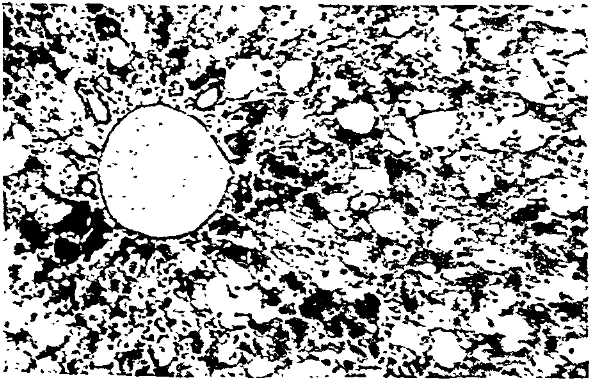
BLOOD VOLUME IN CONGESTIVE FAILURE

J F Ross et al (Boston) had measured the blood volume of dogs before and after the induction of congestive cardiac failure by operative tricuspid incompetence and pulmonary stenosis *Despite the* congestion and increased pressure in the systemic veins the blood volume, as measured by the radioactive chromium tagged red cell method, and by the Evans blue dye method, or by viviperfusion to remove all vanced fibrosis of the whole group but also presented vere cellular changes.

In contrast to the widespread cellular alterations in is group were the practically negligible changes seen the control rats receiving cortisone without carbon trachloride. Vacuolation, if present, was minimal in ctions stained with hæmatoxylin and eosin, and ballooning" was completely absent (fig. 4).

DISCUSSION

The bromsulphalein-retention test, as used here, can be pplied even to hæmolysed or turbid sera (Ahmad and razer 1952). An increase in turbidity caused by cortisone, milar to that of "fasting sera" observed in patients Adlersberg et al. 1952) or in rabbits (Rich et al. 1951) eated with cortisone or with adrenocorticotropic ormone, can therefore be discounted as an explanation f the increased retention values found in the animals eceiving cortisone and carbon tetrachloride. Antopol 1950) has described necrotic foci in the liver parenchyma f mice receiving large doses of cortisone. No such changes were observed in the cortisone-treated control rats in the present experiment; nor did cortisone have any deleterious effect on the elimination of bromsulphalein in that group of rats. This is in keeping with the experience of clinical observers that neither liver function, tested by the standard tests now in use, nor liver structure is much altered in cortisone-treated patients (Holmes et al. 1950, Goldner et al. 1950). Since, therefore, cortisone alone appears to have no obvious effect at the levels given in the present experiment, and since the impairment of liver function in rats receiving cortisone with carbon tetrachloride is considerably more severe than in those treated with carbon tetrachloride alone, the conclusion appears justified that cortisone, in the doses given here, increases the rats' susceptibility to chronic poisoning with carbon tetrachloride. This conclusion is confirmed by the histological observation that, at the cellular level, the liver lesions in both groups differ only in degree but not in kind.


ig. 3—Rat no. 6 (twenty-one injections of carbon tetrachloride; cortisone 50 mg. in ten days): extension of lesions to the cells round portal tract. (5% formol-saline solution. Hæmatoxylin and eosin. ×100.)

The characteristic zonal distribution of the lesion produced by carbon tetrachloride has been considered to be due to the vascular architecture of the liver. Increasing the dose of carbon tetrachloride only leads to an extension of the lesions (Glynn and Himsworth 1946, Himsworth 1947). The mosaic-like character of the lesion produced by carbon tetrachloride given with cortisone makes it increasingly difficult to trace this peculiar pattern, which suggests that the vascular factor may have been supplanted by some other factor. Several possible ones spring to mind in an attempted explanation of this effect of cortisone. It is well known that overdoses of this hormone in the rat lead to decreased consumption of food, rapid loss of weight, a negative nitrogen balance, an activation of fat-metabolism, and, according to Meites (1952), an increase in nutritional requirements. Sufficient experimental evidence is available to show that all these factors, either singly or combined, can increase the susceptibility of the rat towards carbon-tetrachloride poisoning (Forbes et al. 1941, Post et al. 1942, György et al. 1946, Drill 1952). Probably a better understanding of the way in which these factors act would clarify the effect of cortisone described here.

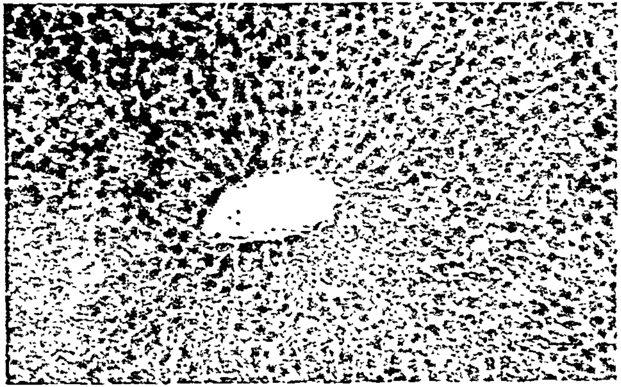


Fig. 4—Rat no. 26 (cortisone 90 mg. alone in ten days): liver cells show minimal changes. A central vein is seen in centre of section. (5% formol-saline solution. Hæmatoxylin and eosin. × 100.)

SUMMARY

Cortisone has little effect on the bromsulphalein-retention test in the normal rat, but produces considerable deterioration if given to rats treated with carbon tetrachloride for seven weeks.

The histological picture showed more widespread liver damage in these rats than in a control group treated with carbon tetrachloride only.

Cortisone increases the susceptibility of the rat's liver to chronic damage by carbon tetrachloride.

We wish to thank the Medical Research Council for the cortisone, and Mr. M. Sharradd for his technical assistance.

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"... although our surgeons are as keen on early post-operative ambulation as those in the United States, this does not apply to the obstetric service. ... Strict bed rest for the parturient mother is still insisted upon. Ostensibly, this is because more importance is laid upon obtaining rapid involution of the uterus than upon the danger of venous thrombosis, but my friend suspected that there is a more subtle reason: he believes that we British doctors are more subservient to our nursing colleagues than we care to admit.—Dr. JOHN LISTER, *N. Engl. J. Med.* 1952, 247, 914.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Fitness to Drive a Vehicle

THE section of general practice met on Dec 17, under the chairmanship of Dr E P SCOTT, president of the section, to discuss Fitness to Drive a Vehicle

Dr R D SUMMERS, a divisional police surgeon in the Metropolitan area, said that in Great Britain during 1951 there had been 1309 road accidents thought to be caused by drivers who were under the influence of alcohol Many such drivers escaped conviction because the reluctance of the courts to find the accused guilty made the police unwilling to press the charge He himself did not certify some 35% of drivers referred to him as being under the influence of alcohol The charge, under section 15 of the Road Traffic Act of 1930, was concerned with being under the influence of alcohol or drugs to such an extent as to be unable to take proper charge of a motor vehicle The phrase about being in charge was sometimes rather unfairly interpreted, for a motorist who felt himself the worse for drink and who stopped his car to get into the back seat for a sleep was still technically in charge of the vehicle and could therefore be convicted of an offence The police surgeon, or the private doctor whom the accused person could call to examine him, must make a complete and thorough examination For this the consent of the accused must be obtained, and it was wise to have a witness to this consent and to the subsequent examination It was not unknown for the accused to assault the police surgeon or to attempt to escape from custody The pulse-rate should be taken at both the beginning and the end of the examination, during alcoholic intoxication the pulse was full and bounding, with a rate between 100 and 140 Full notes should be taken at the time, and every system thoroughly examined, particular attention being paid to any impairment of muscular coordination, the state of the pupils, and general behaviour It should be remembered that defending counsel could completely destroy the value of a careful clinical examination by disclosing, during cross examination, some gap in the doctor's observations For instance, the doctor might have made careful notes of the state of the pupils, but a jury would be led to think his evidence worthless if he had to admit in court that he did not know the colour of the eyes The history of any previous illnesses should be noted, and the events leading up to the accident, especially the taking of food and drink, should be investigated Evidence of the present mental state, speech, gait, and writing should be recorded Dr Summers usually asked the accused to copy a section of the Highway Code relevant to his charge, it was important to produce any specimen of handwriting in court The doctor must confine himself to the condition of the accused at the time when he examined him, and refuse to be drawn into speculations about his state at the time of arrest, which might be an hour or more previously The accused might ask for his own doctor or any other doctor to be called to examine him, as a defence against the findings of the police surgeon Such additional examinations did not come under the provisions of the National Health Service, and any doctor was entitled to refuse, or to charge a fee for his attendance If the police surgeon, having examined the accused, did not consider him to be under the influence of drink, the police very seldom prosecuted When the driver was found to be under the influence, the charge was heard next day in a magistrate's court The accused might be granted a remand to apply for legal aid, or he might elect to go for trial by judge and jury at the County Court, or to be tried by the magistrate

Dr F E CAMPS said that he thought the main duty of the doctor was to exclude the presence of organic disease, for if no disease was found to account for abnormal behaviour, and it could be proved that the person had taken alcohol, then it was a reasonable inference that his inability to control a vehicle was due to the alcohol Several drugs simulated the effect of alcohol on judgment and coordination, but it was equally an offence to be under the influence of drugs unless it could be shown that they had been taken in normal dosage in the ordinary course of medical treatment The barbiturates, nowadays widely prescribed, were commonly blamed for inability to control a vehicle, and lately the anti histamines had joined them, whilst diabetics taking insulin often pleaded hypoglycæmia in defence In one case alkalosis had been brought forward as defence by a man suffering from a gastric ulcer who had taken several spoonfuls of sodium bicarbonate—and also a large quantity of whisky

Any organic nervous disease causing incoordination, such as states of chronic cerebral contusion ("punch drunk"), acute concussion, epilepsy, vertigo from any cause, and Ménière's disease, might be the basis of a defence

Dr Camps thought that the behaviour of the accused at the time of examination was the most important point for the police surgeon to note Most private doctors were for obvious reasons, loth to attend even when they were asked to see their own patients They also were afraid of being involved in a legal case, mainly because of having to face cross examination by counsel—which should be no cause for worry Others, however, disliked hanging around courts waiting for the case to be heard, this could be avoided by approaching the clerk if necessary

Mr L C NICKOLLS, director of the New Scotland Yard laboratory, spoke of the value of the tests for estimating alcohol in blood and urine, which were chiefly corroborative of common-sense observation If a graph were drawn of the percentage of alcohol in the blood of drivers charged with being "drunk in charge," the peak of the curve would be at about 0 3%, for at this stage of intoxication a driver would draw attention to himself by swerving about the road or hitting something, for higher concentrations the curve declined, because at this stage the driver would be in the ditch or in coma Mr Frederick Mead, a Metropolitan magistrate, used to say that there was nobody like an experienced police sergeant for judging whether a man was drunk The doctor had to remember that he contributed only part of the procedure, it was for him to give his medical evidence, but it was the court's responsibility to decide whether the accused was under the influence of drink

Mr Nickolls agreed with Dr Camps that the occasional drinker who had a few too many was a much worse menace than the habitual toper He had known drivers who were drunk when they learnt to drive and would probably have been completely unable to drive if they had ever been sober

If blood or urine was collected for an alcohol estimation, it was essential to make sure that the receptacle had not been cleansed with spirit or 'Dettol', the same applied to hypodermic syringes and needles

There was great difficulty in obtaining convictions unless one had a cast iron case Magistrate, judge, and juryman were all reluctant to convict, for each one felt "There but for the grace of God " One had literally to shame them into giving a conviction, and the doctor should remember that he had a duty to the public

Dr R D LAWRENCE spoke of the diabetic driver In 1927 he and Dr Otto Leyton had discussed with high police officials the question of the diabetic's fitness to drive, and it had been decided that patients taking insulin were safe as drivers From time to time hypoglycæmia gave rise to a road accident, but such cases were relatively infrequent Any diabetic on insulin, especially if he was taking the long acting zinc protamine blood from the body, showed no increase. These results provoked considerable discussion, since they were contrary to clinical experience of congestive failure in man. It was pointed out, however, that this condition of pure right-sided heart-failure without pulmonary disease or anoxia did not have its counterpart in man and results in the two species were not directly comparable.

BIOCHEMICAL CHANGES IN HYPERTENSION

L. TOBIAN and J. BINION (Boston) had clinically analysed various tissues of rats in which hypertension had been induced by operative stenosis of the renal artery. Whereas brain and skeletal muscle tissues showed insignificant changes after the induction of hypertension, the media and intima of the aorta showed much increase in water, sodium, and potassium, and decrease in magnesium. There was evidence that these changes were predominantly intracellular. They could be discovered in operated animals even before hypertension was apparent, and therefore seemed to have some causal relationship to the increased vascular tone and tension in this condition. G. A. PERERA (New York) had found that potassium-deficient diets produced a small but significant amelioration of hypertension in man, and the beneficial effects of sodium restriction in this disease are well known.

PERIARTERITIS

M. A. BLANKENHORN et al. (Cincinnati) gave a classification of the forms of arteritis, and gave reasons for distinguishing classical periarteritis nodosa from hypersensitivity arteritis of the kind that could be induced experimentally in animals and occasionally followed sulphonamide ingestion in man. They believed that the difference was important prognostically, hypersensitivity having the better outlook. In this latter condition the arterial lesions were widespread, were all of the same age, and were found equally throughout the parenchymatous tissues of organs as well as in the hilar region, which was the classic site for periarteritis. In this condition eosinophilia did not occur, whereas in periarteritis nodosa it did. By these and by various other criteria the two conditions could be sharply differentiated.

HYPERTENSION DUE TO VASCULAR RENAL LESION

J. E. HOWARD et al. (Baltimore) read an interesting paper describing *four instances of malignant hypertension*, due apparently to a vascular lesion of one kidney, which cleared up completely when the kidney was removed. Ordinary tests of renal function might fail to reveal any impairment, or impairment of function in the affected kidney might be minimal. In one case the only evidence of abnormality was a constriction of the renal artery on arteriography; even microscopically the kidney that was removed showed no detectable changes. The maximum time between the apparent date of onset and cure by nephrectomy was about nine months.

Miscellaneous

OBSERVATIONS ON OSTEOPOROSIS

P. E. HENNEMAN and his associates (Boston) presented studies in which five patients with osteoporosis received 50 g. of human serum-albumin daily for from nine to thirty days. After twenty days the urinary output of calcium had fallen almost to zero, and metabolic studies suggested that all the retained calcium had been converted into bone. The mechanism of this action was not understood, but albumin might be a transport form of bone-matrix precursor. The amount of calcium retained, which varied from 41 to 199 mg. per day, compared favourably with figures for postmenopausal osteoporosis treated by œstrogen.

INFECTIOUS HEPATITIS

Two carefully controlled studies on infectious hepatitis were presented by a Harvard group working at the American Army Hepatitis Centre at Kyoto, Japan. They had tested: (1) enforced vigorous exercise early in convalescence as against exercise late in convalescence; (2) strict bed rest as against "ad-lib." bed rest; and (3) an enforced diet supplemented by extra choline, fat, protein, and vitamins as against an "ad-lib." hospital diet. Patients were assigned to the treatment groups at random and their progress was followed by carefully standardised clinical and laboratory observations. Patients on the supplemented diet convalesced seven days earlier than the others: the enforcement of exercise or of strict bed rest made no apparent difference to the outcome. In another study it was found that the improvement caused by the supplemented diet was due solely to the higher proportion of protein that it contained; and this was effective in the first week of treatment.

SYNDROME WITH ECK FISTULA

W. MCDERMOTT and R. D. ADAMS (Boston) reported a syndrome of episodic stupor and coma in a man with an *anastomosis between the portal circulation and the inferior vena cava* that had been produced at operation for carcinoma of the head of the pancreas. This appeared to be the first time that this type of anastomosis (an Eck fistula) had been produced in a patient who did not have either liver disease or an established collateral circulation. Convalescence was punctuated by a series of episodes varying from impairment of consciousness to deep coma. The onset was acute, and without obvious cause. The condition might last a few days, then clear up entirely and rapidly. Distinct electro-encephalographic changes, also reversible, occurred. The only consistent biochemical alteration was in the blood-ammonia, which rose sharply at the onset of each episode of stupor. The condition could be precipitated by giving ammonium salts, urea, or a high-protein diet, and in this respect resembled the so-called meat intoxication sometimes seen in Eck-fistula dogs. Protection against these attacks was afforded by a low-protein diet and by phthalylsulphathiazole to suppress intestinal *urea-forming organisms*. Elevation of the blood-ammonia content could not as yet be regarded as the cause of this condition, although it was a constant accompaniment of it. The condition might be allied to the so-called hepatic coma.

Reviews of Books

Proteins and Enzymes

Lane Medical Lectures. KAJ ULRIK LINDERSTROM-LANG. Stanford, Calif.: Stanford University Press. London: Oxford University Press. 1952. Pp. 116. 24s.

Dr. Linderstrom-Lang has been well known all over the world for many years for his ingenious studies of the distribution of enzymes inside single amœbæ, sea-urchin eggs, and other microscopic cells. From the *chemistry department of the Carlsberg Laboratory* in Copenhagen, which he directs, have come investigations of the enzymes present in the intestine of the clothes-moth larva, which enable it to digest hair and wool, and surveys of the distribution of pepsin and certain peptidases in different cells and layers of the gastric and duodenal mucosa. At the same time he has pursued the problem of the structure of proteins and the precise way in which such enzymes as pepsin exert their digestive action. These five lectures, given at Stanford University, California, in October, 1951, summarise the contributions of his school in these twin fields of enzyme biochemistry and relate them to the work of others. They provide a useful introduction to micro-techniques which permit the measurement of the quantities of different enzymes in as little as $^1/_{50}$ of an amœba, and which can be applied to liver biopsy specimens and other pathological material. They also contain many suggestions stimulating for the biochemical specialist, who will find the book gracefully written. But all medical research-workers, and particularly pathologists, may find something of value. As biochemical knowledge grows, and histochemistry develops in step, the post-mortem histology of the routine hospital pathologist is likely to give place to enzyme assays on cells and tissue sections which will provide a more dynamic functional picture of what has gone wrong. Dr. Linderstrom-Lang has laid much of the groundwork for this development.

Manual of Clinical Allergy

JOHN M. SHELDON, M.D., professor of internal medicine, University of Michigan; ROBERT G. LOVELL, M.D., instructor in internal medicine; KENNETH P. MATHEWS, M.D., assistant professor of internal medicine, University of Michigan Medical School. Philadelphia and London: W. B. Saunders. 1953. Pp. 413. 42s. 6d.

OWING to the close relation between experimental and clinical allergy most textbooks and reference books suitable for the allergist contain detailed discussions of both aspects. This book provides a common-sense

E II R

June 2, 1953

When all the people with one voice
Acclaim the Coronation day,
Each craft and calling fitly may
In its own way
Rejoice,
And its especial homage pay.

Our forefathers' untutored art
Sought healing in the touch of kings,
Yet truth lay at their legend's heart,
For we have felt the touch that brings
Health to the nation, we have seen
The greatness and the grace
Of Britain in her Queen

God save the Queen!
What meaning has that prayer
For us who know that monarchs wear
An unseen crown of care,
That kingship's tasks
Are lifelong, and through life is paid the price
Unceasing service asks?

How better can we pray
Than that, when she shall come
At close of day
Into the gay serenity of home,
There she may ever find
The best of medicines the spirit knows—
A quiet mind
And, at the heart of everything, repose?

W R B

practical survey of the clinical approach. The objective is somewhat blurred, however, for the useful 51-page discussion of pollen identification belongs rather to a reference work, while the scanty 4-page discussion of the basic mechanisms could have been extended to cover the basic facts essential for an adequate understanding of a growing subject. The value of the clinical material is enhanced by the omission of references to much vague and unsatisfactory clinical literature which are found in larger volumes. With allergy, indeed, comprehensiveness seldom aids comprehension, particularly by those who are not engaged in this field. The practical advice for the identification and handling of the commoner allergens can be applied readily in practice.

A classification of the anti-histamine drugs based on various combinations with the active dimethylamino group is useful for therapeutic trials, and could be improved further by a clear classification of these drugs into sedative and stimulating, and long-acting and short-acting, and by advice on their combined use. The authors correctly point out that palliatives do not replace the "well-established," "cause and effect" investigation, and they might well have added a warning of the dangers of unexpected and unrecognised sedation by the anti-histamine drugs, which may endanger the patient and others. The long lists of trade names quoted for the various anti-histamine drugs illustrate a real source of confusion and the urgent need of a common name for each, to which the manufacturer's mark could be added.

The references have been judiciously chosen and do not hamper smooth reading, but there are unfortunate omissions of contributions from other countries—such as the extraction of a highly purified specific house-dust antigen, and its identification as a polypeptide-polysaccharide complex by Rimington et al., which has obvious advantages in diagnosis and treatment.

Congenital Heart Disease

HENNING GOTZSCHE. Copenhagen: Henning Gotzsche. 1952. Pp. 254. Kr. 25.

Scandinavian authors have produced a number of monographs on congenital heart-disease, and this work from Copenhagen is one of the most comprehensive.

It is based on 200 consecutive cases studied in the medical department of the university. A short historical introduction, a full clinical picture, and an account of detailed diagnostic methods, is accorded to each disorder. The radiographic features and electrocardiographic changes are carefully analysed, and well illustrated, and the more advanced investigations such as cardiac catheterisation, angiocardiography, and phonocardiography are discussed where necessary. The numerous tables and case-reports illustrate the care with which the book has been compiled, and the translator is also to be congratulated.

Diseases of the Esophagus

PHILIP THOREK, M.D., F.A.C.S., associate clinical professor of surgery, University of Illinois College of Medicine. Philadelphia and London: J. B. Lippincott. 1952. Pp. 140. 80s.

THE number of recently published monographs on surgery of the œsophagus show with what interest this subject is being pursued. In this concise and comprehensive work Dr. Thorek emphasises the pathological and surgical aspects. The half-tone illustrations and diagrams are of outstanding quality and of particular value to the surgeon. The sections on congenital defects and diverticula are especially good, but those on achalasia and hernia are less satisfactory. The points that probably require greater emphasis are the risk of regurgitation or reflux from stomach into œsophagus if the so-called sphincter mechanism is inefficient, and the ease with which the cardio-œsophageal junction can ascend into the thorax. Actually some of the operations described in relation to abnormalities in the lower œsophagus and diaphragm are so ornate in name and character as to merit their relegation to a museum, so as to make place for more simple and rational procedures. The treatment of carcinoma is well described and efficiently illustrated, but without reference to immediate or long-term results.

Annual Survey of Psycho-Analysis

A Comprehensive Survey of Current Psychoanalytic Theory and Practice. Vol. I. Editor: JOHN FROSCH, M.D., in collaboration with JACOB A. ARLOW, M.D., NATHANIEL ROSS, M.D., and SIDNEY TARACHOW, M.D. New York: International Universities Press. London: Allen & Unwin. 1953. Pp. 556. 75s.

THIS is the first of a projected annual issue, and it summarises the psycho-analytic literature for 1950. The definition of psycho-analytic is somewhat elastic, and though most of the publications reviewed are American the output of other countries has not been overlooked.

Some twelve authors present the various sections discussing history, critique, methodology, psycho-analytic studies in development, ego psychology, clinical studies, psycho-analysis and psychosomatic medicine, child analysis, psycho-analytic therapy (with four subsections), applied psycho-analysis (in six fields), and psycho-analytic training and practice. A 125-page chapter describes twelve of the more important psycho-analytic books published in 1950. Inevitably, there is some unevenness of style and treatment, and it was hardly to be expected that all the material should be new or profound; but to the practising analyst or the student the book should prove useful for reference.

Brain Surgeon

An Autobiography. WILLIAM SHARPE. London: Gollancz. 1953. Pp. 244. 16s.

THIS autobiography is full of clinical stories told with gusto and "all the tricks of salesmanship" that the author knows, and they are many.

Born of a Scots Presbyterian clergyman and brought up in the slum areas of Pittsburgh, Chicago, and Philadelphia, Dr. Sharpe won his way to Harvard and eventually to Harvey Cushing's clinic at Johns Hopkins where he learnt the craft of neurosurgery. At a comparatively early age he was appointed the first professor of surgery at the Harvard Medical School at Shanghai and his year of office brought much adventure and rich experience. He was invited to advise on the treatment of the President of China's eldest son, who was partially paralysed after a riding accident. In defiance of the opinions of the presidential physicians he operated successfully, and only when he had finished did he learn that, had he failed, his life might well have been taken by the patient's mother.

His main interests are in the relief of hydrocephalus and the occurrence of intracranial hæmorrhage in the newborn, which he believes is responsible for cerebral spastic paralysis.

Sir Cecil Wakeley describes Dr. Sharpe as one of the pioneers of neurosurgery. But, like that of most other pioneers, his point of view is not always the same as other people's; and his account of a demonstration laminectomy will spoil his book for many readers.

Progress in Ophthalmology and Otolaryngology

A Quadrennial Review. Vol. I. Editors: MEYER WIENER, M.D., A. EDWARD MAUMENEE, M.D., PERCY E. IRELAND, M.D., JOSEPH A. SULLIVAN, M.B. New York: Grune & Stratton. London: Heinemann Medical Books. 1952. Pp. 666. £5.

THIS book, containing 35 chapters on ophthalmology and 29 on otolaryngology, aims at covering the literature from 1946 to 1950. Opinions will differ on whether any useful purpose is thereby served. There are four excellent abstract journals in ophthalmology—two in English, one in French, and one in German. In addition, some ophthalmic monthlies carry abstract sections, while others carry critical review articles of recent work on particular subjects; and there is also a yearbook in ophthalmology and otolaryngology. Thus a quadrennial review necessarily tends to become a digest of digests. The standard reached by some of the chapters in this volume is high, but only when the writer has broken away from the stranglehold of abstracting papers published over a given period. Incongruously enough in a publication of this type, some chapters are in the nature of original communications. Most of the book, however, is parochial in outlook and takes little note of anything outside American journals.

The Wider World

THE HEALTH OF A TROPICAL PEOPLE

A Survey in Ceylon

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I METHODS OF ASSESSING HEALTH

Health strictly means wholeness, but, both for individuals and for communities, we need to specify the qualities in which wholeness is desirable The World Health Organisation in 1946 defined health as "a state of complete physical, mental and social well being and not merely the absence of disease or infirmity" This definition, while emphasising that many factors contribute to health, is not sufficiently precise for practical use The scientist in the field requires a definition in terms of qualities which he can measure accurately indeed, he has inevitably confined his assessment to factors which he can record accurately By thus limiting the number of health factors he studies, he has sacrificed comprehensiveness but he has achieved some accuracy of detail

The W H O definition implies at least three qualities in health—physical, mental, and social Physical health has been measured most often, though occasionally it has been studied in relation to some aspect of the gross environment—e g , economic status or sanitation Moreover, usually only some of its many aspects have been studied, the emphasis of the assessment varying with the interests of the observer For example, some workers have analysed the vital statistics of a community, others have assessed the nutritional status of the inhabitants, others have measured the physical development of the people, others, and more rarely, have examined the incidence of sickness

Efforts to standardise the methods for the assessment of health have been made from time to time, and lead to the development of the concept of health indices, about which a report was published by the health organisation of the League of Nations in 1939 This memorandum suggested that the health of a population should be measured by indices of (1) vitality and health, (2) environment, and (3) public-health activity

Standardisation of assessment is helpful in comparing the health of the same community at different times, or the health of different communities But the basis of assessment assumes that certain statistics are both available and reliable Moreover, much of the information demanded even if obtainable, is not applicable to primitive society for the health indices were designed to assess the health of the more advanced countries Thus in many countries of the world vital statistics may not be obtainable or if obtainable they may be of doubtful reliability or cover only major epidemic diseases, such as smallpox typhoid fever, cholera and plague Again even in the better-organised countries the morbidity statistics may relate only to hospital patients

Criteria

Any assessment of the diet of a community presupposes basic or minimal requirements for the various nutrients These requirements are still in dispute in the West, and some of them are probably different for the people of the East Thus the basal metabolic rate varies with climate, being less in the tropics than in temperate climates (Galvao 1948a and b) Moreover, the physique of most people in the East is different from that of people living in Europe or in North America, and so their daily energy requirements are different (Cullumbine 1950a) Because of their smaller stature the calcium requirement of Eastern people will probably be less too, and their calcium intake will vary further with their dietary pattern—e g , polished or unpolished rice—while allowance must be made for adaptation to adverse intakes (Cullumbine 1950b) The pattern of the diet may also influence the required intake of carotene (Hume and Krebs 1949) In other words, nutrient requirements cannot be standardised for the whole world, and local requirements must be established for each major community before the adequacy of diets can be judged

This may necessitate the selection and the study of a subgroup of the population who have shown adequate physical and physiological growth and development within the limits imposed by their environments and their heredity "Adequate" is here used in preference to 'optimal," since the optimal physical and physiological development is an ideal which has yet to be defined Thus, should we aim to achieve men six feet tall or should we be content with a race of five feet men? Is there any advantage in weighing 50 kg in Ceylon or 70 kg in Britain?

Not only has the optimal development to be defined but the significance of the observed range of variation of the physiological characters of the body is but little understood Can we say how the functional capacity of a man with a systolic blood pressure of 125 mm Hg and a blood hæmoglobin of 16 g per 100 ml differs from that of a man with a pressure of 115 mm and a hæmoglobin of 15 g?

Lacking a definition of optimal development, we need some yardstick for assessing not only the adequacy of diets but also the growth potential of the population This yardstick may be data obtained in a more prosperous and advanced country, though this is not always desirable since people may be ethnically different and may live in grossly dissimilar environments Here again we may have to select and study a subgroup of people within the same community, the selection is usually made from people who have a sufficient income (both monetary and in kind) to provide an adequate diet and who have sufficient education and intelligence to insist upon adequate housing, sanitation, and medical care

This yardstick population will itself vary in the factors to be measured, and should *not* be considered as necessarily a "*normal*" population In fact the concept of "normality" must be used with care As Sinclair (1949) has stated, its meaning may be different for different observers To a statistician it may indicate *that* a variate is within ± σ of the mean for a given population Such a definition may be useful when comparing subsections of a population, but it may not agree with the physiological concept of normal For example, it would class dental caries as being normal in an adult population (Sinclair 1949) Should "normality," therefore, be used to indicate merely the absence of signs and symptoms of disease? The pathologist and the clinician use such a standard and with justification, but it may be too crude a demarcation and ignore the finer gradations of function likely to be found in a large population Nor can "normality" be taken to signify perfection, since the definition of perfection will vary with the circumstances of the study The definition would then approach the physiologists' meaning of normal—viz , adequate function in the environment studied This meaning again requires classification—e g , of the environmental factors considered important, of the functions assessed, and of the qualification 'adequate"

Perhaps all these concepts of normality could be defined as the absence of the signs and symptoms of disease with adequate function under the conditions of study, and with all the measured varieties lying

THE LANCET

LONDON: SATURDAY, MAY 30, 1953

Negative or Positive?

In 1916 Lloyd George appointed a committee to consider means of securing permanent improvement in the relationship of employer and employee and of ensuring that industrial conditions affecting this relationship should be systematically and continuously reviewed. This committee recommended that each of the chief industries should have a representative joint body capable of dealing with matters affecting the welfare of the industry as a whole, and that every factory should have a works committee meeting regularly to deal with its own staff problems. The Whitley machinery devised for these purposes has since played an important part in negotiations between employers and employed not only in industry but in the Civil Service. The joint bodies or councils are named after the committee's chairman, J. H. Whitley, M.P., afterwards Speaker of the House of Commons.

The National Health Service is covered by nine Whitley Councils, each dealing with a particular type of staff, and one General Council.[1] The "management side" consists of officials of the Ministry of Health and representatives of regional hospital boards, boards of governors, executive councils, and local health authorities. The "staff side" consists of representatives of professional organisations and trade unions. The basic principle on which the councils were founded was that management and staff should reach agreement by joint consultation and negotiation, failing which they might agree to arbitration. The application of this principle to the hospital service is generally recognised as desirable; but the experience of the past few years has shown that the mechanism by which it is applied could be considerably improved, and some valuable suggestions to this end are made in a memorandum prepared by a group of hospital administrators.[2] In a service employing some 400,000 persons, whose salaries and wages account for 60% of the total expenditure, some form of central control over rates of pay is unavoidable; but the present system has an inflexibility which causes great difficulty at the periphery, where boards of governors and regional hospital boards have no power to vary national rates to suit local conditions, to reward meritorious services, or to bring exceptional experience to bear on an administrative problem. In some groups of workers, such as technicians in electrocardiography and electro-encephalography departments, unrealistically low rates of remuneration have been fixed and recruitment is consequently difficult. Admittedly the system has important advantages: employees know exactly where they stand, and the Ministry can maintain a large measure of control over the finances and man-power in the hospital services. But management committees and regional boards are increasingly at a disadvantage when they try to act as good employers and to compete with local industry. Moreover the ways in which uniformity can be wasteful have been evident for quite a long time.[3]

When taken over by the nation five years ago, the hospitals were at all stages of development, and judged by the criteria of business many of them fall far short of efficiency. Undoubtedly they still have much to learn from industry. But have they sufficient incentive to constant improvement? A new attitude of mind is badly needed to offset the depressing effects of Treasury strait-lacing, and we could wish that the Ministry of Health showed greater awareness of the need to study, on a research basis, the ways in which hospital administration could be improved. An active research programme, and a wider application of the lessons learnt from the best centres (which would come out very clearly if departmental costing were introduced), might well result in a 15–20% increase in efficiency without extra cost. The immediate need is not so much to establish special recognition of merit at lower levels —which can always be given by promotion—as to introduce exceptional men and women at exceptional salaries to assist in the development of a particular branch of the hospital service, such as catering, laundry, or records. As the hospital administrators' memorandum points out, some of the work they would do could fairly be regarded as research projects; and it might indeed even be financed out of endowment funds, thus circumventing Whitley designations. Again, incentive would be stimulated if exceptional merit could be recognised within the service by a system of monetary prizes awarded to those whose methods would clearly make a contribution to the National Health Service as a whole. The South West Metropolitan Regional Board award annually scholarships for medical research, and there is no reason why the same principle should not apply to the administrative staff; for we already have indices by which to assess their contribution. There is also the occasional individual—e.g., a surgical instrument technician—who has built up a highly specialised and extremely efficient department and whose particular contribution to his hospital is certainly not being properly rewarded by the national scale. It should be within the power of a regional board, when a really strong case has been made out, to sanction an increase in salary. In some aspects of hospital work, experiment is needed with different methods of pay—e.g., rates of pay based on piece-work in laundries.

As for the Whitley Councils themselves, the policy of stimulating maximum efficiency can be fully worked out only if all those serving on the councils are really familiar with the problems at the periphery. At present they are not. The Ministry's officials, living in the shadow of the Treasury, sometimes seem more concerned with outvoting other management representatives in the interests of financial stringency than in stimulating a good-employer policy. Insufficient liaison between these officials on the one hand, and the senior hospital officers or committee members on the other, means that the management side is not always fully briefed on within the limits ± σ of the mean of each variate. This approaches the type of definition which is often given to physical health, and, as I have said, it is usually physical health which has been assessed in health studies. But if a man is a creature of his environment, the study cannot be divorced from the social, economic, physical, and even political aspects of his surroundings. Otherwise the study becomes merely descriptive, and logical cause-and-effect relationships cannot be formulated.

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[1] See *Lancet* 1948, i, 845.

[2] Multigraphed copies obtainable from Mr. J. D. Banks, Royal Cancer Hospital, Fulham Road, London, S.W.3.

[3] *Lancet*, 1949, ii, 201.

The assessment of physical health should include, therefore, at least

(1) A demographic study of the population.
(2) An analysis of the vital statistics for the population.
(3) An analysis of the prevalence of sickness within the population.
(4) A physical and physiological characterisation of the people.
(5) A dietary history of the population and its relationship to available food-supplies.
(6) A statement of the medical (and probably educational) facilities available to the population.
(7) A description of the physical, social, economic, and, possibly, political factors in the environment, at least in so far as these may effect the previous items (1–6 inclusive).

The Ceylon Inquiry

It is on these lines that, in the past four years, we have tried to evaluate the health of the people of Ceylon.

Ceylon is particularly well suited for a study of the health of a tropical people. It is a small island which can be adequately covered by one research group. Within this small space are to be found diverse ethnic, religious, educational, economic, and social characteristics which are broadly typical of Asia as a whole. There is, and has been for some years, a very comprehensive official computation of vital statistics. (The diagnosis of causes of death may be questioned but this will be discussed later.) In proportion to its population Ceylon also has, for Asia, a relatively large number of doctors trained in the Western system of medicine, and fairly good hospital services. The presence of a reliable system for the registration of vital statistics and the provision of a national medical service may be points of distinction from the rest of South-east Asia, but a study of the health experience in Ceylon may be a useful preliminary to an analysis of the health problems of this region.

The preliminary assessment of the health of the Ceylonese included

(1) A complete analysis of the recorded vital statistics for the past twelve years (Cullumbine 1951).
(2) A study of morbidity and disabling illness based on door-to-door interviewing of 17,946 households with 94,128 persons from all districts and communities in Ceylon (Cullumbine 1952).
(3) Anthropometric and physiological surveys involving about 10,000 subjects, with more detailed studies on smaller selected groups.
(4) A survey of the dietary habits of one in every thousand families in the total population (1400 families). This was done on a family basis and the food prepared for consumption by each family was weighed on seven consecutive days (Cullumbine 1951).
(5) An analysis of the food supplies, and of the medical facilities (Cullumbine 1949).

DEATH-RATES

Each of these studies had its own problems of measurement and of interpretation. Thus, though independent checks suggest that there is complete registration of births and deaths in Ceylon, the accuracy of the registered causes of death may be questioned. In selected urban areas the person appointed to be registrar is a doctor and he has a special responsibility for the certification of causes of death. But only about 15% of all deaths are registered with these medically qualified registrars, and a minority of all certifications are made by practitioners of Western medicine. The influence this has on the recorded causes of death is seen from the figures in the table, where the causes of infantile deaths in 1950 in the Kalutara Totamune have been separated into those registered with lay registrars and those registered with medical registrars.

THE PERCENTAGE DISTRIBUTION BY CAUSE OF INFANTILE DEATHS DURING 1950 IN THE KALUTARA TOTAMUNE

Cause of death	Lay registrar	Medical registrar
All causes	100 (364 cases)	100 (221 cases)
Convulsions	62·3	10·9
Prematurity	13·2	24·4
Infantile debility	1·6	20·4
Pneumonia	9·3	0·9
Bronchopneumonia	1·1	17·4
Bronchitis	—	2·3
Malnutrition, &c	2·7	5·4
Toxæmia (worms)	4·1	5·9
Enteritis and diarrhœa	2·2	5·9
Asphyxia neonatorum	—	2·3
Icterus neonatorum	—	0·9
Other causes	3·4	3·3

The two lists suggest that we are dealing with two distinct populations so widely do the recorded causes of death differ. Actually each list applies to people living in the same area, although the medical registrar's district is slightly less rural than the lay registrar's district. Because of the uncertainty about individual causes of death, groups of major diseases rather than specific causes have been considered in the analysis of the vital statistics. It must be remembered, however, that it is usually agreed that Ceylon's vital statistics are more accurate than those of the rest of South east Asia.

SICKNESS-RATES

The study of morbidity in a community is more difficult than the study of mortality. As deaths have to be registered by law, their number can be readily determined; but the incidence of illnesses is a matter for speculation. The cause of death has also to be registered, so that the certifier is faced with the necessity of making a diagnosis. The diagnosis may be wrong, but the onus of officially committing a professional opinion to paper induces a little extra thought and caution and at least provokes some degree of wisdom after the event. An illness, on the other hand, may never be diagnosed, though the patient, his friends, and his medical advisers are usually stimulated to tentative fancies.

As a rule the only morbidity statistics available which possess any degree of accuracy in diagnosis are those from hospitals. These hospital figures do not necessarily bear any relation to the actual incidence of disease or to the total deaths. As a rule, the cases admitted to hospital are those with a serious prognosis or which require skilled or technical treatment. The wishes of the patient and the doctor, the availability of hospital beds, the degree of safety involved in moving a sick person, and many other factors will influence admission. The hospital statistics will indicate, however, the incidence of the major incapacitating diseases in a community and, remembering their limitations, should repay study.

Hospital statistics in Ceylon do not give the age, the normal residence, and occupation, nor other socio-economic details about the patient. It did seem desirable, therefore, to attempt to fill this deficiency by a morbidity survey.

The planning of such a survey is hampered at the outset by the lack of an agreed definition of sickness. Downs and Collins (1940) have described sickness as a "disturbance of health"; but this, as Stocks (1947) has maintained, involves the "mystical word health" for which, again, an agreed definition is still needed. At present it is probably better to give an accurate description of the type of information obtained rather than a the merits of the different cases submitted to the councils. A more positive policy on the management side might well lead to less arbitration and might speed up the work: when it may take eighteen months to get a ruling from a council on a small but important point, much frustration is felt at the periphery. The hospital administrators' memorandum makes out a strong case, too, for strengthening the Staffing Division of the Ministry of Health. This Staffing Division has, in fact, been formed only recently, and we trust that it will be able to ensure not only adequate briefing on individual cases but also the continuous review of policies for recruitment and training and of the effect of existing scales. At present the Ministry, through the Whitley Councils, has a negative rather than a positive influence, and the service thereby suffers. A proportion of work which should be done by the Staffing Division is already done by the independent foundations, the King's Fund and the Nuffield Foundation; but great scope remains, particularly if such a division could be built up with a strong statistical and research section.

The Whitley equivalent of the works council, the joint consultative staff committee, has now been formed in all hospitals, and they are improving the sense of cohesion which is so desirable in any large community. There can be nothing more frustrating than being unable to put forward constructive criticism—a situation commonly found unless there is an alternative to a difficult foreman or departmental head—and such committees can ensure adequate attention to reasonable facilities—e.g., catering, cloakrooms, and rest rooms—which have always existed for the professional staff. These committees undoubtedly make a positive contribution to local morale and thereby improve efficiency, and it seems a pity that the medical staff have been excluded from their constitution. The professional reputation of the hospital and the efficiency of medical care depend largely on the senior medical staff, and it is particularly unfortunate that their medical committees should not have any statutory recognition. Indeed, a curious situation has now arisen whereby management committee members or governors come officially into contact with, and get to know, technical and manual staff, but have no such official opportunity for getting to know senior medical staff.

Angiocardiography

IN 1929 FORSSMANN introduced a ureteric catheter into his own arm, passed it into his heart, and injected 'Uroselectan' into his right auricle; but it was not until 1939 that ROBB and STEINBERG described a relatively safe and practical method of displaying the heart and pulmonary vessels. With this method radiologists had to take a series of films in rapid succession—an exciting challenge to their technique. Not all workers, however, felt the need for multiple films: and many of the pioneer investigations by ROBB et al. were made with only two films, taken at intervals determined by the circulation-time. The usual contrast medium is diodone (70%) and in the conscious patient this produces some very unpleasant sensations.[1] These can be minimised by premedication and forewarning; but not every patient is willing to undergo a second injection, and a medium less toxic and more radio-opaque is greatly needed. As part of the price of this investigation, there has been a small but steady number of deaths,[2] mainly among severely handicapped children.

The period of initial exploration is over, and few abnormalities of the chest have not been investigated by this method. Sometimes the information gained has proved important, but often the method has done no more than dramatically portray the obvious or confirm a probability. Occasionally, however, angiocardiography provides essential information that cannot be procured by any other means. In the investigation of diseases of the lung, it has so far proved disappointing.[3] There seemed no reason why neoplasms of the lung should not alter the pulmonary vascular pattern in some characteristic way, as do neoplasms of the brain. But this is not so; the tumours are not to be seen, and the most that can be expected is evidence of some displacement of the vessels or of involvement of the pulmonary artery or venæ cavæ. So far as the lung is concerned, it is only in investigation of possible vascular abnormalities that angiocardiography is justified. Arteriovenous fistulæ can be beautifully demonstrated, but the diagnosis is usually made by clinical examination and can often be confirmed by plain radiography and tomography. In this condition the real value of angiography is to make sure that the lesions are not multiple, and that smaller and less obvious foci are not being overlooked. Angiography may be helpful in cases of so-called unilateral emphysema. With plain radiography a very similar appearance can be produced by thrombosis or obstruction of one of the main pulmonary arteries, but an angiogram should at once separate the two conditions. Perhaps the most important use of angiocardiography is in the investigation of mediastinal tumours, when it can usually be relied on to reveal aneurysms of the aorta or pulmonary artery, or to delineate an abnormal course of one of the great vessels or their branches. Occasionally the method may be misleading, as where a clot has formed in an aneurysm, or where the opening into a saccular expansion is too small for much contrast medium to enter: but unless plain films and screening show the tumour clearly separated from the aorta and pulmonary artery, an angiogram is justified. No reliance should be placed on kymography, which many workers have found most deceptive.

In acquired heart-disease angiocardiography is still on trial.[3] In syphilitic aortitis enlargement and irregularity of the calibre of the aorta can be shown early,[4] and the diagnosis of pericardial effusion may sometimes be clinched by showing the extent to which the cardiac outline extends beyond the chambers of the heart.[3] In acquired valvular disease of the heart the method has displayed the enlarged chambers; but so far it has not been possible to demonstrate the valves, and attention has centred on the secondary effects in the lung fields.[5] Care, however, is needed precise, but debatable, definition of illness (Bransby 1948)

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[1] van Diggelen, H. T. *Lancet*, 1947, ii, 64.

[2] Dotter, C. T., Jackson, F. S. *Radiology*, 1950, 54, 527.

[3] Dotter, C. T., Steinberg, I. Angiocardiography. Vol 20, Annals of Roentgenology. London, 1952.

[4] Steinberg, I., Dotter, C. T., Peabody, G., Reader, G. G., Heinoff, L., Webster, B. *Amer. J. Roentgenol.* 1949. 62, 655.

[5] Goodwin, J. F., Steiner, R. E., Lowe, K. G. *J. Fac. Radiol., Lond.* 1952, 4, 21.

Information on sickness can be obtained either from doctors or lay people The first source should give more accurate information about the causes of sickness, but it limits the survey to illnesses treated by doctors and to people who seek medical aid If lay people are questioned then a more representative sample of the population will be obtained, but the reported causes of sickness will be less accurate, and the information will depend on the memory of the individual and his psychological attitude towards illness

Despite these difficulties a morbidity survey provides data on the incidence and social distribution of sickness which are necessary for the evaluation of the health of the people and for the planning of health services

The survey in Ceylon was designed to answer two questions

(1) How many of the working population were unable to attend their regular duties on the day of the survey because of disablement ?

(2) How many people had been ill during the past year ?

We realised that a year is a long time to expect people to remember their illnesses, but information on this point, however crude, was needed for other purposes The investigation of disablement was made as objective as possible in order to increase the accuracy of recording for the lay interviewers

ANTHROPOMETRIC AND PHYSIOLOGICAL SURVEYS

The anthropometric and the physiological surveys collected data on the physical and physiological growth of the Ceylonese from all districts, economic groups, ethnic groups, and communities Exercise tests were also performed by many of the subjects and, from all these collected data, correlations were derived between (1) each physiological character measured and the exercise performance indices, (2) various anthropometric indices and the exercise indices, and (3) each physiological character and certain anthropometric indices

The nutritional data were related as far as possible to "standards" obtained from selected groups of Ceylonese Thus, from studies of basal metabolic rates, calorie requirements were computed for various age groups Mineral and nitrogen balance studies gave evidence for basal intakes of these nutrients Investigations of the foodstuffs consumed by middle class schoolboys indicated what and how much healthy boys were eating

It was possible to analyse all this physical, physiological, mortality, morbidity, and dietary information according to age, sex, community, district of residence, family income, &c , and thus to compose a coherent picture of the health of the Ceylonese within their social environment It would be more difficult to do this in a larger and more complex society, but it could be attempted in other small, selected regions Before health problems can be solved these problems must first be described and their magnitude defined In many areas of the world the mortality, morbidity, and nutritional data are fragmentary, but active health programmes are being applied on this incomplete information Investigation should precede correction

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Special Articles

THE WORLD'S FOOD-SUPPLY

On April 22 the nutrition panel of the food group of the Society of Chemical Industry held the final meeting of the series[1] on Food and the Future The subject under discussion was Synthetic Potentialities

Mr W F J **CUTHBERTSON**, PH D (Glaxo Laboratories Ltd), discussed the general possibilities of supplementing our food supply by synthetic substances The direct synthesis of bulk foods—the fats, carbohydrates, and amino acids—was not likely to play a material part The process would require enormous quantities of energy, and if the problem were to be projected into the speculative future, our reserves of oil and coal, and even atomic energy, must be considered as strictly limited and diminishing assets On the other hand, chemical transformation of natural products could perhaps lead to the production of large quantities of food from inedible crop residues The greater part of our plant production was composed of polysaccharides and lignin, and little energy would be required to transform these into carbohydrates or fats The potentialities of this method were shown by the industrial production of dextrose from sawdust, which was carried out with reasonable efficiency

Synthetic chemistry was far more likely to play its part in the preparation of essential substances which were required in relatively small amounts Already all the vitamins had been synthesised, and most of them were produced on the factory scale for supplementing the human diet Although few of the amino acids could yet be synthesised in bulk, the two in which foods were so often deficient, methionine and lysine, were fortunately being produced on a large scale The value of supplementing the human diet with synthetic vitamins had been well illustrated in the Philippine Islands, where fortification of polished rice with synthetic thiamine had resulted in the abolition of beriberi

In animal nutrition these synthetic substances offered great possibilities We knew most, if not quite all of the various food factors required to maintain health and rapid and economic growth of our farm animals Unfortunately high-yielding food crops all showed some degree of deficiency of one or more of the essential food factors, thus, wheat lacked vitamin D and ascorbic acid, and maize was poor in vitamin B$_{12}$ and tryptophan The procedure had been to grow higher-quality crops of lower yield to supplement these deficient foods or to use costly materials, now difficult to obtain for this purpose, such as milk, fish meal, or meat meal Now that synthetic additives were available, it was possible to grow the most efficient crops, in terms of calories per acre, and to raise the quality of the food with these supplements Already, in the U S A , synthetic riboflavine, at the rate of 2 g per ton of diet, had replaced 20–100 lb of dried milk or whey solids, vitamin B$_{12}$, produced by fermentation, had replaced part of the requirements of milk and fish products, maize and soya were supplemented with synthetic methionine, wheat and cotton seed were fortified with lysine, and synthetic vitamins and choline were added to the diet As a result it was now possible to rear chickens to 4 lb weight in ten weeks on a total food intake of 10–15 lb, instead of twelve or thirteen weeks on 16–20 lb of food These supplements might be added directly to human food A completely vegetarian diet would be far more economical than our usual diet, but we did not yet know whether it would be adequate When all the food factors had been identified, the synthetic chemist might be able to make a wholly vegetarian diet which was fully adequate in drawing conclusions about the state of the vessels or the pulmonary blood-pressure from isolated snapshots of the lungs. The method has been much used in congenital cyanotic heart-disease. GOODWIN et al.[5] point out that even here *it is only an auxiliary* investigation which should not be used indiscriminately in all cases. Not every blue child need be subjected to angiocardiography and safe cases must be selected wit. [illegible] whether a child liable to syncopal attacks should ever be submitted to this manœuvre, for the profound fall in blood-pressure always induced by the injection may easily prove fatal.[6] The investigation can be useful, not only for diagnosis (commonly the diagnosis has already been made) but for the information it gives about the anatomical disposition of vessels available for anastomosis, and also about any additional defects and complications hitherto unsuspected. Nevertheless angiocardiography can be positively misleading, and its evidence should seldom be preferred to the findings from cardiac catheterisation. It may be no easier to assess the pulmonary vascularity when the vessels are full of contrast medium than with plain radiography, and on occasion the contrast medium appears to stream past one pulmonary artery and thus gives a false impression of abnormality. This investigation is most likely to be helpful in distinguishing pulmonary stenosis plus an atrial septal defect from a simple Fallot's tetrad; in demonstrating the abnormal origins of the great vessels in cases of transposition; and in showing whether any pulmonary arteries are present in cases of pulmonary and tricuspid atresia. *Angiocardiography plays no part in the diagnosis of* coarctation of the aorta; but by no other means can the narrowing be so well displayed, and most surgeons now like to see an angiogram before operating. If the aorta is not shown well enough by a venous angiocardiogram, the contrast medium may be injected through a catheter introduced into the aorta through the right radial or brachial artery; and a similar selective angiogram can be obtained with a catheter in the right ventricle, in an attempt to throw more light on an infundibular or valvular stenosis. These methods are, however, perhaps especially risky.

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[1] See *Lancet* 1952 ii 1269 *Ibid* March 14 1953 p 538 *Ibid* May 9, 1953, p 911

So much time and money has been invested in angiocardiography that undue emphasis may have been laid on the information that it yields; and one suspects that occasionally the patient may have been sacrificed to the machine. The next technical advance will almost certainly come through screen cinematography, and has been brought much nearer by the introduction of a practical screen-image intensifier. This apparatus can already increase the brightness of the screen a thousandfold, and it should not be long before ciné films can be safely taken without risk to the patient of overexposure.

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[6] Howarth, S. *Brit. med. J.* 1950, ii, 1090.

Annotations

GENESIS OF GLOMERULONEPHRITIS

HÆMOLYTIC streptococci were once feared for their invasiveness: erysipelas or lymphangitis could cause grave anxiety, but now these respond rapidly to chemotherapy, and death from septicæmia is rare. But streptococci are still dangerous because of the peculiar sterile inflammations they sometimes provoke—namely, glomerulonephritis and rheumatic carditis. These disorders both involve tissues not invaded by the organisms and follow rather than accompany the infection; both may continue to advance long after the infection has gone. The relation of the infection to these sterile inflammations is mysterious: one naturally looks for some mechanism common to both, but there are a number of differences which restrain generalisation. For example, complement is raised or normal in rheumatism but is lowered in acute nephritis,[1] and there are some interesting epidemiological contrasts.[2] The incidence of acute rheumatism varies with class and climate, but within a given community it complicates a fairly steady fraction of streptococcal infections. It is common for different members of a family to be affected at different times, and only too common for one patient to have repeated attacks. Acute glomerulonephritis does not show the same geographical variations, but its incidence in outbreaks of streptococcal infections varies greatly even in one locality, sometimes being so high that it appears itself as an epidemic disorder. Apart from episodes of this type the relatives of patients are not especially at risk, and after complete recovery second attacks are rare.

An explanation of these differences is suggested by recent bacteriological studies.[3–5] Some, but by no means all, group-A streptococci may be placed in distinct serological types, of which about 50 have been described. It has been found that the frequency of these types in association with acute nephritis does not correspond at all with their general frequency: a great excess of type 12 has been found and a smaller excess of a few other types. On the other hand, outbreaks due to type-12 are not always followed by a high incidence of nephritis, so the existence of a factor correlated with, but separable from, the type specificity is suggested.

Typing is an expert matter. The importance of these findings is not in any promise of early help in controlling the disease but in the insight they give into its genesis. The suggestion is that a peculiarity of the streptococcus is important, and perhaps necessary, for the development of nephritis after infection; and this would explain the epidemiological features. The different behaviour of acute rheumatism suggests that in this disease peculiarity of the host is more important than that of the streptococci.

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[1] Fischel, E. E., Gajdusek, D. C. *Amer. J. Med.* 1952, 12, 190.

[2] Seegal, D., Earle, D. P. jun. *Amer. J. med. Sci.* 1941, 201, 528.

[3] Rammelkamp, C. H. jun., Weaver, R. S. *J. clin. Invest.* 1953, 32, 345.

[4] Westheim, A. R., Lyttle, J. D., Loeb, E. N., Earle, D. P., Seegal, B. C., Seegal, D. *Ibid*, p. 359.

[5] See Dingle, J. H., Rammelkamp, C. H. jun., Wannamaker, L. W. *Lancet*, April 11, 1953, p. 736.

GROWTH HORMONE AND CHRONIC ARTHRITIS

THE explanation of some forms of chronic arthritis as the result of overproduction or imbalance of adrenal cortical hormones arises from Selye's conception that a disordered pituitary-adrenal response to stress is largely responsible for this type of disease. The ability of cortisone, an adrenal glucocorticoid, to ameliorate arthritic conditions, both clinically and experimentally, supports this view, for hydrocortisone is a natural product of the adrenal cortex, its release is stimulated by pituitary corticotrophin, and its action may be interpreted as a means of redressing the hormonal balance. Selye's work,[6] and that of others,[7 8] has shown that mineralocorticoids, such as deoxycortone, can exert, experimentally, an opposite effect to that of

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[6] Selye, H. *Brit. med. J.* 1949, ii, 1129.

[7] Schaffenburg, C., Masson, G. M. C., Corcoran, A. C. *Proc. Soc. exp. Biol., N.Y.* 1950, 74, 358.

[8] Hughes, C. D., Swenson, M. J., Underbjerg, G. K. L., Hughes, J.S. *Science*, 1952, 116, 252.

Mr P N **Williams** (Lever Bros and Unilever, Ltd) discussed the possibilities of "synthetic fats" These were produced on an industrial scale during the war in Germany, but there were many drawbacks to their use Synthetic fats contained the unnatural odd numbered carbon chain fatty acids, and it had been suggested that these were harmful There was, however, good evidence that this was not so But other criticisms were valid synthetic fats contained branched-chain fatty acids which were toxic and resulted in restriction of growth, and they also contained dibasic acids which led to the excretion of dibasic acids in the urine, which was said to harm the kidneys Both of these toxic substances could be removed from the fat, but only at high cost

There was certainly insufficient evidence from which to argue for the consumption of synthetic fats by man The only nutritional tests which had been made were carried out in Germany, and the results were conflicting Apart from this, Mr Williams was very pessimistic about the possibilities of synthetic fats making a reasonable addition to our food-supply because of the cost and the quantities required The German process reached the stage of industrial production, but the output was only 2000 tons per year, compared with the world consumption of 18,500,000 tons of natural oils

Fats produced by moulds and yeast were more likely to be of value They could be grown on waste carbohydrate, and the fats produced should be nutritionally similar to vegetable fats, although they had not yet been tested

DISCUSSION

Mr N W **Pirie**, F R S, questioned the value of estimates of the life of our fuel reserves He suggested that the supplementation of foods by synthetic materials was a catalytic process, catalysing the efficiency with which foods were used

Mr A L **Bacharach** pointed out that synthesis might be an indirect means of supplementing the world's food-supplies, depending upon how much edible oil was at present used for industrial purposes He criticised the pessimism about synthetic fats because of their cost by pointing out that increasing demands for vegetable oils, together with the rising standards of living in tropical countries, might well raise the price of natural fats, while technological improvements might reduce the cost of synthetic fat

Mr H **Greene** PH D, said that the demand for a higher standard of living among the inhabitants of underdeveloped countries caused a demand for books, films, and textiles, and only a small demand for food, which could usually be met with no great difficulty

Mr H **Pritchard** said that unnatural fatty acids gave rise to toxic end-products of metabolism, such as oxalic acid, and in the case of elm fat, sebacic acid

Mr H **Moult** suggested that fat supplies could be eked out by the addition of small amounts of linseed and castor oils He said that the Indian government was seriously considering the use of ground-nut oil as tractor fuel

After the discussion, Mr **Norman Wright**, D SC (Ministry of Food), summarised the four meetings The unconventional foods, with the exception of leaf protein, had been disappointing In particular, food yeast which was being produced commercially, was finding little favour as human food Far more investigation into their possibilities was required and they must be regarded as long term projects For example, chlorella culture might become essential in an emergency, but its cost must be calculated in terms of human activity Even after the technical production problems had been solved, there still remained the problem of converting a structureless and insipid material into a palatable food

The progress in conventional methods was also disappointing Several speakers had emphasised the need for planning, but there were inadequate data For example, we did not know the possibilities of increasing areas under cultivation and yields of crops, we did not even know the potentially cultivable area in the world Fawcett had estimated that climatically there were 5 acres of land available per head, of which one third was cultivated, but we had no knowledge of the extent to which this area could be increased

Dr Wright concluded by saying that the solution of the problem needed determined and imaginative leadership, together with the intelligent application of the available knowledge by the rank and file of the world's agricultural people Science could only give an aid, it rested with man himself to determine what use he made of it

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TERMS OF SERVICE OF HOSPITAL STAFFS

The terms of service of hospital staffs were discussed at a meeting of Committee B of the Medical Whitley Council on May 12

CLAIM FOR A REVIEW

Ten months ago the staff side notified the management side of Committee B of its intention to seek a review of the remuneration of hospital medical staffs, in order to secure full and proper implementation of the recommendations of the Spens report on the remuneration of consultants

Discussions were held with the management side in October and again in January, and the staff side has submitted at least three comprehensive memoranda on the subject So far the management side has not replied to the representations put forward and has not indicated its attitude towards the claim Nearly four months ago the staff side submitted a memorandum to the management side in reply to certain questions and referring to a number of important principles arising out of the Spens report

At the meeting on May 12 the staff side learnt that the management side are still not in a position to enter into discussions A very strong protest was made at the continued delay on the part of the management side, and an assurance was given that an early meeting would be held—in probably a month's time—when the management side's reply would be available

ALLOWANCES FOR WHOLE-TIME OFFICERS

During the past two years the staff side has repeatedly urged the management side to reconsider the allowances paid to whole-time members of hospital staffs, and to relate them to the clear intentions of the Spens Committee These discussions have covered such items as mileage allowances, rental for telephone, membership of learned societies, and allowances towards the expenses incurred in the purchase of textbooks and professional journals The management side has so far declined to make any amendments to the existing terms of service

On May 12 these matters, and also the question of domiciliary consultations, were raised again, and the case was presented by representatives of whole-time consultants specially coopted to the staff side, three of whom were appointed by the Association of Whole-time Consultants The management side pointed out that all the points made by the deputation of whole time officers had already been put to them very forcibly by the staff side itself They indicated, however, that they did not feel able to accede to any request which would place whole time members of medical staffs in a privileged position and on a different basis from other whole-time members of hospital staffs They therefore held out little hope for any concession in regard to mileage allowances and telephone rentals, but they agreed to consider whether anything could be done to assist whole-time cortisone; for example, in rats they aggravate both scorbutic arthritis and formalin periarthritis in animals sensitised to their action by unilateral nephrectomy and an increased salt intake. This type of experimental "adaptation disease" can only be produced when the adrenal cortex is intact. In further experiments,[9] Selye showed that lyophilised anterior pituitary increased the sensitivity of the rat to the effects of mineralocorticoids, and he attributed this to a direct sensitisation of the tissues. He identified the pituitary factor with growth hormone and pointed out the analogy with A.C.T.H. and cortisone. An explanation of chronic arthritis along these lines, therefore, supposes the existence of an intact pituitary-adrenal mechanism.

Reinhardt and Li[10] have lately reported results which suggest a different significance of pituitary hormones in experimental arthritis. They found that administration of growth hormone over a period of several months to adrenalectomised and ovariectomised guineapigs (fed on 1% NaCl and stock diet) produced definite chronic arthritis with bony changes, and 1 of 10 normal animals given growth hormone also showed arthritic lesions; but none of the untreated normal controls were affected. These results suggest that growth hormone itself may be directly responsible for chronic arthritis, for they were obtained independently of the adrenal gland and its hormones. They also suggest that cortisone exerts its anti-arthritic effects by suppressing secretion of growth hormone, or, as Selye suggested, by antagonising its local effects in the tissues. Reinhardt and Li make it clear that they have not so far excluded non-specific sensitisation to pituitary hormone as a possible explanation of their results. It has already been suggested[11] that insufficient heed was given to the possible effects of hypersensitivity in interpreting Selye's experiments. These latest results in this complex subject both amplify and challenge our present views on the place of the adrenal cortex in the development of arthritis.

ALLERGY TO ACRYLIC RESINS

A CASE recently heard by a tribunal in Edinburgh[12] raises a matter of interest and importance to doctors and dentists—allergy to acrylic resins. The facts were these. A patient who had worn an upper denture for some eight years without trouble began to have pain and swelling in the mouth within two days of having the denture relined. A doctor whom she consulted told her that her mouth might always remain sensitive, and the appeal was then brought, not against the dentist concerned, but against Edinburgh Executive Council, which had refused any grant towards charges incurred by the patient for private dental treatment. During the hearing it was stated that 1 in about 5000 patients was allergic to acrylic resins.

The cause of such allergy is still undetermined. In the past, soreness of the mouth developed with vulcanite dentures; but this was almost certainly due to small amounts of mercury salts in the red or pink colouring-matter of the rubber. It has been suggested that with acrylic resins it is not the polymethyl methacrylate itself that causes the trouble, but rather the presence of such plasticisers as dibutyl phthalate which are added to improve its working properties. Early in the late war there were several instances of dermatitis under the side-pieces of spectacles, and this was traced to the plasticiser used during manufacture; but there is little evidence that the same cause holds with denture materials. At present the allergic reaction is usually held to be caused by traces of unpolymerised monomer in the finished denture. Evidence for this view is rather slight; but these unpleasant reactions have commonly been observed after the use of auto-polymerising resins for relining, and it is quite possible that the Edinburgh case comes into this category. When these auto-polymerising resins are used for conservative dentistry, there is often a transient, and usually harmless, hyperæmia of the tooth-pulp. Fortunately, a patient who cannot tolerate acrylic resin alone will be quite happy with a vulcanite denture faced with acrylic resin, or even an acrylic-resin denture with a stainless-steel lining. A reaction seems to arise only when there is actual contact with the palate or the mucosa over the alveolar ridge.

Meanwhile, the dermatologist faces a pretty problem in the patient who must wear rubber gloves in order to avoid severe dermatitis when handling monomeric and polymeric acrylic, and yet can wear an acrylic-resin denture without trouble.

COLICINES AND BACTERIOPHAGES

THAT certain strains of *Bacterium coli* and other enterobacteriaceæ can produce antibiotic substances or "colicines" active against other coliform organisms, has been known since 1925.[1] The colicines are proteins or polypeptides, and their production and antibiotic action resemble in many ways those of bacteriophages. The relation between these two types of biological agents has been studied extensively in the last few years by Fredericq[2] and his colleagues in Belgium, and by workers in Lwoff's laboratory at the Pasteur Institute.[3]

Bacteriophages differ from colicines in that they possess both desoxyribonucleic acid (D.N.A.) and protein portions, and reproduce themselves in the sensitive bacteria they kill. Both phages and colicines can be characterised by the spectrum of their activity on different bacterial strains; and, just as plaque formation may differentiate one phage from another, so the type of clearing produced on a plate by a colicine may be a characteristic of it. Resistance or susceptibility of bacteria to phage and colicine action depends on the absence or presence of specific cell receptors to which these agents can attach themselves. In some cases the same receptor is used by a phage and a colicine; and a mutant, becoming resistant to a certain phage through loss of this receptor, will also become resistant to a colicine at the same time.

Both colicines and temperate phages are produced in bacteria—in colicinogenic and in lysogenic strains, which are themselves resistant to the agents they release. Some of these strains can be made to produce colicines or phages in large amounts by irradiation with ultraviolet light or treatment with certain mutagens and carcinogens. In both cases, during the latent period before the release of these agents residual growth takes place, respiration continues to increase, ribonucleic-acid metabolism proceeds, and the formation of adaptive enzymes or virulent phage can take place in the bacteria. In induced colicinogenic strains, however, D.N.A. production continues, while in lysogenic strains this is blocked for the first part of the period, perhaps because of the presence of induced phage D.N.A.

If in their production colicines simulate temperate phages, in their action on sensitive bacteria they imitate virulent ones. Only one particle of each is necessary for their lethal action on bacteria, and their adsorption constants are of the same order. Whereas, however, in bacteria infected with a virulent phage those processes necessary for phage reproduction continue, colicines inhibit all synthetic activities.

Although in many ways colicines and phages resemble one another no serological relationship has yet been proved, perhaps because colicines are poor antigens;

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[9] Selye, H. *Brit. med. J.* 1951, i, 263.
[10] Reinhardt, W. O., Li, C. H. *Science*, 1953, 117, 295.
[11] *Brit. med. J.* 1951, 285.
[12] *Glasgow Herald*, April 10, 1953.

[1] Gratia, A. *C.R. Soc. Biol. Paris*, 1925, 93, 1040.
[2] Fredericq, P. *Ann. Inst. Pasteur*, 1953, 84, 294.
[3] Jacob, F., Siminovitch, L., Wollman, E. L. *Ibid*, p. 313.

consultants, who, like their part-time colleagues, are required to keep themselves abreast of current trends and developments in medicine but are unable to claim income-tax relief on the expenses involved

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GENERAL MEDICAL COUNCIL

SESSION MAY 19–20

THE General Medical Council met on May 19 and 20, and its session was followed by the sittings of the Medical Disciplinary Committee

PRESIDENTIAL ADDRESS

Prof **DAVID CAMPBELL** said that the *British Pharmacopœia, 1953*, published in March, will become official from Sept 1 Among the many changes in this 8th edition is the abandonment of Latin in the main titles of the monographs—a break in the tradition established in 1535 when Valerius Cordus at the early age of 27 published his *Dispensatorium* in the city of Nuremberg, the first pharmacopœia to have civil authority "But the break was inevitable The ever-increasing number of new drugs made it extremely difficult to coin suitable Latin titles for new monographs without running the risk of making confusion worse confounded"

Referring to the rules made in 1945 for courses of study and examinations for diplomas in public health, the President said that these were to a certain extent experimental, being designed to meet the changing circumstances of the public health services at that time They provided for a preliminary course, after which a certificate in public health may be granted, and a final course, designed especially for future medical officers of health, followed by an examination open only to holders of the certificate

"Since these rules were adopted, great changes have occurred in the conditions of medical practice The National Health Service, introduced five years ago, has altered considerably the scope of the work of medical officers of health, while the institution within the last six months of a compulsory year of house officer service will affect practitioners in the early years of their careers It is not a matter for surprise, therefore, that those most directly concerned are disposed to think that the rules made in 1945 might profitably be reviewed at this stage in the light of the changed conditions and the experience now available"

Jan 1, 1953, was the appointed day on which the provisions of the Medical Act, 1950, which require proof of special experience as a condition of full registration, were put into effect "In anticipation of the introduction of the new conditions," said the President, "more than a thousand practitioners holding Commonwealth diplomas applied to be registered, and the great majority were able to obtain registration before the appointed day" The total number of names on one register at the beginning of this year was 83,914 Twenty years ago the number was 56,741 "The striking increase during the past two decades must mean that many more avenues of employment have been opened up to duly qualified and registered practitioners of medicine That is highly satisfactory But it prompts the question as to whether this is likely to continue, and whether there will be a limiting factor to a further increase"

DISCIPLINARY CASE

The council completed its last penal case

This was the case of *Garden Hepburn Swapp*, M B Aberd (1928), registered as of 8, Bath Street, Stonehaven, Kincardineshire, against whom the council had found proved convictions relating to drunkenness when in charge of a motor car Judgment had been postponed until the present session In view of the testimonials produced by Dr Swapp, the Registrar was not directed to erase his name from the Register

The **PRESIDENT** recalled that during the last two years the council had had, under the Medical Act, 1950, to complete cases which it had already begun In future all disciplinary business would be a matter for the Medical Disciplinary Committee

BUSINESS OF THE COUNCIL

At its meeting last November the council asked the Executive Committee to report on the mode of election of the Medical Disciplinary Committee, to ensure that as far as possible all members of the council took part in its work

The **PRESIDENT**, presenting the report of the Executive Committee, explained that it agreed with the opinion expressed by several members of the council that the present method tended to result in the re election of existing members It regarded the work of such importance that as far as possible all members should be afforded an opportunity of serving on the Medical Disciplinary Committee or the Penal Cases Committee The Executive Committee recommended in regard to the former that there should be a rota with a certain number of retiring members deemed ineligible for re election for a period of one year Explaining the proposed method, the President remarked that it was important to ensure substantial continuity, and he revealed that the Medical Disciplinary Committee had given up the practice of postponing judgment for two years, it now postponed judgment for six months or one year

The council approved the proposals for the new form of election, which is to come into operation next year The Executive Committee is to consider and report on a similar arrangement for the election of the Penal Cases Committee

Dr **H GUY DAIN**, presenting the report of the Pharmacopœia Committee, stated that 17,453 copies of the *British Pharmacopœia, 1953*, which comes into force on Sept 1, had already been sold

The problem of approved names was, he said, a very difficult one When a new substance was put on the market the person who made it chose a name The American Medical Association and the World Health Organisation might or might not choose the same name, and the Pharmacopœia Commission had to choose a name for a substance which had already got a name It was necessary to find appropriate names for the "flood" of new substances From the *Pharmacopœia* point of view, a name was wanted which did not convey any suggestion of the use of the substance The Pharmacopœia Commission had given the Committee their ideas as to the way in which the names were chosen, they endeavoured to keep them as short as possible Substances were submitted to the Pharmacopœia Commission to be named, and names were attached to them as soon as possible This applied to substances which might never come into use or get into the *Pharmacopœia*

The selection committee had learnt with much pleasure that Prof D M Dunlop, the chairman of the Pharmacopœia Commission, 1948–53, would be prepared to continue his services as chairman The council confirmed the appointment, and also the appointment of the members of the new commission

Dr **J P HEDLEY**, the senior treasurer, referred to the satisfactory financial position of the council at the end of the year This was mainly due to the large number of Commonwealth registrations of persons becoming registered before new regulations for the intern year came into operation For 1952 the council had a total excess of income over expenditure of £25,271

DIPLOMAS AND CERTIFICATES IN PUBLIC HEALTH

The council considered the annual returns of the results of examinations held in 1952 for certificates in public health and diplomas and degrees in sanitary science, public health, or State medicine, and information received from licensing bodies Members had had circulated a memorandum expressing the personal views of Prof Walter Schlapp and Dr Fraser Brockington, professor of public health at Manchester

The **PRESIDENT** observed that in general the numbers of those who took the certificate in public health in 1952 but antibacterial serum protects cells from the lethal action of both. In certain cases phages can kill bacteria without multiplying in them, and phage "ghosts" deprived of their D.N.A. by "osmotic shock"[4] can also destroy cells in a manner very similar to that of colicines. At least one strain produces both a bacteriophage and a colicine.

Perhaps when the D.N.A. of a phage enters a bacterial cell[5] it takes over the colicine-synthesising mechanism and diverts it for the production of its own protein coat. Whatever the exact relation between these agents, both are obviously involved in reactions which are proceeding along very similar lines, although self-reproducing units are formed only by bacteriophages.

TREPONEMAL IMMOBILISATION TEST

At present the treponemal immobilisation test for syphilis is being investigated at some 26 laboratories throughout the world.[6] This test, described by Nelson[7] in 1949, rests on the immobilisation of *Treponema pallidum*, in a special medium to ensure its survival when exposed to syphilitic serum and complement. The test is receiving especially close attention in France.[8] [9]

Touraine[9] takes the view that in primary and secondary syphilis the clinical diagnosis can be confirmed much more easily and quickly by dark-ground examination and the usual serum tests—a contention that is supported by the figures of other workers. In the early stages of the disease these serum tests become positive before the immobilisation test, but in the later stages the immobilisation test discloses latent syphilis in cases where the serum tests give no clue: in congenital and latent syphilis the immobilisation test is always positive. In tertiary mucocutaneous syphilis this test is positive in 98–100% of cases, compared with 48% for serum tests; and the proportions are much the same for late visceral syphilis. As regards neurosyphilis, in tabes dorsalis the immobilisation test is much the most useful; in one series cited by Touraine, it was positive in 33 out of 35 cases, in 18 of which serum tests were negative or doubtful.

Apparently the immobilisation test is specific; when it is positive—provided the other treponemal diseases, such as yaws and pinta bejel, have been excluded—syphilis can be diagnosed with some confidence. Touraine observes, however, that relatively little research has been carried out on the test's specificity; for instance, the possibility that leprosy gives a positive result has not yet been definitely excluded. With serum tests non-syphilitic positive reactions have been reported in infective mononucleosis and atypical pneumonia; and Touraine suggests that it is premature to conclude that with the *immobilisation test similar non-syphilitic* reactions do not occur. During treatment a steady decline in the degree of immobilisation suggests that therapy is succeeding. When, however, the patient has been insufficiently treated, or where treatment is started late in the disease, the test does not reflect the value of the therapy.

Touraine remarks that the technique of the test is complex and laborious; and the opportunities for technical error are much greater than with serum tests.

Treponemes are inoculated into the testis of a rabbit, and the testis must be removed at the right time. If it is removed too early, too few treponemes are obtained; and if too late, the test is vitiated by "auto immobilisins" produced by the animal. It has been suggested that the latter difficulty can be overcome by means of nitrogen mustard or X-radiation. Further difficulties can arise with the medium used in the test. The survival of the Nichols strain of treponemes used in the test depends on the medium being made up freshly from reliable components, and above all on the exclusion of oxygen during the incubation period. Success also depends on the density of the treponemes in the emulsion used (5 treponemes per dark-ground field), the serum concentration (10% in the final mixture), and the concentration of complement, on which the sensitivity of the test depends. The incubation period used is 18 hours, at a temperature of 37·5°C. The reading of the test is laborious, and one observer is not able to deal with more than 35 sera in a batch. If 50% or more treponemes are immobilised the test is reported as positive; if 20–50%, as doubtful; and if less than 20%, as negative. According to Nelson, if the control tube registers more than 30% immobilisation, the test should be reported as "inconclusive," or as "no valid test."

Touraine notes that in parallel periodic tests in a single case, the results of the immobilisation test may fluctuate whereas those of serum tests remain stable. Olansky et al.[10] showed that the test gave inconstant results with sera from malarial patients who had been inoculated with *Plasmodium vivax*.

Touraine declares that at present the immobilisation test should not be brought into general use; thus it will not become the focus of the arguments, errors, and hopes and disappointments that originally surrounded "sérologie classique." Clearly, before the test can be introduced into routine work, its specificity must be confirmed, and the technique simplified.

INTERNATIONAL HOSPITAL CONGRESS

No whit daunted by the thought of working when most others were enjoying a public holiday, participants in the Eighth International Hospital Congress came together from some forty countries in London last Monday for a week of discussions on the theme Preventive Medicine as a Major Function of the Hospital. This congress, like its predecessors, has been organised by the International Hospital Federation; and like its predecessors it had much of the air of a family reunion. The family is mixed; for the federation attracts as members not only doctors, but nurses, architects, administrators, and others concerned with designing and operating hospitals as well as those interested in central or local government. Perhaps the unusual opportunity for workers from different fields to exchange views breeds a happy expansiveness. The congress, under the chairmanship of Dr. René Sand, the federation's president, was opened by Mr. Iain Macleod, Minister of Health.

Prof. H. W. C. Vines contributed to the first plenary session a paper in which he rued "the academic blunder of the divorce of Preventive from Clinical Medicine, its forced marriage to Public Health, and the subsequent relegation of the unhappy pair to the isolation of a faintly depressed specialism." He drew attention to impediments in the way of preventive practice: these included the patient's reluctance to admit to illness until this was fully established (though the increasing cost of sickness might precipitate the requirement that all insured persons should be regularly examined), and the "curative" outlook of the medical profession. Hospitals, he suggested, should aim at improved coöperation with the domiciliary services, and should make a serious effort to prevent patients being admitted for trivial reasons. Hospitals tended to be obsessed with beds, regarding their outpatient departments as unwelcome appendages. Their preoccupation should be with outpatient departments where the patient could be treated while "still ambulant, still living his life with some semblance of normality among his own people, still perhaps able to were the same as those who took the diploma (except at University College Dublin), indicating that those who took the certificate proceeded to take the diploma.

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[4] Herriott, R. M. *J. Bact.* 1951, 61, 752.

[5] See leading article, *Lancet*, April 25, 1953, p. 833.

[6] World Health Organisation Communication, DC VD SERO 8 TPI Test, Sept. 10, 1952.

[7] Nelson, R. A., Mayer, M. M. *J. exp. Med.* 1949, 89, 369.

[8] Colloque Annuel Société Française de Dermatologie et de Syphiligraphie, Marseilles, Oct. 17–19, 1952.

[9] Touraine, A. *Pr. méd.* 1953, 61, 77.

[10] Olansky, S., Harris, A. Hill, J. H. *Amer. J. Syph.* 1953, 37, 23.

Professor SCHLAPP said that the first point was the time before a candidate could enter for the certificate. Under present conditions this was a minor matter because most candidates had to do two years National Service after qualifying. It seemed that the rules were not fulfilling the purpose for which they were drawn up. The original idea was that the C.P.H. candidates should be more numerous than those for the D.P.H. He wondered whether the division into certificate and diploma courses was best educationally.

Sir ANDREW DAVIDSON said that it seemed clear that the intentions of the advocates of the C.P.H. were not being fulfilled. This certificate was no better than the old part I of the D.P.H. rules.

"I think the most important thing we have to ask ourselves is 'What are we training a person for?'" continued Sir Andrew. "If we are going to educate people in public health we must know what functions that person will have to perform, and adjust the education to those functions. It seems to me that a case could be made out for a revision of the rules but I did feel that the setting up of a committee just now might be a little premature—on the other hand it might act as a stimulus to the people who have to supply us with information."

Sir Andrew believed that, on balance, the council would be justified in setting up a committee to consider a revision of the rules and at the same time to advise the council on the recognition of Commonwealth diplomas under the 1950 Act.

Dr R. M. F. PICKEN agreed that the case for having a committee was a strong one. He thought that there was a case for abolishing the statutory requirement of the diploma in public health for posts. He had never been satisfied with any D.P.H. course prescribed by the General Medical Council: it was a mixture of incompatibles. It was clear that a number were taking the course who never needed it statutorily; that was one of the reasons why the certificate was invented. Wales always had far more C.P.H. students than D.P.H. students. In Wales they made it clear to an intending student that if he would not need the diploma statutorily, it would be better if he took something else—for example, the diploma in child health or the diploma in obstetrics.

Prof. A. P. THOMSON said that at Birmingham the policy was to avoid all diplomas, and they were unlikely to provide a course. They held that postgraduate training of this kind was a matter for a higher degree in medicine; they had no objection to theses in public health being submitted for the M.D. degree. Birmingham University considered that if the authorities insisted on a diploma, this was the affair of the Colleges.

The PRESIDENT remarked that the council was charged with the supervision of the diploma and it must carry out this duty. In view of the difficulties, a change in the law was unlikely.

The council agreed to set up a special committee on the lines indicated by Sir Andrew Davidson.

PROVISIONAL REGISTRATION

The council considered a report of a special committee on provisional and full registration. This contained an opinion from the legal assessor on provisional registration and a letter from the British Medical Association relating to house officers' salaries which also raised the question of appeal in the case of an individual who at the end of his period of service or during his service did not get a certificate of satisfactory service.

The PRESIDENT commented that this was a matter for licensing bodies. He thought that each individual licensing body, if it got an unsatisfactory certificate, would inquire into the reasons. It would be difficult to go behind an unsatisfactory certificate; it would be impossible to hold anything like a judicial inquiry. If the individual went to the West Indies to an approved post, for example, how could the licensing body find out what was satisfactory or not? They would be bound to accept the certificate as it was.

The council approved the revised form of certificate of satisfactory service, and authorised the president to sign the necessary order. The certificate as revised includes the name of a member of the consultant or specialist staff under whom the individual has worked.

The council approved reciprocal registration arrangements under section 1 (*b*) of the Medical Act, 1950, with the Province of Alberta.

Medical Disciplinary Committee

The committee began its sitting on May 20, with the President in the chair.

APPLICATIONS FOR RESTORATION

Charles Lockley Bikitsha applied for his name to be restored to the Register. Mr B. B. Gillis, his counsel, said that Mr Bikitsha's name was erased in 1952 following his conviction at Birmingham Assizes in July, 1951. The matter arose largely as a result of the sympathy which he felt for two women who sought him out and represented to him that their pregnancies were due to men of his own race.

The committee did not think fit to direct the Registrar to restore Mr Bikitsha's name to the Register.

Mr H. Brown, counsel representing *Ram Kissoon Nandlal*, who applied for restoration, said that Mr Nandlal had been removed from the Register in 1951 for having had intercourse with a woman patient.

The Chairman announced that the committee had not seen fit to restore the name of Ram Kissoon Nandlal to the Register.

Mohammed Farid was represented by Mr N. Leigh Taylor, solicitor, who explained that the applicant was in Mecca. His name was erased in 1943 following a conviction for manslaughter.

The committee did not restore Mohammed Farid's name.

The committee restored to the Register the name of *Brendan O'Carroll*, which was erased in 1948.

James Albert Scarers also applied successfully for the restoration of his name, erased in 1947.

Mr F. P. Winterbotham made a statement about the application for restoration by *Henry Charles Coutts Hackney*. Letters and certificates sent in support of the application were not written by the persons from whom they purported to come. A letter had been received from the applicant saying that owing to a septic foot he would be unable to attend.

After the committee had resolved not to restore to the Register the name of Henry Charles Coutts Hackney the Chairman said: "The question arises whether we should take any further action." The committee considered this matter in camera.

ADULTERY

Charles Kingsley Colwill, registered as of Richmond House, Aldenham Road, Bushey, Herts, M.R.C.S. (1924), M.B. Camb. (1926), was charged with infamous conduct in a professional respect for committing adultery with a married woman with which woman he had stood in professional relationship at all material times.

The Registrar was directed to erase from the Register the name of Charles Kingsley Colwill. This is subject to appeal to the Privy Council within twenty-eight days.

Nicholas Lupkovics, registered as of Compton Lodge, Higher Compton, Plymouth, M.D. Chile (1938), was summoned to appear on the charge of having been convicted of unlawfully making an untrue statement to procure a passport and of committing adultery with a married woman with whom he was alleged to have stood in professional relationship.

The practitioner had not been traced, and the committee, which decided to proceed with the inquiry, found the conviction proved and ordered the erasure from the Register of the name of Nicholas Lupkovics. He has twenty-eight days in which to enter an appeal to the Privy Council.

ADJOURNED JUDGMENT

In May, 1952, the committee postponed judgment for one year on *John Howard Crawford*, registered as of 16A Wimborne Road, Bournemouth, M.B. Leeds (1937), against whom they found proved charges relating to forms purporting to relate to certain persons which he sent to the local executive council work, and still in a condition perhaps where his complaint can be arrested." Professor Vines thought that the future outpatient department, or polyclinic, might be in the centre of the town, whereas its related inpatient department would be at the periphery. The hospital, forsaking "the silences of intellectual snobbery," should also be a centre of instruction on healthy living.

Prof. C. A. Romanzi (Genoa) declared that for effective preventive action the hospital must be integrated with the other health services. Dr. E. L. Crosby, president of the American Hospital Association, also insisted on this need, and on the need "for the education of the patient and his family while he is being treated in the hospital." Prof. G. Portmann (Bordeaux) was impressed by the possibilities of the outpatient department for prevention; but he sadly reflected, as have others, that "it is difficult to make the authorities see that a programme of preventive medicine is in fact a profitable investment."

THIRST

WE all know thirst as a blessing when we can pleasantly satisfy it, and a curse when we cannot. Anyone, however, who sets out to define the physiological mechanism and the clinical importance of thirst is likely to sympathise with the American who replied to a questionary on this subject with the words: "I could save you lots of time and useless research. It seems silly to spend money to learn information so simple it cannot be comprehended."[1] Is thirst produced by dryness of the mouth or throat, or is it due to a more general desiccation of cells, either throughout the body or in some special receptor analagous to, and possibly even identical with, Verney's osmoreceptors?[2] Cannon[3] suggested that dryness of the mouth was the cause, and demonstrated a decrease in salivary secretion; but this hardly amounts to proof, since thirst and diminished salivary secretion might be independent consequences of general tissue dehydration. Perhaps the strongest evidence against the buccal theory is that thirst is not relieved by the tantalising procedure of sham-drinking, in which water given freely by mouth is allowed to escape from an œsophageal fistula.[4] Thirst is readily produced by the injection of hypertonic solutions either of salt[5] or of sorbitol, sodium sulphate, and acetate.[6] Substances, such as urea, which enter cells have a much less striking and rapid effect, although their diuretic action may later lead to water-drinking. These experiments would suggest that a rise in the osmotic pressure of body-fluid is a potent thirst stimulus; a rise in serum-sodium is usually present, but thirst can be induced by other agents (sorbitol, for example) with which the osmotic pressure is increased but the serum-sodium reduced. The introduction of hypertonic solutions into the blood-stream is likely to have two effects on intracellular fluid—shrinkage in volume, and increase in osmotic pressure. When shrinkage in volume without increase in osmotic pressure of intracellular fluid was induced by potassium depletion, thirst was not observed.[7] Increase in osmotic pressure of body-fluid therefore seems to be the most firmly established thirst stimulus; but local factors may play some part in the mechanism, for thirsty men have been found to make good only part of their water deficit[8] and hypertonic saline diminishes salivary secretion.[9]

Despite large lacunæ in our understanding of thirst, its presence or absence can help us in assessing clinical problems; and Holmes and Montgomery[1] have reviewed thirst as a symptom. They, like Marriott,[10] regard thirst as pointing to predominant water depletion; and, again like Marriott, they comment on the absence of true thirst in salt depletion. Some patients do complain of thirst when depleted of sodium; but it must be difficult for untrained observers to distinguish between ordinary thirst and the unpleasant metallic taste observed by McCance[11] in salt depletion. It is also difficult to explain the thirst of patients with cardiac œdema, who quite often have a low serum-sodium[12]; Holmes and Montgomery suggest diminished salivary blood-flow and intracellular dehydration as alternative explanations. They make some interesting observations on the salivary flow in patients with diabetes insipidus and with functional polydipsia. In normal people and those with functional polydipsia pitressin either decreases the salivary flow or leaves it unaltered; in patients with diabetes insipidus pitressin causes a striking increase in salivary flow, which also results from forcing fluids beyond the level of urinary output. Hæmorrhage does not occasion thirst unless it is severe enough to lead to shock. Thirst, or at least dryness of the mouth, can also be produced by emotion.

The interesting review by Holmes and Montgomery should stimulate further clinical observations on thirst; and these workers point out that, apart from its practical value, inquiry about thirst always leads to a good story, for "everyone has had some particular experience with thirst, which he loves to recount."

RESEARCH ON POLIOMYELITIS

LABORATORY research on poliomyelitis is an expensive business, but recent progress in technique has made it possible to dispense with the costly monkey and to bring this work within the means of laboratories in the lower income groups. At a meeting of the epidemiological section of the Royal Society of Medicine on May 15, Dr. A. P. Goffe described some of these changes, and particularly those that followed the work of Enders et al.[13] on the growth of poliomyelitis viruses in tissue culture. He gave a demonstration of how he had been applying these techniques to the serological typing of poliomyelitis virus strains recovered in this country. Unfortunately, facilities in this country for laboratory investigations of poliomyelitis outbreaks are at present very limited, and Dr. F. O. MacCallum pleaded for the use of the available resources in studying one or two hand-picked problems, rather than testing all specimens submitted for examination. Which questions are to be investigated largely depends on how wide an expansion of laboratory facilities is contemplated. Perhaps the best argument for intensifying the attack on poliomyelitis by research in this country is the great progress made in the U.S.A. towards successful vaccines.[14] There are good reasons for hoping that practical vaccines will be available within the next few years, and until then there are many technical matters in the production and use of vaccines which would repay immediate investigation. The demand for vaccines is certain to be heavy and the cost of producing them high; and if they are to be manufactured in this country, it will be necessary to train people in the specialised techniques required for this exacting work. This work alone is clearly capable of absorbing a large proportion of the available laboratory facilities, and there are many other promising lines of

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1. Holmes, J. H., Montgomery, A. V. *Amer. J. med. Sci.* 1953, 225, 281.
2. Verney, E. B. *Proc. roy Soc.* B. 1947, 135, 25.
3. Cannon, W. B. *Proc. roy. Soc.* 1918, 90, 283.
4. Towbin, E. J. *Amer. J. Physiol.* 1949, 159, 533.
5. Wolf, A. V. *Ibid*, 1950, 161, 75.
6. Holmes, J. H., Gregersen, M. I. *Ibid*, 1950, 162, 326.
7. Black, D. A. K., Milne, M. D. *Clin. Sci.* 1952, 11, 397.
8. Pitts, G. C., Johnson, R. E., Consolazio, F. C. *Amer. J. Physiol.* 1944, 142, 253.
9. Holmes, J. H., Gregersen, M. I. *Ibid*, 1947, 151, 252.
10. Marriott, H. L. Water and Salt Depletion. *Oxford*, 1950.
11. McCance, R. A. *Lancet*, 1936, i, 823.
12. Squires, R. D., Singer, R. B., Moffitt, G. R., Elkinton, J. R. *Circulation*, 1951, 4, 697.
13. Enders, J. F., Weller, T. H., Robbins, F. C. *Science*, 1949, 109, 85.
14. See leading article, *Lancet*, April 18, 1953. p. 777.

After considering testimonials the committee found him not guilty of infamous conduct in a professional respect

ALLEGED ASSAULT UNDER HYPNOSIS

Sidney Linton, registered as of Bentley House, Meanwood, Leeds 6, M R C S (1945), was charged with (1) having behaved improperly to, and committed adultery with, a single woman, and (2) that he stood in professional relationship with her at the material times

The committee determined that the facts alleged against Dr Linton under head one of the charge had not been proved to their satisfaction They accordingly found him not guilty of infamous conduct in a professional respect

CONVICTIONS FOR DRUNKENNESS

Florence Joseph O'Driscoll, registered as of 8, Moss Lane Orrell Park, Liverpool 9, M B N U I (1928), was charged with having been fined 10*s* at Liverpool on Feb 24, 1949, for disorderly behaviour whilst drunk, and of being fined 10*s* at the same court in 1953 for being found drunk

The Chairman announced that the committee had decided to postpone judgment until May, 1954

NAME NOT ERASED

In May, 1952, the committee postponed for one year judgment on *Daniel Topping Gemmell*, registered as of 81, Madison Avenue, Ward End, Birmingham, 8, L R C P E (1924) He had been fined £5 after being convicted at Bottisham Petty Sessions of an act of indecency

In view of the testimony to his conduct, the committee determined that the Registrar should not be directed to erase his name

DRUNKENNESS CHARGE

Patrick Aloysius Gallen, registered as of 355, Garscube Road, Glasgow, M B Glasg (1929), was charged with having been convicted of offences involving being in charge of a motor car whilst under the influence of drink

The committee postponed judgment for one year

CONVICTION FOR PROCURING DRUGS

Joseph Henry Bentley, registered as of Littlewick, Limpsfield, Surrey, L M S S A (1935), admitted conviction at the Magistrate's Court, Portsmouth, on Nov 7, 1952, of procuring morphine, contrary to the Dangerous Drugs Regulations, 1937, and of failing to keep a register of drugs

The committee postponed judgment for one year

DRUNKENNESS IN CHARGE OF CAR

At the sitting in May, 1952 the committee postponed judgment for one year in the case of *Thomas Patrick Smyth*, registered as of 32, Market Street, Atherton, Manchester, L A H Dubl (1939), who had been convicted in 1948 and 1951 of being in charge of a motor car when under the influence of drink or drugs

The Registrar was not directed to erase his name

Roger Keith Hayden, registered as of 4, Graham Road, Hendon Central, London, N W 4, M R C S (1943), was charged with having been convicted at Chelmsford on Nov 20, 1952, of driving a motor vehicle when under the influence of drink, of assaulting two police constables, and of committing wilful damage to cell windows He was further charged with having been convicted at Chelmsford on Dec 4, 1952 on five counts of obtaining cyclobarbitone, amphetamine, and codeine, by false pretences

Judgment was postponed for one year

Patrick Laurence Lyons, registered as of Highland Lodge, Kilkelly, co Mayo, L A H Dubl (1948), L.R F P S Glasg (1948), had been convicted in 1951 of driving or attempting to drive, or being in charge of, a motor vehicle when under the influence of drink or a drug

The committee postponed judgment for one year

POSTPONED JUDGMENTS

Thomas Leven, registered as of 2, Beech Avenue, Irvine, Ayrshire, L R C P E (1945), had been summoned to appear before the committee in November, on a charge of having been admonished at the Sheriff Court of Ayr in June, 1952, after having pleaded guilty to procuring in cumulo 567 grains of morphine sulphate by presenting, in the name of patients, prescriptions therefor to chemists

The committee postponed judgment for one year

The Registrar was directed not to erase from the Register the name of *Alan McKerlie*, registered as of 238, Upper Chorlton Road, Manchester, 16 M B Aberd (1937) Judgment in his case was postponed from May, 1952, when he had been found to have been convicted of being drunk and disorderly, of driving a motor car whilst under the influence of drink, and of assault

Patrick Kennedy, registered as of 53 East Dulwich Road, London, S E 22, L R C P I (1926), appeared before the committee In December, 1951, judgment against him was postponed for one year He was not present in November, 1952, and the committee postponed judgment until May, 1953 Dr Kennedy was now present He was told by the chairman that in view of the absence of satisfactory evidence as to his conduct, the committee had determined to postpone judgment for a further six months

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LONDON TEACHING HOSPITALS

Boards of Governors

THE Minister of Health has made the following appointments, to fill vacancies caused by the retirement of a third of the members, to the boards of governors of the 26 London teaching hospitals Of 215 appointments, 164 are reappointments of retiring members There are 9 appointments outstanding The names of medical members are shown in bold type Those appointed will hold office until March 31, 1956

ST BARTHOLOMEW'S HOSPITAL

Reappointed Sir Herbert Cohen, O B E, **E R Cullinan**, F R C P, Prof J F Lockwood, PH D, Alexander McL Niven, J P, Sir Denis Truscott, **O S Tubbs**, F R C S, R R J Turner, O B E, J S Weatherley

New members **Geoffrey Keynes**, F R C S, F R C P, Lord Hardinge of Penshurst (until March 31, 1954)

LONDON HOSPITAL

Reappointed Sir Thomas Creed, K B E, M C, M A, Q C, Lieut Commander Horace Denton, O B E, R N retd, Mrs R C Littlejohn, **D. W C Northfield**, F R C S, Colonel V C Ponsonby, M C, Lieut Colonel W M Pryor, D S O, **Hermon Taylor**, F R C S, C S B Wentworth Stanley

New member Miss Irene Dowling

ROYAL FREE HOSPITAL

Reappointed Prof Winifred Cullis, C B E, D SC, W E Ford, **J D McLaggan**, C V O, F R C S, **Clifford Morson**, O B E, F R C S, Lady Bowen Thomas, Miss **B E Turner**, O B E, F R C O G

New members Miss M E Craven, Hon Mrs Gilmour, Prof **Esther Killick**, M R C P

UNIVERSITY COLLEGE HOSPITAL

Reappointed Mrs I M Bolton, Prof **S J Cowell**, F R C P, B Ifor Evans, **E A Gregg**, L.R C P I, J P, Mrs M Harvey, J P, Major General J C F Holland, C B, D F C, Sir Cosmo Parkinson, G C M G, K C B, O B E, A Shefford, O B E, one appointment outstanding

MIDDLESEX HOSPITAL

Reappointed Sir Eric Gore Browne, D S O, C G Izard, O B E, J C Maude, Q C, W B Morrison, S Whitbread

New members **H Wilkes Harvey**, F R C S E, J P, **F D Howitt**, C V O, F R C P, **R V Hudson**, F R C S, **Clifford Morson**, O B E, F R C S

CHARING CROSS HOSPITAL

Reappointed Mrs E O Lindgren, Howard Marshall, Sir John W Morris, C B E, M C, G A Pargiter, M.P, **David Trevor**, F R C S, Sir John Stewart Wallace, C B

New members Lieut Colonel C E G B Gond, M C Prof **W J Hamilton**, M D, Harry Hutchinson

ST GEORGE'S HOSPITAL

Reappointed J Bennie J P, Hon Mrs Reginald Coke, E O Durlacher, Mrs Helga Feiling Alderman W D Little Brigadier H L Roy Matthews **M F Nicholls**, C B E, F R C S Hon Sir Frank Soskice, Q C, M.P

New members Prof **T Crawford**, M D, **V H. Riddell**, F R C S

WESTMINSTER HOSPITAL

Reappointed Viscount Addison, Hon Mrs S Assheton, A N H Baines, **R Coyte**, O B E, F.R C S, **C J Gavey**, F R C P, Mrs M High, Henry Solomons, Sir Harry Vanderpant, two appointments outstanding

investigation to be attended to. One of them was indicated by Dr. J. Stevenson Logan at the Royal Society of Medicine when he described the high prevalence of paralytic attacks of poliomyelitis in school-teachers. This observation suggests an opportunity for the laboratory to help in tracing the precise path of infection in a particular school. For one thing, preventive measures could be planned more rationally if we knew whether the virus was spread by direct contact or by droplet infection.

The meeting was very interested in the possible uses [illegible] Dr. Goffe used some sobering [illegible] his view that gamma-globulin could be used only in small numbers of cases. Indeed, Hammon et al.,[15] who described the promising gamma-globulin trials in the U.S.A., do not believe that its widespread application is practicable.

ACNE VULGARIS

ACNE vulgaris is almost a normal accompaniment of puberty; but if it is severe, or if it persists beyond the 'teens, then some reason has to be found. According to Wittkower[16] people with acne are arrested in their emotional and psychosexual development at the stage of puberty, with no corresponding delay in physical development: the menarche, for example, does not vary from the normal. This suggests that acne is caused by emotional disturbances connected with puberty as well as the physiological processes of maturation.

Lorenz et al.,[17] postulating that in acne emotional influences must operate by quantitative or qualitative alterations in sebum secretion, have devised a method of collecting sebum specimens for study. They obtain their material from that sebum-rich area—the angle of the nose. The skin is first cleaned with ether so that the quantity of sebum subsequently collected represents the amount reappearing on the skin-surface in a given time. The apparatus consists of a hollow glass rod, the ground end of which is applied to the skin under a pressure of 400 g. for 5 seconds by means of a piston-shaft with a metal sleeve at one end for holding the glass rod and with a coiled spring in its hollow handle at the other end. They find that the "control" level of facial sebum output is much the same in acne and in normal patients, and that facial sebum secretion is stable during periods of tranquility although there are day-to-day fluctuations.

In patients with acne, however, sebaceous glandular function is labile, with abrupt fluctuations in facial sebum output under stressful circumstances. These patients have a labile affect, highly characteristic and stereotyped. They respond periodically with feelings of intense anger for brief periods, promptly followed by more prolonged feelings of remorse (guilt and depression), usually set up by conflict with some figure of authority, especially a parent. The daily lives of these patients are punctuated by distinct swings in affect. There is a close association between this emotional lability and fluctuations in sebum output, and the rapid phasic mood-swings are closely related to the number of facial pustules. Stressful interviews with such patients were associated with increased sebum secretion when anger was elicited, and with decreased sebum secretion when the patient responded with remorse. No significant changes in sebum secretion arose from non-stressful interviews with these patients, nor during stressful interviews in a control group of patients without acne. Lorenz and his colleagues suggest that abrupt phasic alteration in the rate of sebum secretion is an important factor in comedone formation; stasis, inspissation, and other physiochemical changes, they say, occur in the hyposecretory phase and lead to impaction of sebum in the next hypersecretory phase, so that the acne is exacerbated after 24–48 hours. Skin-temperature may influence the viscosity of sebum and hence stasis and plug formation, and Lorenz et al. believe that the pronounced vasomotor changes associated with variations of mood may cause wide fluctuations of temperature in the skin. It is perhaps significant that acne vulgaris mainly affects the face, upper chest, and back—the "blush" areas of the body.

The sebaceous glands are not under direct nervous control, but they respond to endocrine stimuli. The nervous control of the sweat-glands can, however, to some extent influence the spread of sebum on the surface of the skin, hyperhidrosis leading to more emulsification and spread of the skin fat. Aron-Brunetière[18] suggests that the neuro-endocrine pathogenesis of acne is somewhat as follows: a disequilibrium in the hypothalamo-pituitary mechanisms disturbs the production of pituitary gonadostimulins with the result that the balance of the steroid hormones is upset towards an excess of androgens (and, in women, progesterone) over œstrogens. Haskin et al.[19] have shown that in the rat the administration of progesterone produces an increase in sebaceous-gland size comparable to that induced by testosterone; and these workers, too, suggest that adolescent acne in the female is related more to progesterone/œstrogen imbalance than to androgen/œstrogen levels.

NOVO ZINC INSULIN

RECENT clinical trials[20] [21] in this country have done much to confirm the claims of the Danish Novo Terapeutisk Laboratories that their new insulin represents an advance on all previous insulins. Hallas-Mollerd an his colleagues[22] made the relatively simple discovery that the addition of small quantities of zinc to dissolved crystalline insulin in acetate buffer precipitated the insulin over a wide range of pH, including that of the body-fluids. This fact had previously been obscured because phosphate is sometimes used as a buffer for insulin, and added zinc is precipitated as zinc phosphate rather than combined with the insulin. There have been suggestions of an interesting relation between zinc and insulin for a long time; for example, it was known that the pancreas contained a higher proportion of zinc than any other organ, and that the addition of large amounts of zinc to soluble insulin[23] or small amounts to protamine insulin[24] prolonged their respective actions. The Danish zinc insulin precipitate also has a long-continued action. Zinc insulin crystals form when zinc chloride is added to dissolved crystalline insulin, buffered with acetate to a pH of between 4·5 and 5·8, whereas outside this pH range the precipitate is amorphous. The fact that the zinc insulin crystals, once formed, are stable over a wide range of pH is of great practical importance. The duration of the effect of these insulins depends largely on the size of the particles in the precipitate. Thus, zinc insulin crystals 100 μ long exert a hypoglycæmic action for more than thirty hours in man, whereas the finer amorphous zinc insulin particles act for some twelve to fourteen hours. The Danes have also made up an intermediate variety containing both crystalline and amorphous forms of zinc insulin, and this lasts about twenty-four hours. Each variety contains nothing but thrice

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[15] Hammon, W. M., Pittsburgh, P. H., Coriell, L. L., Comden, M. J., Wehrle, P. F. *J. Amer. med. Ass.* 1953, 151, 1272.
[16] Wittkower, E. *Brit. J. Derm.* 1951, 63, 214.
[17] Lorenz, T. H., Graham, D. T., Wolf, S. *J. Lab. clin. Med.* 1953, 41, 11.
[18] Aron-Brunetière, R. *Brit. J. Derm.* 1953, 65, 157.
[19] Haskin, D., Lasher, N., Rothman, S. *J. invest. Derm.* 1953, 20, 207.
[20] Lawrence, R. D., Oakley, W. *Brit. med. J.* 1953, i, 242.
[21] Stowers, J. M., Nabarro, J. D. N. *Proc. R. Soc. Med.* (in the press).
[22] Hallas-Moller, K., Petersen, K., Schlichtkrull, J. *Science*, 1952, 116, 394.
[23] Scott, D. A., Fisher, A. M. *J. Pharmacol.* 1935, 55, 206.
[24] Scott, D. A., Fisher, A. M. *Ibid*, 1936, 58, 78.

ST MARY'S HOSPITAL

Reappointed **Richard Doll,** MD, I M Gluckstein, A H Lee, Lord McGowan, KBE, Prof **W D Newcomb,** FRCP, Lady Plummer, Miss **Esther Rickards,** FRCS, H L Smedley

New members **D F Hutchinson,** OBE, MRCS, **G L M McElligott,** MRCS

GUY'S HOSPITAL

Reappointed S B Askew, R H Burslem, JP, E V Evans, OBE, DSC, Prof **T B Johnston,** CBE, MD, K I Julian, CBE, Richard Newton, Prof **W R Spurrell,** FRCS, **F S Warner,** MRCS, FDSRCS

New members Brigadier Archer Clive, A. E Orchard Lisle

KING'S COLLEGE HOSPITAL

Reappointed **Ralph Cocker,** MB, FDSRCS, **Terence East,** FRCP, Squadron Leader G Edgar, G Hart, H Lock Kendell **Sidney Thomson,** FRCP, Hon Mrs Charles Tufton, O.BE

New member Mrs M E Davis, JP, one appointment outstanding

ST THOMAS'S HOSPITAL

Reappointed R J Sainsbury, MA, ACA, Mrs D A Thomas, Sir Herbert Thompson, CIE, MA, **N E Waterfield,** OBE, FRCS, S W Whiffen, C R N Winn, C.B, OBE, MA, LLM, **J M Wyatt,** FRCOG

New members **R H. Boggon,** FRCS, Mrs Margaret Mitchiner, **J S Richardson,** MVO, FRCP

HAMMERSMITH, WEST LONDON AND ST MARK'S HOSPITALS

Reappointed Prof **Ian Aird,** FRCS, E G Anthony, J.P, J Bennie, JP, Mrs M Griffith, Dame Katherine Jones, DBE, RRC, SRN, Mrs R K Judges, **H R Thompson,** FRCS

New member **R H Franklin,** FRCS one appointment outstanding

HOSPITAL FOR SICK CHILDREN

Reappointed Mrs B A Beaumont, JP Hon Margaret Bigge, **W C V Brothwood,** MD, **I A B Cathie,** MD Mrs E M Fell, **G H Macnab,** FRCS, Lady Thomas

New member Edith Batho

NATIONAL HOSPITAL FOR NERVOUS DISEASES

Reappointed **Macdonald Critchley,** FRCP, Hon Mrs Lyttelton, Countess of Rothes, Sir Norman Strathie, W H Taylor

New members Sir **Charles Symonds,** K.BE, CB, FRC.P, **Harvey Jackson,** FRCS, Sir John Woods

MOORFIELDS, WESTMINSTER AND CENTRAL EYE HOSPITAL

Reappointed N E Behrens, **F W Law,** FRC.S, Bryn Roberts, A P D Smyth, Miss V Spenser Wilkinson, Sir John Stainton, KBE, QC

New members **P McG Moffatt,** FRCS, Lady Dunbar Nasmith, CBE

BETHLEM ROYAL AND MAUDSLEY HOSPITALS

Reappointed W J Bourne, Prof **A J Lewis,** FRCP, Prof **Alfred Meyer,** MD, **T A Munro,** MD, E V M Stockdale, Sir Frederick Wells

New member T S Stigger, one appointment outstanding

ST JOHN'S HOSPITAL FOR DISEASES OF THE SKIN

Reappointed **F R Bettley,** FRCP, **G M Frizelle,** MD, Sir **Archibald Gray,** CBE, FRCP, H. Gutteridge, MIMECHE, H Whitbread, MA

HOSPITAL FOR DISEASES OF THE CHEST

Reappointed Mrs M G Burton, J H Cooke, **A Hope Gosse,** FRCP, Sir **Bennett Hance,** KCIE, OBE, MD, A. J Newman, **F H. Young,** OBE, FRCP

New members Hon Michael Astor, J W Randall Naton, JP, one appointment outstanding

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL

Reappointed A E Reneson Coucher, FRICS, **A T Fripp,** FRCS, Sir Howard Kerr, KCVO, CMG, OBE, Miss Grace Rattenbury, M.A., **H J Seddon,** CMG, FRCS, Lady Sherwood

New member Angus Mackinnon, DSO, MC (until March 31, 1955)

NATIONAL HEART HOSPITAL

Reappointed **R C Brock,** FRCS, **J Maurice Campbell,** OBE, FRCP, L H Watts, Mrs E V Whiter, one appointment outstanding

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL

Reappointed Mrs D E Clark, A G Farr, G F Higginson, Prof **F. C Ormerod,** FRCS, J R Roselli, Mrs A Rye

New member A C Crouch

ROYAL CANCER HOSPITAL

Reappointed **A Lawrence Abel,** FRCS, D E W Gibb, D A J Jackman, MBE, JP **E E Pochin,** FRCP, W G Wilsher, F Griffiths Woollard, DL, BSC, JP

New member Sir Edgar Sylvester, KBE, FCA

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS

Reappointed **Frank Cook,** FRCS, Admiral J H Godfrey, C.B, Hon Mrs E Hodgkin, Frank Ramseyer, **J M Wyatt,** FRCOG

New members **Briant Evans,** FRCS, **S G Clayton,** F.RCOG (until March 31, 1955), R D Forshaw

EASTMAN DENTAL HOSPITAL

Reappointed Sir **Allen Daley,** FRCP J G Girdwood, OB.E, Prof **W E Herbert,** MRCS, Miss K G **Lloyd Williams,** MD

New member I R H Kramer, L.D.S

ST PETER'S AND ST PAUL'S HOSPITALS

Reappointed H Lythgoe, Colonel A R Martin, H M Tobin, **R Ogier Ward,** OBE, FRC.S

New members **A W Badenoch,** FRCS, **J D Fergusson,** FRCS one appointment outstanding

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Parliament

QUESTION TIME

Medical Appointments in the Civil Service

Dr A D D Broughton asked the Financial Secretary to the Treasury what information he had received from the British Medical Association with regard to its refusal to publish advertisements of vacant medical appointments in the Civil Service, what was the subject at issue that had given rise to this decision, and what action he was taking to remedy the situation —Mr J A Boyd Carpenter replied The British Medical Association indicated some time ago that, if advertisements of these posts were offered for insertion in the *British Medical Journal,* they would not be accepted, and I received on May 7 a letter from the association saying that they still adhere to that decision Vacancies are not now being advertised and therefore no question of refusal to insert advertisements at present arises The reason, I understand, for the British Medical Association attitude is that they do not regard as satisfactory the present salaries, which are those recommended by an independent committee under Sir Harold Howitt's chairmanship in 1951 I have discussed the matter several times with a joint committee of the British Medical Association, the Medical Staff Association of the Ministry of Health, and the Institution of Professional Civil Servants, and I offered to reconvene the Howitt Committee to review the present salaries This offer was rejected I have made other suggestions for settling this matter, but so far without result

Consultants in the N H S

In answer to a question Mr Iain Macleod, the Minister of Health, stated that the number of whole time consultants in England and Wales at Dec 31, 1952, was 1800 The corresponding numbers for 1950 and 1951 were 1529 and 1650 The number of part time consultants doing maximum sessions was not available The percentage of whole time specialists among all consultants had climbed steadily in each of the last three years Although there had been an increase in the number of part timers the percentage was less than the increase of the whole timers crystallised insulin combined with zinc (2 mg. per 1000 units) and suspended in saline and acetate buffer to bring the pH to 7·2. Each of the three varieties can be mixed with either of the others, but not with the commercial insulins which contain phosphate. Moreover, mixtures of the different varieties are stable and can therefore be premixed in vials for each patient's individual needs.[21]

The Danes claim that 90% of all diabetics needing insulin can be successfully treated with a single daily injection of an appropriate zinc insulin preparation; the insulin requirements of the other 10% show such wide and spontaneous fluctuations that no one-injection régime would be satisfactory. A similar claim has been made for NPH insulin, which has a duration of action that suits most diabetics. There is, however, the important factor of the individual response to a given diet and insulin dose, and this response is surprisingly variable. If the action of NPH insulin proves to be too long delayed, the time can easily be shortened by mixing in a proportion of soluble insulin. But if the action of NPH is too short, nothing can be done to lengthen it; and here lies one of the main advantages of the new series of zinc insulins which can be graded to cover a wide range of action. Another advantage is their purity and freedom from added protein, which makes local skin sensitisation unlikely. In fact no cases of skin sensitivity to these insulins have so far been reported, in spite of their use in patients known to be sensitive to other insulins.[21] The simplicity of the ingredients of the Novo zinc insulins means that uniformity of action from batch to batch is more likely, and preliminary studies by Oakley [25] suggest that this is so. It would at present only complicate matters to add the three grades of Novo zinc insulin to the three types of insulin already in this country, but few would claim that our present insulins are ideal. It seems reasonable, therefore, to give a wider trial to Novo zinc insulins, under carefully controlled conditions, to provide adequate data on which to decide whether they can replace globin and protamine zinc insulin altogether.

LA MÉDIASTINOGRAPHIE GAZEUSE

THE display of a mass by X rays is chiefly determined by the contrast between it and its immediate surroundings. Apart from fat, and structures containing much calcium, the density of all body tissues is approximately the same; and, no matter how large a lump may be, unless at least a part of it is surrounded by shadows of different density it will be very difficult or impossible to define.

In the study of mediastinal abnormalities this handicap is particularly severe, and a group of French workers [26] have been trying to improve the accuracy of diagnosis in this field by injecting air into the mediastinum, to supply the necessary contrast. The air is introduced into the deep tissues of the neck through a needle transfixing the trachea. This method has been used in over 50 cases without serious mishap. There have been no air-emboli, and the authors claim that caval compression does not occur since the air can easily escape up into the neck and down into the abdomen. Up to 700 c.cm. is introduced; and then a *full radiographic* examination is made, including if necessary barium swallow, tomography, and cardioangiography.

This method certainly yields startling pictures, but it seems unlikely to help in answering the two questions most important to the surgeon—namely, is the lesion malignant, and is it operable? Thus the method is unlikely to supplant thoracotomy.

MAXIMUM BREATHING CAPACITY

MAXIMUM breathing capacity is usually measured by causing the patient to breathe for a quarter of a minute as deeply and quickly as possible to and from a recording spirometer with a light aluminium bell and without a CO_2 absorber.[1] The result, obtained from a kymograph tracing of the movements of the bell, is expressed in litres per minute or in litres per minute per square metre of body-surface. Various modifications of this technique have been described.[2]

The difference between the maximum breathing capacity (M.B.C.) and pulmonary ventilation—the breathing reserve—is normally more than 90% of the M.B.C. when the patient is at rest. When the reserve falls to 60–70% of the M.B.C., either by restriction of the M.B.C. or increase in ventilation, dyspnœa is felt. In health this only happens during exercise, but in the patient with pulmonary disease it may occur at rest [3]; and in this event not only is the M.B.C. low but ventilation is often high. The M.B.C. is the dynamic equivalent of the vital capacity, which may be regarded as a static measurement of the bellows action of the thorax and lungs. The relationship between these two measurements has lately been examined,[4, 5] and a close correlation has been established between the volume of the first part of a maximum expiration, which is delivered most rapidly, and the M.B.C. This fact allows a fairly accurate prediction of the M.B.C. to be made from tracings of the vital capacity; moreover estimates made in this way are less liable to be influenced by subjective error or practice effects, particularly when questions of compensation are at stake.

In normal people the maximum ventilation during exhausting exercise is not as great as the M.B.C.,[6] but, by contrast, in some severely incapacitated patients the M.B.C. is actually less than the maximum ventilation on exercise. It has recently been shown that the work done in ventilating the lungs is less when the ventilation is brought about by exercise than by a voluntary hyperventilation, owing to a decrease in the viscous resistance of the lungs during exercise.[7]

Within wide limits pulmonary ventilation varies directly with increase in oxygen consumption or external work. The relation between these two, however, is not identical from subject to subject; for a given increase of oxygen consumption one patient may ventilate much more than another, and his breathing reserve be less in terms of the work he can do. Thus, even if in two such cases the breathing reserve at rest is identical the amount of effort which they can put out may differ.[8]

Only when maximum breathing capacity is much impaired is the patient's activity noticeably limited. Thus, whereas an athletic young man may have a M.B.C. of 150 litres per minute, many who consider themselves normal have M.B.C.s of about half this or even less: patients with M.B.C.s of 70 litres or more per minute are usually free from troublesome dyspnœa on ordinary effort. Although fundamentally the M.B.C measures only the bellows function of the lungs it is usually diminished by any functional disturbance of the respiratory system even when this is not primarily mechanical. Thus, like the vital capacity, the M.B.C. may be used as a non-specific indicator of progress in the functional evolution of disease.

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In England Now

A Running Commentary by Peripatetic Correspondents

AT the annual meeting of the National Association of Malingerers, held this week in London, Dame Lydia Languish was elected to the chair in succession to Baron Münchausen, who has been appointed adviser extraordinary to the Persian Plenipotentiary

The council noted with pleasure the loyal greetings sent by the Malades Imaginaires de France, but they regretfully decided that they could not offer hospitality for the Coronation to their Gallic colleagues Their own members were going to have difficulty in getting a good view of the procession despite the general lending of televiewers to hospitals "Many hospital R M O s," commented Dame Lydia, "are unsympathetic to our members, and outpatient E C T has proved a deterrent to many who could normally have expected a comfortable bed from which to view the ceremony "

A ballot of the members was taken for the allocation of the Hyde Park Corner zone to three members A general discussion followed as to the techniques to be employed by those successful in the ballot In an acute abdomen, it was suggested, the onset of pain should not be too early, as this could mean postoperative transfer to a country branch before June 2 Too late, it could involve the patient in postoperative pain, gastric suction, and other procedures which, although satisfying in themselves, could mask the interest the procession should demand Status epilepticus was likewise regarded with suspicion, as psychiatrists are often on hand in the hospital, and it again carries a risk of transfer It was finally decided that one member should develop renal colic and another status asthmaticus on June 1

Miss Lily Hepar, the association's consultant on pernicious anæmia, advised the pallid third ballot-holder to faint in the Underground, while protesting violently that she was quite well Miss Hepar offered to lend her own subicteral eye-drops to her colleague for the occasion She doubted whether the hæmaglobin could be checked the same evening Other members suggested an acute slipped disc, but it was pointed out that this could involve a mirror view

Dame Lydia emphasised that other members were on their honour not to trespass on the ballot-holders' field She thought, however, that any member who held the association's diploma could probably achieve the front row by performing near the Boy Scouts

* * *

The smallpox in the West Riding is virulent where the unvaccinated are concerned and precautions against its spread are strict A "contact" who had had a small boil on his leg the previous week was sent home from the colliery where he worked because he was not feeling very well When he presented a certificate of incapacity for work on the grounds of being a "smallpox contact" the local National Insurance office with admirable presence of mind and coolness burnt the contaminated piece of paper in the interests of public safety Not until he could produce a new and healthier certificate for a boil could the unfortunate collier get his money

* * *

You and I, gentle reader and gentle writer respectively, manage to get along nicely without the word "Methodology" We would willingly take the pledge never to let it pass our lips, or ginger up our graffiti The first time I came across it, it conjured up a picture of a plump woman in a large hat playing a harmonium and singing a sacred song Tears were running down her face (But that was one of my schizophrenic fancies Association of ideas—portmanteau word Methodist-Doxology Query—Primitive Methodology or Wesleyan ditto ? In either case, why the tears ? I dunno) Unfortunately it doesn't mean that at all Oddly enough although American scientific writers have made a corner in it, and will expend it five times in the second paragraph of an article, it is in fact an English word, and is registered in the 1929 edition of *Chambers's Dictionary* There it is defined as the "Science of method in scientific procedure" A splendid idea I wonder why we don't take to it We sometimes ask ourselves—"How can such-and-such best be accomplished ?" and proceed to discuss ways and means But can that be the same thing ? One can't be *quite certain*.

Quite a lot of splendid words crop up in Scientific American for which an American-English dictionary would be essential, did such a book exist As it is, one has to guess the meaning, check it roughly by the context, and hope for the best If it is an adjective, of course, one mentally removes it from the sentence to see if anyone is any the poorer Such an adjective is "Organizationalized," which is *not* in *Chambers's* and which one never meets here even in bureaucratic circles, but which may easily occur three times in five lines (usually at the beginning) of an American article Obviously it has no synonym, or who would use it and go on using it ? One has a vague idea as to what it may mean, but no exactitude

More and more I am forced to recognise that English and American are two different languages Their deceptive similarity sometimes plunges the English reader into disastrous misinterpretation, but more often leaves him with a wretched margin of uncertainty about the exact translation We ought to be warned by our French experiences of these homonymous pitfalls Think of the difference between "assister à une opération" and "assist at an operation" In the good old days it might have been as much as twenty guineas

* * *

The bad habit of adding a second serpent to the staff of Asclepios is often deprecated on the grounds that it suggests that our proper deity is Hermes, god of travellers, merchants, and liars But are we not being over-hasty in disowning Hermes ? Listen a moment to Guerber on the *Myths of Greece and Rome* "Hermes escorted the souls of the departed to Hades, and in that character was called Psychopompus, under the name of Oneicopompus he was regarded as the lord of dreams and visions" Surely the psycho-analysts are the modern guides through purgatory to the Elysian fields of the integrated personality, and they, at least, are entitled to the two-snaked caduceus and the patronage of Psychopompus himself

* * *

I've just met my most uncommunicative patient The battle went thus

"Good morning," I said, "tell me what you've noticed wrong with yourself"

"Nothing," she said

"Are you perfectly fit ?"

"Yes"

"Then why are you in the hospital ?"

"Because I got a telegram telling me to come"

"Then why," I continued, "did you come to the outpatients in the first place ?"

"Doctor sent me"

This line of approach was not proving exactly helpful I tried another "Have you any pain ?" I asked

"Oh yes," she said

"How long have you had it ?"

"I don't know"

"I'm sure you must know—is it a day, a week, or what ?"

"Oh no," she said

"Oh no what ?"

"I mean 'yes'"

"Well how long then ?"

"A long time"

"How long is that ?" I asked

"Quite a while," she said

As she made no further offer as to time, I suggested "Is it a week, a year, or ten years ?"

With the conviction of an expert witness she said "Yes"

As a matter of interest she proved to have hypertension, angina pectoris, and deep-vein thrombosis of the calf

* * *

News from Hospital—Counsel cross examining night sister at the Medical Disciplinary Committee Do you make any records of visits by doctors ?

Sister No I'm afraid we don't consider them important *enough* pe, should be warned to take carbohydrate in adequate mounts and not to miss a meal or a mid-morning or id-afternoon snack when on the road. He was more ubious about the suitability of a diabetic for driving a ublic vehicle or for piloting an aeroplane. He strongly issented from the view of another speaker that a lawyer as entitled to pick holes in the police surgeon's evidence, o get his client off.

Dr. G. M. KERR said that attention should be paid to oss of judgment and increased reaction-time, both of hich preceded motor incoördination and might result n serious errors in driving.

Dr. LINDSEY BATTEN said that the legal casuistry nvolved in quibbles about the colour of the accused nan's eyes was calculated to keep any but the most stout-hearted doctor from venturing into court.

Dr. G. J. V. CROSBY said that it was often an invidious task for a doctor to dissuade elderly private patients from continuing to drive. One of his patients who drove a high-powered car at a reckless speed was extremely annoyed at the advice that he should give up driving after he had had three blackouts in a year and had been found to have petit mal.

MANCHESTER MEDICAL SOCIETY

Pituitary Adenomata

AT a meeting of the section of medicine of the Manchester Medical Society, on Dec. 3, Sir GEOFFREY JEFFERSON, F.R.S., spoke on the Varying Behaviour of Pituitary Adenomata. He said that some pituitary adenomata behaved in a toxic fashion, while others were inert. The "toxic adenomata" produced gigantism, acromegaly, and basophilism—although he shared the general doubt about basophilism being primarily a pituitary disorder. The chromophobe adenomata produced varying degrees of hypopituitarism; some eventually caused a drift towards Simmonds's disease.

Sir Geoffrey based his remarks on 316 adenomata. He had operated on 250; 11 showed locally invasive properties. Sugar-tolerance curves had not shown any significant trends, though the toxic adenomata were more liable to give rise to glycosuria. Neither the metabolic-rate nor the eosinophil-count showed any uniform change. On the whole the urinary output of gonadotropins was more often reduced than that of the 17-ketosteroids. The dangers of operation were related more to hypothalamic disturbances than to acute stress syndromes. The enlarged sella turcica seen in radiographs gave an inadequate idea of the actual size of the adenomata, of which sizeable supra-sella extensions were extremely common—a fact easily demonstrated by pneumo-encephalography.

DEVON AND EXETER MEDICO-CHIRURGICAL SOCIETY

Outpatient Problems

AT a meeting of the Devon and Exeter Medico-Chirurgical Society on Dec. 18, Dr. W. A. LISTER spoke of common outpatient problems.

The first was that of the child who persistently coughed at night. This cough started about the age of 2, often after pertussis and pneumonia. The patient was intelligent, quick, alert, impatient, growing fast, and rather pale. Associated complaints were abdominal pains and persistent nasal catarrh. Inquiry revealed that the mother had taken the child to many doctors, hospitals, and clinics; but still the cough continued. In the causation these were the main factors: (1) an infective focus in the throat, nasopharynx, or sinuses; (2) a psychosomatic factor (the patient was often the only child of anxious parents); and (3) a dietetic factor, usually an intolerance of fat. If these patients are recognised as early asthmatics other things fell into place. Focal infection must be dealt with; this would improve but not cure the patient's condition. The psychological side should receive attention, perhaps at a child-guidance clinic. Dietetic measures consisted in reducing intake of fat and increasing intake of carbohydrate. Skin tests were disappointing; but common allergens, such as feathers, hair, and pollen, should be avoided as far as possible: the removal of the domestic cat sometimes produced striking improvement. The breathing exercises advocated by the Asthma Research Council were of great help.

Dr. Lister's second problem was that of the mild melancholic. Such patients often complained of vertical headache or pressure, or of boring pain in the temporal region. The condition was apt to follow the receipt of bad news and to occur in elderly men with an enlarged prostate. A carefully recorded history would often elicit evidence of previous attacks. Skin rashes, night waking in the small hours, and withdrawal of interest from customary occupations were characteristic. Organic disease must, of course, be carefully excluded before melancholia was diagnosed. Treatment consisted in attacking the night waking with phenobarbitone and countering the consequent morning hangover with '*Benzedrine*.' (*The* depression was worse in the morning.) If these measures failed electroconvulsive therapy often succeeded.

Dr. Lister's third problem was that of back strain producing persistent and otherwise inexplicable pain. Such pain might be due to minor degrees of root irritation on the concave side of a scoliosis. Poker-back followed prolonged and unnecessary decubitus. Both types responded well to physiotherapy.

Dr. CHARLES WROTH deplored the lack of liaison by which the same patient might be repeatedly and unnecessarily examined radiographically in various clinics and hospitals, or even in the same hospital.

Reviews of Books

Heredity in Uterine Cancer

DOUGLAS P. MURPHY, M.D., F.A.C.S., assistant professor of obstetrics and gynæcology and research associate, Gynecean Hospital, Institute of Gynecologic Research, University of Pennsylvania. Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1952. Pp. 128. 16s.

Dr. Murphy is right in thinking it important to determine whether heredity plays a part in the ætiology of uterine cancer, not only from the point of view of the woman whose mother has died of the disease, and who is therefore apprehensive for herself, but also from the point of view of those who have to diagnose and treat it. This book describes a well-planned, controlled investigation into the cancer incidence of near female relatives (mothers, sisters, female first-cousins, and their mothers) of 201 women suffering from cancer of the uterus, no attempt being made to distinguish cancer of the cervix from that of the body. The author concludes "that there is evidence for a rôle of inheritance in uterine cancer"; but that the quantitative effect is small and has not been measured with high precision. He is also of the opinion that the factors which predispose to uterine cancer do not predispose in any significant degree to cancer in other sites, but that hereditary factors do play a part in the ætiology of cancer elsewhere in the body. No significant tendency to concentration in particular families could be detected. The study is similar in plan to that of Brobeck,[1] made in 1949, and in general the results are similar.

The data took nearly three years to collect and at least four years to analyse. Four field workers were employed, and 890 patients diagnosed as having cancer of the cervix were visited, in order to secure records of 201 cancer family groups. The

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[1] Brobeck, O. Heredity in Cancer Uteri: A Genetical and Clinical Study of 200 Patients with Cancer of the Cervix Uteri and 90 Patients with Cancer of the Corpus Uteri. Aarhus, Denmark, 1949.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Fitness to Drive a Vehicle

THE section of general practice met on Dec 17, under the chairmanship of Dr E P SCOTT, president of the section, to discuss Fitness to Drive a Vehicle

Dr R D SUMMERS, a divisional police surgeon in the Metropolitan area, said that in Great Britain during 1951 there had been 1309 road accidents thought to be caused by drivers who were under the influence of alcohol Many such drivers escaped conviction because the reluctance of the courts to find the accused guilty made the police unwilling to press the charge He himself did not certify some 35% of drivers referred to him as being under the influence of alcohol The charge, under section 15 of the Road Traffic Act of 1930, was concerned with being under the influence of alcohol or drugs to such an extent as to be unable to take proper charge of a motor vehicle The phrase about being in charge was sometimes rather unfairly interpreted, for a motorist who felt himself the worse for drink and who stopped his car to get into the back seat for a sleep was still technically in charge of the vehicle and could therefore be convicted of an offence The police surgeon, or the private doctor whom the accused person could call to examine him, must make a complete and thorough examination For this the consent of the accused must be obtained, and it was wise to have a witness to this consent and to the subsequent examination It was not unknown for the accused to assault the police surgeon or to attempt to escape from custody The pulse-rate should be taken at both the beginning and the end of the examination, during alcoholic intoxication the pulse was full and bounding, with a rate between 100 and 140 Full notes should be taken at the time, and every system thoroughly examined, particular attention being paid to any impairment of muscular coordination, the state of the pupils, and general behaviour It should be remembered that defending counsel could completely destroy the value of a careful clinical examination by disclosing, during cross examination, some gap in the doctor's observations For instance, the doctor might have made careful notes of the state of the pupils, but a jury would be led to think his evidence worthless if he had to admit in court that he did not know the colour of the eyes The history of any previous illnesses should be noted, and the events leading up to the accident, especially the taking of food and drink, should be investigated Evidence of the present mental state, speech, gait, and writing should be recorded Dr Summers usually asked the accused to copy a section of the Highway Code relevant to his charge, it was important to produce any specimen of handwriting in court The doctor must confine himself to the condition of the accused at the time when he examined him, and refuse to be drawn into speculations about his state at the time of arrest, which might be an hour or more previously The accused might ask for his own doctor or any other doctor to be called to examine him, as a defence against the findings of the police surgeon Such additional examinations did not come under the provisions of the National Health Service, and any doctor was entitled to refuse, or to charge a fee for his attendance If the police surgeon, having examined the accused, did not consider him to be under the influence of drink, the police very seldom prosecuted When the driver was found to be under the influence, the charge was heard next day in a magistrate's court The accused might be granted a remand to apply for legal aid, or he might elect to go for trial by judge and jury at the County Court, or to be tried by the magistrate

Dr F E CAMPS said that he thought the main duty of the doctor was to exclude the presence of organic disease, for if no disease was found to account abnormal behaviour, and it could be proved that t person had taken alcohol, then it was a reasonable infer- ence that his inability to control a vehicle was due to alcohol Several drugs simulated the effect of alco on judgment and coordination, but it was equally offence to be under the influence of drugs unless it co be shown that they had been taken in normal dosage the ordinary course of medical treatment The barb turates, nowadays widely prescribed, were commo blamed for inability to control a vehicle, and lately anti-histamines had joined them, whilst diabeti taking insulin often pleaded hypoglycæmia in defence In one case alkalosis had been brought forward as defence by a man suffering from a gastric ulcer who had take several spoonfuls of sodium bicarbonate—and also large quantity of whisky

Any organic nervous disease causing incoordinatio such as states of chronic cerebral contusion ("punch drunk"), acute concussion, epilepsy, vertigo from an cause, and Ménière's disease, might be the basis of defence

Dr Camps thought that the behaviour of the accu at the time of examination was the most important poin for the police surgeon to note Most private doctors were for obvious reasons, loth to attend even when the were asked to see their own patients They also we afraid of being involved in a legal case, mainly becau of having to face cross-examination by counsel—whic should be no cause for worry Others, however, dislike hanging around courts waiting for the case to be heard, th could be avoided by approaching the clerk if necessary

Mr L C. NICKOLLS, director of the New Scotland Yar laboratory, spoke of the value of the tests for estimatin alcohol in blood and urine, which were chiefly corrobora tive of common-sense observation If a graph were draw of the percentage of alcohol in the blood of driver charged with being "drunk in charge," the peak of th curve would be at about 0 3%, for at this stage of intoxi cation a driver would draw attention to himself b swerving about the road or hitting something, fo higher concentrations the curve declined, because a this stage the driver would be in the ditch or in coma Mr Frederick Mead, a Metropolitan magistrate, used t say that there was nobody like an experienced police sergeant for judging whether a man was drunk Th doctor had to remember that he contributed only par of the procedure, it was for him to give his medica evidence, but it was the court's responsibility to decide whether the accused was under the influence of drink

Mr Nickolls agreed with Dr Camps that the occasiona drinker who had a few too many was a much wor menace than the habitual toper He had known driver who were drunk when they learnt to drive and would probably have been completely unable to drive if the had ever been sober

If blood or urine was collected for an alcohol estima tion, it was essential to make sure that the receptacle had not been cleansed with spirit or 'Dettol', the same applied to hypodermic syringes and needles

There was great difficulty in obtaining convictions unless one had a cast iron case Magistrate, judge, and juryman were all reluctant to convict, for each one felt "There but for the grace of God " One had literally to shame them into giving a conviction, and the doctor should remember that he had a duty to the public

Dr R D LAWRENCE spoke of the diabetic driver In 1927 he and Dr Otto Leyton had discussed with high police officials the question of the diabetic's fitness to drive, and it had been decided that patients taking insulin were safe as drivers From time to time hypo glycæmia gave rise to a road accident, but such cases were relatively infrequent Any diabetic on insulin especially if he was taking the long acting zinc protamine

Letters to the Editor

PRESCRIBING OF SOPORIFICS

SIR,—A recent account in the daily press must have caused dismay to medical readers. If correctly reported, it appears that a coroner has commented on, and by implication censured, a medical practitioner for allowing the issue of 40 'Seconal' capsules to a patient, thus giving four times the lethal dose into her possession.

Now this is a normal practice. and the only one which is possible for general practitioners or consultants in hospital or private practice. To issue a few sleeping-tablets each week would not deter a determined would-be suicide from carrying out his intent. It is a simple matter to save up the requisite quantity of capsules to procure a fatal dose. Even if all drugs were refused, is it seriously contended that a patient in despair could not take his life? Are we to expect legal strictures on the Gas Board for issuing in unlimited quantities a deadly and insidious poison to the populace?

Note that in the case reported the woman was in hospital because she had taken an overdose of drugs; yet she killed herself by jumping from a third-floor window.

London, W.1. A. H. DOUTHWAITE.

TUBERCULOSIS IN GLASGOW

SIR,—Dr. Brailsford's letter (May 9) shows that even a leader of our profession need not be immune from a common confusion of thought about tuberculosis. It is certainly true that overcrowding will assist the dissemination of tuberculous infection, or of any other infection, and that malnutrition will increase the severity of the individual case; but there is no evidence that "good housing and a good standard of living will eradicate the disease." It is here that the confusion arises, and as a result the early eradication of tuberculosis has been confidently predicted by doctors from time to time over the past fifty years. The reason their prediction has not so far been fulfilled is that environmental improvements, while reducing the incidence and mortality of tuberculosis, cannot eradicate it, because the tubercle bacillus is an extremely resilient organism, and it is against the bacillus itself that the final assault must be made.

Dr. Brailsford's "public health" approach to the disease has not, I think, been consciously used by doctors as a means of escape from a difficult situation; but in fact it has served as such, because if tuberculosis is a disease which can be eradicated by an evolutionary process of social improvement, our responsibility as doctors is considerably lightened. We can be grateful that we ourselves have been strong enough to escape a serious tuberculous lesion and pray that succeeding generations will contain higher and higher proportions of well-nourished people living in airy surroundings. It is because of this argument that it has been easy for some of us to push tuberculosis towards the social worker and politician, out of the field of medical science, to object to our "slender resources" being used to treat tuberculosis in "elaborate chest hospitals," and to dissuade our daughters from nursing in them.

Medical science, however, has at last caught up with tuberculosis. The discovery of streptomycin, *p*-amino-salicylic acid, and isoniazid, and the exploitation of these drugs by the thoracic surgeon in evolving almost miraculous therapeutic techniques, have made tuberculosis one of the most curable of all diseases. The use of these drugs and the development of thoracic surgery and mass radiography have resulted, in the United Kingdom during the past five years, in the most rapid and spectacular fall in the death-rate from tuberculosis which has yet been seen in the long history of the disease. In the same period the price of food has steadily increased; and although the standard of living may not have deteriorated greatly, it certainly has not risen. It seems just possible that because of the revolution in treatment the control of tuberculosis is becoming independent of social conditions. If tuberculosis is a serious problem in Glasgow, it follows that there are not enough chest hospitals in Glasgow and not enough consulting chest physicians.

Thousands of tuberculous patients in the United Kingdom will die this year, not because they have been undernourished or lived in slums, but simply because they were unfortunate enough to become infected with tubercle bacilli and could not be admitted soon enough to a chest hospital. If they were suffering from acute appendicitis, hospitals and operating-theatres would be improvised in disused cowsheds, if necessary, to save their lives; but because they have a disease which so many believe can be eradicated by good food and good housing, their deaths will be merely statistics in annual reports.

We must leave the standard of living and the provision of houses to those sincere men and women to whom we give responsibility for these matters, influencing their actions when we feel it necessary to do so as enlightened citizens; and as doctors we must accept tuberculosis as a challenge to medical science, because if we do not, it will always be with us.

Dungannon Chest Hospital,
co. Tyrone, Northern Ireland. E. F. JAMES.

TREATMENT OF TUBERCULOUS MENINGITIS WITH STREPTOMYCIN

SIR,—In April, 1949, an interim report of a sub-committee of the Scientific Advisory Committee[1] was published summarising the results obtained at five Scottish centres which had been set up for the treatment of tuberculous meningitis. That report contained an analysis of the first 81 patients, of whom 52 had been observed for a minimum period of seven months. Among this latter group 61% had died, and of those who survived the majority were progressing favourably.

Although the numbers were too small to allow of accurate statistical analysis, certain tentative deductions were made regarding the main factors which appeared to govern the prognosis. The most important of these were: (1) the most favourable results were obtained in the age-group 4–17 years; (2) patients who were classified as "early" according to a prearranged clinical grouping,* had a better recovery-rate than those classified as "intermediate" or "late"; (3) the observation of the presence of choroidal tubercles was associated with a higher fatality-rate; and (4) in those cases of meningitis where the chest radiograph showed a "snowstorm" appearance, the outlook was also less favourable. Finally, it seemed that the administration of streptomycin by both the intramuscular and the intrathecal route was essential for success, since none of the patients had survived who had received only intramuscular treatment.

When this analysis was made, it was decided to extend the study to include a larger number of patients who would be followed up for a longer period. Accordingly, it was arranged to include in a further analysis all those patients with tuberculous meningitis admitted between September, 1947 (when the units were opened) and September, 1949. During this period a total of 266 patients was dealt with, which, of course, includes the 81 patients who formed the subject of the earlier report. The records of all these patients were reviewed during

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[1] Tuberculous Meningitis Treated with Streptomycin. H.M. Stationery Office, 1949. See *Lancet*, 1949, i, 618.

* Clinical grouping: *Early*=Minimal physical signs; no neurological signs; not badly confused. *Intermediate*=Definite meningeal and neurological signs present; confused but able to be roused. *Late*=In coma; many neurological signs.

TREATMENT OF WHOOPING-COUGH WITH ANTIBIOTICS

A REPORT BY THE WHOOPING-COUGH SUBCOMMITTEE OF THE ANTIBIOTICS CLINICAL TRIALS (NON-TUBERCULOUS CONDITIONS) COMMITTEE OF THE MEDICAL RESEARCH COUNCIL*

DURING 1950–51 a controlled investigation of the value of chloramphenicol and aureomycin in the treatment of whooping-cough was made in eight infectious-diseases hospitals in England, Scotland, and Northern Ireland.

Plan of the Investigation

Children 0–5 years of age admitted to the eight hospitals with *uncomplicated* clinical pertussis within 21 days after the onset of the earliest symptoms were included in the trials. On admission the patients were divided by sex and placed in one of three age-groups—0–11 months, 12–35 months, and 36–59 months. They were then allocated to one of three treatment groups—the chloramphenicol group, the aureomycin group, or the control group. Children in the control group were given a mixture of lactose and quinine. The drugs were dispensed in cachets, and, as the chloramphenicol was white and the aureomycin yellow, half the control cachets contained white powder and half yellow powder. To make it more difficult for the observer to detect which drug was being given to an individual patient each of the three drugs was made up under three different letters. The order in which patients were allocated to the treatments was determined by placing the nine letters in a randomly determined sequence. A separate sequence was constructed for each series of 9 patients in each age and sex group.

All the cases were given the appropriate treatment for the first 7 days of the observation period, but the amount of the drug differed for each age-group. Children aged 0–11 months were given 1·0 g daily, children aged 12–35 months 1·5 g daily, and children aged 36–59 months 2 g daily. The drugs were administered twice a day in equally divided doses. Administration presented some difficulties because of the bitter taste. Each hospital devised its own methods, and the powder from the cachets was mixed into honey, jam, fruit purée, milk, sweetened condensed milk, or other suitable excipient.

Each child was to be observed for 20 days. Observations were first recorded on the first day of treatment. Each day notes were made of the number of paroxysms observed by the day staff and the night staff, and at the end of each day the sister of the ward was asked to record whether the paroxysms in each case had been on the whole mild, moderate, or severe. Records were made of the frequency of vomiting during or after paroxysms, but the recorded incidence was low, and in the analysis no useful information was obtained. The occurrence of toxic effects of the drugs was also noted, including vomiting immediately after administration.

It was expected that, though only uncomplicated cases were to be taken into the investigation, some children might develop complications during the period of treatment and observation. For the purpose of the inquiry, a complication was defined as any infective condition associated with whooping cough which the physician in charge considered to be severe enough to require immediate treatment with sulphonamides or antibiotics. In such cases when they occurred during the 7 day treatment period the administration of the trial drugs was stopped. The physicians treated the cases as they thought best. Observations on the number and severity of the paroxysms were continued and all the complicated cases were included in the analysis.

Description of Treatment Groups

Numbers of Cases.—Altogether records were completed for 317 patients, but the records for 23 cases were excluded.

In 7 the appropriate drug was not available at the time of admission or the wrong dosage scale was used, in 3 the diagnosis was doubtful, 1 child had been treated with chloramphenicol and 1 with aureomycin before admission, 2 children developed salmonella infections and 1 developed Sonne dysentery within 4 days of the start of treatment; these patients were removed to other wards. 1 child was found to be infected with *Hæmophilus parapertussis*. 3 children were removed from hospital by their parents early in the observation period. 4 children (3 on aureomycin and 1 on chloramphenicol) vomited the drug repeatedly and attempts to continue administration had to be abandoned.

The analysis was therefore made on the records for 294 cases. The distribution of cases by age and by treatment group is given by hospitals in table I. 98 patients were in the chloramphenicol group, 96 in the aureomycin group, and 100 in the control group. The number in each treatment group was similar for all hospitals together and for each hospital separately. The number of children treated in Neasden, St Ann's General, and Northern Ireland Fever Hospitals was small and these hospitals were grouped together.

TABLE I—NUMBERS OF CASES TREATED, DIVIDED BY AGE, HOSPITAL, AND TYPE OF TREATMENT

Hospital	Chloramphenicol group				Aureomycin group				Control group			
	0–11 months	12–35 months	36–59 months	*All ages*	0–11 months	12–35 months	36–59 months	*All ages*	0–11 months	12–35 months	36–59 months	*All ages*
Edinburgh	5	8	2	*15*	6	8	5	*19*	5	7	3	*15*
Fazakerley	4	8	7	*19*	4	7	1	*12*	2	7	7	*16*
Monsall	4	1	6	*11*	6	5	4	*15*	7	4	5	*16*
Ruchill	15	10	6	*31*	16	10	5	*31*	15	11	6	*32*
Seacroft	6	1	0	*7*	5	1	0	*6*	3	3	3	*9*
Neasden, St Ann's, Northern Ireland	5	7	3	*15*	5	6	2	*13*	3	5	4	*12*
All areas	39	35	24	*98*	42	37	17	*96*	35	37	28	*100*

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* The members of the subcommittee were ROBERT CRUICKSHANK, professor of bacteriology, St Mary's Hospital Medical School, London (chairman); T ANDERSON, reader in infectious diseases, University of Glasgow; E C BENN, consultant in infectious diseases, Seacroft Infectious Diseases Hospital, Leeds; A BRADFORD HILL, professor of medical statistics, London School of Hygiene and Tropical Medicine; A B CHRISTIE, consultant in infectious diseases, Fazakerley Infectious Diseases Hospital, Liverpool; A JOE, medical superintendent, City Hospital, Edinburgh; F F KANE, medical superintendent, Northern Ireland Fever Hospital, Belfast; D C LIDDLE, consultant in infectious diseases, Monsall Hospital, Manchester; W F TWINING McMATH, physician superintendent, Neasden Hospital, London; A C RANKIN, formerly physician superintendent, South Middlesex Infectious Diseases Hospital; R SWYER, consultant in infectious diseases, St Ann's General Hospital, London; and W C COCKBURN, director, Epidemiological Research Laboratory, Central Public Health Laboratory, Colindale (secretary).

TABLE I—RESULTS AFTER OBSERVATION OF AT LEAST 2 YEARS AND 3 MONTHS IN CASES OF TUBERCULOUS MENINGITIS WITHOUT AND WITH "SNOWSTORM" APPEARANCE OF CHEST RADIOGRAPH

—	No. of patients treated	Results		
		Died	Unsatisfactory	Good
Without "snowstorm" lung	181 *(100%)*	94 *(52%)*	16 *(9%)*	71 *(39%)*
With "snowstorm" lung	85 *(100%)*	47 *(55%)*	4 *(5%)*	34 *(40%)*
Total	266 *(100%)*	141 *(53%)*	20 *(8%)*	105 *(39%)*

December, 1952—i.e., after a minimum follow-up period of 2 years and 3 months.

Table I gives the results of treatment for the two main groups of cases—namely, patients with tuberculous meningitis without an accompanying "snowstorm" radiograph of the chest, and patients who, at any time during their treatment, presented evidence of both manifestations of the disease. It will be observed that for the series as a whole and for each of the two groups the proportion of results classified as "good" is the same—namely, approximately 40%.

Subdivision of the cases into the three grades—early, intermediate, and late—has confirmed the original impression that the best results have been obtained in those patients who were regarded as "early" on admission, for in this group the proportion of satisfactory recoveries approaches 60%. The general validity of this clinical assessment as a prognostic guide is supported by the fact that, in those assessed as "early" on admission, death was unusual during the initial period of treatment, whereas in those assessed as "late" a high proportion of the deaths occurred during the first 4 weeks in hospital (table II).

Table II shows the number of deaths, the weekly fatality-rate, and the number of survivors at intervals following admission to hospital. As would be expected, the mortality among survivors in each period progressively diminishes with the passage of time.

This analysis may be briefly summarised. During a period of 2 years, 266 patients with tuberculous meningitis were treated with streptomycin at five Scottish centres. A follow-up of these patients 2 years and 3 months after the admission of the last case shows that 105 (39%) were alive and regarded as excellent recoveries; a further 20 patients were alive although their condition was regarded as unsatisfactory; and the remainder—141—have died.

It seems desirable to correct an earlier impression regarding the importance of the demonstration of a "snowstorm" radiograph in patients with meningitis. In this larger series, such a finding seems of little prognostic value. On the other hand, the assessment of the patient when treatment is begun, despite the fact that it is based on somewhat imperfect clinical data, does constitute a useful prognostic guide. It is apparent that the clinical findings used in making this assessment reflect a gradation of "severity," and that in a proportion of the "late" cases the administration of streptomycin produces little alteration in the steady deterioration of the patient.

TABLE II—DEATHS, FATALITY-RATES, AND SURVIVORSHIP

Weeks after admission	—1	—2	—4	—8	—16	—52	—116
No. of patients alive at beginning of period	266*	247	232	217	205	175	129
Deaths during the period E	0	0	1	2	6	17	2
I	6	5	4	7	16	24	2
L	13	10	10	3	8	5	0
	19	15	15	12	30	46	4
Average weekly fatality-rate (%) among survivors	7	6	3	1·4	1·8	0·7	0·05

*In the series 28% were classified as "early," 49% as "intermediate," and 23% as "late."

D. M. DUNLOP
Chairman
T. ANDERSON
D. BELL
STANLEY GRAHAM

D. G. MCINTOSH
G. L. MONTGOMERY
J. D. ROSS
G. J. SUMMERS
I. M. MACGREGOR
Medical Secretary.

CIRRHOSIS: LIGATION OR ANASTOMOSIS?

SIR,—Professor McFadzean and Mr. Cook (March 28) plead that hepatic-artery ligation has been developed in an attempt to find a safe and effective substitute for portacaval anastomosis. They admit that portacaval shunts prevent the recurrence of hæmatemesis and have a favourable effect on the ascites in the majority of these cases. Similar remarks were made in your editorial last year.[1]

I do not believe that any operation should be advocated simply because it is technically difficult, but neither should an effective operation be abandoned because of its difficulty. If this view were adopted we would all still be doing gastrojejunostomy instead of gastrectomy for chronic duodenal ulcer! Furthermore, I believe that the difficulties and dangers of portacaval anastomosis have been grossly overestimated. The early results in this unit have been reported elsewhere[2] and it was then noted that the operation carried a high mortality-rate in patients in whom splenectomy had not been performed, but that in the first 9 patients in whom splenectomy had been performed as a preliminary measure there had been only 1 operative death. Since these cases were reported 6 further direct portacaval shunts have been done without operative death. The operation can be completed within two and a half hours. Only 1 patient, operated on four years ago, has had hæmatemesis, and the results of treatment on the whole have been very satisfactory.

Against this background must be considered the results of hepatic-artery ligation as reported, and also as carried out in this unit. The clinical material in McFadzean and Cook's series is presumably similar, for in Hong-Kong it is largely chance which determines whether the patient finds his way into the medical unit and has his hepatic artery tied, or into the surgical unit to get an Eck fistula.

In this unit 4 patients have been subjected by way of a trial to hepatic-artery ligation. The first died with portal vein thrombosis, and the remaining 3 went steadily downhill. It was noted at operation that the fall in portal pressure, measured directly with a manometer, was quite inconstant after ligation of either splenic or hepatic arteries. Furthermore, it must be remembered that the peripheral resistance within the liver is increased in cirrhosis and flow is therefore dependent on maintenance of an adequate pressure. If the pressure in the portal vein falls and the hepatic arterial supply is removed, the total flow through the liver must fall. If the portal vein only is interrupted, blood continues to reach the liver at a high pressure through the hepatic artery and in these circumstances maintenance of adequate liver function in man is possible.

It is well known that in a certain number of patients with cirrhosis splenectomy alone improves the clinical condition, and I am not yet convinced that the improvement which follows ligation of the hepatic artery, combined

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1. *Lancet*, 1952, i, 1097.
2. Stock, F. E. *Ann. R. Coll. Surg. Engl.* 1952, 10, 187.

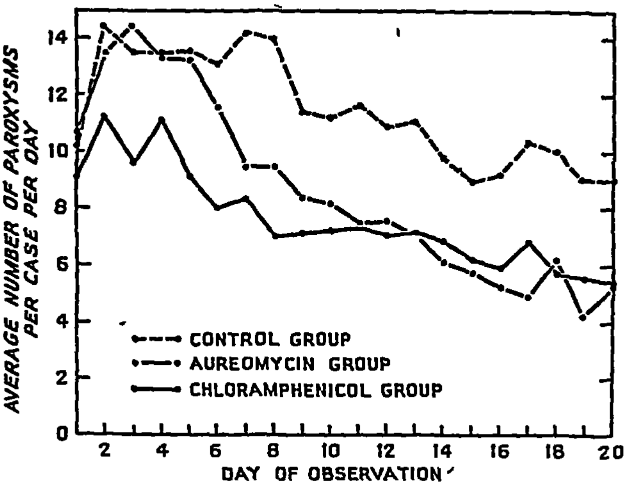

Fig 1—Early cases

Sex distribution—More females than males were treated in the investigation In the chloramphenicol group 53 1% were females, in the aureomycin group 56 3%, in the control group 55 0%, and in all groups together 54 8% As the proportion of females in each group was similar, no separate analysis by sex was made From inspection it did not appear that females fared better or worse than males

Confirmation of Diagnosis—All suitable cases which on clinical grounds were considered to be suffering from whooping cough were taken into the investigation In order to confirm the clinical diagnosis swabs were taken on admission and an attempt was made to get a history of other cases in the family or neighbourhood *H pertussis* was isolated from 47% of the cases—44% in the chloramphenicol group, 49% in the aureomycin group, and 47% in the control group A history of associated cases was obtained from 60—59% in the chloramphenicol group, 65% in the aureomycin group, and 56% in the control group

Duration of Observations—The intention was to observe each case for 20 days from the beginning of treatment, but some patients were discharged before the full period of observation was completed The numbers lost at various stages in each group were similar (see table III) The records of these cases were included up to the time the patients left hospital

Results

The results in the three groups were assessed by analysing (*a*) the number of paroxysms per case per day, (*b*) the severity of the paroxysms, (*c*) the number of complicated cases, (*d*) the number of deaths, and (*e*) the bacteriological findings at intervals during the period of observation The cases were divided into three types depending on the duration of symptoms before treatment was begun

Early cases were defined as those with symptoms for 1-8 days before treatment began There were 85 early cases—28 on chloramphenicol, 29 on aureomycin, and 28 controls

Intermediate cases were defined as those with symptoms for 9-15 days before treatment began In this category there were 147 cases—50 on chloramphenicol, 49 on aureomycin, and 48 controls

Late cases were defined as those with symptoms for 16-21 days before treatment began 62 were placed in this category —20 on chloramphenicol, 18 on aureomycin, and 24 controls

The date of the beginning of the illness was taken as the day on which the earliest symptoms—cough or coryza —began, and *not* as the day when the cough became paroxysmal Complete accuracy in ascertaining the day of the onset of the first signs of illness was not always possible, but cases on all three treatments were subject to the same degree of error

A separate analysis of the records of children on chloramphenicol and aureomycin was made No clear difference between the effects of the two antibiotics was observed, this is illustrated in the graphs Except for consideration of complications and deaths, the two groups were combined and are referred to as the "treated group"

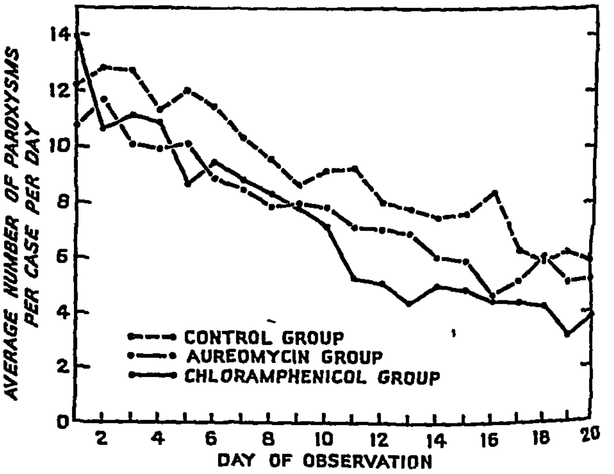

Fig 3—Late cases

NUMBERS OF PAROXYSMS

The average number of paroxysms per case was calculated separately for each of the 20 days of observation The results for each day are shown in the graphs and by 4 day periods in table II The average number of paroxysms per case in the treated group was less than in the control group for the early, intermediate, and late cases, and the differences were consistent throughout the period of observation In the day-by day analysis, the differences in the average number of paroxysms per case on days 6, 7, 8, and 9 (i e, around the end of the treatment period on day 7) were for early cases 3 2, 5 2, 5 7, and 3 7, for intermediate cases 1 0, 1 9, 1 4, and 1 6, and for late cases 2 3, 1 8, 1 5, and 0 8 The only large differences were those observed in the early cases where for example on day 8 the [illegible] 5 7 paroxysms This finding was [illegible] (difference/standard error = 3 2) In the intermediate and late cases the treated children had on the average about 2 paroxysms per day less than the control children

The information on paroxysms was then analysed by calculating for the 2nd, 8th, 14th, and 20th days of observation the percentages of cases with 0-9, 10-19 and 20 or more paroxysms (table III) By this method

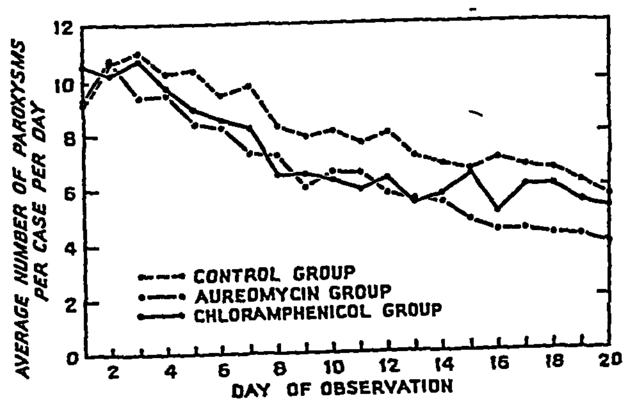

Fig 2—Intermediate cases

with splenectomy is due to the ligation rather than to the splenectomy.

These considerations have led me to discard the operation of ligation of the hepatic artery and I continue to advocate splenectomy followed by portacaval anastomosis for any patient with cirrhosis, splenomegaly, and œsophageal varices.

University of Hong-Kong. **FRANCIS E. STOCK**
Professor of Surgery.

CONTRACEPTIVE TECHNIQUE

SIR,—The letter from the managing director of Ortho Pharmaceutical Ltd. should not satisfy anyone in charge of a birth-control clinic, and does not satisfy me, though it advertises further the contraceptives I am warning people about. The "diaphragm and jelly" Mr. George praises I have long shown to be a not entirely satisfactory technique.[1] Though theoretically it would be very nice to have a suppository or substance that would do away with the necessity for any diaphragm cap or barrier, there are reasons which make this unlikely of achievement. Mr. George claims that their advertised product —'Preceptin Vaginal Gel'—is safe without any barrier.

First let me say it has to be placed with an applicator, and for general contraceptive use I condemn all methods involving the use of an applicator, which has many bad features. Further, a method involving the use only of a jelly-like substance ignores the fact that in coitus the sperm may be ejaculated directly into the uterus, when none of the substance's alleged unique capacity to destroy sperms would be able to take effect.[2]

The Ortho Research Foundation speaks of "thousands of patients." What degree of safety after at least one year's, and preferably two years', consistent use of this as the only contraceptive do they claim? We should be given also one or two addresses of recommended clinics in this country where this contraceptive has been consistently used, and the degree of success they record.

C.B.C. Birth Control Clinic,
108, Whitfield Street,
London, W.1.

MARIE C. STOPES
President and Founder.

THE BRACHIAL-PALSY HAZARD

SIR,—Though the Law may have to concern itself with a particular injury or an isolated event, doctors must try to regard the whole patient and his whole welfare. Recent interest in brachial-plexus injury subsequent to certain operating-table positions seems to illustrate this matter.

Let us, for argument's sake, admit that there is a risk of brachial-plexus injury following maintained abduction of the arm under anæsthesia. I believe that there are instances when the risk should forthrightly be accepted in the patient's interest.

Sometimes the continuance of an intravenous infusion is of critical importance to the patient because of collapse. Sometimes sudden and unpredicted interruption of the flow of the infusion might disrupt the smooth course of anæsthesia given by the method judged best for the patient's survival, and such sudden disruption at a critical point in the operation could have grave consequences. In patients in a shocked state veins in the leg are often unsatisfactory, and an infusion into a forearm vein can easily fail unless the arm is accessible so that attention can be given immediately when needed. Unless the arm is abducted such attention is either impossible or imperfect. If the arm be only a little abducted the surgeon may be hampered by it and the patient's interests thereby damaged.

Even though it may expose me to the risk of being deemed negligent, I shall continue as occasion requires to place an infusion in a forearm vein, and abduct the arm onto an arm-board so that I can be as sure as humanly possible that the flow continues. I shall do this because I believe that the conscientious application of knowledge and judgment to the patient's whole welfare will not infrequently demand it; though I shall be fully aware of the small risk to his brachial plexus.

Department of Anæsthesia,
Royal Victoria Infirmary,
Newcastle upon Tyne.

E. A. PASK.

⁂ Dr. Pask can, we believe, pursue his course safely for the patient if he makes one small concession to the brachial plexus: by using the Jackman arm-rest[1] he can prevent the abducted arm from falling below the coronal plane of the body. At the same time, we should point out that many other devices for protecting the brachial plexus are already in successful use.[2]—ED. L.

INTESTINAL OBSTRUCTION IN INFANTS

SIR,—It was never the intention in my letter of April 4 to decry in any way the invaluable part played by special centres in the advancement of neonatal surgery, and I question whether such an interpretation is justified. Pædiatric surgical centres in Boston, Liverpool, and Stockholm, among others, have in a few years turned a mortality-rate of 75% in intestinal obstruction of the newborn (excluding meconium ileus) into a survival-rate of 75% or better—truly a remarkable achievement.

Progress in medicine and surgery characteristically follows a pattern by which one or more main centres develop new methods of treatment or new surgical techniques, which are later successfully adopted by others. Surely this process can be profitably applied to abdominal surgery in the newborn, where early diagnosis and treatment are essential.

Halifax General Hospital. **W. P. SWEETNAM.**

PEPTIC ULCERATION

SIR,—I was interested in Dr. Csato's account (May 16) of treatment of peptic ulceration with injections of chorionic gonadotropin.

Some time ago I was struck by a statement by a patient with duodenal ulcer that her symptoms always remitted when she was pregnant. As she had failed to respond to the usual medical remedies, I gave her a course of ethinylœstradiol sublingually (to avoid the irritant effect of the drug on the gastric mucosa). There was an immediate resolution of symptoms in 2–3 days; but when she suffered a further exacerbation some 6 months later, there was complete failure to reproduce the same effect. Neither did she respond to ethisterone given in like manner. Since then I have tried both hormones in 5 other cases, and methyltestosterone in 3 male patients. Symptoms have been completely relieved by ethisterone in 1 case, and by ethinylœstradiol in another; but in the remaining 6 cases there was no effect. In 1 case methyltestosterone greatly aggravated the pain. In view of Dr. Csato's observations, I intend to treat some further cases with injections of progesterone, as opposed to the less reliable oral preparation.

There is, perhaps, a slight tendency to take for granted the natural history of diseases, without inquiring more deeply into possible causes for spontaneous remissions and variations. Thus pregnancy has often been classed as one of many intercurrent conditions which may cause remission in such diverse diseases as peptic ulceration, disseminated sclerosis, and rheumatoid arthritis. Yet this observation on rheumatoid arthritis was one of the factors leading directly to the discovery of cortisone.

Twickenham, Middlesex. **DAVID WHEATLEY.**

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[1] Stopes, M. C. *Med. World, Lond.* Nov. 23, 1951.
[2] Stopes, M. C. *Clin. Med. Surg.* March, 1931.

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[1] Wilson, E. F., Murphy, T. T. P., Angel, R. E. *Lancet*, 1951, i, 511.
[2] Ewing, M. R. *Ibid*, 1950, i, 99; Kiloh, L., pp. 103, 121; Galley, A. H., Gray, A. J., p. 184; Finnie, W. J., p. 228; Lunn, M., Clutton-Brock, J., Clarke, S. H. C., Gusterson, E. R., p. 229; Lee, M., p. 277; Browne, J. C. M., Roberts, H., p. 278; FitzGerald, T. B., p. 326; Ward, R. O., Rollason, W. N., p. 423; Sinclair, A. D., p. 592.

TABLE II—AVERAGE NUMBERS OF PAROXYSMS PER CASE PER DAY IN 4-DAY PERIODS

—		Days 1–4 C*	Days 1–4 T†	Days 5–8 C	Days 5–8 T	Days 9–12 C	Days 9–12 T	Days 13–16 C	Days 13–16 T	Days 17–20 C	Days 17–20 T
ALL CASES	Average number of paroxysms per case per day	11 5	10 7	10 9	8 6	9 0	6 7	7 9	5 5	7 1	5 0
	Difference	*0 8*		*2 3*		*2 3*		*2 4*		*2 1*	
EARLY CASES	Average number of paroxysms per case per day	14 9	11 6	13 6	9 6	11 2	7 5	9 7	6 2	9 5	5 4
	Difference	*3 3*		*4 0*		*3 7*		*3 5*		*4 1*	
INTERMEDIATE CASES	Average number of paroxysms per case per day	10 3	10 0	9 4	7 9	7 9	6 2	6 9	5 3	6 3	5 0
	Difference	*0 3*		*1 5*		*1 7*		*1 6*		*1 3*	
LATE CASES	Average number of paroxysms per case per day	12 3	10 8	10 9	8 8	8 7	6 8	7 8	5 2	6 0	4 7
	Difference	*1 5*		*2 1*		*1 9*		*2 6*		*1 3*	

* C = control group † T = treated group

also the differences between the control and treated groups were greatest in the early cases For instance on day 2 the percentages of early cases with 0–9, 10–19, and 20 or more paroxysms were similar in the two groups, but on days 8, 14, and 20 respectively 72%, 80%, and 90% of the treated children had fewer than 10 paroxysms per day compared with 40%, 58%, and 64% of the control children These differences were statistically significant (differences/standard errors = 2 6, 2 2, and 2 7)

SEVERITY OF PAROXYSMS

As mentioned earlier, the sister of the ward, who did not know which drug was given to individual patients, was asked to record each day during the observation period whether she considered the paroxysms in each case had been on the whole mild, moderate, or severe For the analysis of this information the 20 day observation period was divided into the five 4-day periods The results for the early, intermediate, and late cases are given in table IV The greatest differences between the treated and control groups were in the early cases For example the proportion of early control cases in which the paroxysms were described as absent or mild increased from 22% in the first 4 day period to 29% in the fifth 4 day period, but in the treated cases the percentages increased from 17 to 66 Between the first and fifth 4 day periods the proportion of control cases with severe paroxysms fell from 41 to 23% while the proportion of treated cases fell from 27 to 4%

In the early cases the differences between treated and control groups in the percentages of cases where the paroxysms were absent or mild were statistically significant for the third, fourth, and fifth 4 day periods (differences/standard errors = 4 4, 5 8, and 6 2) In the intermediate cases the differences in the percentages of cases where the paroxysms were absent or mild were statistically significant for the same three periods (differences/standard errors = 2 7, 3 1, and 3 9) It appeared that the drugs influenced the severity of the paroxysms to a greater degree than they affected the numbers of paroxysms in the intermediate cases*

TABLE III—PERCENTAGES OF CASES WITH 0–9, 10–19, AND 20 OR MORE PAROXYSMS ON THE 2ND, 8TH, 14TH, AND 20TH DAYS OF OBSERVATION

Number of paroxysms	Day 2 C*	Day 2 T†	Day 8 C	Day 8 T	Day 14 C	Day 14 T	Day 20 C	Day 20 T
ALL CASES	%	%	%	%	%	%	%	%
0–	45	50	60	74	71	83	74	90
10–	43	41	31	23	26	15	24	9
20 and over	12	9	9	3	3	1	1	1
Number of cases observed	*100*	*194*	*100*	*194*	*98*	*191*	*89*	*169*
EARLY CASES	%	%	%	%	%	%	%	%
0–	43	50	40	72	58	80	64	90
10–	36	33	46	23	35	20	32	10
20 and over	21	18	14	5	7	0	4	0
Number of cases observed	*28*	*57*	*28*	*57*	*28*	*56*	*25*	*50*
INTERMEDIATE CASES	%	%	%	%	%	%	%	%
0–	57	55	71	78	74	82	80	90
10–	38	37	21	20	26	15	20	9
20 and over	6	7	8	1	0	2	0	1
Number of cases observed	*48*	*99*	*48*	*99*	*46*	*97*	*40*	*88*
LATE CASES	%	%	%	%	%	%	%	%
0–	25	37	62	68	79	92	75	90
10–	62	61	33	29	17	8	25	10
20 and over	13	3	4	3	4	0	0	0
Number of cases observed	*24*	*38*	*24*	*38*	*24*	*38*	*24*	*31*

* C = control group † T = treated group

TABLE IV—PERCENTAGES OF CASES WHERE THE PAROXYSMS WERE DESCRIBED AS ABSENT OR MILD, MODERATE, OR SEVERE (IN 4 DAY PERIODS)

Description of paroxysms	Days 1–4 C* %	Days 1–4 T† %	Days 5–8 C %	Days 5–8 T %	Days 9–12 C %	Days 9–12 T %	Days 13–16 C %	Days 13–16 T %	Days 17–20 C %	Days 17–20 T %
EARLY CASES										
Absent or mild	22	17	20	29	15	39	21	54	29	66
Moderate	37	56	40	56	40	54	42	40	48	29
Severe	41	27	40	15	45	6	37	6	23	4
INTERMEDIATE CASES										
Absent or mild	9	12	19	24	30	41	41	55	46	65
Moderate	57	55	54	56	46	49	41	38	37	30
Severe	33	33	26	19	22	10	16	7	15	5
Not stated	0	0	2	0	2	0	2	0	2	0
LATE CASES										
Absent or mild	23	19	25	34	34	49	51	60	54	68
Moderate	54	47	52	49	54	44	42	33	39	27
Severe	23	34	23	17	12	7	7	7	7	5

* C = control group † T = treated group

COMPLICATED CASES AND DEATHS

19 patients developed respiratory complications during the observation period—7 in the control group (3 bronchopneumonia, 2 bronchitis, 1 lobar pneumonia, and 1 pleural effusion with atelectasis), 7 in the aureomycin group (2 bronchopneumonia, 2 bronchitis, 2 lobar pneumonia, and 1 pleural effusion with atelectasis), and 5 in the chloramphenicol group (3 bronchopneumonia and 2 bronchitis) 3 cases in the control group and 2 cases in the chloramphenicol group occurred during the period the drug was being administered All cases in the aureomycin group and the remaining cases in the other groups occurred after the end of the treatment period In addition 3 cases, 1 in each treatment group, were fatal, in the control group a male aged 6 weeks developed bronchopneumonia on the 5th day of observation and in spite of treatment with sulphonamides and penicillin died on the 10th day of observation, in the aureomycin group a male aged 7 months developed convulsions on the 14th day of observation and died the following day, in the chloramphenicol group a female aged 1 year developed widespread collapse of the lungs about the 7th day of observation and died on the 11th day of observation None of the complicated or fatal cases occurred in patients treated within 8 days of the onset of symptoms

BACTERIOLOGICAL RESULTS

Most cases were swabbed on or about the 1st, 2nd, 3rd, 8th, and 11th days of observation In the third

COMPRESSION OF CERVICAL CORD AND CERVICAL SPONDYLOSIS

SIR,—In connection with the article by Sir Charles Symonds (March 7) on the interrelation of trauma and cervical spondylosis in cervical-cord compression, I should like to record the following case.

The patient, aged 71, was admitted to Addenbrooke's Hospital on March 21, 1952. That afternoon he had been for a walk, but felt dizzy and came home by bus. On alighting he fell, but he was unable to give an account of the exact circumstances. Eye-witnesses said that it looked as if he had fainted and had fallen on to his head; it was thought that he had temporarily completely lost the use of his legs and arms. When admitted to the casualty department he could talk and was rational; he said he had lost the use of his arms and legs, and he complained of severe pain in his fingers and hands.

There was a small abrasion over the vertex. Pulse-rate 36 per min.; blood-pressure 160/90 mm. Hg. The patient's arms were held abducted at the shoulders, and the elbows were flexed. There was little voluntary movement of the upper arms apart from weak flexion of the elbows and abduction of the shoulders. Complete paralysis of the lower limbs had been reported, but during this examination he regained some weak power of flexion of the hips and knees. Reflexes were as follows: biceps, triceps, and supinator jerks absent on the right side, just elicited on the left side; abdominal reflexes absent; knee-jerks and ankle-jerks present; plantar reflex equivocal on the right side, extensor on the left side. Neck movements, particularly extension, produced pain in the arms and hands. There was some tenderness over the spinous processes of C3 and C4.

Radiographic examination showed no evidence of dislocation or fracture of the cervical spine. Some diminution of the disc spaces C4–5 and C5–6 was noted; but there was only slight lipping of these vertebral bodies, and there were only slight osteo-arthritic changes.

Lumbar puncture yielded cerebrospinal fluid under pressure of 150 mm. water; protein 55 mg. per 100 ml.; Queckenstedt test indicated partial block on extension, slight relief on flexion.

Electrocardiography showed 2 : 1 heart-block.

Course.—The patient was admitted and rested flat in bed. Power was gradually regained in the lower limbs, but severe paræsthesia in the hands and forearms persisted. Next day there was still little power in the hands or forearms, though the biceps showed some improvement and there was full active movement of the lower limbs. On March 23 pain and temperature sensation were noted absent in his legs, but position sense was unimpaired. Attempts to relieve the pain in the arms by traction on the head only exacerbated it, and retention of urine added to the patient's distress. Despite antibiotics and parental therapy, his general condition gradually deteriorated, and on March 29 he died of uræmia and bronchopneumonia.

Necropsy.—There was almost complete prolapse backwards into the spinal canal of the intervertebral disc between the 4th and 5th cervical vertebræ, narrowing the spinal canal at this point: the narrowing was greater to the left of the midline. There was also incomplete prolapse of the intervertebral disc between the 5th and 6th cervical vertebræ, causing a slighter narrowing of the spinal canal. Some portions of protruded material lay beneath the posterior longitudinal ligament, thus connecting these two prolapsed intervertebral discs. Recent hæmorrhage into the remains of the affected discs suggested that these changes were recent and traumatic. The spinal cord had evidently suffered some compression at the site of the maximum narrowing of the spinal canal, but it showed no gross abnormality to the naked eye. Section of the cord at the level of the disc prolapse showed definite acute degenerative changes consistent with recent trauma; the changes were mainly in the lateral columns.

The lungs showed bilateral severe bronchopneumonia affecting the lower lobes. An infarct was present in the right upper lobe. In the heart there was no gross change apart from some atheroma of the coronary arteries with slight narrowing of the right coronary artery.

In this case there was sudden spinal-cord compression, probably due to an acute injury, associated with prolapse of two intervertebral discs. There is no clear evidence as to whether it was a flexion or extension injury. The cause of the fall may have been heart-block. Apart from narrowing of the intervertebral discs C4–5 and C5–6 there was little radiographic evidence of cervical spondylosis. This discrepancy between the relatively normal radiographic findings on the one hand and the pathological findings on the other corresponds with that found by Brain et al.,[1] who correlated the radiographic and myelographic findings in a number of similar cases. The simultaneous prolapse of two intervertebral discs corresponds with multiple lesions described by Brain et al., but the protrusion of disc material beneath the posterior longitudinal ligaments is unusual. The changes in the lateral portions of the cord may account for the dissociated sensory loss in the legs and the paræsthesia in the arms. This distribution of microscopic changes in the cord is in contrast to those described by Sir Charles Symonds in case 4 of his article, but corresponds quite remarkably with the findings of Bedford et al.[2]; it suggests that they may be related to the attachment of the denticulate ligaments to the lateral margin of the spinal cord.

I would like to thank Mr. T. J. Fairbank, consultant orthopædic surgeon, for permission to publish this case, and Dr. A. M. Barrett, university pathologist, for the description of pathological findings in this case, which he discussed at a clinico-pathological conference of Cambridge University Medical School.

Addenbrooke's Hospital,
Cambridge.

B. J. GROGONO.

THE ILLEGIBLE CANDIDATE

SIR,—I greatly appreciate the timely and humane letter from Sir John Conybeare (May 16).

I should not dream of penalising an examination candidate for bad writing. Indeed, I regard any extra labour involved in reading an illegible script as an opportunity of repaying the debt I owe to my own examiners.

Department of Medicine,
University of Birmingham.

W. MELVILLE ARNOTT.

DIAGNOSIS OF ACUTE MENINGITIS IN INFANCY

SIR,—Dr. Haworth's article is most timely, in view of your recent leading article, Hazards of Lumbar Puncture, and the correspondence it has provoked. However, I do not think pædiatricians are likely to be deterred from resorting to lumbar puncture on the slightest suspicion of meningitis, where the hazards of tardy diagnosis far outweigh any other consideration.

It is good that Dr. Haworth stresses once again the difficulty in diagnosis of acute meningitis in infants, but in giving indications for lumbar puncture he made no mention of convulsions. Ounsted[3] said: "It follows that any small child who has had an *unexplained* febrile seizure should be admitted to hospital, and that, unless some definite contra-indication exists, a lumbar puncture should be done without delay." Profiting by past mistakes, I now make it a rule to perform a lumbar puncture on any infant under twelve months of age who has just had a convulsion for the *first time*. Indeed, I am not deterred by the presence of an obvious focus of infection such as an acute otitis media or pneumonia, for meningitis may well co-exist.

It is noteworthy that, in the series analysed by Dr. Haworth, cases 4, 8, and 11 would have been diagnosed ante mortem if this rule had been applied.

The newborn period is a time of especial diagnostic difficulties, and lumbar puncture must then be considered as part of a routine investigation in an "ill baby." The day seems not far distant when there will be

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1. Brain, W. R., Northfield, D., Wilkinson, M. *Brain*, 1952, 75, 187.
2. Bedford, P. D., Bosanquet, F. D., Russell, W. R. *Lancet*, 1952, ii, 55.
3. Ounsted, C. *Lancet*, 1951, i, 1245.

TABLE V—BACTERIOLOGICAL RESULTS

Intervals when swabbed*	Early cases				Intermediate cases				Late cases				All cases			
	Control group		Treated group		Control group		Treated group		Control group		Treated group		Control group		Treated group	
	Number swabbed	% +ve	Number swabbed	% +ve	Number swabbed	% +ve	Number swabbed	% +ve	Number swabbed	% +ve	Number swabbed	% +ve	Number swabbed	% +ve	Number swabbed	% +ve
I	23	*39·1*	46	*39·1*	37	*37·8*	78	*34·6*	18	*27·8*	31	*29·0*	78	*35·9*	155	*34·8*
II	21	*47·6*	50	*40·0*	37	*32·4*	74	*36·5*	15	*33·3*	22	*27·3*	73	*37·0*	146	*38·4*
III	24	*29·2*	39	*17·9*	35	*25·7*	68	*16·2*	13	*30·8*	23	*4·3*	72	*27·8*	130	*14·6*
IV	21	*19·0*	45	*4·4*	38	*15·8*	81	*3·7*	18	*11·1*	31	*0*	77	*15·6*	157	*3·2*
V	23	*13·0*	48	*10·4*	39	*12·8*	84	*4·8*	16	*0*	27	*0*	78	*10·3*	159	*5·7*

* I = 1st day of observation (day 1) *or* day −1 *or* day −2 *or* day −3
II = 2nd day of observation (day 2)
III = 3rd day of observation (day 3) *or* day 4
IV = 8th day of observation (day 8) *or* day 7 *or* day 9
V = 11th day of observation (day 11) *or* day 10 *or* day 12 *or* day 13

and fourth intervals (see footnote to table v) the percentage of positive cases was less in the treated than in the control groups for early, intermediate, and late cases. The differences for cases of all types at these intervals were statistically significant (differences/standard errors = 2·3 and 3·4). In the treated group of early cases the percentage of cases from which *H. pertussis* was isolated increased from 4·4 in interval IV to 10·4 in interval V. As the same children were not swabbed in the two intervals this did not mean that some cases became swab-positive after treatment had been completed. When the cards were scrutinised it was found that none of the children who became swab-negative were positive when swabbed later.

TOXIC EFFECTS

Presumed toxic effects were noted in 28 cases—12 in the chloramphenicol group, 15 in the aureomycin group, and 1 in the control group. The effects noted were:

Vomiting.—7 on chloramphenicol, 11 on aureomycin, and 1 control.

Anorexia.—3 on chloramphenicol and 2 on aureomycin.

Diarrhœa.—2 on choramphenicol.

Redness of Buttocks.—1 on aureomycin.

Urticarial Rash.—1 on aureomycin.

Summary and Conclusions

In a strictly controlled investigation 98 children 0–5 years of age were treated with chloramphenicol, 96 with aureomycin, and 100 with an inert powder (lactose and quinine). The patients were given the drugs twice daily for 7 days. For 20 days from the 1st day of treatment the number and severity of paroxysms and the occurrence of toxic effects and complications were noted. In addition, swabs for isolation of *H. pertussis* were taken on admission and at intervals afterwards.

When cases which had symptoms for 1–21 days before the beginning of treatment were considered together, the benefit to the treated cases, though consistent during the period of observation, was small. If attention had been directed solely to the straightforward comparison of the whole of the treated and control groups it would have been concluded that the results were disappointing and that chemotherapy failed to produce a clear-cut clinical cure. In cases which were treated within 8 days from the onset of the earliest symptoms the differences between the groups were greater, and some of the differences were statistically significant. Even with early cases, however, the effect of the drugs was not dramatic. No difference was detected between the effect of aureomycin and chloramphenicol.

On the 3rd and 8th days of observation but not on the 1st, 2nd, and 11th days of observation the proportion of patients from whom *H. pertussis* was isolated was greater in the control group than in the treated group.

These findings are in general agreement with those of Wehrle et al. (1951) and LaBoccetta and Dawson (1952), and it may be reasonable to speculate on the significance of the results in relation to our scanty knowledge of the pathogenesis of the disease. In an acute infectious disease it might be expected that elimination of the infecting agent would be followed by rapid disappearance of the signs which that agent initiated. The failure to observe such an immediate amelioration in whooping-cough might support a view that infection with *H. pertussis* sets in train a sequence of events which, once it has started, is not greatly affected by elimination of the pathogen. The present study suggests that early recognition and early antibiotic therapy of whooping-cough may help to reduce the severity of the infection, but that little is to be gained from antibiotic treatment of cases in which even slight symptoms have been present for more than a week.

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Wehrle, P. F., Lepper, M. H., Bundesen, H. N. (1951) *J. Pediatrics*, 39, 435.

FAMILIAL CRETINISM

DOUGLAS HUBBLE
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WHEN cretinism occurs in regions where goitre is not endemic it is known as *sporadic* cretinism. This is the common type of cretinism seen in this country, and it is usually accompanied by no evidence of a goitre. Hilton Fagge, of Guy's Hospital, observed in 1871 that no vestige of a thyroid gland could be found in sporadic cretins, and he contrasted this with the "bronchocele" seen in endemic cretinism. The published reports of the histology of the thyroid gland confirm that there is an atrophy of this gland without any evidence of colloid formation or other active gland structure. It may be assumed, as a working hypothesis, that such atrophy of the thyroid gland could either be due to a primary failure of the thyrotropic hormone or else to some failure in the gland, either developmental or destructive. A primary failure of the thyrotropic hormone has not yet been established as a cause of cretinism. Where there is a primary failure of the gland, it may be assumed that there is an excess of thyrotropic hormone circulating, because the secretion of this anterior pituitary hormone is inversely regulated by the amount of circulating thyroxine. The gland, however, is incapable of response to this stimulus.

Endemic cretinism occurs in regions where goitre is endemic because of a deficiency of naturally occurring iodine. The goitrous thyroid resulting from severe iodine as many quips in pædiatric circles about the neglected lumbar puncture as there are about that old favourite, the rectal examination.

London, S.E.24. R. J. K. BROWN.

ANTIBIOTICS IN CHRONIC RESPIRATORY INFECTIONS

SIR,—The ætiological significance of bacteria found on sputum cultures in bronchial infection is difficult to appraise, as you suggested in your leading article of March 14, which mentions some of our observations.[1]

To determine the bacteriological cause of chronic bronchitis or bronchiectasis is especially difficult when numerous colonies are found on blood-plates. Since the bacteria that produce chronic bronchial infection may also be found in sputum cultures from patients whose expectoration is entirely allergic in origin—for example, the viscid expectoration of patients with asthma due to ragweed pollen—emphasis has been placed on the presence of gross pus or polymorphonuclear leucocytes in sputum smears, in the belief that bacterial infection is more probable only under these circumstances.

We have assumed the pneumococcus to be the cause of both acute and chronic bronchial infections when a purulent sputum becomes mucoid at the same time as the organism disappears from the culture. In cases in which a prolonged symptomatic remission follows antibiotic treatment, the pneumococcus found before treatment does not generally appear on sputum cultures, except when an acute reinfection occurs.

The *Staphylococcus aureus*, however, does not, in our experience, follow the same pattern. This organism has been repeatedly found on cultures over a period of two to nine years, especially in cases of bronchiectasis. Antibiotic treatment, either by aerosol, penicillin, or the broad-spectrum antibiotics, has often been followed by conversion of sputum from purulent to mucoid, with temporary disappearance of the organism on culture in some cases; in others, *Staph. aureus* may still be present, though in a less abundant growth than before treatment. *Staph. aureus* appears to be the only gram-positive organism that has developed resistance to penicillin and often to terramycin; under these circumstances, the sputum becomes grossly purulent, with abundant growth of staphylococci on blood-plates. When the organism is eradicated by penicillin aerosol (1 million units daily) or by carbamycin, its importance in these cases is demonstrated, provided symptomatic improvement is also noted.

Streptococcus viridans has seemed to us to be pathogenic in cases of chronic bronchial infection in which disappearance of this organism was accompanied by a decrease or elimination of pus in the sputum and by clinical improvement. In some of these patients, the stoppage of antibiotic treatment was followed by reappearance of purulent sputum with apparently the same organism again found in abundant growth on blood-plates. But our therapeutic programme may have suppressed a *Hæmophilus influenzæ*; though this organism did not grow it may have been responsible for some of these cases.

In the treatment of patients with bronchiectasis by aerosol penicillin continued for two to nine years, the sputum may be predominantly mucoid with few or a moderate number of polymorphonuclear leucocytes on smear, and, on culture, a variety of gram-negative organisms without, however, evidence of active infection. When invasion by gram-negative organisms, such as *Bacterium pneumoniæ*, does take place, as shown by purulent sputum and symptoms of bronchial infection, the broad-spectrum antibiotics are generally effective in eliminating this secondary infection. The use of the broad-spectrum drugs is also valuable in the treatment of acute infections with the common gram-positive bacteria, but prolonged treatment of chronic respiratory disease may result in new infections with bacteria previously known more as contaminants than pathogens—namely, proteus, *Bact. aerogenes*, *Pseudomonas pyocyanea* and colon and paracolon bacilli.

Since *Hæmophilus influenzæ* is at times the cause of chronic bronchial infection (though found less commonly in our cultures than reported by Mulder et al.[2]) the latest antibiotics, carbamycin and erythromycin, assume increasing importance. These drugs are now preferred to broad-spectrum drugs, primarily because they do have a more limited range—i.e., against gram-positive bacteria. Furthermore, carbamycin and erythromycin seem to be generally effective in infections due to staphylococci resistant to penicillin and terramycin. In addition, the increasing incidence of allergic reactions to penicillin encourages the trial of these agents in place of penicillin for bronchopulmonary infections with gram-positive organisms. Our knowledge of the part played by the bacteria that are found in sputum cultures may be increased by the use of drugs of limited range, rather than broad-spectrum antibiotics which are effective against both gram-negative and gram-positive organisms.

It is evident that further investigation is required to determine with precision the rôle of the various organisms in maintaining chronic bronchial infection. The interpretation of sputum cultures calls for smears, stained from the same sputum and examined for polymorphonuclear leucocytes. The correlation between the disappearance of pus and the disappearance of bacteria on culture does not always give the bacteriological answer, but this approach, combined with the clinical result, seems to offer more promise than any other. Admittedly, at times, a contaminating organism, such as proteus, may overgrow a blood-plate and obscure the true cause such as a staphylococcus. This seems to have happened in three of our cases in which penicillin was effective in clearing pus from the sputum; although in vitro the proteus organism was highly resistant to penicillin.

New York. ALVAN L. BARACH.

THE EXPERT WITNESS

SIR,—The position of the expert witness was discussed in your annotation of Jan. 10, and it has been caustically satirised by A. P. Herbert.

In a recent case the court heard two expert witnesses, both psychiatrists of consultant status, giving directly conflicting opinions on vital points, particularly with reference to the question of insanity under the McNaughten rules. That the McNaughten rules themselves constitute an archaic and unsatisfactory yardstick for the assessment of insanity is irrelevant at the moment. As a medical (non-psychiatric) witness in this case, I myself found considerable difficulty in forming a sincere opinion of the accused's mental state after evidence had been given on this matter. How great must have been the confusion in the minds of the jurymen?

Surely the time has come—is indeed overdue—for the establishment of court experts or panels of experts, medical and otherwise, owing allegiance to neither Crown nor defendant but trying to assess the difficult technical problems which arise, according to their merits. Clearly the present system can only bring public ridicule to our profession and embarrassment to jurymen, and generally impede the execution of what is in many other ways one of our incomparable assets—British justice.

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[1] Barach, A. L., Bickerman, H. A., Beck, G. I. *Arch. intern. Med.* 1952, 90, 808.

[2] Mulder, J., Goslings, W. R. O., van der Plas, M. C., Lopes Cordozo, P. *Acta med. scand.* 1952, 143, 32.

deficiency can fail to produce thyroxine,* at any time in the patient's life, owing to the exhaustion of the completely disordered gland. When an iodine deficiency goitre has been present in more than one generation, the thyroid of the fœtus may be thus early exhausted, and the child will in consequence be born a cretin with a large degenerate goitre. The enlarged thyroid of iodine deficiency has been shown by radioactive studies to be avid for iodine. Atrophy of the thyroid may also be associated with endemic cretinism, and de Quervain (1924) observed that retardation of development (in all systems except the central nervous system) was greater in cretins with atrophic thyroids than in cretins with goitres. This introduces the useful notion, supported by several other clinical observations, that the deficiency of thryoxine production may be quantitative, and that a relative insufficiency does occur. Endemic cretinism must be rare in England, but Murray et al. (1948) referred briefly to two families in which endemic cretinism may have occurred.

Sporadic cretinism or hypothyroidism is rarely associated with a goitre. Still more rare is *familial cretinism* (outside endemic goitre regions), and it appears from the published reports that these cases are associated with a goitre.

Lerman et al. (1946) described two cretinous brothers, both with goitres. Biopsy specimens of the thyroid glands showed areas of hypoplasia. The uptake of radioactive iodine was high, and the concentration of iodine in the removed thyroid was low.

Stanbury and Hedge (1950) reported from Boston the investigation of four cretinous children in one family. The parents were first cousins and their first three children were not hypothyroid, nor had they goitres. The succeeding four children were all goitrous cretins. As a result of radioactive iodine studies Stanbury and Hedge conclude that the thyroids of their patients could extract iodide from the blood but could not incorporate it into thyroxine.

McGirr and Hutchison (1953) describe the results of their radioactive iodine investigations in seven children with goitrous cretinism from three related families and in two half sisters of a fourth family, and conclude that their patients could link iodine to protein and release it into the circulation in an organic form which was not thyroxine. They postulate an intrinsic defect in the final synthesis of the thyroid hormone which is sometimes familial.

I describe here a family of four cretins. In the thyroid gland and in the plasma of the eldest girl the presence of thyroxine was shown, and radioactive iodine studies in the second cretin, a boy, have shown an overactive gland capable of taking up iodine, binding it to protein, and releasing the protein-bound iodine into the circulation.

These four children, G. W. K., G. K., P. K., and J. K. (fig. 1), were first sent to the hospital when their ages were 17 years, 13 years 4 months, $8^1/_2$ years, and $6^1/_2$ years.

Their father and mother are not related. Their father was born at Bentley, Yorks, and their mother at Shirebrook, Notts. The father is an engineer, and the mother worked, before her marriage, on farms at Reddington, Mansfield, and Retford. In all these farms the drinking-water came from a well. Neither parent has had a goitre at any time, nor has there been any thyroid disorder in either of them or in their families. The father has eleven siblings, all of whom are healthy, and his father and mother had no relevant diseases. The mother has three siblings, all of whom are well. The father's height is 5 ft. 3 in., and the mother's 5 ft. 1 in.; in the appearance of neither is there any suggestion of hypothyroidism.

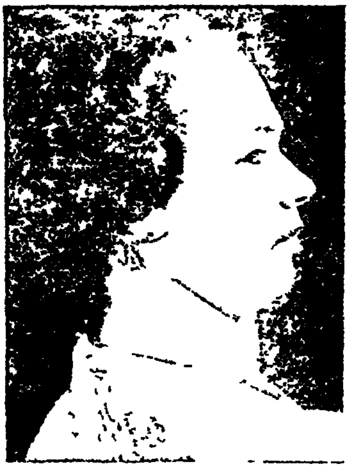

Fig. 2—Profile of G. W. K., showing degree of thyroid enlargement when all thyroid therapy had been stopped for six months.

The family has not lived in an area where goitre is endemic, nor is there anything in the history which suggests the implication of a goitrogenic substance.

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* For the sake of convenience "thyroxine" will be used to indicate the active secretion of the thyroid gland. It is not intended to imply that other substances, such as triiodothyronine (Gross and Pitt Rivers 1952), may not be active.

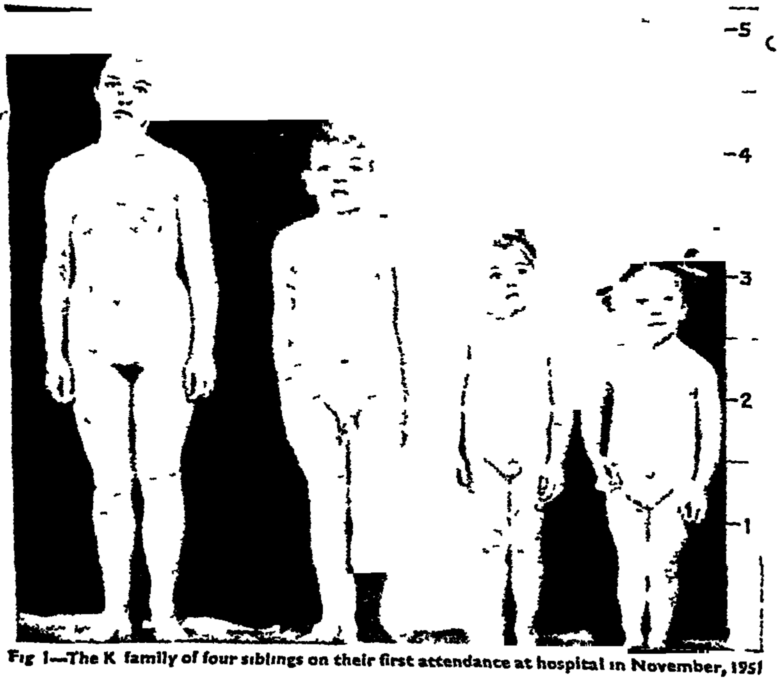

Fig. 1—The K. family of four siblings on their first attendance at hospital in November, 1951.

CASE-RECORDS

G. W. K.—Female, aged 17 (fig. 2). Hypothyroidism was probably diagnosed at the age of 8 years. She is said to have walked and talked at 2 years. She could not read at the age of 7 years but could count up to ten; her intelligence quotient was then reported to be 69%; her height was $36^1/_2$ in. (more than 20% below average). She continued to take thyroid gr. $^1/_2$ thrice daily until May, 1951, when her mother noticed that the neck was swelling. The thyroid therapy was stopped, and the swelling increased steadily in size. Her menses began at the age of 14 and are regular.

When she was examined on Nov. 17, 1951, her facial appearance suggested myxœdema. Her voice was harsh, her intonation guttural, and her speech slow. Her thyroid gland was large and nodular. Her height was 4 ft. 8 in. at 17 years.

Blood cholesterol was 316 mg. per 100 ml., and the basal metabolic rate (B.M.R.) was −23%.

Blood count.—Red cells 4,300,000 per c.mm.; Hb 12.1 g. per 100 ml.

Radiography.—The scale epiphyses of ischium and ilium had not appeared. This retardation, together with evidence elsewhere, gave a bone age of 15 or 16 years.

Electrocardiography showed low voltage throughout, with well marked flattening of P and T waves in all leads.

LOCALISED MUSCULAR ATROPHY IN DIABETES

SIR,—I read with some interest the article by Dr. Hirson (May 16). I have been interested for some time in insulin lipodystrophy, and it appears to me that he is in fact describing the very common condition of insulin fat atrophy. His conclusions are largely drawn from the fact that the areas of atrophy are not "habitually" used for insulin injection by the patient. This is, of course, no proof that these atrophic areas are not in fact directly due to insulin, because even one or two insulin injections, particularly early in the régime, may give rise to quite definite atrophy many months later. In his case 3, I agree that the area over the right masseter is unlikely to have been used for insulin injection, but is it not possible that this is an area of ectopic fat atrophy, which, as he states, has been described by observers in the past? It also appears rather unlikely that, in the case of long skeletal muscle, atrophy would present itself as small elliptical or circular areas; surely one would have expected atrophy to have occurred in the longitudinal axis of the muscle? The photographs he presents are in fact fairly typical of pronounced insulin fat atrophy.

It is possible that a series of biopsies taken from these areas might have helped to prove his case of muscular atrophy, but I feel that it is highly probable that they would show the presence of a fat atrophy without involvement of muscle.

Sheffield. J. N. HARRIS-JONES.

ALCOHOL AND THE MOTORIST

SIR,—At the international conference on alcohol and traffic, held at Stockholm in 1950, Dr. A. Simpson Wells, a South African representative, stated[1] that "recently legislation has been passed in the Union of South Africa permitting a medical officer to take samples of blood to determine the blood alcohol concentration . . . the consent of the driver involved in the accident is not necessary." This statement was quoted in the *British Journal of Addiction* in 1950,[2] and again in your correspondence columns in 1951,[3] when Dr. Pullar-Strecker said:

> "According to Dr. A. Simpson Wells, the Union of South Africa has quite recently added to its legal code a law which permits a medical man to take a sample of blood from anyone who is suspected of being under the influence of alcohol and who has been involved in a road accident. This is quite an innovation; as recently as 1949 attention was drawn to the fact that chemical tests for determining intoxication have never been used in South African courts, because of the common-law principle which protects the accused from giving any evidence which may incriminate him."

Since my return to the Union of South Africa, I have drawn the attention of a representative of the Attorney-General's office to the above statements, and with his permission I quote his comments:

> "The above statements are incorrect. There has been *no recent* legislation permitting the taking of a sample of blood. What happened was that there appeared last year (1952) a Bill which set out a proposed amendment to the Criminal Procedure Act; this amendment would have provided for the taking of blood samples. Unfortunately this Bill was not proceeded with, and the amendment never became law.
>
> "Though there has been no recent legislation and, while there is no specific provision for the taking of blood, I have always held the view (which I know to be shared by at least one counsel of repute) that under present legislation this can be done.
>
> "Sec. 2 (1) Act 39 of 1926 provides that a medical officer of a gaol or any district surgeon may take such steps as he may deem necessary in order to ascertain whether the body of any person . . . shows any condition. I take it that drunkenness is a condition of the body, and if so then to my mind the district surgeon is entitled to take a blood sample to enable him to ascertain that condition. I may add that I have never been able to persuade a district surgeon that he has the power!"

I am bringing the above to your attention, because it is my opinion that the taking of blood samples to determine the degree of intoxication is of a significance analogous to that of X-ray examination in the case of bone injuries —i.e., sometimes confirmatory and sometimes even conclusive.

Johannesburg. J. J. PRAG.

INACCURACY IN THE LABORATORY

SIR,—In the last few years there has been an increasing appreciation amongst clinical pathologists of the extent to which quantitative laboratory investigations may be inaccurate. In your leading article (March 7) you discuss some aspects of the problem. Dr. Harrison (April 18) suggests that the calibration of glassware, especially of pipettes, and the purity of chemicals are important causes of the errors.

We use grade "B" glassware as a routine and repeated checks in the past have not shown serious errors. Dr. A. Pomerance and Mr. D. A. Podmore have carried out a special examination of 22 pipettes taken at random from those in daily use, with the following results:

(1) *Bulb pipettes* (*one mark*).—15 pipettes (capacity 1–20 ml.).

Amount delivered excessive: 9 pipettes (range of error + 0·09 to + 0·8%; mean error + 0·28%).

Amount delivered deficient: 6 pipettes (range of error − 0·05 to − 0·8%; mean error − 0·40%).

(2) *Straight pipettes calibrated throughout the whole length.*—7 pipettes (capacity 1–25 ml.) on which 16 tests from one mark to another were carried out (amounts delivered 1–10 ml.).

Amount delivered excessive: 5 tests (range of error + 0·06–1·4%; mean error + 0·86%).

Amount delivered deficient: 11 tests (*range of error* −0·16–1·4%; *mean error* −0·67%).

These results make it seem unlikely that inaccurate glassware is responsible for the variation which Dr. Wootton and Professor King found between the results of different laboratories (March 7).

Many reagents can now be prepared from chemicals of known standards of purity; experience suggests that these standards are reliable. It is unlikely that lack of purity of chemicals is causing gross inaccuracies.

There are other causes of error to be considered. Many laboratories use accurate, but unsuitable, glassware with resultant loss of accuracy in the manipulations; the straight, calibrated pipettes, tests with which are described above, are a good example. In the choice of suitable glassware the studies of Professor Conway[1] deserve more attention than they have received.

For several years control solutions and bloods have been exchanged between two laboratories in Sheffield and one in a neighbouring town; the results have shown a good deal of variability although the methods have been carefully studied. I have found it impossible to resist the conclusion that the biggest errors are caused by lack of care in the various manipulations; confirmation of this view has been provided by replicate determinations. Better results are obtained by experienced staff and by staff who are not harassed and overburdened with excessive work.

Quantitative laboratory methods have been studied extensively, but the results are scattered through the literature; much remains to be done. Published methods frequently demand considerable modification before they are applicable: the laboratories concerned may not have the time to undertake the necessary studies, and there is uncritical use of the methods without adequate controls. Clinical pathologists need to have at their disposal detailed accounts of well-tried methods

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[1] Proceedings of the First International Conference on Alcohol and Traffic. Stockholm, 1950; p. 162.

[2] *Brit. J. Addict.* 1950, 47, 46.

[3] Pullar-Strecker, H. *Lancet*, 1951, i, 1369.

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[1] Conway, F. J. Microdiffusion Analysis and Volumetric Error. London, 1950.

Electro encephalography (Dr. F. Graham Lescher) showed in all channels slow activity of raised amplitude and varying from 2 to 6 cycles per sec.

Treatment and Progress.—The thyroid gland was removed by Mr. J. R. Ratcliffe in January, 1952 (see below). The patient has lost the appearance of myxœdema with a dose of thyroid gr. 1 twice daily. Her voice remains guttural. Her blood cholesterol level has fallen to 125 mg. per 100 ml. Electrocardiography now shows normal voltage. She has grown 2 in. in a year. She is well and working happily as a polisher in a pencil factory.

G. K.—Male, aged 13 years 4 months. Birth weight 10 lb. He walked at 2 years. There were other evidences of physical and mental retardation, but his mother did not notice anything wrong. He was aged 4 years 4 months when his sister's hypothyroidism was diagnosed; he was taken to the school clinic, and cretinism was also diagnosed in him. There is no evidence that enlargement of the thyroid gland was observed. Thyroid therapy was started with gr. $^1/_2$ daily; the daily dose was later increased to gr. 1 and gr. $1^1/_2$ alternately. He attended the clinic till 1948, when attendance ceased.

In November, 1951, his appearance was hypothyroid. He disliked cold weather and was wearing two woollen sweaters. His voice was harsh and his speech guttural. His extremities were cold and pale. His height was 48.5 in. (average height for his age 59.8 in.). This represented a retardation of more than 20% and a height age of 7 years. The ratio of upper segment to lower segment was 1 : 1. His weight was 73 lb. (average for age 100 lb.). His head circumference was 22 in. and the length of his penis was 3 in. Both testes were in the scrotum. There was a small soft enlargement of the thyroid gland, which was just visible.

Blood cholesterol level was 266 mg. per 100 ml.

Blood-count.—Red cells 4,500,000 per c.mm.; Hb 82%.

Radiography showed no olecranon process in the ulna and no trochlear centre in the humerus; the bone age was 9 years.

Electrocardiography normal except for a conduction defect in lead V_1.

Electro encephalography (Dr. F. Graham Lescher) gave an abnormal record with much slow activity, 5–6 cycles per sec. from all channels, with some occasional slower activity, 3–4 cycles per sec. of increased amplitude.

Intelligence quotient (Dr. Flora Macdonald) 81.

Treatment and Progress.—The patient is now (November, 1952) having thyroid gr. 1 thrice daily. He has grown 3 in. in a year, and there is considerable quickening of activity, intelligence, and body warmth. His blood cholesterol level is now 146 mg. per 100 ml. and his bone age 11 years.

For the radioactive iodine studies see below.

P. K.—*Female, aged* $8^1/_2$ years. Thyroid therapy was started at the age of 1 year. She continued to take no more than gr. $^1/_2$ daily. She has a family reputation for quick-wittedness.

When examined on Nov. 17, 1951, her height was 40 in. (average for a girl of her age 51 in.). Her height was that of a girl aged $4^1/_2$ years, and her retardation was more than 20%. The ratio of upper segment to lower segment was 1.1 : 1. Weight 43 lb.—i.e., 20 lb. below average for girls of her age. The abdomen was protuberant and there was a small umbilical hernia. The skin was dry. The extremities were cold but there was no cyanosis. There was an increase of hair growth on the extensor surfaces of the arms. The thyroid gland was soft but enlarged in both lobes, palpably but not visibly.

Blood cholesterol 284 mg. per 100 ml.

Blood count.—Red cells 3,200,000 per c.mm. Hb 72%.

Radiography of Carpus.—Hamate and capitate only had appeared. Bone age 2–3 years.

Electrocardiograms within normal limits.

Electro encephalogram (Dr. F. Graham Lescher) within normal limits.

Intelligence quotient (Dr. Flora Macdonald) 73.

Treatment and Progress.—Her height has increased by $4^1/_4$ in. in a year (November, 1952). Her bone age is now 4 or 5 years. Her thyroid is no longer palpable. She is having thyroid gr. $^1/_2$ thrice daily—a larger dose gives her a headache and makes her fretful. The blood cholesterol is 125 mg. per 100 ml.

J. K.—Female, aged $6^1/_2$ years. Thyroid therapy was started at the age of 1 year.

When examined on Nov. 17, 1951, her height was 37.5 in.—8 in. (17%) below average. The ratio of upper to lower segment was 1.2 : 1 (average at $4^1/_2$ years). Her lips were pink and her extremities cold. The abdomen was not so protuberant as that of P. K., and there was no umbilical hernia. The skin was dry, and the extensor surfaces of the arms were hairy. There was a small soft enlargement of both lobes of the thyroid.

Blood cholesterol 239 mg. per 100 ml.

Blood count.—Red cells 3,900,000 per c.mm.; Hb 85%.

Radiography of Carpus.—Hamate and capitate only had appeared. Bone age 2–3 years.

Electrocardiograms within normal limits.

Electro encephalogram (Dr. F. Graham Lescher) abnormal. There was much slow activity, of raised amplitude and from all channels. The rate was 3–6 cycles per sec.

Intelligence quotient (Dr. Flora Macdonald) 69.

Treatment and Progress.—She is having thyroid gr. $^1/_2$ thrice daily (November, 1952). She has grown $4^1/_4$ in. in a year, the thyroid gland is not now palpable, and the blood cholesterol is 140 mg. per 100 ml.

DIAGNOSTIC STUDIES

G. W. K.—The thyroid gland was removed on Jan. 22, 1952. Dr. G. R. Osborn reported on its histology as follows (see fig. 3):

> "Microscopically the normal lobular pattern is present except in the nodules; it is obscured by the degenerations which are present, however. The acini present vary greatly in size, though many are within normal limits. Very few contain any colloid; when present it is polychromasic and dense. The acinar cells are mostly flattened or cuboidal, the shape is mainly affected by the extraordinary degree of nuclear variation which is present. Many nuclei are upwards of 4–6 times normal size; they are hyperchromatic and not unlike those seen at the height of thiouracil action. There is some fibrous replacement of acini; much of this is slight, but some is extensive. Large numbers of cysts about the size of a pin's head appear to be the result of distension of acini with serous fluid; very few of these contain colloid. The nodules which are present appear to have arisen in the usual way, but they show nuclear variation of lesser degree and much larger serous cysts. Lymphocytic infiltration is inconspicuous. Arteriosclerosis is present, but early."

The histological appearances of this thyroid gland do not greatly differ from the degenerate areas in the much larger glands removed from the goitrous cretins described by Stanbury and Hedge (1950), who regarded the

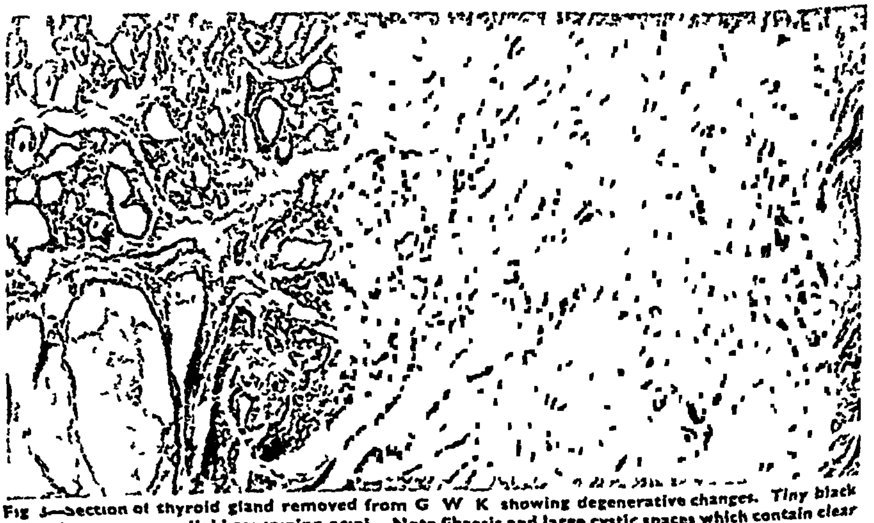

Fig. 3—Section of thyroid gland removed from G. W. K. showing degenerative changes. Tiny black circular areas are colloid-containing acini. Note fibrosis and large cystic spaces which contain clear serous fluid but no colloid. (×90.)

giving full indications of the difficulties likely to be encountered, of the precautions needed, and of the type of apparatus (e.g., pipettes) to be used.

In discussing these problems a statistical approach is essential. Replicate determinations and comparisons between different laboratories yield answers whose random variation is commonly greater than many pathologists are willing to admit.

The suggestion, in your leading article, of a review of these problems is timely and valuable. It is to be hoped that the Association of Clinical Pathologists, in collaboration with the other bodies you mention, will undertake the task.

Sheffield. ARTHUR JORDAN.

MEPHENESIN IN RHEUMATISM

SIR,—The considerable number of reports recently published regarding the toxicity of phenylbutazone ('Butazolidin'), and the very wide use of this drug in various skeletal complaints unconnected with rheumatoid arthritis, prompt the following comments on the results achieved with another agent, mephenesin. I used this in between 20 and 30 cases of "rheumatic" complaints, which included periarthritis and various forms of "fibrositis" with and without neuritic involvement.

The drug was supplied in 0·5 g. tablets as 'Tolserol' by E. R. Squibb & Sons.

A woman of 70, suffering from chronic fibrositis, refused to continue to take the tablets "because they were too big," and was excluded from this group.

All the remaining patients improved considerably within a short period, and the following examples illustrate typical results:

A man, aged 46, suffering from acute spasm at the sacro-iliac junction, reported much benefit within three to four days and complete relief after one week.

A man, aged 50, with acute lumbago and sciatica-like pain in the right leg, was free from symptoms after one week's treatment.

A housewife, aged 32, who had suffered from chronic low backache for six or seven years, with exacerbation following the birth of a child two years ago, had complete remission within two days.

A woman, aged about 50, with chronic fibrositis, mainly of the trapezius, and some low back pain of five years' standing, was able to look over both shoulders after four days' treatment, although she had been unable to do this for about five years.

A woman, aged 40, with anxiety neurosis and chronic fibrositis of the shoulder, was much relieved within four days. Greater improvement resulted when treatment with methylphenobarbitone was combined with mephenesin, though the barbiturate caused some feeling of lassitude.

A woman, aged 40, with a history of sciatica following a divorce five years ago, had a second attack thought to be due to a domestic disturbance in August, 1952. She had been admitted to hospital where a prolapsed intervertebral disc was diagnosed, although not shown by X-ray examination. She had sciatica of the right leg and severe sacro-iliac spasm but no clinical evidence of prolapsed disc. After four days' mephenesin, she was able to walk naturally, but full therapeutic response necessitated the administration of 6 g. daily for sixteen days.

The optimum daily dose was usually 4—6 g., given in divided doses every four hours, except during the night. Most patients responded satisfactorily within from two to seven days, and in severe chronic cases, where there may be a tendency for the symptoms to recur, it would probably be advisable to give periodic short courses as necessary, rather than to prolong treatment in the hope of permanently eradicating the disease. 2 patients had very slight vertigo, but no other toxic effects were encountered, in the cases treated with tolserol.

Mephenesin is a muscle relaxant and its blocking action breaks the spasm-pain cycle, but the drug does not appear to have any direct analgesic effect; but in my series it was not necessary to use any other drug to relieve pain, for the response to mephenesin was rapid. When this drug is used in the treatment of patients with neuroses, a suitable barbiturate can be given at the same time. But 2 patients with anxiety neurosis and definite hypertension became decidedly worse when mephenesin was *substituted* for barbiturates in the treatment of their neuroses.

In general, acute cases respond more rapidly than chronic conditions; but mephenesin appears to be very effective in a variety of fibrositic disorders, and its virtual freedom from toxicity by the oral route makes it suitable for routine use.

Worthing, Sussex. J. R. B. PECKOVER.

CIRCUMCISION OF THE NEWBORN

SIR,—The question raised by Dr. Morris (May 2) concerning bleeding from hæmorrhagic disease of the newborn following immediate circumcision—and indeed hæmorrhage due to other causes after this operation—is answered by the work of Miller and Snyder.[1] They advocate operation only upon normal, healthy, full-term infants. In their series no babies with icterus, erythroblastosis, or purpura were circumcised: the rhesus state of the mother had previously been determined; and they were able to show, from a study of 700 bleeding and coagulation times taken after delivery, that there was no inherent defect of the clotting mechanism at birth. Postoperative bleeding was of import in 0·3% of the children and was due to faulty technique.

Dr. Morris's suggestion that circumcision was delayed until the eighth day of life because of the dangers of bleeding finds confirmation in the writings of Maimonides[2] and also in the *Talmud*.[3] But hæmorrhage itself would have been no deterrent to the ritual, rather the reverse, for the shedding of blood was of significance [4] and was often all that was demanded.

The age at which circumcision is done varies so much throughout the world and is so connected with the origins of the act that (even excluding savage races and manhood-initiation ages) no one reason can be given. Among the Jews the eighth day was chosen, for in the first week of life neither animal nor man could be offered to God.[5] [6] In people of other sects or cultures, circumcision might be at the end of the seventh day of life, as in the Falashas, in the first month among the South-western Arabs, in the second month among the Mazequas, in the third year among the Persian Mohammedans, or in the seventh year among the Christian Copts.[7] The Arabs circumcised when the child was 13, for at that age Ishmael was thus operated upon. Some Islamite tribes performed the rite when the child was old enough to be able to quote religious tracts or profess his faith, and others when the boy was at an age (variously and curiously defined) of reason.

Benenden, Kent. THOMAS MARMION.

Public Health

Smallpox

No further cases have been reported from Lancashire and the West Riding where the outbreak of smallpox has so far involved 30 people, 8 of whom have died. A fortnight has now gone by without a new case. At the Chesterfield Royal Hospital, Derbyshire, precautions have been taken pending the result of investigations into the death of a 19-year-old youth on May 24.[8]

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1. Miller, R. L., Snyder, D. C. *Amer. J. Obstet. Gynec.* 1953, 65, 1.
2. Moussa Ben Maimon. On Circumcision. I.
3. *Talmud.* Jebamoth. 646.
4. *Leviticus*, XVII, 11.
5. *Genesis*, XVII, x-xii.
6. *Leviticus*, XXII. xxvii.
7. Jewish Encyclopedia. Edited by I. Singer. London, 1904; vol. IV, p. 97.
8. *Manchester Guardian*, May 26, 1953.

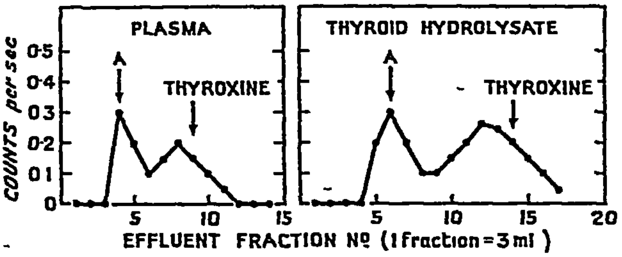

Fig 4—Result of iodine fractionation in plasma and thyroid gland of G W K by Mrs Pitt Rivers and Dr Jack Gross. Fraction A is an artefact of the process. No quantitative estimation of thyroxine was made and amounts of thyroxine in plasma and in gland are not comparable, because aliquots were used.

changes as the sequel to compensatory hyperplasia. The steady enlargement of the gland when thyroid administration was stopped in the six months before coming to hospital supports this theory. Twenty-four hours before the gland was removed, a dose of 107 µC of radioactive iodine (I^{131}) was given, and the gland, together with blood taken at the time of the operation, was sent to Mrs Pitt-Rivers and Dr Jack Gross at the National Institute for Medical Research. They reported as follows:

"The thyroid was hydrolysed in 2 *N* sodium hydroxide by refluxing for 17 hours. It was then brought to pH 1–2 and extracted with butanol. The butanol extract was concentrated to a very low volume and put on the kieselguhr column. The plasma was acidified and extracted with butanol, and the butanol extracts were evaporated (Gross and Pitt Rivers 1951, 1952) and put on the kieselguhr NaOH column.

UPTAKE AND URINARY EXCRETION OF RADIOACTIVE IODINE IN CASE G K

Date	Time to half-peaks (min.)	4 hr	12 hr	24 hr	48 hr	72 hr
			Gland content			
*Jan. 1, 1952 (fig 5)	90	48%	60%	59%	54%	52%
†Oct. 28, 1952 (fig 6)	70	52%	61%	57%	49%‡	40%‡
			Urinary excretion			
Jan 1, 1952				12.7%	15.1%	
Oct 28, 1952				17.4%	23.2%	29.7%

All percentages are of total dose.
*Dose 26.3 µC of I^{131}.
†Dose 21.2 µC of I^{131}.
‡Following administration of thiocyanate 2 g at 26 hr.

Thyroxine was identified in the radioactivity in both extracts (fig 4). Fraction A of radioactivity is an artefact of this process. The amount of thyroxine present was not estimated."

G K was investigated by radioactive-iodine techniques in Prof E J Wayne's department in Sheffield in January and October, 1952. Dr H Miller, Dr A G Macgregor, and Dr R S Weetch conducted the investigations. The first investigations were made when thyroid therapy had been stopped for more than three weeks, and before the second series all thyroid medication had ceased for twenty-four days. The results are shown in the accompanying table.

The peak uptake in both tracer tests was about 60%. The thyroid clearance rate, on the first occasion, was 75 ml per minute at one hour, and on the second occasion 76 ml per minute at one and-a-half hours. The plasma activity forty-eight hours after the tracer dose on Jan 1, 1952, was 0.91% per litre, and of this 0.64% per litre was in the protein-bound fraction. Thus 70% of the iodine fraction was in the protein-bound form. On the second occasion the patient was given potassium thiocyanate 2 g at twenty-six hours. At this time his plasma activity was 0.59% per litre, and the protein-bound iodine was 0.40% per litre, giving 68% of the radioactivity in a protein-bound form.

Potassium thiocyanate is a goitrogenic substance and discharges from the gland any radioactive iodine which is not linked to protein (Vanderlaan and Vanderlaan 1947). The result is shown in fig 6, which shows that there was only a small reduction of gland activity immediately after the dose of thiocyanate, but Dr Miller observes that "this appears to be a genuine effect and probably represents a small fraction of I^{131} in inorganic form turned out into the blood and later reabsorbed to some extent." The curve should be compared with the curve of gland activity obtained in January (fig 5), and on this difference Dr Miller comments: "The biological elimination following thiocyanate administration appears to be significantly quicker than that observed in the first test. This could be explained if the thiocyanate did have some interference on the rate of reabsorption of I^{131} from the blood to the gland."

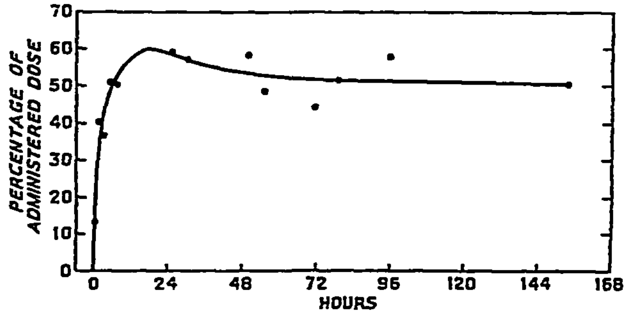

Fig 5—Gland content of I^{131} in G K. in January, 1952, after a dose of 26.3 µC. Rapid uptake of iodine falls within hyperthyroid range.

DISCUSSION

It has been shown that the thyroid gland of the eldest child of this family of four cretins can both synthesise thyroxine and liberate it into the plasma. Studies with I^{131} in the second child have shown that his gland can synthesise protein-bound iodine and liberate it into the plasma. Moreover, the activity of his gland is such that, whether judged by the time of the half-peak uptake, the twenty-four-hour urinary excretion, the clearance-rate, the total gland activity or the protein-bound plasma activity, these radioactive-iodine tests taken alone indicate hyperthyroidism in him (Goodwin et al 1951). Nevertheless the indisputable clinical evidence is that these children have hypothyroidism. These results confirm the reports by Lerman et al (1946),

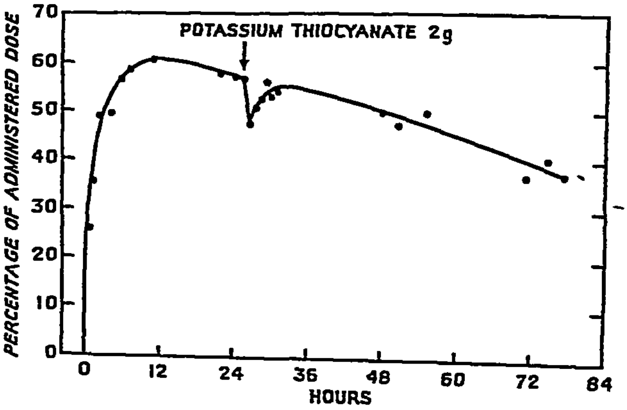

Fig 6—Radioactive-iodine uptake and discharge in G K. in October 1952. At 26 hr thiocyanate 2 g was given, and increased rate of fall compared with fig 5 may be attributed to interference with rate of reabsorption of I^{131} from blood to gland. Note that this curve is quite different from that obtained by Stanbury and Hedge (fig 7).

Notes and News

THE ROYAL SOCIETY

At the society's conversazione on May 21, the National Institute for Medical Research and the M.R.C. Blood Transfusion Research Unit from the Postgraduate Medical School of London set out some of the results of their work on the preservation of living cells in the frozen state. In the deep-freeze, red cells can be stored for months at − 79°C. Many technical difficulties have been overcome, but a few remain to be solved before the full promise of the method in blood-transfusion work is fulfilled; a rather lower temperature may prove best in the end. Moreover, there is still much to learn about what happens to the red cell under various conditions of storage. In the past it has been hard to store for more than a few days bull spermatozoa for artificial insemination in breeding experiments; but semen, deep-frozen in glycerol, has been stored for up to a year and used successfully.

Archæologists applauded and forgers fled before Mr. E. T. Hall's X-ray spectrometer from the Clarendon Laboratory; for this beautiful machine will identify in a moment or two the metals in a Roman brooch or a doubtful coin. The specimen is irradiated and, as the crystal of the spectrometer turns, the peaks of characteristic radiation in the secondary beam are picked out; and the critical wave-lengths of these peaks identify the element responsible. Of course, this method of analysis is not new, but the deftness of control and the rapidity with which this spectrometer records the results and counts the constituents of the secondary beam are impressive additions to the technique. As well as protecting the archæologist's treasures from cruder analysis and dismaying the counterfeiter, it may prove useful in industries where a quick answer is needed—for example, when the composition of a melt must be known within a few minutes.

The rare metal, germanium, has an odd and, as far as is known, unique property: when an electric current is passed through a germanium crystal under suitable conditions the transparency of the crystal to infra-red light changes. The current, it seems, increases the density of free electrons in the crystal, and more electrons mean more absorption in the infra-red part of the spectrum. This effect was very neatly demonstrated by Dr. A. F. Gibson and Mr. R. Lawrence, of the Telecommunications Research Establishment at Great Malvern. The current through the crystal came from a gramophone, and a tungsten lamp shone an infra-red beam through it too, so that the intensity of the emerging beam varied in response to the changes in the current from the gramophone. Thus, the sounds of the orchestra on the record were transformed into an infra-red beam of varying intensity, which was in effect a radio beam of extremely short wavelength. The infra-red music then disappeared into a photoelectric cell connected to a loudspeaker. And so the orchestra emerged. As the demonstrators modestly observed, the quality of their infra-red radio link was about the same as that of the B.B.C.

Mr. L. R. O. Storey, of the Cavendish Laboratory, also had a gramophone. He played a record of some alarming atmospherics—just like those exasperating noises that crackle and whine out of some loudspeakers as the announcer is reading the latest Test score. Lightning flashes are to blame for the brittle clicks, which are local phenomena; but the more melodious "whistlers" may reach the receiver by a roundabout path from a very long way off. The waves from a local click set off in a giant arc along the Earth's magnetic lines of force, pass over the Equator about 7000 miles up, and come to earth in the opposite hemisphere. During their journey through the ionosphere, the waves of high frequency travel faster than their companions of low frequency, so they arrive a few seconds earlier. What started off as a click, therefore, comes out of the receiver as a long falling note of astonishment. And the whistler may bounce to and fro along the lines of force, producing a series of strains with a dying fall on both sides of the Equator, just as though Nature were whistling incredulously at the success of her prank as she withdraws to prepare another programme in the ionosphere. The properties of these atmospherics have shown, among other things, that the Earth's atmosphere extends to a much greater height than we imagined.

Bees lead well-ordered lives, and Mr. C. R. Ribbands, of the Rothamsted Experimental Station, explained some of their social and domestic arrangements. He showed how the life of the bee community has evolved by simple stages to its present complexity. All the available food is shared among the community, and this unselfish distribution means, for one thing, that all the bees smell to each other of the same flowers, so that unlucky bees can seek out the scent of likely crops and the colony can forage as a unit.

There were plenty of animals about, and the Marine Biological Association of the United Kingdom brought along a mixed bag of sea creatures. The starfishes and brittle-stars are attractive enough, but they are unpopular for their interference with man's pleasures. The starfish likes oysters and mussels, and the lethargic brittle-star takes up a lot of bedspace that would otherwise be a feeding-ground for more appetising fare.

The most disconcerting exhibit was undoubtedly the one demonstrating the effect of an echo on a speaker. Dr. E. C. Cherry and Mr. A. J. Fourcin, of the Imperial College of Science and Technology, put the nimblest speaker out of his stride by returning his own words to him through headphones $^1/_5$ second after they had been uttered. Normally he hears his words almost as soon as he speaks, and, if he is wise, his thoughts run slightly ahead of his words. The delicate speech mechanism has been built up under these conditions, and if he is reminded in this way of what his past experience has conditioned him to forget, everything may go awry. The effect in this experiment was certainly devastating: commentaries that ran confidently for a few seconds were cut short by hesitancy or complete silence, and sometimes by unintelligible stammering or slurring. Clearly the device would have its uses in curbing the less engaging after-dinner speakers.

WORLD HEALTH ASSEMBLY

The sixth World Health Assembly, which is meeting in Geneva, is to consider a recommendation that the production of heroin be abolished throughout the world. The proposal has been put before the assembly by the committee on programme and budget, and, if approved, it will be passed to the Economic and Social Council of the United Nations and its commission on narcotics. The abolition of legally produced heroin would do much to facilitate the control of its illegal use. The committee also asked for a study of the steps necessary to launch a campaign against smallpox. Governments and regional committees of W.H.O. will be asked about their views before the executive board begins its study, the results of which will be presented to next year's assembly.

MINISTRY OF PENSIONS HOSPITALS

Three months ago the Prime Minister announced that the Ministry of Pensions would be amalgamated with the Ministry of National Insurance to form a new Ministry of Pensions and National Insurance, and that the medical treatment it has undertaken—including the management of hospitals and the supply of artificial limbs, surgical appliances, and invalid vehicles—would be transferred to the Ministry of Health and the Department of Health for Scotland.

Since the National Health Service was set up in 1948, war pensioners, like other members of the community, have been entitled to the care of practitioner and hospital without charge, and have had less need of separate care: indeed, of some 35,600 war pensioners receiving inpatient treatment in the year ended in March, only 14,200 had it in Ministry of Pensions hospitals compared with 21,400 in N.H.S. hospitals, including sanatoria and mental hospitals. The Ministry of Pensions hospital service has accordingly contracted; four hospitals, with a total of about 1600 beds, have been transferred to the N.H.S.; and in the eight hospitals which, with certain units elsewhere, the Ministry of Pensions has retained, about 3000 N.H.S. patients have been treated during the past year. Even so it has been difficult to keep these eight hospitals full, and it is hoped that their closer integration with the N.H.S. will increase the occupancy of their beds.

A white-paper[1] sets out the proposed transfer of functions. The hospitals now to be transferred to the health departments are: Queen Mary's, Roehampton; Chapel Allerton, Leeds; Mossley Hill, Liverpool; Dunston Hill, Gateshead; Rookwood, Cardiff; Mount Pleasant, Chepstow; Edenhall, Edinburgh; and Leopardstown Park, Dublin. In England and Wales the hospital staffs and the headquarters staffs engaged in hospital administration will be transferred to the Ministry of Health, and in the first instance the hospitals will be directly administered by that department, though it is

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[1] Cmd. 8842. 1953. H.M. Stationery Office. Pp. 11. *6d.*

Stanbury and Hedge (1950), and McGirr and Hutchison (1953) that children with familial goitrous cretinism have very active thyroid function

When the chemical results of this thyroid overactivity are considered, a very different picture emerges The three cretinous siblings described by Stanbury and Hedge (1950) could extract iodide from the blood, but, when thiocyanate was administered at four hours, 70–90% of the radioactive iodine was discharged into the blood two hours later, indicating that nearly the whole of the iodine had not by this time become organically bound (fig 7) The nine familial goitrous cretins described by McGirr and Hutchison (1953) could bind iodine to protein, and six of them were proved to be capable of releasing the organically *bound iodine into the blood* These workers concluded that part of the protein-bound fraction in two of their cases might be diiodotyrosine, and in the plasma of a third patient Mrs Pitt-Rivers and Dr Gross excluded the presence of thyroxine and triiodothyronine In one of the four children reported here the same workers identified thyroxine in both the gland and the plasma, though they could not estimate its amount

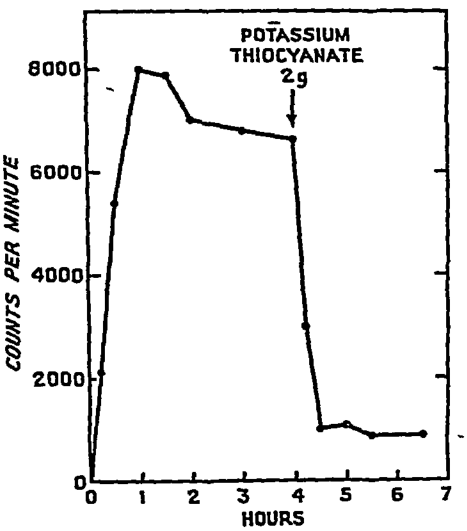

Fig 7—Curve from Stanbury and Hedge (1950), in counts per minute and not in percentage of administered dose, shows immediate fall in gland content of radioactive iodine which occurs in goitrous cretinism when little iodine has become protein bound

Clinicians will be grateful for any help which can be obtained from radioactive iodine studies in doubtful cases of thyroid overactivity or underactivity It is apparent from these results that the diagnosis of hypothyroidism and cretinism must remain predominantly a clinical problem All who have studied the records will agree that these familial goitrous cretins had hypothyroidism, and they responded normally to the administration of thyroid There was in them no peripheral resistance to the utilisation of thyroid

In none of the published cases, except G W K, has thyroxine been identified, but in none of the published cases, except case 5 of McGirr and Hutchison (1953) and then only in the plasma, has it been proved to be entirely absent Hamilton et al (1943), in their pioneer radioactive iodine studies of hypothyroidism in children, investigated two severely hypothyroid children with goitres and discovered thyroxine in the removed glands It may eventually be shown that the thyroid glands of all these goitrous cretins, whether familial or not have at one time been capable of making thyroxine, but in inadequate amounts It is obvious from the published cases that the degree of cretinism varies being severe in the cases of Stanbury and Hedge (1950) and no more than moderate in mine The full clinical account of the cases reported by McGirr and Hutchison (1953) will be awaited with interest, but from the details of height age and bone age already given, it appears that in their cases too the degree and the time of onset of hypothyroidism varied greatly

From the histological appearances of the thyroid gland removed from G W K it can be assumed that the production of thyroxine would be progressively impaired, and that the clinical picture of hypothyroidism would develop gradually This agrees with the observation of de Quervain (1924) that the retardation in endemic cretinism is slower in the patients with goitres than in those with atrophic thyroid glands It is usual to attribute the late diagnosis of cretinism to parental negligence or to medical ineptitude This concept of a progressive and relative hypothyroidism in goitrous cretinism permits a more charitable opinion In G W K the diagnosis was made at the age of 8 years, and in G K at the age of 4 years, and in P K and J K not until the age of 1 year, despite the previous recognition of hypothyroidism in the older children In the two brothers described by Lerman et al (1946) symptoms were first noticed at the ages of 10 years and 5 years Thyroid therapy was given intermittently and, as in the family described here, when thyroid therapy was stopped the thyroid gland enlarged Reduction in the size of the gland when adequate thyroid therapy was instituted was observed in the K children, but such an observation could obviously not be expected in cases where the gland was large and degenerate In the cases described by Stanbury and Hedge (1950) cretinism was diagnosed in infancy and thyroid therapy was started then Enlargement of the gland was not observed until the ages of 7 and 13 years in their two cases in which this fact was reported These facts make probable the hypothesis that the gland does not enlarge unless the circulating thyroxine, whether produced in the body or administered, is insufficient to depress the secretion of the thyrotropic hormone An enlarging thyroid gland indicates that the dose of administered thyroid is inadequate It may be assumed that the deficiency in the synthesis of thyroxine in these cases occurs at different stages, either in the binding of iodine to protein—inability to form the "diiodotyrosine like" fraction of Chaikoff and Taurog (1949)—or in the conversion of diiodotyrosine to thyroxine (Harington 1926, Harington and Barger 1927) or to triiodothyronine (Gross and Pitt Rivers 1952)

CONCLUSIONS AND SUMMARY

A family of four hypothyroid siblings is described In the eldest child, in whom thyroid therapy had been stopped for six months, a moderate sized goitre developed In the younger children, in whom thyroid therapy had been inadequate, small soft enlargements of the thyroid gland were present which disappeared when adequate therapy was instituted

Thyroxine was present both in the plasma and in the removed thyroid gland of the eldest child In the second child considerable thyroid activity was proved by radioactive-iodine studies This dissociation between the clinical diagnosis (hypothyroidism) and the radioactive iodine diagnosis (hyperthyroidism) has been noted by other workers

In these children it is assumed that the amount of thyroxine formed must be inadequate for their needs It is suggested that the clinical records of goitrous cretinism, both endemic and sporadic, often denote a relative and progressive, rather than an absolute, insufficiency of thyroxine The enlargement of the gland is an index of the degree of thyroxine inadequacy

The stage at which these chemical defects in thyroxine formation occur obviously varies in the published cases of goitrous cretinism In some, as in the cases described here, the deficiency may be quantitative and not qualitative

Dr P Hay Heddle rescued these children from their hypothyroid state I am grateful to Sir Charles Harington, F R S Mrs Pitt Rivers, and Dr Jack Gross for their chromatographic studies, and to Prof E J Wayne, Dr H Miller, Dr A G Macgregor, and Dr R S Weetch for their radio

intended that "as and when appropriate" they shall be entrusted to regional hospital boards and management committees. When this is done, war pensioners will still have first call on the services of these hospitals, and, so long as a hospital is substantially used for war pensioners, the management committee will be specially constituted. Administration of the Scottish hospital will be entrusted from the outset to the appropriate regional board and board of management. The Roehampton Hospital, with its international reputation for the treatment of certain disabilities, and its own board of governors, will require special arrangements if and when it is brought within the N.H.S.

ACCIDENTS AT HOME

"SAFE at home," like "safe in bed," is one of those common sayings which do not stand up to examination. We think the total of those who die from accidents on the roads—about 48,000 yearly—sufficiently appalling, but those who die from accidents in the home easily outnumber them: the average during the years 1940–49 was 60,000 yearly. These figures appear in a new Home Office report,[1] from the Standing Interdepartmental Committee on Accidents in the Home; they refer only to fatal accidents because no accurate assessment is available of non-fatal accidents. More than a quarter of those who die are under 15 and more than half over 65; and more children under 15 die from home accidents than from any single infectious disease. The commonest accidents are falls, accounting for 58% of the total, burns and scalds causing 13%, suffocation 12%, and coal-gas poisoning 8%. About nine-tenths of the falls happen to old people, and so do over half the burns and scalds and nearly two-thirds of the coal-gas poisonings. Nearly all the suffocations are of babies sleeping on down pillows.

Surveys have shown that faulty design of equipment is responsible for less than 10% of domestic accidents; some 20% were due to poor maintenance, particularly of flooring, stair-treads, and hand-rails, and to bad lighting. But most of the accidents happened in the course of ordinary domestic jobs, particularly at busy times: more than half happened in the kitchen or living-room while cooking or washing was being done, or tea being made. Fireguards were shockingly scarce: in over 1000 houses where a coal fire was burning, a fireguard was in use in only just a third of those containing children under 6; and only 7% of households containing old people over 70 used guards. "It is hardly surprising," the report notes, "that so many children and old people are killed, crippled, and disfigured from burns each year."

Legislation already does something to enforce the use of guards. The Children and Young Persons Act, 1933, has a provision aimed at preventing people in charge of children under 7 from allowing such children to be in a room with an inadequately protected fire; and the age has now been raised to 12, and the wording changed to cover "any heating appliance liable to cause injury to a person by contact therewith." Guards have also been made compulsory on prescribed kinds of gas and electric fires and oil heaters sold to the public. People are also getting some teaching on the prevention of fires by the fire prevention officers who arrange exhibitions and demonstrations, give talks, and show films. The British Standards Institution are doing their part by laying down principles of good workmanship and safe design for domestic gear, and these have been adopted by reputable manufacturers. But the final responsibility for preventing accidents must always lie with individuals, and in an appendix the committee list some common causes of accidents which all of us should have in mind. These include a dustpan and brush left on an ill-lighted staircase, a loop of flex across a living-room floor (which may give a shock or prove a trip-wire), a loose mat on a slippery floor, loose stair carpets, unguarded bedroom fires, a saucepan handle sticking out beyond a stove where a child can reach it, a loose table-cloth which a child can tug, an electric fire or radio in the bathroom, medicines or garden chemicals left within reach of a child, and down pillows for babies. The committee add some precautions for those leaving the house. See that your cigarette is out, the electric iron unplugged, the gas-taps turned off, fires guarded, and television and wireless disconnected.

Empire Rheumatism Council

Sir Henry Cohen will deliver a Coronation lecture at 1, Wimpole Street, London, W.1, on Thursday, July 2, at 8.15 P.M. He will speak on the Concept of Collagen Disease.

University of London

The governing body of the British Postgraduate Medical Federation has approved the award of postgraduate travelling fellowships for 1953–54, tenable for one year, to the following:

M. B. McIlroy, M.R.C.P., of St. Bartholomew's Hospital (respiratory function, U.S.A.).

D. Marrack, M.D., of the Postgraduate Medical School of London (biochemistry, U.S.A.).

T. A. J. Prankerd, M.R.C.P., of University College Hospital (hæmatology, U.S.A.).

P. Story, M.D., of St. Bartholomew's Hospital (hæmatology, U.S.A.).

University of Leeds

On June 25, on the occasion of the meeting of the British Association of Urological Surgeons in Leeds, the honorary degree of D.SC. will be conferred on Prof. Charles Huggins (Chicago) and Mr. R. Ogier Ward.

Dr. H. N. Green has been appointed professor of experimental pathology and director of cancer research.

Professor Green graduated as M.B. at the University of Sheffield in 1924. In 1925 he obtained the degree of B.SC., with first-class honours, and a year later took the degree of M.SC. He became M.D. in 1927. From 1926 to 1933 he worked in Sheffield as clinical assistant to Sir Edward Mellanby at the Royal Infirmary and as research assistant in the university department of pharmacology. In 1933 he was appointed lecturer in pathology at the University of Cambridge where he remained until 1935, when he returned to the University of Sheffield as professor of pathology. Alongside his professorial duties he has directed cancer research in the university. He has also directed a Medical Research Council team which has investigated the nature and mechanism of shock; and from 1944 to 1945 he held the rank of lieut.-colonel in the British Traumatic Shock Unit II of the R.A.M.C. and served abroad in North-west Europe. His publications include *Biological Actions of the Adenine Nucleotides* which appeared in 1950.

Major C. K. Anderson has been appointed research fellow in genito-urinary pathology, and Dr. P. G. Keates research fellow in radiodiagnosis.

University of Birmingham

The following appointments are announced: Dr. J. H. Cort and Dr. K. White, lecturers in physiology; Dr. Constance Ross, research fellow in the departments of pædiatrics and child health and of pharmacology.

The title of honorary part-time lecturer in medicine has been conferred upon Dr. O. L. Wade, senior registrar in the medical professorial unit, United Birmingham Hospitals, during the tenure of his present appointment. The title of university research fellow, for the duration of their present appointments, has been conferred upon the following: Dr. H. Bickel, Dr. J. D. Blainey, Dr. J. P. Bull, Dr. D. S. Rowe, and Dr. I. D. Singh.

Mr. Stanley Way will give the Ingleby lectures for 1953 on Thursday and Friday, June 18 and 19, at the Medical School at 4 P.M. He is to speak on the Ætiology of Carcinoma of the Body of the Uterus.

Queen's University, Belfast

At the summer graduation the honorary degree of LL.D. will be conferred on Dame Hilda Lloyd.

Royal College of Physicians of Edinburgh

The college has approved of regulations permitting suitably qualified persons to read in, and borrow from, the library. The college library, the use of which has hitherto been restricted to fellows, was founded in 1681 and is the oldest medical library in Scotland. It is almost entirely restricted to medicine and contains nearly 200,000 volumes.

Royal College of Surgeons of Edinburgh

At a meeting of the college held on May 20, with Prof. Walter Mercer, the president, in the chair, the following were admitted to the fellowship:

A. J. C. Allison, A. E. Amoils, Ebenezer Sunderaraj Chellappa, A. F. G. C. Christie, D. C. Cooke, E. C. Edwards, J. C. Foster, J. D. Fraser, D. R. Gunn, I. A. Harris, H. H. Martin, Jit Shrimukh Mehta, M. N. Menzies, Lumir Louis Ptak, Kazimierz Rubinstein, Upendra Narain Shahi, Mohammed Raza Shirazi, J. D. C. Sim, I. M. Stewart, Gulabbhai Gopalji Vashi, R. D. Venn, W. F. Walker, Ian Wilson.

Woodberry Down Health Centre

A joint committee of the London Executive Council and the London Local Medical Committee have selected six general practitioners to work at this health centre.

Royal Medical Benevolent Fund

The annual general meeting of the fund will be held at 11, Chandos Street, London, W.1, on Tuesday, June 9, at 5 P.M., with Lord Webb-Johnson, the president, in the chair.

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[1] London: H.M. Stationery Office, 1953. Pp. 11. *6d.*

active iodine estimations All of these workers, together with Dr J H Hutchison, have by their discussions helped my understanding of these problems

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RADIOACTIVE-IODINE STUDIES IN NON-ENDEMIC GOITROUS CRETINISM

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Radioactive iodine has become widely used in the study of thyroid disorders since the original investigations with I^{128} (half life 25 minutes) were made by Hertz et al (1938), and with I^{131} (half-life 8 days) by Hamilton and Soley (1939) Goodwin et al (1951) discussed the relative merits of the various methods and reached the conclusion, supported by their own experience, that the amount of protein-bound iodine in the plasma 48 hours after the administration of radioactive iodine gives more valuable information about thyroid function than does either the uptake of iodine by the thyroid gland or its excretion by the kidneys

High values for the thyroid uptake of radio iodine have been observed not only in thyrotoxicosis but also in other thyroid disorders They have been found in non-toxic goitre of recent development (Raben and Astwood 1949) and in cretins with non-endemic goitre (Hamilton et al 1943, Lerman et al 1946, Stanbury and Hedge 1950, Stanbury 1951) They have been produced experimentally by deprivation of iodine, by blocking the utilisation of iodine with anti-thyroid drugs (Raben and Astwood 1949), and by the injection of thyrotropin (Stanley and Astwood 1949)

Abnormally large amounts of protein-bound I^{131} are found in the plasma characteristically in thyrotoxicosis, and occasionally persist in successfully treated thyrotoxic patients who no longer show any clinical evidence of hyperthyroidism (Blomfield et al 1951) Abnormally large amounts of non-radioactive iodine I^{127} have also been found in similar cases (Engstrom et al 1950, Man et al 1951) and in a patient with a simple goitre (Man et al 1951)

We have found abnormally large amounts of protein-bound I^{131} in the plasma of patients with non-endemic goitrous cretinism, who are of particular clinical interest because they presented with the unusual combination of hypothyroidism and thyroid enlargement unrelated to iodine deficiency or to the action of any known goitrogen

MATERIAL

The ages of the 12 patients ranged from 2 years and 9 months to 20 years, 5 were males and 7 females, 4 were members of one family, and 3 were closely related to them, 2 were members of another family, and 3 were unrelated to either family or to each other The patients, each of whom had an enlarged thyroid gland, presented the typical features of hypothyroidism These cases are summarised in table I The ages of onset of recognisable symptoms were sometimes difficult to determine but varied from a few months to 3 years Since the distinction between cretinism and juvenile myxœdema appears artificial in these cases, most of which occurred in the one family group, and for the sake of brevity, the patients are classified as cretins None of the patients came from an area of endemic goitre, and in none was there a history of deprivation of iodine or of exposure to a goitrogen

TABLE I—SUMMARY OF 12 CASES OF NON-ENDEMIC GOITROUS CRETINISM

Case no	Sex	Age (yr)	Height (cm)	Bone age (yr)	Cholesterol (mg per 100 ml)	Electrocardiogram	State of thyroid	Teleradiograph of heart	Previous thyroid treatment	
1	M	$15\,^{7}/_{12}$	136 (*151 2*)	7–8	200	Low voltage, flat P and T	Diffuse firm goitre	C R 52%	—	
2	F	$11\,^{7}/_{12}$	108 (*141 6*)	4–5	321	Low voltage, flat P and T	Firm nodular goitre	C R. 61%	—	
3	M	$10\,^{1}/_{12}$	112 (*132*)	4–5	223	Low voltage flat P and T	Diffuse firm goitre	C R 65%	—	
4	F	$8\,^{3}/_{12}$	100 (*123 7*)	3–4	318	Low voltage, inverted T_1 and T_2	Diffuse goitre	C R 65%	—	
5	F	$7\,^{7}/_{12}$	93 (*119 9*)	2–3	184	Low voltage inverted T_3	Diffuse firm goitre	C R 60%	—	
6	F	20	149 8	16–17	400	Low voltage	Diffuse firm goitre	No enlargement	—	
7	M	16	123 (*157 8*)	13	500	Low voltage	Diffuse firm goitre	No enlargement	—	
8	M	$4\,^{8}/_{12}$	68 (*99*)	Under 1	150	Low voltage, flat P and T	Slightly enlarged	No enlargement	—	
9	M	$2\,^{9}/_{12}$	82 5 (*87 5*)	1	260	Low voltage inverted T_2	Slightly enlarged	No enlargement	—	
10	F	4	87 (*96 7*)	Under 1	236	Low voltage flat P and T	Slightly enlarged	C R 57%	—	
11	F	$6\,^{1}/_{2}$	98 (*112*)	3	139	—	Diffuse firm goitre	No enlargement	Yes $^{6}/_{12}$	Stopped $^{2}/_{12}$ before I^{131} studies
12	F	$3\,^{1}/_{2}$	88 (*93*)	3	122	—	Diffuse firm goitre	No enlargement	Yes $^{8}/_{12}$	

Notes —Cases 1 2 3 and 4 are siblings Case 5 is a cousin of 1–4 6 and 7 Cases 6 and 7 are siblings and cousins of 1–5 Cases 11 and 12 are half-sisters (same mother) Previous to thyroid treatment cases 11 and 12 showed much delayed ossification and hypercholesterolæmia (Dundee Royal Infirmary)

Height —Italic figures in parentheses are the average normal heights for children of the respective ages (taken from Holt s *Diseases of Infancy and Childhood*, 1911)

Teleradiograph of heart —C R =Cardiothoracic ratio

St. Thomas's Hospital Medical School

The 1953 edition of the list of old students can now be obtained from the medical school beadle (price 5*s.* 3*d.*, including postage).

Symposium on Stammering

A symposium on the speech re-education of the stammerer is to be held at Goldsmiths' College, New Cross, London, S.E.14, on Thursday, June 11, at 6.45 P.M., when students from the college's classes in speech correction will discuss the problems of the stammerer.

Allergy to Penicillin

Because she is allergic to penicillin, a midwife at Scunthorpe has had to leave her employment. Alderman George Canty, chairman of the health committee, reported to Lindsey County Council that the nurse had tried wearing rubber gloves and other remedies, but none was of any help. Asked if there was no possibility of her finding work in another field of nursing, Alderman Canty replied that penicillin was so widely used that she would find it difficult to avoid coming into contact with it.

Conference of Prison Medical Officers

This annual conference was held at the Home Office on May 22, with Dr. H. K. Snell, director of medical services, Prison Commission, in the chair. Dr. N. J. deV. Mather, consultant psychiatrist at Crumpsall Hospital, Manchester, read a paper on Schizophrenia in Relation to Criminal Behaviour; and Dr. W. J. Gray, medical officer to H.M. Prison, Maidstone. and Dr. D. A. Ogden, medical officer to H.M. Borstal Institution, Portland, opened a discussion on the Management of the Homosexual in Prisons and Borstal Institutions.

Society of Apothecaries of London

Welcoming the Lord Mayor and Sheriffs at a livery dinner held at Apothecaries' Hall on May 19, Sir Wilson Jameson, the master, described the society as the best cross-section of the medical profession. Having separated from the Grocers' Company in 1617, it now had one of the largest liveries; and all had joined it "for no other reason than that we love the old institutions of this country." In his response the Lord Mayor (Sir Rupert De la Bère, M.P.) spoke of the value of tradition, and of the spirit of fellowship and friendliness evident in the society. Of the future of this country he said that "the rest of the world will believe in us as long as we believe in ourselves." Dr. H. Seaward Morley, the senior warden, proposed The Guests, coupled with the name of Mr. Justice Danckwerts—which name, he said, was greatly honoured in the households of general practitioners. In such homes it was already attached to a number of objects, and it might well be further commemorated by the profession keeping St. Danckwerts' Day, perhaps on Jan. 1 or April 1. Mr. Justice Danckwerts, in reply, regretted the inhibitions of his judicial office: he might not comment on his own judgment; he might not indulge in politics; he could offer no views on corporal punishment; and he must not even talk about that sacred cow, the National Health Service. So he contented himself with comparing the times of our fathers with the present day, when, in Medicine as in Law, manners have become milder, and people less eccentric. Finally, Sir Wilson Jameson, in proposing the Master's Toast, reviewed the society's affairs: he mentioned the retirement of Mr. Dearman (bedel since 1946) after 52 years' service; the course of lectures held last November, which would be followed by another next November; the religious service to be held on Sunday, Oct. 25; the ladies' dinner on June 16; and the soirée on July 21, when Sir William Gilliatt would be made a master of midwifery and Sir Charles Harington, F.R.S. would receive the society's gold medal in therapeutics for his work on the synthesis of thyroxine. The society had been very happy in the past few months to give accommodation to the new College of General Practitioners. During the year large sums had been spent in maintenance but it was a duty and privilege to maintain a building which had stood some 300 years and had withstood two world wars. The present was a season of rejoicing; and despite all the stress and trouble afflicting the world we could catch glimpses of a more hopeful future—of which it was just possible that this year would see the beginning. He proposed, in the traditional words, The Worshipful Society of Apothecaries of London, may it flourish root and branch—bringing help to all—till time ceases.

International Congress of Rheumatic Diseases

This congress will be held in Geneva from Aug. 24 to 28, under the auspices of the La Ligue Internationale contre le Rhumatisme. Further particulars may be had from Prof. K.-M. Walthard, Institut de Physiatrie, Hôpital Cantonal, Geneva, Switzerland.

Diary of the Week

MAY 31 TO JUNE 6

Wednesday, 3rd

Postgraduate Medical School of London, Ducane Road, W.12
2 P.M. Dr. J. C. Broom: Leptospirosis.

Royal Society of Medicine, 1, Wimpole Street, W.1
5 P.M. *Section of History of Medicine.* Dr. J. Zelmanowits: Historical Note on the Simple Dementing Form of Schizophrenia. Dr. Henry J. John (Ohio): Jan Evangelista Purkinje, Czech Scientist and Patriot (1787–1869).

Thursday, 4th

Postgraduate Medical School of London
4 P.M. Dr. B. Ackner: Depression. (First of three lectures.)

Royal Society of Medicine
5 P.M. *Section of Endocrinology.* Dr. Patricia Benedict (Boston): Idiopathic Hypercalciuria. Dr. Felipe A. de la Balze (Buenos Aires): Klinefelter's Syndrome.

London Jewish Hospital Medical Society
8.30 P.M. (11, Chandos Street, W.1.) Prof. David Slome: Experimental Surgery.

Honyman Gillespie Lecture
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Mr. G. A. Pollock: Cerebral Palsy.

University of St. Andrews
5 P.M. (Medical School, Small's Wynd, Dundee.) Prof. A. D. Peacock, D.SC.: Animal Parthenogenesis.

Friday, 5th

University of London
5 P.M. (Westminster Medical School, 17, Horseferry Road, W.1.) *Dr. de la Balze: Morphology and Histochemistry of* Normal Adult Testes: Changes under Œstrogens Therapy.

Postgraduate Medical School of London
2 P.M. Mr. W. R. Merrington: *Carcinoma of Breast.*
4 P.M. Prof. Robert Kark (Illinois): Albumin Exchange *in Health and Cirrhosis.*

Institute of Dermatology, St. John's Hospital, W.C.2
5.30 P.M. Dr. G. B. Dowling: Tuberculosis of Skin.

Institute of Obstetrics and Gynæcology
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Mr. J. Wrigley: Problem of Dysmenorrhœa.

Saturday, 6th

Institute of Obstetrics and Gynæcology
10 A.M. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Mr. C. MacIntosh Marshall: Joseph Price oration.

Appointments

Falkman, S. C. J., L.R.C.P.E., D.P.H.: asst. county M.O. and M.O.H., Sedgley urban district and Tettenhall urban district.

Johnson, F. H. W., M.B. Lond.: appointed factory doctor, Bawtry, Yorkshire.

Kennedy, A. R., M.B., B.SC. Manc., D.P.H.: asst. county M.O. for Staffordshire and M.O.H., Seisdon rural district.

Laughlin, John, M.B. Camb.: appointed factory doctor, Three Bridges, Sussex.

Ritchie, Jean, B.A., B.M. Oxfd, D.M.R.T.: radiotherapist, Colonial Medical Service, Malaya.

Weir, I. B. L., M.B., B.SC. Glasg., D.P.H.: M.O.H., Dundee.

East Anglian Regional Hospital Board:

Bennett, L. B. G., M.B. Camb.: surgical registrar, Great Yarmouth and Gorleston Hospital.

Luck, L. C., L.R.C.P.E.: anæsthetic registrar, West Suffolk General Hospital.

Lumsden, J. D., M.D. Manc.: anæsthetic registrar, united Norwich hospitals.

Prouse, F. H., M.D.: orthopædic registrar, East Suffolk and Ipswich Hospital and Ipswich Borough General Hospital.

Births, Marriages, and Deaths

BIRTHS

Herst.—On May 8, at Guy's Hospital, to Pamela Herst, M.B. (née Green), wife of Edward R. Herst, M.B.—a son (Ian Malcolm).

TABLE II—UPTAKE OF THE RADIO IODINE BY THYROID GLAND

Case no	Percentage of dose in thyroid at hours after administrations									Potassium thiocyanate		
	1	2	3	4	5	6	24	48	72	Time (hr)	Amount (g)	Immediate effect
1	25	70	79	—	—	—	24	14	9	48	2	Nil
2	79	88	—	88	—	—	—	—	—	4	2	Nil
3	64	71	—	78	—	80	77	60	50	24	2	Nil
4	90	—	90	90	—	—	38	—	—	4	2	Nil
5	—	—	—	—	—	—	49	—	—	—	—	—
6	—	—	—	—	—	—	44	—	—	—	—	—
7	24	40	—	—	—	—	36	—	—	—	—	—
8	—	—	—	—	—	—	75	70	—	48	1	Nil
9	—	—	—	—	—	—	23	—	—	—	—	—
10	—	—	—	—	—	—	12 5	—	—	—	—	—
11	40	66	71	73	75	75	38	—	—	—	—	—
12	36	51	56	62	74	70	31	—	—	—	—	—

METHODS

Carrier-free radioactive I^{131}, prepared by the Atomic Energy Research Establishment, Harwell, was administered in water as a drink to each patient 2 hours after food The dose was 30–200 µC

The amount, corrected for decay, of I^{131} which accumulated in the thyroid gland was estimated by a simple technique

A Geiger Müller counter (General Electric Co type ' G M 4 '), shielded laterally and distally with 2 cm of lead, and standard electronic counting equipment (power unit, amplification and quench unit, and scaler) were used The number of gamma rays emitted in 5 minutes by the dose in 10 ml of water in a universal container placed 30 cm from the counter was determined At various intervals after the dose was given the number of gamma rays emitted by the thyroid gland was counted (table II) The patient was placed with the upper margin of the sternum 30 cm distant from the lower and anterior surface of the counter shield, and the anterior surface of the neck was held vertically Additional lead shielding (0 5 cm) intervened between the patient's trunk and the counter

In cases 1–4 and 8 the effect of an oral dose (1 or 2 g) of potassium thiocyanate on the amount of radio-iodine in the thyroid gland was observed

The urine was collected in divided periods over 48 hours in 8 of the 12 cases (table III) The bladder was emptied at the end of each period except in cases 8 and 9, in which urine was collected continuously through a Paul's tube fixed to the penis Samples of urine were counted in the beta liquid counter designed by Veall (1948) The amount of radioactive iodine excreted in each period was expressed as a percentage of the dose administered, a dilution of the stock radio iodine solution used being kept for estimation of the dose

Samples of blood were taken off into oxalated bottles at 24 hours in 4 cases and at 48 hours in 9 cases The plasma was separated by centrifuging, and the total radioactivity present in 5 ml samples made up to the counter volume (10 ml) was determined in the beta liquid counter and the result expressed as the percentage of dose administered per litre of plasma (table IV) The radioactivity of the protein-bound iodine of the plasma was determined by precipitation by trichloracetic acid (Sheline and Clark 1950, Goodwin et al 1951) 5 ml samples of plasma were used, and the proteins were precipitated by 10% trichloracetic acid, the precipitate was washed twice with 2% trichloracetic acid, redissolved in 2N NaOH and the volume made up to the counter volume Counts for at least 10 minutes were made on the total plasma-iodine samples, and 20 minutes on the protein-bound iodine samples

TABLE III—URINARY EXCRETION OF RADIOACTIVE IODINE

Case no	Percentage of radioactive iodine excreted in various periods (hr)						
	0–6	6–12	12–18	18–24	0–24	6–24	24–48
1	9 3%	—	—	—	59 6%	50 3%	27 0%
2	—	—	—	—	—	—	—
3	15 0%	—	—	—	27 0%	14 0%	14 0%
4	—	—	—	—	—	—	—
5	5 5%	0%	25 7%	14 8%	46 0%	40 5%	19 8%
6	8 5%	10 0%	5 8%	11 3%	35 6%	27 1%	23 0%
7	11 9%	8 9%	12 3%	17 2%	50 3%	38 4%	17 6%
8	7 0%	0%	9 0%	4 0%	20 0%	13 0%	5 4%
9	2 2%	0 3%	37 1%	15 4%	55 0%	52 8%	14 4%
10	20 4%	11 8%	9 0%	6 8%	48 0%	27 6%	4 0%
11	—	—	—	—	—	—	—
12	—	—	—	—	—	—	—

3 ml samples of plasma from cases 11 and 12, who received 125 µC of I^{131}, were examined for butanol extractable iodine by a modification of the method of Taurog and Chaikoff (1948) The iodine was extracted by three washings of n butyl alcohol, the extract was treated twice with a solution of 5% Na_2CO_3 in 4N NaOH, and the mixture was allowed to separate The alcohol layer was separated and concentrated by heat to counter volume Counts were made for 20 minutes on the fraction of plasma extractable by butyl alcohol but not re extractable by treatment with the solution of 5% Na_2CO_3 in 4N NaOH

Samples of plasma from cases 5, 6, and 7, who received 200 µC of I^{131} were submitted to Dr J Gross and Mrs R Pitt-Rivers at the National Institute for Medical Research, Mill Hill, London, for analysis by chromatography of the radioactivity in a butanol extract of the plasma (Gross and Pitt-Rivers 1952)

TABLE IV—PERCENTAGE OF I^{131} PRESENT AS TOTAL PLASMA IODINE (T P I), PROTEIN-BOUND IODINE (P B I), AND BUTYL ALCOHOL EXTRACTABLE IODINE (B E I)

(Results expressed as per cent of dose per litre of plasma)

Case no	24 hr			48 hr			
	T P I	P B I	$\frac{\text{P B I} \times 100}{\text{T P I}}$	T P I	P B I	$\frac{\text{P B I} \times 100}{\text{T P I}}$	B E I
1	—	—	—	0 95	0 50	52%	—
2	—	—	—	—	—	—	—
3	—	—	—	—	—	—	—
4	—	—	—	—	—	—	—
5	2 50	0 43	17%	1 02	0 49	48%	—
6	1 00	0 13	13%	0 45	0 10	21%	—
7	2 89	1 38	47%	1 78	1 12	62%	—
8	—	—	—	1 54	1 00	65%	—
9	—	—	—	1 68	0 58	34%	—
10	1 28	0 74	58%	1 28	0 87	68%	—
11	—	—	—	1 35	0 49	36%	0 36%
12	—	—	—	1 32	0 40	30%	0 25%

RESULTS

The uptake by the thyroid gland, the excretion by the kidney, and the amount in the plasma of radioactive iodine are shown in tables II, III, and IV respectively It will be seen not only that the thyroid glands of these patients accumulated radio-iodine from the blood stream, but also that most of them did so with abnormal rapidity and in excessive amounts The glands did not retain the radio-iodine but released it into the circulation, some of it in a chemical form which could be precipitated by trichloracetic acid and extracted by butyl alcohol

Dr Gross and Mrs Pitt Rivers reported that radioactivity was present in butyl alcohol extracts of plasma samples withdrawn from cases 6 and 7 at 24 and 48 hours, but the amount was insufficient to give an autoradiograph allowing identification of its origin Radioactivity was present in the butyl-alcohol extract from case 5 which was examined on a kieselguhr column The radioactivity was not elutable with 20% chloroform in butyl alcohol equilibrated with 0 05% NaOH but was removed from the column with water Its chemical identity remained unknown It was neither thyroxine nor triiodothyronine

DISCUSSION

Thyroid Uptake

In general the uptake of iodine by the thyroid gland suggests hyperthyroidism Direct comparison with the pe, should be warned to take carbohydrate in adequate mounts and not to miss a meal or a mid-morning or id-afternoon snack when on the road. He was more ubious about the suitability of a diabetic for driving a ublic vehicle or for piloting an aeroplane. He strongly issented from the view of another speaker that a lawyer as entitled to pick holes in the police surgeon's evidence, o get his client off.

Dr. G. M. KERR said that attention should be paid to oss of judgment and increased reaction-time, both of which preceded motor incoördination and might result n serious errors in driving.

Dr. LINDSEY BATTEN said that the legal casuistry nvolved in quibbles about the colour of the accused nan's eyes was calculated to keep any but the most tout-hearted doctor from venturing into court.

Dr. G. J. V. CROSBY said that it was often an invidious ask for a doctor to dissuade elderly private patients from continuing to drive. One of his patients who drove a high-powered car at a reckless speed was extremely annoyed at the advice that he should give up driving after he had had three blackouts in a year and had been found to have petit mal.

MANCHESTER MEDICAL SOCIETY

Pituitary Adenomata

AT a meeting of the section of medicine of the Manchester Medical Society, on Dec. 3, Sir GEOFFREY JEFFERSON, F.R.S., spoke on the Varying Behaviour of Pituitary Adenomata. He said that some pituitary adenomata behaved in a toxic fashion, while others were inert. The "toxic adenomata" produced gigantism, acromegaly, and basophilism—although he shared the general doubt about basophilism being primarily a pituitary disorder. The chromophobe adenomata produced varying degrees of hypopituitarism; some eventually caused a drift towards Simmonds's disease.

Sir Geoffrey based his remarks on 316 adenomata. He had operated on 250; 11 showed locally invasive properties. Sugar-tolerance curves had not shown any significant trends, though the toxic adenomata were more liable to give rise to glycosuria. Neither the metabolic-rate nor the eosinophil-count showed any uniform change. On the whole the urinary output of gonadotropins was more often reduced than that of the 17-ketosteroids. The dangers of operation were related more to hypothalamic disturbances than to acute stress syndromes. The enlarged sella turcica seen in radiographs gave an inadequate idea of the actual size of the adenomata, of which sizeable supra-sella extensions were extremely common—a fact easily demonstrated by pneumo-encephalography.

DEVON AND EXETER MEDICO-CHIRURGICAL SOCIETY

Outpatient Problems

AT a meeting of the Devon and Exeter Medico-Chirurgical Society on Dec. 18, Dr. W. A. LISTER spoke of common outpatient problems.

The first was that of the child who persistently coughed at night. This cough started about the age of 2, often after pertussis and pneumonia. The patient was intelligent, quick, alert, impatient, growing fast, and rather pale. Associated complaints were abdominal pains and persistent nasal catarrh. Inquiry revealed that the mother had taken the child to many doctors, hospitals, and clinics; but still the cough continued. In the causation these were the main factors: (1) an infective focus in the throat, nasopharynx, or sinuses; (2) a psychosomatic factor (the patient was often the only child of anxious parents); and (3) a dietetic factor, usually an intolerance of fat. If these patients are recognised as early asthmatics other things fell into place. Focal infection must be dealt with; this would improve but not cure the patient's condition. The psychological side should receive attention, perhaps at a child-guidance clinic. Dietetic measures consisted in reducing intake of fat and increasing intake of carbohydrate. Skin tests were disappointing; but common allergens, such as feathers, hair, and pollen, should be avoided as far as possible: the removal of the domestic cat sometimes produced striking improvement. The breathing exercises advocated by the Asthma Research Council were of great help.

Dr. Lister's second problem was that of the mild melancholic. Such patients often complained of vertical headache or pressure, or of boring pain in the temporal region. The condition was apt to follow the receipt of bad news and to occur in elderly men with an enlarged prostate. A carefully recorded history would often elicit evidence of previous attacks. Skin rashes, night waking in the small hours, and withdrawal of interest from customary occupations were characteristic. Organic disease must, of course, be carefully excluded before melancholia was diagnosed. Treatment consisted in attacking the night waking with phenobarbitone and countering the consequent morning hangover with 'Benzedrine.' (The depression was worse in the morning.) If these measures failed electroconvulsive therapy often succeeded.

Dr. Lister's third problem was that of back strain producing persistent and otherwise inexplicable pain. Such pain might be due to minor degrees of root irritation on the concave side of a scoliosis. Poker-back followed prolonged and unnecessary decubitus. Both types responded well to physiotherapy.

Dr. CHARLES WROTH deplored the lack of liaison by which the same patient might be repeatedly and unnecessarily examined radiographically in various clinics and hospitals, or even in the same hospital.

Reviews of Books

Heredity in Uterine Cancer

DOUGLAS P. MURPHY, M.D., F.A.C.S., assistant professor of obstetrics and gynæcology and research associate, Gynecean Hospital, Institute of Gynecologic Research, University of Pennsylvania. Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1952. Pp. 128. 16*s*.

Dr. Murphy is right in thinking it important to determine whether heredity plays a part in the ætiology of uterine cancer, not only from the point of view of the woman whose mother has died of the disease, and who is therefore apprehensive for herself, but also from the point of view of those who have to diagnose and treat it. This book describes a well-planned, controlled investigation into the cancer incidence of near female relatives (mothers, sisters, female first-cousins, and their mothers) of 201 women suffering from cancer of the uterus, no attempt being made to distinguish cancer of the cervix from that of the body. The author concludes "that there is evidence for a rôle of inheritance in uterine cancer"; but that the *quantitative effect is small* and has not been measured with high precision. He is also of the opinion that the factors which predispose to uterine cancer do not predispose in any significant degree to cancer in other sites, but that hereditary factors do play a part in the ætiology of cancer elsewhere in the body. No significant tendency to concentration in particular families could be detected. The study is similar in plan to that of Brobeck,[1] made in 1949, and in general the results are similar.

The data took nearly three years to collect and at least four years to analyse. Four field workers were employed, and 890 patients diagnosed as having cancer of the cervix were visited, in order to secure records of 201 cancer family groups. The control families, 215 in number, were obtained from a dental clinic (113), women's clubs (82), and volunteers (20) An investigation of this kind cannot be lightly undertaken—it takes time, costs money, and when completed leaves gaps which detract from the value of any conclusions which may be drawn However careful the planning of the inquiry—and this was done with the utmost care—uncertainties due to lack of verified information, death of the patients or their relatives inequalities of cancerous and control groups, and many other hazards are certain to creep in.

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[1] Brobeck, O. Heredity in Cancer Uteri: A Genetical and Clinical Study of 200 Patients with Cancer of the Cervix Uteri and 90 Patients with Cancer of the Corpus Uteri. Aarhus, Denmark, 1949.

Even when such investigations point strongly to possible ætiological factors, the final proof must lie in biological experiment with material in which all or most of the factors can be controlled

The Principles and Methods of Physical Diagnosis

SIMON S LEOPOLD, M D, associate professor of clinical medicine, school of medicine and graduate school of medicine, University of Pennsylvania Philadelphia and London W B Saunders 1952 Pp 430 37*s* 6*d*

IN this book Dr Leopold has set out to describe the methods of physical examination with an account of how and why such methods achieve their purpose—in other words, to provide a physiological or pathological explanation of the mechanisms at work It is indeed a most laudable object and he has approached it with skill, producing a text full of clear and practical information supported by nearly 400 photographs, pictures, and diagrams It is a new and useful departure to include a chapter on the acoustic principles of the sounds from the thorax, written from the physicist's point of view, by a professor of electrical engineering This does not make very easy reading for the student, but will certainly, as the writer hopes, stimulate in him "a continual consciousness of the complexity of sounds in physicodiagnostic procedures" Not all the smaller books on physical diagnosis are such a direct guide to the first principles of clinical methods

The Infirmities of Genius

W R BETT, M R C S London Christopher Johnson 1952 Pp 192 18*s*

DOES genius depend upon some external stimulus, such as alcohol, illness, or drugs, or upon some abnormality of character, to produce its most brilliant results? The author discusses this question in a penetrating survey of the lives of fifteen famous literary figures, examining the work of each and relating it to his physical weakness or mental instability The essays are written with a nice choice of language, and have a charm and an interest that will delight the reader even though most of the subjects were hardly pleasant people

Carlyle's life was an endless conflict, unresolved and unresolvable Shelley was morbidly hypersensitive and drank large quantities of laudanum, his cruelty to his first wife drove her to suicide Swinburne was a drunkard who had epileptiform seizures, Poe fought the intolerable morbidity of his manic depressive state of mind by taking refuge in opium and alcohol, De Quincey, the self confessed opium eater, would consume an ounce of opium in a day Beaudelaire was a syphilitic with a taste for opium and hashish, he died paralysed and speechless The gentle, peaceful Charles Lamb in his youth had a mental breakdown that necessitated his temporary restraint, Balzac wrote his best works after he had developed symptoms of hypertension, Keats died riddled with tuberculosis Burns was a victim of rheumatic fever, Byron's life was blighted by a congenital club foot, Alexander Pope, a tiny hunchback, was a martyr to headaches and to asthma

But what glorious things they wrote! Unsuccessful authors may console themselves with the thought that the price they paid was high

Dictionnaire français-anglais anglais-français des termes médicaux et biologiques

PIERRE LÉPINE chef de service à l'Institut Pasteur London H K Lewis Paris, Éditions Médicales Flammarion 1952 Pp 830 63*s*

AT last we have a really good dictionary of medical and biological terms to facilitate communication between the French-speaking and the English-speaking worlds The French side of it is based on the 1949 edition of Garnier and Delamare, and the English on the 10th edition of *Dorland's American Pocket Medical Dictionary* and the 1945 edition of *Gould's Medical Dictionary* Consequently the spelling of English words is American, there is thus no item "œdema" (except under "edema") and these little catches have to be borne in mind Between the two alphabetical sections are useful lists of equivalent weights, measures, and temperatures The whole work has taken about five years to prepare and appears to have been very carefully done, but there are still a few errors and omissions

Lancisi's Aneurysms

Translated by WILMER CAVE WRIGHT, emeritus professor of Greek, Bryn Mawr College New York Macmillan 1952 Pp 362 $7 50

THE name of Giovanni Maria Lancisi, physician to three Popes and the greatest Italian clinician of the early 18th century, is remembered chiefly through his editing and publication, in 1714, of the remarkable anatomical plates of Eustachius which had been lost for 160 years His main work, however, was *De Aneurysmatibus*, posthumously published in 1728 and never previously translated in full into a modern language The translator has done her work well, giving the Latin text on the left-hand pages, opposite her very readable English translation She has also provided informative notes

Lancisi uses the term aneurysm to mean dilatation of the heart as well as dilatation of the arterial wall Some of his case notes and necropsy findings seem to relate to hypertensive heart failure He appreciates the relation of syphilis to aortic aneurysm and other forms of heart disease, and regards the prognosis as good "In order that I might extend immediate relief to the patient, I asked him whether he had ever been afflicted with the French disease, and when he replied that as a youth he had once been attacked by virulent gonorrhœa which ceased of itself, then I was inspired with the most confident hope that the sick man would soon convalesce from this terrible malady, that is, if he would for his part undergo the treatment with mercurials just as it has turned out so fortunately for me in other cases" He gives a clear description of right heart failure, the chronic bronchitis and asthmatic spasm impeding the flow of blood through the lungs

Lancisi was clearly a pioneer in the pathological study of heart-disease, and his book is a classic which will delight cardiologists

Any Questions ?

A Selection of Questions and Answers published in the BRITISH MEDICAL JOURNAL Second series London British Medical Association, Tavistock Square, W C 1 1952 Pp 195 7*s* 6*d*

THIS second series of answers to questions from doctors, like the first bears a superficial and disconcerting resemblance to those little volumes of likely questions and appropriate replies which the more anxious types among us used to con on the way to the examination rooms But a second glance removes this impression the questions are so much more perspicacious, searching, and practical than those set by examiners, and the replies come from informed and expert quarters A third thought which crosses the mind is that examiners might do worse than study this little book when deciding what to ask the student taking finals

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Gas and Air Analgesia in Midwifery (2nd ed London *Staples Press* 1952 Pp 78 10*s* 6*d*)—Dr G H J Stown in the new edition of his little book, has despaired of describing every kind of anæsthetic machine now in use in this country though he has done his best to include pictures of most if not all of them By omitting the descriptions he has made room, without increasing the size of his little book, for a very short chapter on 'Trilene' (trichlorethylene), and a longer one on the care of the unconscious patient and the resuscitation of the newborn infant The cost of the book has doubled with the rising costs of publishing since 1946, but it is still within reach of modest purses It is designed to explain to midwives the principles underlying gas and oxygen analgesia, and to give them practical advice on its management, but it can also be read with profit by medical students results of other workers is difficult owing to considerable variations in the techniques used. By any standards, however, it is obvious that the thyroid glands of cases 1–4, 11, and 12, in which serial measurements were made, accumulated iodine more rapidly than normal, and that the greatest uptake was well above the normal range. The initial observations were incomplete in case 7 but suggested a similar trend. The uptake at 24 hours was abnormally high—i.e., above 55% (Werner et al. 1949, Goodwin et al. 1951) in only 2 of the 11 patients so studied (cases 3 and 8), but it is obvious that the peak uptake was often past by this time (cases 1, 4, 11, and 12). None of the patients showed an inability to take up iodine from the blood-stream into the thyroid gland. The administration of potassium thiocyanate, which leads to the discharge of any inorganic iodine present in the thyroid gland (Vanderlaan and Vanderlaan 1947), did not produce any detectable alteration in the radio-iodine content of the glands (cases 1–4 and 8). These results indicate that the thyroid glands could take up inorganic iodine from the blood and convert it into an organic form. They suggest also that the glands could release this organic iodine into the circulation.

Urinary Excretion

In contrast with the uptake of iodine by the thyroid gland, in no case did the amount of iodine excreted in the urine suggest hyperthyroidism. The amounts excreted in 24 hours were within the range reported in normal and hypothyroid people—i.e., 20–65% (Goodwin et al. 1951). Of the 8 patients so studied 6 excreted more than 25% of the ingested dose in 6–24 hours. Mason and Oliver (1949) consider that this result is characteristic of hypothyroidism. The large amount of iodine excreted in the urine in the period from 24 to 48 hours by at least 4, and probably 6, of these 8 patients also indicates hypothyroidism according to the findings of Arnott et al. (1949). So far as the present investigations are concerned, the amounts of iodine excreted in the urine are more consistent with the clinical state of the patient than are the amounts of iodine taken up by the thyroid gland. None the less, the intrinsic unreliability of urine collections and the particular difficulties met with in this type of patient detract from the value of studies of urinary excretion.

Plasma Radioactivity

The results of the plasma-radioactivity studies are unexpected in hypothyroidism. The total radioactivity present in the plasma at 48 hours exceeded 0·7% per litre in 8 of 9 patients. Goodwin et al. (1951) found that 0·7% per litre was the upper limit of normal. They found values in excess of 0·7% per litre in patients with thyrotoxicosis and toxic adenoma, in 1 patient with a cervical lipoma overlying the thyroid gland and a normal basal metabolic rate, and in 1 patient with Hashimoto's thyroiditis who had a basal metabolic rate of −20%. High values for total plasma activity at 24 hours were found in the 4 patients we examined. Williams et al. (1949) recorded similar results at 24 hours in both thyrotoxicosis and myxœdema.

Our results for protein-bound iodine obtained at 48 hours by precipitation by trichloracetic acid—0·1–0·5% per litre in 5 patients, and more than 0·5% per litre in 4 patients—are important. They should be compared with the figures found by Goodwin et al. (1951), in whose 2 cases of hypothyroidism protein-bound activity at 48 hours was negligible, and in only 2 of whose non-toxic subjects did it exceed 0·2% per litre. These workers consider that, if the amount of radio-iodine present in protein-bound form at 48 hours exceeds 0·5% of the dose per litre, the patient should be regarded as thyrotoxic, with the important reservation that abnormal results may be obtained in thyrotoxic patients who have been successfully treated and no longer show any clinical evidence of thyrotoxicosis. They report, but do not discuss, the result in the case of Hashimoto's thyroiditis, where the protein-bound activity at 48 hours was 2·3% per litre. Of the 4 patients in whom we estimated protein-bound activity at 24 hours the results were in the thyrotoxic range in 3 and in the normal range (Freedberg et al. 1949) in 1.

The value of the study of protein-bound iodine by a precipitation method as an index of thyroid function is based on the assumption that the protein-bound iodine so separated and estimated is essentially a measure of the thyroxine content of the plasma (Goodwin et al. 1951). Though the assumption is generally true it is not universally so (Blomfield et al. 1951). Our results in these cases of cretinism also discredit the general applicability of such an assumption.

The exact chemical composition of the compounds included with the protein-bound iodine fraction is unknown, but it appears that some diiodotyrosine may be precipitated with the proteins (Man et al. 1951). Rall (1950) has reported a case of myxœdema in which 27% of the plasma radioactivity at 48 hours was present as diiodotyrosine. The likelihood that diiodotyrosine is the basis of the radioactivity in the protein-bound iodine fraction in our cases has therefore to be carefully considered.

The results, in cases 11 and 12, of the butanol-extraction method, which is stated to remove any inorganic iodine and diiodotyrosine, but not thyroxine, from the butyl-alcohol extract (Taurog and Chaikoff 1948), are important. It is obvious that radioactivity persists in the butyl-alcohol extract, but the amount is less than that precipitated by trichloracetic acid. Clearly only a proportion of the radioactivity found by precipitation can be due to diiodotyrosine. The chemical basis of the remainder is unknown. On clinical grounds it is not thyroxine. The patients presented with the clinical picture of hypothyroidism and showed a striking response to dry thyroid given orally. There is therefore no evidence of tissue insensitivity to the thyroid hormone. The chromatographic studies of Dr. Gross and Mrs. Pitt-Rivers in case 5 support the opinion that the thyroid hormone, whether it be thyroxine or triiodothyronine, was not being released into the circulation. Though its chemical identity remains unknown, it is reasonable to assume that the radioactivity is present in a small organic molecule, probably in a protein molecule.

The plasma studies confirm the conclusions reached from the studies of thyroid uptake that the thyroid glands could take up inorganic iodine from the blood and convert it to an organic iodine compound. In addition they show that the glands could release iodine in an organic form into the circulation.

CONCLUSIONS

The thyroid uptake and plasma content of radioactive protein-bound iodine in our cases of non-endemic cretinism add to the anomalous results reported in other investigations of thyroid disorders by similar isotope techniques. They emphasise how important it is that no laboratory test should take precedence over clinical assessment of the patient. Most of the amounts of iodine taken up by the thyroid glands and some of the amounts of protein-bound iodine found in the plasma in our cases suggested hyperthyroidism and might readily, without reference to the clinical picture, have been interpreted as indicating thyrotoxicosis. The amounts of iodine excreted in the urine were most consistent with the clinical state. These results add weight to the advice offered by Goodwin et al. (1951) that, when radio-iodine is used, it is worth while to investigate every patient as fully as possible; but the conclusion of these workers that "the estimation of the protein-bound plasma activity 48 hours after a tracer

STEVENS-JOHNSON SYNDROME

REPORT OF A CASE

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FOLLOWING the original description of erythema multiforme exudativum by Hebra in 1866, Alibert and Bazin (1862) described lesions of the mouth, associated with general symptoms, and they distinguished a herpetic lesion of the iris. In 1922, Stevens and Johnson stated that the criteria for diagnosis were a generalised maculopapular eruption associated with ulceromembranous stomatitis, purulent conjunctivitis, and fever. In 1937 Klauder described a new symptom complex known in the French literature as ectodermosis erosiva pluriorificialis, and in 1938 Low and Davies reported a case "dermato-stomatitis" (Baader) complicating manic depressive insanity. In 1940 Behcet described a "triple symptom complex" consisting of aphthous ulcers in the mouth and on the genitalia and erosion of the cornea with iridocyclitis, associated with erythema nodosum. Lever (1944) described the development of cicatricial conjunctivitis and keratitis. Whatever the name used in these and other descriptions the conditions were very similar, varying only slightly from Hebra's original account. In fact certain authors (e.g., Billow and Lowen 1952, Thomas 1950) have suggested that the various synonyms should be dropped and Hebra's original title used. More recently upper respiratory and pulmonary complications (Finland et al. 1948) and severe anæmia (Alexander 1949) have been reported.

Anderson et al. (1949) tried to identify a virus by scarifying the eyes of rabbits with fluid from the vesicles. A conjunctivitis developed and cytoplasmic inclusion bodies were demonstrated, but this has not so far been confirmed by other workers. Finland et al. (1948) noticed lesions in the lungs resembling virus pneumonia in severe cases. Klauder (1937) pointed out similarities to foot-and-mouth disease but he was unable to identify the virus. Murray (1947) and Alexander (1949) isolated *Staphylococcus aureus* from the eyes, throat, and urethra, as was done in the case reported here. Certain authors have suggested allergy as a cause, but the evidence has not been convincing except perhaps in two instances. Thomas (1950) described a case which relapsed four times after a small dose of sulphonamide on each occasion, and Straus (1948) reproduced the syndrome by giving sulphonamides. On the other hand, Billow and Albin (1946) did not find any cases in a large number of people given sulphadiazine for a period of five weeks, but a fatality has been reported following the use of sulphadiazine (Nellen 1947).

The condition is commonest below the age of 30 but may occur at any age, and there is a preponderance of male patients (Ashby and Lazar 1951). The duration of the rash is usually about eighteen to twenty-one days (Nellen 1947). Recurrences and fatalities have been reported (Billow and Lowen 1952, Thomas 1950).

Treatment has in general been unsatisfactory and mainly symptomatic. In favourable cases the condition usually clears in three to four weeks. Claims have been made for sulphonamides and penicillin (Wright et al. 1947) but they have not proved of great value. Church (1950) and Lynas (1950) found that aureomycin produced dramatic improvement. A patient treated topically with cortisone did well (Fishman 1951), and adrenocorticotropic hormone (A.C.T.H.) has also been successful (Caldwell 1953).

CASE RECORD

A soldier, aged 20, reported to the skin department of a military hospital. He had been vaccinated for the first time ten days previously. The day before admission he had noticed a rash on his arms, legs, hands, feet, and body. He had felt unwell the previous night, and in the morning he felt shivery and his gums and tongue were painful. He had had no previous skin disease or serious illness. He had not been taking any drugs. His family history was negative.

He was a well built man who looked flushed and ill. The temperature was 100·8°F, pulse-rate 94, and respiration-rate 22. He had no generalised lymphadenopathy, but there were some palpable glands in the left axilla, presumably due to the vaccination. His tongue looked red and sore and was ulcerated in places. The gums were inflamed. The lips showed vesiculation and some crusting. The fauces were inflamed, with a few vesicles and small ulcers. He did not complain very much about his throat. The eyes, although he made no complaint about them, showed definite conjunctivitis with a slight purulent discharge and blepharitis. Over the insertion of the left deltoid there was a large crusted infected vaccination mark surrounded by a large area of erythema. Purulent material exuded from the edges of the crust.

The arms, forearms, palms, thighs, legs, and soles were covered with a diffuse erythematous eruption with numerous vesico papules. The lesions tended to coalesce at the wrists and there were many lesions scattered over the chest, abdomen, and back. Examination of other systems revealed no abnormality.

The day following admission he complained of irritation of the glans penis, frequency of micturition, and slight dysuria. He had a purulent balanitis and white urethral discharge.

Investigations.—Hb 94% (Sahli), red-cell count 5·2 million per c.mm., white-cell count 14,000 per c.mm. (polymorphs 82%), platelets 350,000 per c.mm. Clotting-time and bleeding-time normal. Blood-urea 24 mg. per 100 ml. Plasma-proteins normal. Blood culture negative. Erythrocyte-sedimentation rate 21 mm. in 1st hour (Westergren). W.R. negative. Swabs from throat, mouth, conjunctivæ, and vaccination grew *Staph. aureus*. Urethral smear showed gram-positive cocci, pus cells, and epithelial cells, and a culture grew *Staph. aureus*. The urine was cloudy with a heavy deposit in the first specimen in a two-glass test. It contained a few pus cells, and the deposit was urates. Fluid from one of the vesicles was sterile. Biopsy of a lesion showed changes consistent with a diagnosis of erythema multiforme. X-ray examination of the chest showed no evidence of disease.

Progress and Treatment.—Treatment was started with 'Sulphatriad,' 2 g. at once and 1 g. six-hourly. He had hydrogen peroxide mouth-washes, and a 1% aqueous solution of gentian violet was applied to the lips and gums; 10% 'Albucid' (sulphacetamide) drops to the eyes. The balanitis was treated with 1 in 4000 potassium permanganate. All these local applications were used frequently. Calamine cream was applied to the skin. He showed no response to the chemotherapy in forty-eight hours, so penicillin (200,000 units six-hourly) was given in addition. The pyrexia continued, ranging between 100° and 102°F, and he appeared to be becoming more toxic. He found difficulty in eating, but continued to take food and fluid by mouth. After a further three days, the mouth and eyes had improved slightly, and the balanitis was not so troublesome, though the urethral discharge remained the same. In spite of this improvement his general condition was unchanged. The skin lesions had in some areas begun to fade but fresh crops appeared, some of them hæmorrhagic. As his general condition was not responding, it was decided to stop the penicillin and sulphatriad, and to give a course of chloramphenicol. The dosage was 1 g. to start with and 500 mg. four-hourly, supplemented by vitamin B_1 (6 mg. four-hourly). This produced an almost dramatic response, and within thirty-six hours his temperature was normal and remained so. Within three days, the urethral discharge had cleared, the balanitis had almost gone, the mouth and eyes had much improved, and the skin lesions were drying up and flaking off, the palms and soles being last to clear. After five days the dose of chloramphenicol was reduced to 250 mg. eight-hourly, and stopped altogether after eight days when all signs had gone except for slight flaking of the skin on the palms and soles. Ten days later he was discharged from hospital, and when seen one month later he was well and had had no recurrence.

DISCUSSION

This case showed the commoner signs necessary for a diagnosis of Stevens-Johnson syndrome—i.e., a rash dose of radioactive iodine is essentially a measure of the amount of circulating thyroxine" must be accepted with even greater reserve than they suggest.

The results of our investigations confirm the American reports (Hamilton et al. 1943, Lerman et al. 1946, Stanbury and Hedge 1950, Stanbury 1951) that the thyroid glands of cretins with non-endemic goitre are hyperactive and accumulate radio-iodine administered orally more rapidly and to a greater degree than normal. In some of the American cases there was definite evidence that the thyroid glands could not convert inorganic iodine into an organic form (Stanbury and Hedge 1950, Stanbury 1951), and in others there was evidence that the thyroid glands could form thyroxine but could not release it into the circulation (Hamilton et al. 1943). Our patients clearly differ from those described by Stanbury and his colleague in that the glands converted the inorganic iodine into an organic form. We have not had the opportunity to examine any of the glands after removal by operation, because we have not found thyroidectomy to be necessary in any of our patients. We cannot therefore state dogmatically that our patients differ from those described by Hamilton and his associates, since we have no information about the chemical form in which the iodine is present in the glands. Probably our patients do differ. Our results suggest that our patients could release the radio-iodine in an organic form into the circulation.

Our investigations indicate that non-endemic goitrous cretinism may be caused by an inability of the thyroid gland to complete the synthesis of the thyroid hormone. The defect which we have discovered has apparently not been previously described. The nature and cause of the defect are obscure. It is probably intrinsic, and there is evidence that it may be familial.

SUMMARY

The results obtained with radioactive iodine (I^{131}) in 12 cases of non-endemic goitrous cretinism are recorded and discussed.

Most of the amounts of I^{131} taken up by the thyroid gland and some of the amounts of protein-bound iodine found in the plasma suggested hyperthyroidism, and might readily, without reference to the clinical picture, have been interpreted as indicating thyrotoxicosis, whereas the amounts of iodine excreted in the urine were most consistent with hypothyroidism.

The thyroid glands of the patients took up inorganic iodine from the blood-stream and incorporated it into an organic form. An organic iodine compound, not thyroxine, was released into the circulation. Its chemical nature is unknown, but it is present in that fraction of the plasma which is extractable by butyl alcohol but not re-extractable by treatment with the solution of 5% Na_2Co_3 in 4N NaOH.

It has been shown that non-endemic cretinism may occur in the presence of a thyroid gland which is able and eager to take up and convert inorganic iodine to an organic form, and it is postulated that in such cases there may be an intrinsic, probably familial, defect in the final synthesis of the thyroid hormone.

Thanks are due to Prof. J. L. Henderson for allowing us to study cases 11 and 12; Dr. J. Gross and Mrs. R. Pitt-Rivers for the chromatographic studies; the Board of Management, Glasgow Royal Infirmary, and the Rankin Fund, Glasgow University, for defraying the expenses of the radio-iodine studies; and the nurses of the two hospitals for their coöperation.

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PERIPHERAL BLOOD PICTURE AFTER OPERATION FOR PORTAL HYPERTENSION

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MANY hæmatologists have come to accept the idea that the spleen may influence hæmatopoiesis. This concept has arisen from studies of the peripheral blood

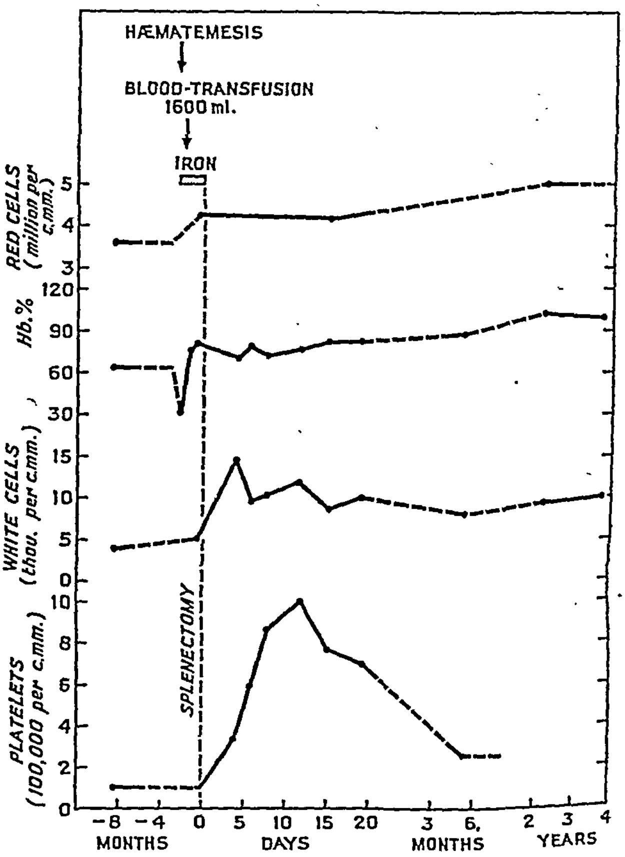

Fig. 1—Blood picture before and after splenectomy in portal hypertension with intrahepatic obstruction (hepatolienal fibrosis).

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like erythema multiforme, stomatitis, conjunctivitis, and urethritis The interesting points are the preceding vaccination and the response to chloramphenicol

Common Lesions—Eye lesions are almost always present—usually a conjunctivitis with exudate and usually bilateral There may be œdema of the lids and blepharitis Cases of keratitis severe enough to cause blindness have been reported (Lever 1944), although with the use of chemotherapy this may be reduced (Goldfarb 1946) The lips are always involved and show erythema, swelling, fissuring, ulceration with hæmorrhage, and residual crusting Buccal lesions are almost always present, and may show a pseudomembrane or ulceration and vesiculation involving the tongue, palate, fauces, and pharynx Penile or vulvo-vaginal lesions with erythema, œdema, and vesiculation, with or without non-specific urethritis, are also common The rash is most often maculopapular, vesicobullous, or hæmorrhagic It is usually generalised in distribution but the scalp often escapes

Rarer Signs—Pneumonic lesions have been reported in the U S A by the Commission on Acute Respiratory Diseases (1946), Finland et al (1948), and Billow and Lowen (1952), and in this country by Church (1950) Sore throat, with or without dysphagia, and joint pains are occasional features, and erythema nodosum sometimes appears

Differential Diagnosis—The condition has to be distinguished from the other bullous and vesicular dermatoses and exanthemata These include the pemphigus group, dermatitis herpetiformis, the herpes group, bullous erythema multiforme, Kaposi's varicelliform eruption, vaccinia, varicella, and variola Drug eruptions should be considered, such as those due to arsenic, barbiturates, bromides, iodides, phenolphthalein, and quinine

I can find no report of the syndrome following vaccination, although a case of erythema multiforme complicating vaccination has been reported

The cause of this condition is still unidentified, and the treatment is mainly symptomatic, although chemotherapy will reduce secondary infection and probably prevent serious eye complications In the future cortisone and A C T H may provide the answer (Fishman 1951)

SUMMARY

A soldier, aged 20, fell ill with a case of Stevens-Johnson syndrome ten days after vaccination He was successfully treated with chloramphenicol

I am indebted to Dr P D C Kinmont for his helpful criticism

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Fertilisers versus Organic Manures

THE section of comparative medicine met on May 20, with Prof C L OAKLEY, the president, in the chair

SIR WILLIAM OGG (Rothamsted Experimental Station, Harpenden) explained the history of fertiliser development While manure was used from ancient times, liming came very much later, and it was only after 1842, when John Bennett Lawes, the founder of Rothamsted, patented his water-soluble superphosphate fertiliser and showed it was better than the ground bones previously used, that research began into the best way to use different fertilisers for different crops on different soils This coincided with a time of great increase in population, and the urbanisation of Britain, which in turn meant that sewage from the towns went into the sea instead of restoring valuable chemical elements to the land Now the motor car had replaced the horse, and the quantity of animal feeding-stuffs imported annually had fallen to half the pre-1939 figure England and Wales now made about 35 million tons of farmyard manure a year, which represented about a third of all the nitrogen, a quarter of the phosphate, and half the potash actually added to the soil by farmers today Most of the recent increase in British food production was due to better fertiliser practice, and a survey had shown that many farmers still had a great deal to learn and could further increase their yields by using the correct fertiliser in the right time and place Before the war Holland used five times as much fertiliser annually as did Britain, and other European countries had similar figures

Proponents of "organic" farming differed in their degree of opposition to the use of chemical fertilisers some would permit basic slag (just as some teetotallers drink invalid port), but they all believed that manure had a vital principle lacking in all chemicals, and therefore that plants grown without it were inferior in nutritive quality and in resistance to disease The scientific evidence did not support this view Many plants could be grown in pure mineral solutions (hydroponics) even when special precautions were taken to eliminate soil bacteria on their roots Soil diseases were distributed quite differently from the areas of greatest use of fertilisers, and Rothamsted experiments had shown that nitrogenous fertilisers actually made wheat more resistant to some diseases Nor did fertiliser increase soil erosion The broad balk field at Harpenden had been heavily dressed with chemicals for the past 110 years, yet crops were still good, root and stubble organic matter was still available for ploughing in, and the soil microbe count was high (although in general very high counts did not necessarily mean better crops)

Fertilisers were essential for large crops because manure and compost could never supply much more than 10% of the need Town refuse and sewage sludge were inferior to good dung and too bulky to transport far To grow crops specially for composting was very uneconomic in land and labour This stated the British position, but it had to be remembered that soils in many parts of the world were naturally deficient in phosphorus, potash, or trace elements, and agriculture only became possible when these lacks had been made good with chemicals

Fertilisers were flexible in use, but required intelligent application, mistakes were possible Organic manures worked more slowly and sometimes gave the wrong balance of nutrients, but were nearly foolproof The two were not mutually exclusive but were complementary, and the best farming practice employed both

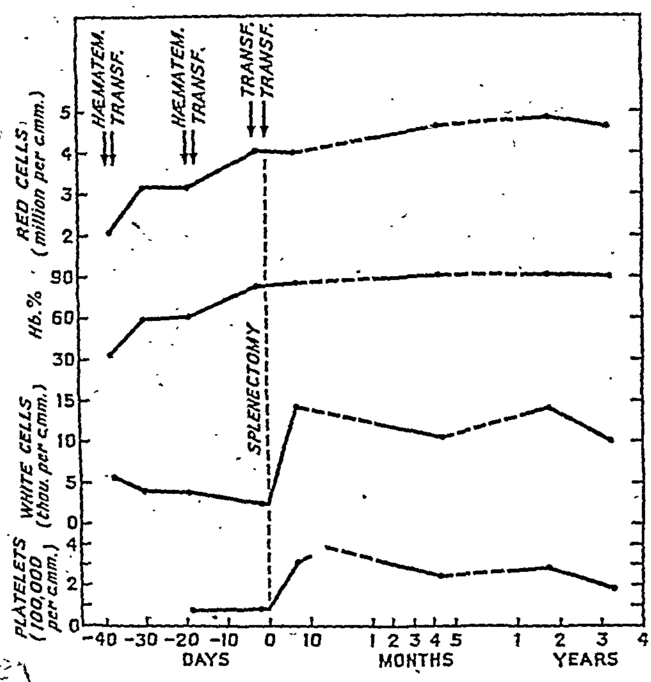


Fig. 2—Blood picture before and after splenectomy in portal hypertension with extrahepatic obstruction.

and of the bone-marrow in conditions associated with enlargement or increased activity of splenic tissue, such as may be observed in portal hypertension or in idiopathic thrombocytopenic purpura.

The term "hypersplenism" has been applied to the clinical picture in which it is believed that overactivity of the spleen results in reduction of one or more of the formed elements of the peripheral blood or delayed maturation of their precursor cells in the bone-marrow. This rôle of the spleen has been discussed by Limarzi and Schleicher (1940) Limarzi et al. (1943), Dameshek and Estren (1947), Robson (1949), and Schatken (1952). In certain cases it has been shown that splenectomy can bring about rapid and lasting improvement in the abnormal hæmatological picture.

The syndrome of portal hypertension is now well recognised. It is characterised by splenomegaly and peripheral blood changes, of which the commonest are granulopenia and thrombocytopenia; in most cases by evidence of hepatic cirrhosis; and by a tendency to recurrent bleeding into the gastro-intestinal tract. These hæmorrhages, which usually present as hæmatemeses sufficiently severe to threaten the life of the patient, occur from veins in the cardio-œsophageal area which have become dilated and congested in an attempt to provide alternative channels by which blood may return from the obstructed portal bed to the general circulation.

TABLE I—CLINICAL DETAILS OF CASES IN WHICH THE SPLENIC ARTERY WAS TIED

Case no.	Disease	Main symptom	Site of ligature	Clinical effect
1	Hepato-lienal fibrosis	Ascites and hæmatemesis	Main trunk near hilum	No effect on progress of disease
2	Hepato-lienal fibrosis	Hæmatemesis	Main trunk above pancreas	Bleeding recurred 12 mos. later, no change in spleen size
3	Extra-hepatic block	Hæmatemesis	Main trunk and left gastro-epiploic	No bleeding in 18 mos., no change in spleen size
4	Hepato-lienal fibrosis	Hæmatemesis	Main trunk and left gastro-epiploic	Bleeding recurred 2 yr. later, spleen showed central infarct
5	Cirrhosis	Ascites	Main trunk above pancreas	No effect on progress of disease or on spleen size. Hæmatemesis 18 mos. later

In portal hypertension the main objective of surgical treatment is to prevent the recurrence of serious hæmorrhage by reducing the portal venous blood-pressure or by diverting the portal blood from the dangerous cardio-œsophageal region. Such operations as splenectomy and ligation and division of the splenic arterial supply may lower the portal venous pressure by reducing the volume of arterial blood entering the portal bed. Other operations are designed to establish a large portal-systemic venous communication, such as is provided by anastomosis of the portal vein to the inferior vena cava, or of the splenic vein (after splenectomy) to the left renal vein; these, when successful, achieve the double purpose of lowering portal pressure and of diverting portal blood from the site of the varices. Excision of the varix-bearing area in the lowest 6–8 cm. of the œsophagus and the adjoining fundus and lesser curvature of the stomach is another procedure designed to remove the source of the hæmorrhages, probably without significant reduction of the portal pressure. Splenectomy is done at the same time if the spleen has not already been removed.

A second aim of surgical treatment is to improve the blood picture where there is persistent and severe reduction in the number of circulating leucocytes and platelets.

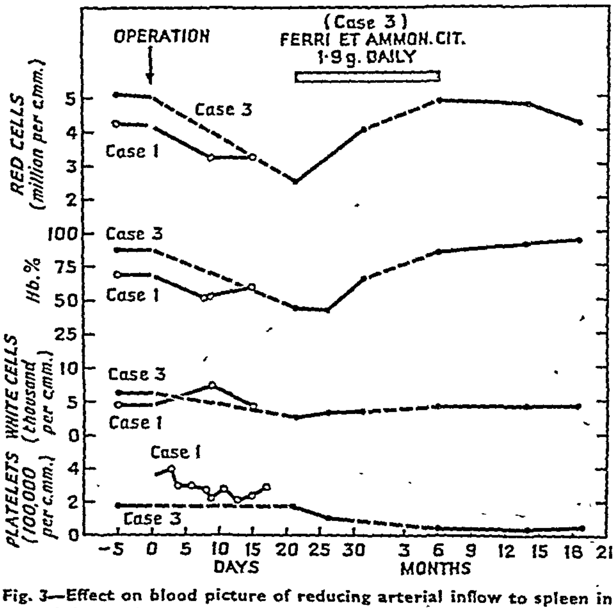


Fig. 3—Effect on blood picture of reducing arterial inflow to spleen in case 1 (hepatolienal fibrosis) and case 3 (extrahepatic obstruction).

HÆMATOLOGICAL CHANGES

It is with certain hæmatological problems of the portal hypertension syndrome that this paper is concerned. 12 cases of portal hypertension are reported in which the surgical treatment did not involve splenectomy: in 7 of these cases the aim of operation was to relieve the portal hypertension by anastomosing the portal vein to the inferior vena cava; and in 5 to reduce the splenic blood-flow by ligation of the splenic artery. In these 12 cases the changes in the peripheral blood picture after operation are compared with those observed after operation in 46 cases of portal hypertension in which splenectomy was done either as the only procedure or as a preliminary to spleno-renal anastomosis.

Mr G C **Ainsworth** PH D (University College of the South-West, Exeter), discussed factors in plant health and growth All agriculture was artificial since it forced plants to grow in pure culture instead of in the associations of mixed species characteristic of different soils and climates in Nature While some plants grew very well in inorganic water culture, others needed symbiotic bacteria or moulds for full growth Lucerne seed had to be inoculated naturally or artificially with root-nodule-forming bacteria In afforestation the newly planted young trees usually carried enough of the necessary symbiotic fungus or mycorrhiza on their roots, but sometimes it was necessary to add cultures to the soil Some cultivated plants grew well independently of the microflora of the soil, while others relied on it In the same way no simple generalisation was possible on the beneficial or adverse effects of fertilisers Adding potash to the soil decreased the rate of attack of the fungus causing chocolate spot in broad beans On the other hand green manure, such as grass cuttings, decreased the incidence of fungal potato scab by encouraging the growth of saprophytic fungi which competed with the pathogens and perhaps eliminated them by antibiotic action Plants could absorb antibiotics from the soil, and lettuce, for instance, had thus been made more resistant to grey mould

Dr D. P **Cuthbertson** (Rowett Research Institute, Aberdeen) said that adding excess of potash to the soil lowered the magnesium content of crops and animals feeding thereon were more subject to tetany But in general fertilisers made very little difference to crop quality They might affect the ratios in which certain proteins were made in the plant but they did not change the fundamental amino acid composition of the proteins Cows and other ruminants in any case gained a part of their dietary protein from the synthetic activity of microbes in their forestomachs The vitamin-C content of plants depended mainly on their genetic inheritance and varied to only a trivial extent with climate, soil or fertiliser McCarrison's claim, prior to 1924, that B vitamins were richer in wheat and millet manured with cow dung had not been substantiated by later, statistically sounder, experiments As for human health—a term very difficult to clarify and define—infant mortality was lowest and the expectation of life greatest in countries which used the most synthetic fertilisers, though of course there were many reasons for this hygienic triumph

Sir **James Scott Watson** (National Agricultural Advisory Service, London) pointed out that farming was lore as well as science British agriculture a century ago was world-famous for its success It was the result of about 8000 years of experience and tradition, and the yield of wheat averaged 11 cwt per acre In 1952 the average was 20 cwt, and this increase was due to science Traditional lore often worked well on its native heath but was disastrous when exported unless science was available too The loss of 50 million acres of good U S farming land through soil erosion was the result of attempting to follow Western European farming practice in the totally different climate of America The physical structure of soil determined its water-holding power, its ease of drainage, and the degree of diffusion of oxygen and carbon dioxide to and from plant roots Soil erosion—the washing away of a powdery topsoil by a deluge of rain—could be mitigated by proper land use and engineering by terracing and contour ploughing, sometimes by growing a cover crop at some season merely to break the impact of heavy raindrops or by agreeing that forest was the only practicable cultivation in a particular area Another approach was to study the binding agents in soil which led to a satisfactory crumb structure Decaying organic matter was important here, but unfortunately it was an unstable system Humus formation varied with bacterial activity, which depended on the nitrogen content of the organic matter Straw was low in this and slow to decay, vetch and clover high in it and fast to decay Good results in practice came from ploughing in certain grass/clover mixtures Plastics had been developed to fix the unstable soil at its best crumb structure, but they were too expensive for farm use Much older was the custom of mixing clay with sandy soils, or marling (adding clay and limestone), or mixing in subsoil by deep ploughing Present-day emphasis was on soil physics rather than soil biology The microflora seemed on the whole to look after itself, and as Sir William Ogg had pointed out it was weathering and not bacterial action that liberated most mineral nutrients for plant use

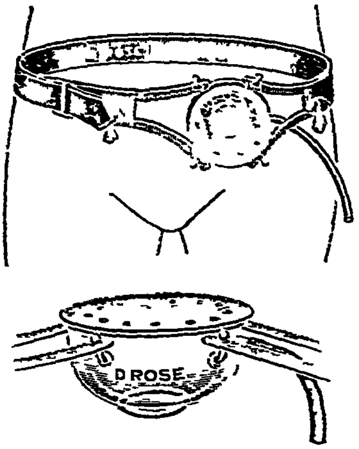
In the discussion the supporters of organic manures presented their views, but most speakers seemed to agree that the scientific evidence was against an extreme stand It seemed in any case to be quite inapplicable to countries such as Australia, where mineral deficiencies in the soil were of prime importance

New Inventions

SUCTION APPARATUS FOR ABDOMINAL FISTULÆ

The apparatus illustrated was originally devised for dealing with a small-bowel fistula opening on the abdominal wall Small-bowel contents rapidly excoriate the skin, and continuous suction applied through a tube placed in the fistula may delay closure

The hole in the base of the cup is centred over the fistula, its special rim ensures watertight closure, and tulle gras can be used to protect the skin within the bottom of the cup The contents are continuously withdrawn through the side-tube by connecting it to an electric sucker The lid is perforated so that no negative pressure is built up



Small-bowel, pancreatic, and biliary fistulæ have all been treated with this simple apparatus It reduces wastage of dressings, and both patient and nurses welcome its use The patient feels dry and comfortable and can sleep undisturbed by frequent dressings

I am indebted to Mr Donald Rose of 36, George Street, Portman Square, London, W 1, for making this apparatus for me

King s College Hospital and
Postgraduate Medical School of
London

Selwyn Taylor
M.CH OXFD, F R C S

" . The prime motive in the creation of a Teaching University at the beginning of the century was to bring examination and thereby instruction into line with research But that meant something more than an opportunity to see that the graduate was informed of the latest discoveries It meant the opportunity to practise at all levels the art of enquiry Our offence is the offence of which academic societies have all too often been guilty, the ancient error of those whose chief distinction it was 'to know and enforce all of the right answers rather than to know or to ask any of the right questions' "—Prof. H. **Hale Bellot**, the vice chancellor, *University of London Gazette*, April, 1953, p 72

Effects of Splenectomy

The effect of splenectomy in such cases is illustrated in figs. 1 and 2 :

In a case of hepatolienal fibrosis with an enlarged spleen the preoperative blood picture showed the characteristic anæmia, granulopenia, and thrombocytopenia (fig. 1). Two months before operation hæmatemesis further lowered the hæmoglobin level, which rose rapidly after transfusion and iron by mouth. Immediately after splenectomy the polymorph and platelet counts increased, the white-cell count reaching a peak on or about the fourth postoperative day, and the platelets on the fourteenth day. Thereafter, over a period of months, the numbers of both the leucocytes and platelets decreased, though in neither case to as few as they had been before operation. The red-cell count and hæmoglobin value gradually increased over a long period.

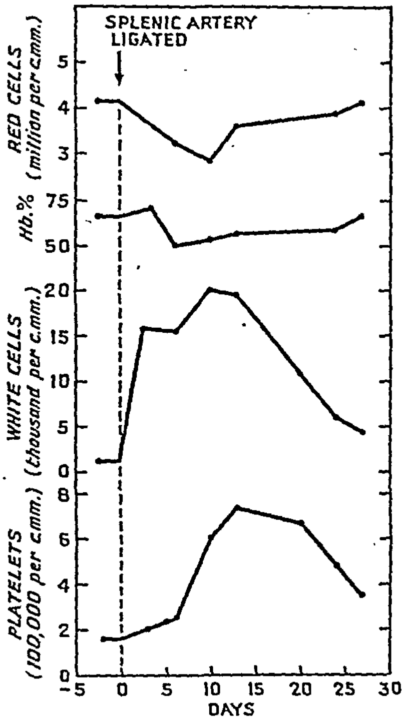


Fig. 4—Blood picture before and after operation in case 4 (hepatolienal fibrosis) in which ligation and division of the splenic and gastro-epiploic arteries caused a massive splenic infarct.

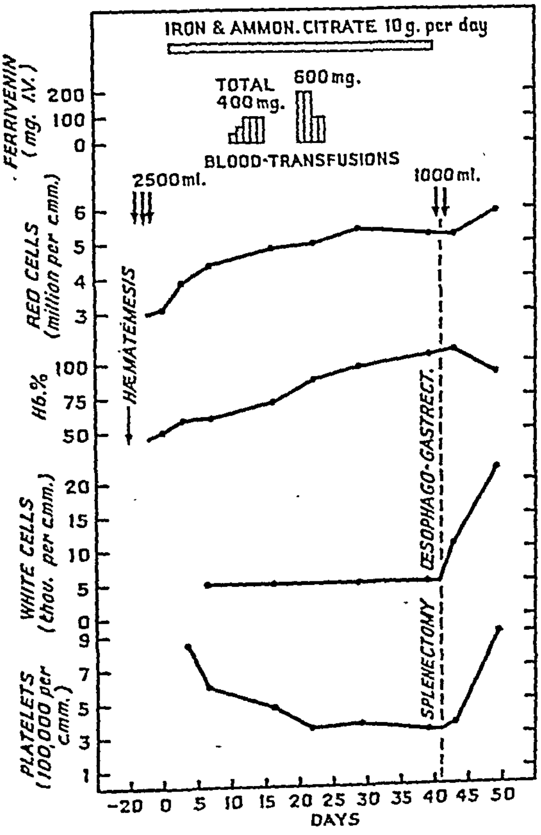


Fig. 5—Blood picture in case 4 twenty-six months after fig. 4, showing response to iron and to splenectomy.

When the splenomegaly and portal hypertension have been associated with extrahepatic portal obstruction, the peripheral blood presents a similar picture and reacts in a similar manner after splenectomy (fig. 2).

Effects of Ligation of Splenic Artery

Where splenectomy is not considered desirable, because of the poor general condition of the patient or the discovery at operation of extensive perisplenic adhesions, ligation of the splenic artery has been advocated as a less formidable operation (Blain 1918). The clinical details of 5 patients in whom such ligation was done are summarised in table I. Three different operations were used : in 2 cases ligation and division of the splenic artery on the upper border of the pancreas ; in 1 case ligation near the hilum of the spleen ; and in 2 cases ligation and division of the splenic and gastro-epiploic arteries. A record of 2 of the patients (case 3 with an extrahepatic block and case 1 with hepatolienal fibrosis), upon whom repeated blood-counts were done after operation, is shown in fig. 3. In both cases there was a postoperative decrease in erythrocytes and hæmoglobin, but in neither was there an increase in leucocytes or in platelets such as occurs after splenectomy. Cases 2 and 5, in which blood-counts were done less frequently, also showed no significant hæmatological changes after operation. In case 3 the continued presence of an enlarged spleen did not prevent a satisfactory response of the anæmia to iron by mouth.

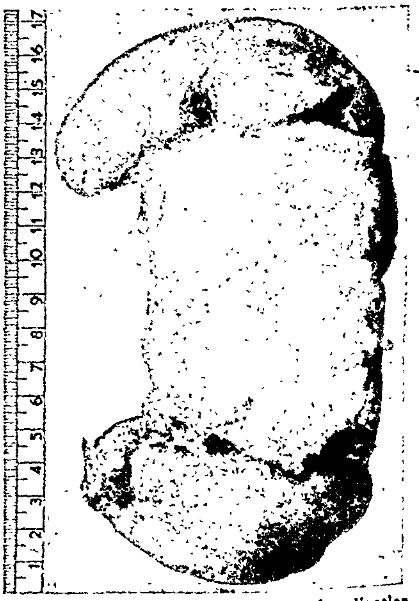


Fig. 6—Spleen removed 28 months after ligation and division of splenic and gastro-epiploic arteries, showing massive central infarct. (Scale in centimetres.)

In only 1 of the abovementioned 5 cases (case 4, with hepatolienal fibrosis) did a noticeable improvement in the peripheral blood picture follow splenic arterial ligation (fig. 4). There was an immediate increase of white-cell and platelet counts to large numbers, but after four weeks they had decreased to figures only slightly greater than those before operation. Two years later hæmatemesis recurred. There was an immediate posthæmorrhagic thrombocytosis, and the anæmia responded quickly and satisfactorily to iron therapy (oral and parenteral) (fig. 5). Splenectomy combined with limited œsophagogastrectomy was followed by typical postsplenectomy changes in the peripheral blood which were similar to those twenty-eight months previously after splenic arterial ligature. The appearance of the spleen removed at operation (fig. 6) provides a clue to the initial response ; there was a large central infarct with, above and below it, segments of living spleen which showed the classical histological changes of hepatolienal fibrosis described by McMichael (1934). Arterial ligations probably seldom produce actual infarction of the spleen or even any material reduction in the volume like erythema multiforme, stomatitis, conjunctivitis, and urethritis The interesting points are the preceding vaccination and the response to chloramphenicol

Common Lesions—Eye lesions are almost always present—usually a conjunctivitis with exudate and usually bilateral There may be œdema of the lids and blepharitis Cases of keratitis severe enough to cause blindness have been reported (Lever 1944), although with the use of chemotherapy this may be reduced (Goldfarb 1946) The lips are always involved and show erythema, swelling, fissuring, ulceration with hæmorrhage, and residual crusting Buccal lesions are almost always present, and may show a pseudomembrane or ulceration and vesiculation involving the tongue, palate, fauces, and pharynx Penile or vulvo-vaginal lesions with erythema, œdema, and vesiculation, with or without non-specific urethritis, are also common The rash is most often maculopapular, vesicobullous, or hæmorrhagic It is usually generalised in distribution but the scalp often escapes

Rarer Signs—Pneumonic lesions have been reported in the U S A by the Commission on Acute Respiratory Diseases (1946), Finland et al (1948), and Billow and Lowen (1952), and in this country by Church (1950) Sore throat, with or without dysphagia, and joint pains are occasional features, and erythema nodosum sometimes appears

Differential Diagnosis—The condition has to be distinguished from the other bullous and vesicular dermatoses and exanthemata These include the pemphigus group, dermatitis herpetiformis, the herpes group, bullous erythema multiforme, Kaposi's varicelliform eruption, vaccinia, varicella, and variola Drug eruptions should be considered, such as those due to arsenic, barbiturates, bromides, iodides, phenolphthalein, and quinine

I can find no report of the syndrome following vaccination, although a case of erythema multiforme complicating vaccination has been reported

The cause of this condition is still unidentified, and the treatment is mainly symptomatic, although chemotherapy will reduce secondary infection and probably prevent serious eye complications In the future cortisone and A C T H may provide the answer (Fishman 1951)

SUMMARY

A soldier, aged 20, fell ill with a case of Stevens-Johnson syndrome ten days after vaccination He was successfully treated with chloramphenicol

I am indebted to Dr P D C Kinmont for his helpful criticism.

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Fertilisers versus Organic Manures

The section of comparative medicine met on May 20, with Prof C L **Oakley**, the president, in the chair

Sir **William Ogg** (Rothamsted Experimental Station, Harpenden) explained the history of fertiliser development While manure was used from ancient times, liming came very much later, and it was only after 1842, when John Bennett Lawes, the founder of Rothamsted, patented his water soluble superphosphate fertiliser and showed it was better than the ground bones previously used, that research began into the best way to use different fertilisers for different crops on different soils This coincided with a time of great increase in population, and the urbanisation of Britain, which in turn meant that sewage from the towns went into the sea instead of restoring valuable chemical elements to the land Now the motor-car had replaced the horse, and the quantity of animal feeding stuffs imported annually had fallen to half the pre-1939 figure England and Wales now made about 35 million tons of farmyard manure a year, which represented about a third of all the nitrogen, a quarter of the phosphate, and half the potash actually added to the soil by farmers today Most of the recent increase in British food production was due to better fertiliser practice, and a survey had shown that many farmers still had a great deal to learn and could further increase their yields by using the correct fertiliser in the right time and place Before the war Holland used five times as much fertiliser annually as did Britain, and other European countries had similar figures

Proponents of "organic" farming differed in their degree of opposition to the use of chemical fertilisers some would permit basic slag (just as some teetotallers drink invalid port), but they all believed that manure had a vital principle lacking in all chemicals, and therefore that plants grown without it were inferior in nutritive quality and in resistance to disease The scientific evidence did not support this view Many plants could be grown in pure mineral solutions (hydroponics) even when special precautions were taken to eliminate soil bacteria on their roots Soil diseases were distributed quite differently from the areas of greatest use of fertilisers, and Rothamsted experiments had shown that nitrogenous fertilisers actually made wheat more resistant to some diseases Nor did fertiliser increase soil erosion The broad balk field at Harpenden had been heavily dressed with chemicals for the past 110 years, yet crops were still good, root and stubble organic matter was still available for ploughing in, and the soil microbe count was high (although in general very high counts did not necessarily mean better crops)

Fertilisers were essential for large crops because manure and compost could never supply much more than 10% of the need Town refuse and sewage sludge were inferior to good dung and too bulky to transport far To grow crops specially for composting was very uneconomic in land and labour This stated the British position, but it had to be remembered that soils in many parts of the world were naturally deficient in phosphorus, potash, or trace elements, and agriculture only became possible when these lacks had been made good with chemicals

Fertilisers were flexible in use, but required intelligent application, mistakes were possible Organic manures worked more slowly and sometimes gave the wrong balance of nutrients, but were nearly foolproof The two were not mutually exclusive but were complementary, and the best farming practice employed both

TABLE II—EFFECT OF PORTACAVAL ANASTOMOSIS ON BLOOD PICTURE

Case no.	Preoperative				Postoperative											
					1 month				6 months				> 12 months			
	Red cells (million per c.mm.)	Hb %	White cells per c.mm.	Platelets per c.mm.	Red cells (million per c.mm.)	Hb %	White cells per c.mm.	Platelets per c.mm.	Red cells (million per c.mm.)	Hb %	White cells per c.mm.	Platelets per c.mm.	Red cells (million per c.mm.)	Hb %	White cells per c.mm.	Platelets per c.mm.
6	3·38	69	4100	—	—	—	—	—	—	—	—	—	4·10	75	4900	139,000
7	3·90	73	7450	130,000	4·30	84	14,750	—	3·80	76	6800	—	—	—	—	—
8	3·00	67	1950	68,000	3·70	73	2900	70,000	—	—	—	—	—	—	—	—
9	4·05	76	3500	152,000	2·80	45	4150	98,000	3·43	60	5600	—	3·66	60	4650	—
10	3·80	63	4400	—	3·20	65	5250	—	—	—	—	—	*4·50	84	4500	96,000
11	3·50	77	3500	198,000	4·40	86	11,050	152,000	*4·50	90	6200	217,000	*4·40	86	6800	150,000
12	4·59	94	5000	106,000	4·40	75	4400	175,000	—	—	—	—	—	76	2400	—

* After adequate iron therapy.

of functioning splenic tissue. Histological examination of the spleen was possible in 3 patients on whom splenectomy was done subsequently. Only in the case already described did infarction occur. The changes observed in the other spleens and in the viable portions of the infarcted spleen were those usually found in portal hypertension. In none of the 5 patients did the spleen decrease in size after ligation of the splenic artery.

Effects of Portacaval Anastomosis

Portacaval anastomosis was done in 7 patients with portal hypertension; their hæmatological records are shown in table II. In 3 cases the spleen was considerably smaller after operation, and in every case there was direct or circumstantial evidence that the anastomosis remained patent. No significant change in the peripheral blood picture, other than that which might be expected from the relief of hæmorrhage and the administration of iron, accompanied these changes in the spleen and portal circulation. In case 8, where the patient presented the typical picture of hepatolienal fibrosis, transfusions effected an improvement in the red-cell count but portacaval anastomosis did not affect the leucopenia and thrombocytopenia (fig. 7). A month later splenectomy was followed by the characteristic and predictable changes in the peripheral blood. Histological examination of the spleen showed that the venous congestion had been completely relieved but that there was an intense cellular hyperplasia of the pulp.

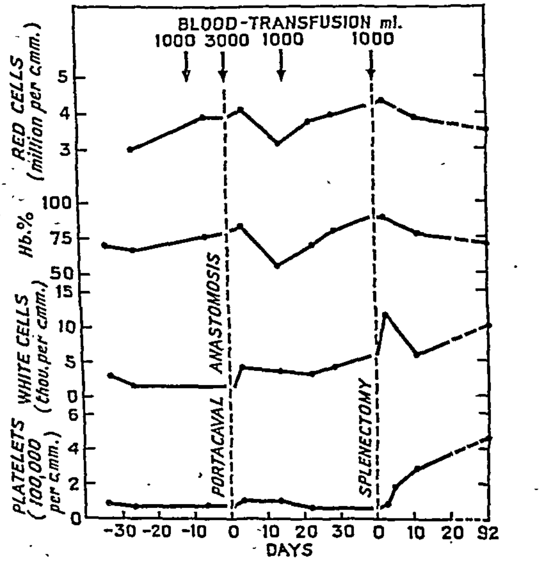

Fig. 7—Effect on blood picture of portacaval anastomosis and splenectomy in case 8 (hepatolienal fibrosis).

CONCLUSIONS

Observations in 46 cases of portal hypertension treated either by splenectomy alone or by splenectomy and splenorenal anastomosis indicate that the persistent leucopenia and thrombocytopenia found in this syndrome are rapidly relieved by splenectomy. These findings suggest a relationship between the levels of the leucocytes and platelets in the peripheral blood and enlargement or functional overactivity of the spleen, and is in accordance with the hæmatological concept of "hypersplenism."

After portacaval anastomosis the spleen became smaller in 3 cases from relief of venous congestion, but the pulp hyperplasia persisted, and in no case was the blood picture improved.

The effects of ligation of the splenic arterial supply by various operations were observed in 5 cases. The spleen did not decrease in size after any of these operations. Histological examination of the spleens of 3 patients in whom the splenic artery had been ligated and divided fifteen, eighteen, and twenty-eight months previously, showed either the typical changes of portal hypertension or complete localised infarction. The generalised atrophy of splenic tissue described by other workers (Watson 1935, Blain and Blain 1950) has not been observed. After splenic arterial ligation no improvement was noted in the blood picture except in 1 case in which there was extensive infarction of the spleen.

Neither relief of portal venous congestion by a portal-systemic venous anastomosis nor reduction in the blood-supply to the spleen by arterial ligation improves the leucopenia or thrombocytopenia characteristic of portal hypertension. In contrast the changes can be regularly relieved by splenectomy. Hence it may be inferred that the reduction in the leucocytes and platelets is directly related to some influence derived from the cellular components of the enlarged spleen.

In no case was there any evidence that any of the operations benefited the red-cell and hæmoglobin levels other than by control and prevention of œsophageal bleeding.

The observations recorded here were made on patients in the Royal Infirmary of Edinburgh and in the Presbyterian Hospital, New York, where one of us (A. I. S. M.) worked with Dr. Arthur H. Blakemore as a Rockefeller Foundation travelling fellow. Most of the hæmatological investigations were made by Miss Sheila T. Lindsay, B.SC.

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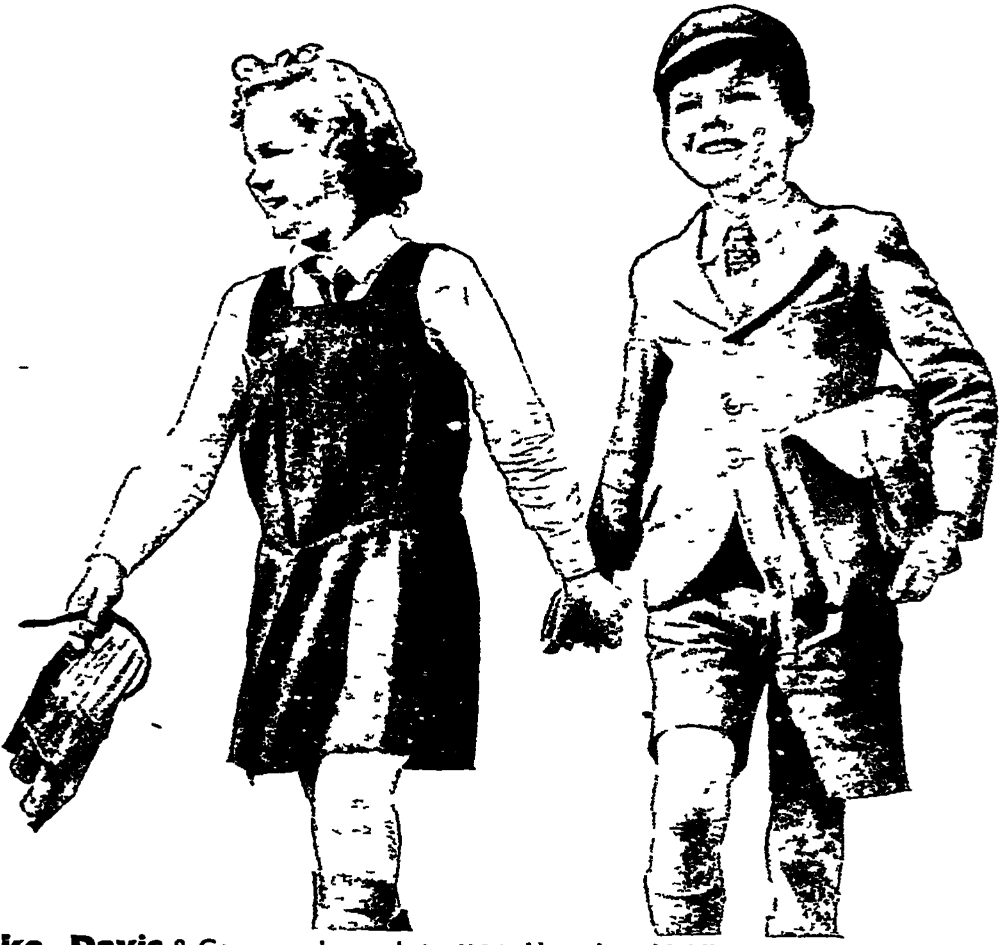

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EXPERIMENTAL ELECTROCARDIOGRAPHY OF THE FŒTUS

C. N. Smyth
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The advantages to the obstetrician of a continuous recorder or indicator of the rate and regularity of the fœtal heart are so evident that attempts have been made to make a satisfactory clinical instrument ever since the electrocardiograph was designed by Einthoven in 1903. Early workers were disappointed with their results, although they tried œsophageal, vaginal, and rectal electrodes and turned their attention to recordings of the equine fœtus and chick embryos in the shell. The advent of the valve amplifier gave a new impetus to the subject, and some recordings were obtained as early as 1923 from the human abdominal surface.

The whole subject is most thoroughly reviewed by Bell (1938) who himself built an equipment in 1938. His conclusions were as follows:

> "One $^1/_3$ of 32 cases showed positive results, but the other $^2/_3$ did not show any wave which could definitely be recognised as fœtal. It is suggested that the failure to secure positive results in all cases is due partly to differences in the electrical properties of the abdominal wall and partly to the electrical disturbances produced by the abdominal muscles."

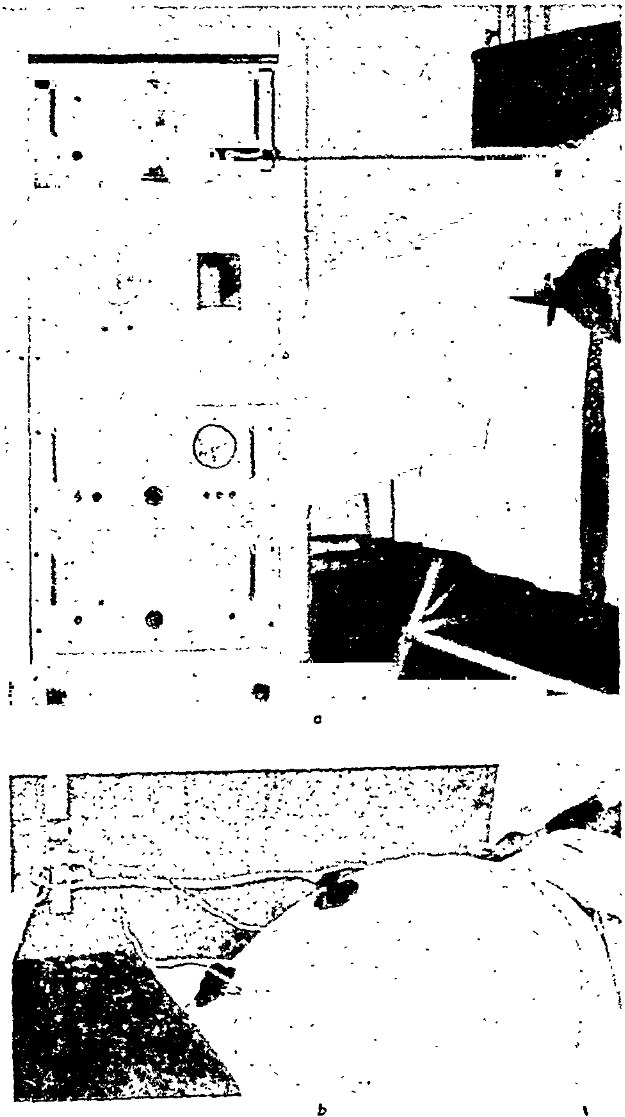

Fig. 2—Apparatus: *a*, fœtal heart 'QRS' electrocardiograph; *b*, electrodes on linea alba and iso-electric belt round waist.

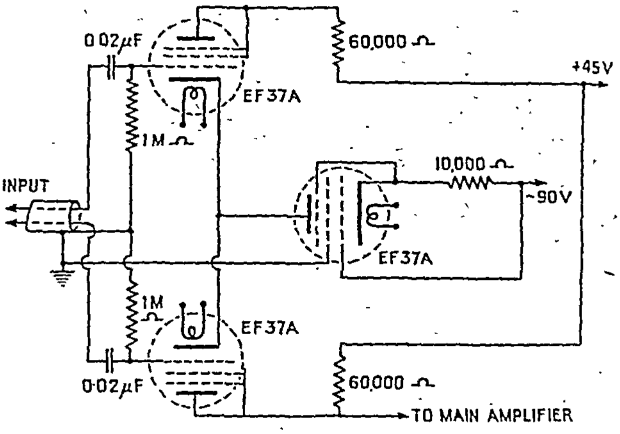

Fig. 1—Pre-amplifier circuit for fœtal electrocardiograph.

In recent years regard to the importance of early recognition of signs of fœtal distress has led to some reduction in the stillbirth-rate—e.g., by cæsarean section in the first stage of labour, by speedy forceps delivery in the second stage, and by simple methods, where they are effective, such as relieving pressure on the presenting part, sedation, and oxygen to the mother. If further improvement is to be obtained, then a more reliable method than occasional listening to the fœtal heart is necessary for the recognition of fœtal distress. Especial interest attaches to automatic recording in addition to the advantages of continuity and of convenience. It has been shown that frequent listening leads to anxiety in the mother, which reflects itself in the fœtal heart-rate as well as disturbing the mother's enjoyment and coöperation in the birth process.

The fœtal heart makes itself evident, as does the adult heart, by sound, by ballistic reaction, and by the electrocardiograph potentials. Sensitive measuring devices based on any of these effects are possibilities, and the selection of the one on which to concentrate a research programme is influenced by considerations of the extraneous disturbing effects which may lead to the production of artefacts in the recorded results, and considerations of the possibility of removing such unwanted disturbances.

Factors which disturb all recordings are maternal heart effects, movements of the mother or of the fœtus, and circulation noises and digestive noises in the patient. In the apparatus there is residual noise due to the discrete nature of valve currents and to thermal agitation, and noise which may be generated by friction or by chemical action between the patient's skin and the measuring device applied to her. Other sources of interference are extraneous room noises from people moving and talking, traffic, door and lift noises, and electrical disturbances from machinery, X rays, diathermy, and broadcasting stations, and frictional electricity from moving clothes, blankets, and trolleys.

Consideration of the practicability of eliminating unwanted effects from the recordings over long periods of time and with the minimum of inconvenience to the patient led us to concentrate on electrocardiography, although we first made preliminary tests with the other two methods to confirm that the supposed difficulties were real.

Our object was to record the heart-rate and irregularity up to and including delivery, so that, besides detecting fœtal distress, we could control the administration of sedatives, anæsthetics, and other drugs, and carefully

Reviews of Books

Contrast Psychology

A Concept of the Movements of the Human Spirit MURDO MACKENZIE, M D, M R C P, consultant physician in psychological medicine, St John's Hospital, Lewisham London Allen & Unwin 1952 Pp 305 21*s*

Dr Mackenzie looks at individual and community problems from his own highly characteristic viewpoint Briefly, he uses the term spirit to denote "the zest or enthusiasm which characterises mental activity at all levels" and believes that personality comprises two distinct components, the first being described as either Immediacy or Deliberation, the second as either Amplification or Simplification Each of these pairs is in irreconcilable contrast to its opposite number but may team up with either one of the other pair This rather rigid schema, inspired by Hegel and A N Whitehead, is applied to the discussion of the community sense of the ancient Greeks and Romans Christian medieval theology, the modern bid for Freedom (from John Locke to Stalin), and the psychology of the Unconscious (Freud, Adler, and Jung) These central chapters, which form the bulk of the book, are written in an eloquent narrative style reminiscent of Carlyle, and present familiar facts in a stimulating and original light The application of the author's cut-and-dried ideas to the consideration of clinical problems in the individual leaves the reader feeling that, somehow, human personality appears more pigeon-holed and docketed by this system of hard-and-fast contrasts than when it is viewed from the unitary standpoint—of psycho-analysis, for example Here are theories in plenty, but the facts and scientific data to confirm or disprove them are nowhere convincingly presented

Atlas of Skull Roentgenograms

BERNARD S EPSTEIN, M D, associate radiologist, Jewish Hospital of Brooklyn, New York, LEO M DAVIDOFF, M D, neurosurgeon Mount Sinai Hospital, New York City London Henry Kimpton 1953 Pp 400 110*s*

THIS book is a collection of X-ray films of the skull, with a short text preceding each section The emphasis is laid on the plain film the special investigations have been excluded It is comprehensive, and many beautiful examples and rare conditions are shown The authors' expressed intention was to keep the text as short as possible but this perhaps has been carried too far Anyone interested in so specialised a subject can be expected to know the essentials, and in many instances more detailed information would be welcome The films are reproduced as negatives, two to a page, and are up to modern American standards, but they do not all convey the very fine detail necessary for the study of skull films As with all atlases, except perhaps the geographical kind, one is left wondering for whom *it* was designed

Vitamin Digest

GUY W CLARK, technical director, Lederle Laboratories Division, American Cyanamid Co Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1953 Pp 254 47*s* 6*d*

THE aim of this book is to give a comprehensive but brief account of both the chemistry and the nutritional importance of all the known vitamins Its 17 chapters range in length from 22 pages about vitamin B_1 down to only 5 pages about *p* aminobenzoic acid After a brief account of the discovery of each vitamin the author attempts to discuss the main scientific developments in its investigation, and completes the picture with information on the allowances which are necessary for adults and children, and on the effects on the vitamin of cooking and food processing

Anyone who is familiar with the wealth of information now available on the vitamins will recognise the difficulty of the task which the author has set himself He must not only be widely read and experienced, but must be able to discriminate in deciding what material to include and what to reject The present work deserves praise at least for providing much valuable information in compact and well-connected narratives The choice of material, however, leaves many fundamental discoveries unmentioned Thus in the chapter on vitamin A no reference is made to the work on its chemical structure for which Karrer earned a Nobel award Steenbock and Black are given no credit for their classical discovery that foods are made antirachitic by ultra violet irradiation, and only one obscure reference is made to Dam's numerous recent contributions to research on vitamin E

Rheumatic Fever

Editor LEWIS THOMAS, M D Minneapolis University of Minnesota Press London Oxford University Press 1952 Pp 349 80*s*

THESE symposia, so often reported to us from the United States, are an admirable feature of American medical life in its academic reaches The local organisers usually pick the distinguished contributors, and a drug firm, or occasionally a charitable organisation (in this case the Minnesota Heart Association), pays their expenses Leading workers in the field under review summarise the position and bring their own up-to-the-minute contributions In a small subject, on which few are working, letter-writing and the reading of one or two journals may achieve the same object less pleasantly though more cheaply, but rheumatic fever demands the attention of cardiologist, pædiatrician, epidemiologist pathologist, bacteriologist, immunologist, chemist, and even surgeon All took part in this symposium, only the geneticist the public-health worker, and the student of comparative medicine seem to have missed their planes Dr Francis Schwentker's paper on the epidemiology of rheumatic fever partly makes up for their absence, but the focus generally is on tissue rather than patient This bias is partly corrected by Duckett Jones and Bland's paper on the natural history of the disease, as well as the studies of Rammelkamp, Denny, and Wannamaker on its epidemiology in the Armed Forces The twenty-odd papers were of high standard, and the discussions were generally apt and entertaining

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Pulmonary Tuberculosis (3rd ed Edinburgh E & S Livingstone 1953 Pp 324 24*s*) —This practical and trust worthy handbook has had a stormy time since the second edition appeared in 1946 for much has happened in the tuberculosis world since then Dr R Y Keers and Dr B G Rigden have had to take their text apart and rewrite it almost completely in order to express modern opinion on the bacteriology, chemotherapy and surgery, aftercare and prevention of this much harassed disease, and even then they have had misgivings lest the whole scene might change before publication date Dr F H Young in his foreword, however, says that this new edition will enable him to recommend this little book *to* his students with even more enthusiasm

Problems of Fertility in General Practice (2nd *ed* London Cassell 1953 Pp 259 18*s* 6*d*) —The first edition of this book, by Mr John Stallworthy, Mr Kenneth Walker, Dr Joan Malleson, and Dr Margaret Hadley Jackson, appeared in 1948 and was well received Since this new edition is identical in form and virtually unaltered in content, it must be assumed that the authors have considered that none of the recent contributions to the literature are worthy of comment in a book designed primarily for general practitioners Nevertheless, it would have been well to include some later references, and to comment on recent work, even if only to indicate to the practitioner that not every contribution to this subject should be accepted uncritically The chapter on "coital problems" remains an admirable exposition of this difficult aspect of infertility, while the section on abortion is again disappointing too much space being given *to* the Rh reaction, which is not really important in connection with abortion It is satisfactory to note the references to the actual cost of hormone therapy The useful appendix now includes a reference to the work of Mann and Parsons on the fructose content of seminal fluid The comments on the nature of approved contraceptives are *more* detailed than they were and the list of Family Planning Association clinics has been brought up to date, but the appendix could have been improved by the addition of a list of the hospitals both in London and in the provinces where complete investigation of infertility cases is undertaken relate obstetric procedures, such as cæsarean section and forceps delivery, to fœtal welfare.

The results to date of our efforts to achieve this objective are published now in the belief that they may be of use to many others who are attempting the same task, and in the hope that the remaining difficulties enumerated may be solved or turned to clinically good use. They are grouped into a brief description of the apparatus (adequate for those working on this side of the problem), a description of the results obtained, a statement of the remaining difficulties, and finally some suggestions arising from our work.

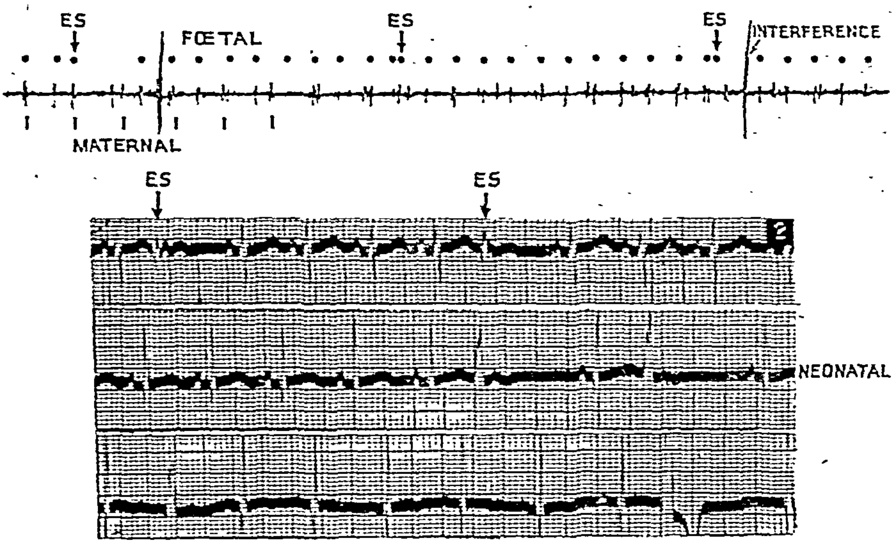

Fig. 6—Fœtal electrocardiogram showing congenital extrasystoles, with confirmation in recording made after birth.

APPARATUS

The recorder used for the investigations comprised a direct writing electrocardiograph of conventional design, preceded by a balanced preamplifier operated from batteries and arranged as shown in the circuit in fig. 1. The complete unit had an equivalent noise level of 3 µV when operating from a source impedance of 20,000 ohms. The frequency response was adjusted to cut off below 30 c.p.s. and above 100 c.p.s.

Connections to the patient were made by fine-silver electrodes placed on skin which had been cleaned and moistened with saline solution. The most satisfactory size was found to be 1¼ in. diameter.

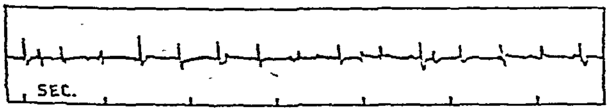

Fig. 3—Fœtal electrocardiogram: electrode of fine silver wire passed into amniotic cavity through polythene catheter during surgical induction of labour at full term.

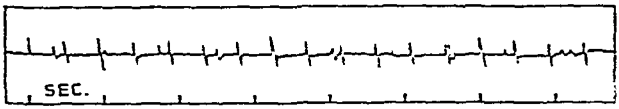

Fig. 5—Fœtal electrocardiogram: abdominal electrodes, fœtus at 20 weeks' gestation.

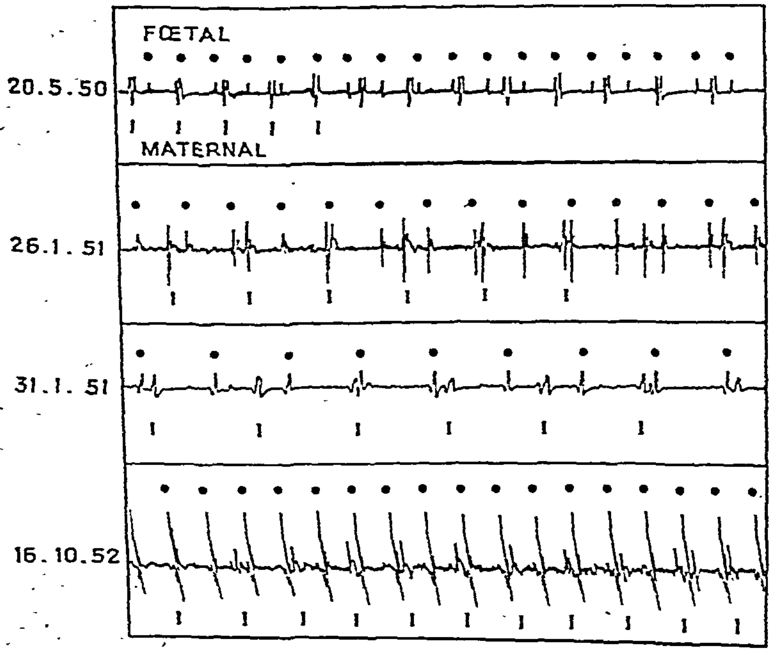

Fig. 4—Typical electrocardiograms made between 1950 and present date.

The preamplifier was of the balanced-input type, being sensitive to differences in potential between the two electrodes and very much less sensitive to potentials between either electrode and earth.

The most important improvement made in electrode connections was the addition of a metal braid belt placed round the mother's waist half-way between the xiphoid process and the fundus uteri. It was connected to earth. It had the effect of making the abdominal skin nearly iso-electric for maternal heart potentials. In men and non-pregnant women the effect of the belt was practically complete, but in pregnant patients there was a considerable difference between cases, a difference which may perhaps be related to uterine blood-supply or to placental position. The electrocardiograph is shown in fig. 2a, and the electrodes (covered with black cloth to make them clear in the photograph) in fig. 2b.

The electrocardiograph also included an integrator for registering fœtal heart-rate, and a neon tube which flashed synchronously with the fœtal heart-beats, and these worked well in cases where the fœtal-heart recordings were dominant over unwanted signals.

RESULTS

More than 100 patients have had fœtal electrocardiographic recordings; the fœtal Q R S complex was recognised in all but 2, and in these the fœtus was dead. In only about 20%, however, was the fœtal Q R S of greater amplitude than the maternal; in about a further 20% it was equal; and in the rest it was smaller but always recognisable.

The recordings confirmed Bell's (1938) suggestion that the linea alba was a favourable site for the electrodes. We placed one just above the umbilicus for vertex presentations, or at the fundus

THE LANCET

LONDON SATURDAY, JUNE 6, 1953

Bed Rest in Tuberculosis

REST in bed is the least disputed treatment of pulmonary tuberculosis But this simple measure was not always popular In the time of HIPPOCRATES it was recommended for treating hæmoptysis, and it was expected to cure the patient if he was not too emaciated Other allusions to rest are, however, few in ancient medical literature The great SYDENHAM advised horse-riding as a specific even " after wasting, night sweats and colliquative diarrhœa have signified the approach of death provided only that the journeys are long enough and the beds at night well aired " Subsequently physicians prescribed such exercise only for the more robust, but it was not until late in the 19th century that strict rest in bed began to be valued In 1863 JOHN HILTON in his book *On Rest and Pain*, recorded that a young girl with tuberculosis of the hip and lungs ceased to cough and improved in general health while remaining in bed with the hip splinted It seems that the importance of his observation was not generally appreciated, and in 1873 EDWARD TRUDEAU, when told that he had phthisis, followed the advice of his doctor and went to the Adirondacks to live out of doors and ride When this failed he rested, and the sanatorium he founded at Saranac is a memorial to the efficacy of rest in pulmonary tuberculosis

At Trudeau Sanatorium MITCHELL [1] has studied the results of bed rest in " minimal " pulmonary disease by analysing 589 cases of limited uncavitated tuberculosis which were treated between 1927 and 1946 As the mortality-rate was low—5% in twenty years—he used the relapse-rate to measure the effect of treatment, which basically consisted in rest in bed for all but three or four hours a day The duration of rest appeared to have no effect on the frequency of relapse Thus, of 310 patients who were in bed for only one or two months, 22 3% relapsed within five years, while of 109 who had six or more months in bed 22% relapsed As would be expected, the prognosis was significantly affected by the extent of the disease, but this could not explain the lack of correlation between duration of rest and relapse, for it did not appear to have been an important factor in determining the duration of rest Moreover, those who spent the shortest time in the sanatorium seemed to have done no worse than those who spent the longest MITCHELL then investigated the late results in patients with pleural effusions [2] The relapse-rate within five years of discharge was found to be influenced by the presence of minimal pulmonary disease and by its extent But, once more, the duration of bed rest or stay in the sanatorium had no obvious effect The interpretation of such retrospective investigations is, as MITCHELL emphasises, very difficult, and he wisely presents the facts without drawing conclusions The absence of a clear relationship between duration of treatment and liability to relapse might well be due to the many variables that cannot be measured For instance, it is impossible to evaluate or record all the factors that make the physician decide to start getting a patient up, and radiographic appearances and the bacterial content of the sputum are very crude indices of the patient's state Moreover, the patient's fate after discharge is probably determined much more by himself and his environment than by the treatment he has received in hospital

CHRISTOPHER BENNET [3] wrote in 1654

> " The manner of lying at Night and sleeping is by no means to be neglected Lying on the Left side is most hurtful to those who have the Lungs burdened by a thin Suffusion, and they who lie on their Backs are most incommoded if they are offended by a Distillation "

It seems that, although there may not nowadays be a " thin suffusion," lying on the left side can be harmful for patients with a tuberculous cavity on the right HELM [4] investigated the sleeping habits of a group of patients with unilateral cavities and found that spread to the other lung was commoner in those who habitually slept on the healthy side Sleeping on the side is thought to promote aspiration into the lower lung of infected material from a cavity in the upper. Such aspiration spread is probably a common mode of progression, and recently SCHWARTZ [5] has claimed that another common route is by the bronchial lymphatics The infection passes along the chain of lymph-nodes and may reach the opposite side by the mediastinal lymphatic communications, segmental tuberculous pneumonia follows from rupture of a node into the bronchus and aspiration of the caseous contents It seems that posture in bed may also affect the size of cavities Over thirty-five years ago WEBB et al [6] [7] in the U S A advised that patients should be nursed on their affected side, and recorded many good results from this simple postural treatment Little more was heard of it until 1948, when DILLWYN THOMAS [8] reported that it was useful for some patients with large cavities who were being prepared for thoracoplasty Since then several others [9–12] have written favourably of this treatment, which has been variously termed reversed postural drainage, postural retention, or postural reduction The benefit from it has been ascribed to decrease in the volume of the dependent lung and changes in its blood-flow, lessened respiratory movement, and retention of secretions within the cavities or (by others) improved drainage of cavities

BENNET sought to explain his observations in the idiom of his time by means of " distillations," " fizzy serum," and " acrid humours " In his day he can have seen few cures, and he himself died of consumption a year after his book was published It is interesting to recall his long-forgotten advice, for the manner of lying is by no means neglected in the modern treatment of pulmonary tuberculosis by rest in bed for breech cases, and the other close to the symphysis pubis (fig. 2b). Vaginal and rectal electrodes cause discomfort of the perineum with consequent increase in perineal action potentials which disturbed the recordings. Œsophageal electrodes were not tried. In one case a fine silver-wire electrode was passed into the amniotic sac through a 'Polythene' catheter which had been previously positioned at a high artificial rupture of membranes, and the result was superior to abdominal recording by a factor of five times in fœtal-heart potential to all unwanted potentials (fig. 3).

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[1] Mitchell R S *Amer Rev Tuberc* 1953, 67 401
[2] Mitchell, R S *Ibid*, p 421
[3] Bennet C The Nature and Cure of Consumptions London, 1720
[4] Helm W H *Thorax* 1951 6 417
[5] Schwartz P *Amer Rev Tuberc* 1953 67 440
[6] Webb G B Forster A M Houck, F M *J Amer med. Ass* 1916 67 1422
[7] Webb G B Forster A M Burton, G G *Ibid* 1921, 76, 846
[8] Thomas D *Tubercle* 1948 29 216
[9] Dormer B A, Greathead E Pirrie, G, Smit, P Randall, T, Van Rensberg M *Dis Chest* 1951, 20, 407
[10] Deshmukh, M D, Williams E H *Tubercle* 1951, 32, 240
[11] Aslett, E, Erin, L *Ibid* 1952 33, 206
[12] Lyons, J P *Ibid* 1953 34, 87

Four typical recordings from the abdominal surface taken between May, 1950, and the present date are shown in fig. 4. Fig. 5 shows a similar recording from a patient only 20 weeks pregnant.

The remaining difficulties are to eliminate the maternal heart-beat potential from the fœtal record and to make the apparatus less responsive to action potentials from voluntary muscle. An additional amplifier working in antiphase to the fœtal electrocardiograph and collecting potentials from the maternal heart only would make it possible to eliminate the maternal trace from the record, but the method involves applying more electrodes to the mother, and the process becomes cumbersome. Interference from voluntary-muscle action potentials may be further reduced by a sharper frequency cut-off to the amplifier top frequency characteristic.

The work has shown that the apparatus may give information on two subjects other than that for which it was originally designed: (1) the amplitude and distribution of maternal heart potentials upon the abdominal surface below the iso-electric belt may be correlated with records taken in cases of retained placenta or cæsarian section to give some indication of the position of the placenta; and (2) the presence of action potentials on the recordings gives immediate indication of the patient's ability to relax between contractions, and can be used, if coupled to a loud-speaker, to obtain the patient's coöperation.

The variation of fœtal heart-rate during contractions, during administration of oxygen or of sedatives to the mother, or when the mother is placed in an attitude which removes pressure from the presenting part, may give information leading to a classification of fœtal distress which will give a rational basis for treatment.

Fig. 6 shows the fœtal and neonatal electrocardiograms of a child with congenital extrasystoles.

Professor Nixon, director of the obstetric unit, proposed this investigation and has given much practical encouragement. The work was made possible through the generosity of the Board of Governors of University College Hospital.

ADDENDUM

Since this article was written, the author has had the help of Messrs. Muirhead Ltd., in making energy-frequency analyses of the QRS complex of adult, newborn, and fœtal hearts. The conclusions were that:

(1) The energy is widely distributed in frequency but is maximal in the normal adult between the frequences 10 and 20 c.p.s.

(2) In both the newborn and the *fœtus* the energy is greatest between 20 and 40 c.p.s.

Furthermore it has been shown that if the frequency response of the recording apparatus is limited to 40 c.p.s., the interfering effects from gross muscle action potentials are substantially reduced.

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ERYTHEMA MULTIFORME EXUDATIVUM MAJOR

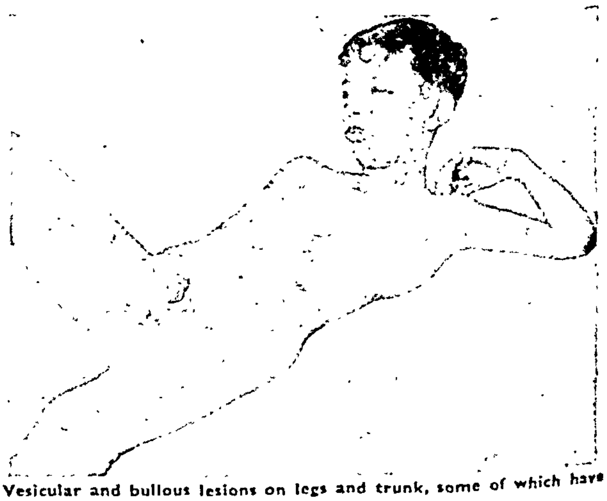
(STEVENS-JOHNSON SYNDROME)

D. M. DAVIES
M.R.C.S.
MEDICAL REGISTRAR, BOLINGBROKE HOSPITAL, LONDON

ERYTHEMA multiforme exudativum major (Thomas 1950, Ashby and Lazar 1951), the so-called Stevens-Johnson syndrome, is a familar disease to dermatologists and ophthalmologists, but it is not so well known to others; nor does it receive the attention it deserves in general medical textbooks.

In the past the subject has been confused, for several diseases, having important features in common, have been described as separate entities. More recently, however, it has become customary to regard these as different forms of one disease (Ashby and Lazar 1951, *Journal of the American Medical Association* 1951, Billow and Lowen 1952). Thus, Hebra (1860) first described "erythema multiforme exsudativum" as an illness characterised by pleomorphic lesions confined to the skin without systemic disturbance; though later (Hebra 1866) he described a case in which the typical rash was associated with pneumonia. Later, others described cases in which the pleomorphic skin rash was accompanied by a more severe illness, with ulceration of the eyes, mouth, and genitalia, and, in some cases, urethritis and an abacterial pneumonia. Some of these cases were described under such names as "ectodermosis erosiva pluriorficialis" (Rendu 1916, Klauder 1937), "dermato-stomatitis" (Baader 1925), "the new eruptive fever" (Stevens and Johnson 1922), "the triple complex" (Behcet 1940), and "the mucosal-respiratory syndrome" (Stanyon and Warner 1945). Recently it has been argued that all these diseases should be included within Hebra's original erythema multiforme exudativum (*Journal of the American Medical Association* 1951, Billow and Lowen 1952); while others (Thomas 1950, Ashby and Lazar 1951) have subdivided the disease into minor and major forms, the minor form corresponding to Hebra's original description, and the major form to the type of illness described by Stevens and Johnson and others.

In the minor form the skin rash may show macules, papules, vesicles, or bullæ, or a mixture of two or more. The lesions, which are usually deep red at first and later purplish, are typically distributed on the sides of the face and neck, and on the extensor surfaces of the limbs. There is little systemic disturbance. The major form has



Vesicular and bullous lesions on legs and trunk, some of which have broken down

Are you

...taking your iron regularly?

It is generally agreed in Medical circles that a sufficient intake of iron is of paramount importance during pregnancy

To prescribe iron, in some form, to expectant and nursing mothers is a simple procedure, but can you always be sure that it will be taken?

How many times do patients confess, under gentle pressure from their doctor or nurse, that they somehow forgot to take their tablets after breakfast or lunch?

You can ensure that your patients are receiving an adequate dosage of iron if you prescribe PRENATALAC for them This food, prepared specially for expectant and nursing mothers, contains 50 mgms of Fe et Amm Cit to the ounce, thus ensuring an adequate intake

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a prodromal period of about a week during which such symptoms as general malaise, cough, vomiting, and epistaxis may appear. These symptoms are followed by the rash which may involve the eyes, mouth, and genitalia, as well as the skin of the face, trunk, and limbs. The scalp is almost invariably spared. Urethritis and pneumonia may also be present. The illness may last from two weeks to two months and usually ends in complete recovery, though it is sometimes fatal. Corneal scarring may produce blindness.

The cause is unknown. In some cases it has been associated with underlying visceral disease; in others, allergy to foods, bacterial toxins, or drugs—especially sulphonamides—has been suggested as a cause; while some writers have suggested that a virus is responsible (Finland et al. 1948, Anderson et al. 1949).

As might be expected, there is no general agreement on treatment. Success has been claimed for sulphonamides and penicillin (Wright et al. 1947), and for aureomycin (Church 1950, Lynas 1950). Others deny the specificity of these drugs, but agree that one or other should be given to combat secondary infection, especially of the eyes and lungs (Billow and Lowen 1952). Cortisone has been tried recently with encouraging results (Fishman 1951); and adrenocorticotropic hormone (A.C.T.H.) is sometimes very effective (Caldwell 1953).

CASE-RECORD

This case illustrates unusually clearly the main features of erythema multiforme exudativum major.

A boy, aged 10, was admitted to the Bolingbroke Hospital on Aug. 19, 1952. On Aug. 9 he had an attack of migraine, to which he was subject. The headache gradually subsided the next day, but the day after that he had a cough, which gradually became worse in the next few days, and he became listless and feverish. On Aug. 15 he lost his appetite, vomited several times, and slept poorly. Next day his cough was very much worse, and he became flushed and irritable. His mouth became sore, his lips swollen, and his eyes red and watery. One or two irritating spots appeared on the trunk and limbs. Treatment with sulphonamides was begun, but that night his condition deteriorated and he became delirious. There was quite severe bleeding from the mouth, followed by four severe epistaxes. The spots became more profuse and the eyes purulent. On Aug. 18, the day before his admission, sulphonamides were stopped and penicillin by injection was started.

When he came to hospital, he was profoundly ill, with a temperature of 103°F, a pulse-rate of 130 per minute, and a respiratory rate of 36 per minute. The lips were swollen, ulcerated, and encrusted with dried blood. The gums, tongue, and buccal mucosa were red, ulcerated, and bleeding. There were several small vesicles on the conjunctivæ, which were inflamed and purulent; the corneæ were not affected. The rash consisted of vesicles and bullæ which had broken down in places, leaving ulcers set on purplish patches of skin. On the upper limbs the rash involved mainly the extensor aspects of the arms, forearms, and hands. On the lower limbs the lesions were most numerous on the front and medial surfaces of the thighs (see figure), the medial surfaces of the legs, and the dorsal surfaces of the feet. All surfaces of the trunk were involved; but the axillæ, palms, and soles escaped. The scrotum, prepuce, glans penis, and meatus were ulcerated, and there was a scanty urethral discharge. In the chest, there were scattered rhonchi in all areas, with fine crepitations at the right base.

Investigations.—A radiograph of the chest showed patchy consolidation of the right lower perihilar region. Hb 92%; white-cell count 10,300 per c.mm. (polymorphs 71%, lymphocytes 15%, monocytes 12%, and plasma cells 2%); erythrocyte-sedimentation rate 56 mm. in 1st hour (Westergren). Blood-culture sterile. Examination of the contents of the bullæ showed a few pus cells, but the culture was sterile. Swabs from the nose and throat showed no significant pathogens. The urine showed no abnormality, the urethral discharge being short-lived.

Progress and Treatment.—The morning after admission the temperature fell to normal, but rose in the evening to 104·2°F. It gradually subsided during the next five days, and, apart from one rise to 99·6°F on Aug. 30, it then remained normal. Treatment with penicillin was continued after admission, and chloramphenicol was also given. On Aug. 21, though his temperature had fallen, he appeared so ill that sulphadiazine (total dosage 28 g.) and aureomycin (total dosage 24 g.) were substituted, but they had no dramatic effect. On Aug. 28 the condition of his eyes gave rise to anxiety, and cortisone eye-drops (6·25 mg. to 1 ml. of saline solution) were instilled for seven days. His condition then gradually improved, and he was discharged on Sept. 18.

SUMMARY

A boy, aged 10, showed the main features of Stevens-Johnson syndrome (erythema multiforme exudativum major) unusually clearly.

He was treated successively with sulphonamides, penicillin, chloramphenicol, and sulphadiazine and aureomycin. Cortisone eye-drops were also given. He recovered completely.

I am indebted to Dr. R. Ewing Rodgers for permission to publish this case, and to Mr. D. M. Thomas for the photograph.

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STEVENS-JOHNSON SYNDROME TREATED WITH A.C.T.H

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Stevens-Johnson syndrome is thought to be a variety of erythema multiforme exudativum. Robinson (1951) includes this disease, along with erythema multiforme, ectodermosis erosiva pluriorificalis, Behcet's disease, and Reiter's disease, in the term "ocular mucous-membrane syndrome." It was first described as a separate entity by Stevens and Johnson (1922).

The syndrome consists of a skin rash associated with lesions of the mucous membranes (such as stomatitis, vaginitis, or urethritis), the eye, and the respiratory tract. The skin lesions may be macular, papular, iris-type, vesicular, or bullous. The ocular lesions consist of conjunctivitis, iritis, or keratitis. Corneal ulceration may occur and lead to total blindness. In the respiratory tract there may be an acute bronchitis or pneumonitis, but this system is not always attacked (Finland et al. 1948). The onset is usually abrupt and systemic disturbance may be considerable. Untreated, the disease usually runs a course of about three weeks, ending in recovery, though it is occasionally fatal. The chief danger, however, is damage to the eyes.

Treatment of the disease has varied. Only fair results have been claimed with sulphonamides (Givner and Ageloff 1941, Erger 1944, Kove 1945, Wright et al. 1947, Wentz and Seiple 1947, Thomas 1950) and *penicillin* (Kove 1945, Wright et al. 1947, Thomas 1950). The course of the disease has hardly been shortened by these drugs, though complications may have been controlled.

THE LANCET

LONDON SATURDAY, JUNE 6, 1953

Bed Rest in Tuberculosis

REST in bed is the least disputed treatment of pulmonary tuberculosis But this simple measure was not always popular In the time of HIPPOCRATES it was recommended for treating hæmoptysis, and it was expected to cure the patient if he was not too emaciated Other allusions to rest are, however, few in ancient medical literature The great SYDENHAM advised horse-riding as a specific even " after wasting, night sweats and colliquative diarrhœa have signified the approach of death provided only that the journeys are long enough and the beds at night well aired " Subsequently physicians prescribed such exercise only for the more robust, but it was not until late in the 19th century that strict rest in bed began to be valued In 1863 JOHN HILTON in his book *On Rest and Pain*, recorded that a young girl with tuberculosis of the hip and lungs ceased to cough and improved in general health while remaining in bed with the hip splinted It seems that the importance of his observation was not generally appreciated, and in 1873 EDWARD TRUDEAU, when told that he had phthisis, followed the advice of his doctor and went to the Adirondacks to live out of doors and ride When this failed he rested, and the sanatorium he founded at Saranac is a memorial to the efficacy of rest in pulmonary tuberculosis

At Trudeau Sanatorium MITCHELL [1] has studied the results of bed rest in " minimal " pulmonary disease by analysing 589 cases of limited uncavitated tuberculosis which were treated between 1927 and 1946 As the mortality-rate was low—5% in twenty years—he used the relapse-rate to measure the effect of treatment, which basically consisted in rest in bed for all but three or four hours a day The duration of rest appeared to have no effect on the frequency of relapse Thus, of 310 patients who were in bed for only one or two months, 22 3% relapsed within five years, while of 109 who had six or more months in bed 22% relapsed As would be expected, the prognosis was significantly affected by the extent of the disease, but this could not explain the lack of correlation between duration of rest and relapse, for it did not appear to have been an important factor in determining the duration of rest Moreover, those who spent the shortest time in the sanatorium seemed to have done no worse than those who spent the longest MITCHELL then investigated the late results in patients with pleural effusions [2] The relapse-rate within five years of discharge was found to be influenced by the presence of minimal pulmonary disease and by its extent But, once more, the duration of bed rest or stay in the sanatorium had no obvious effect The interpretation of such retrospective investigations is, as MITCHELL emphasises, very difficult, and he wisely presents the facts without drawing conclusions The absence of a clear relationship between duration of treatment and liability to relapse might well be due to the many variables that cannot be measured For instance, it is impossible to evaluate or record all the factors that make the physician decide to start getting a patient up, and radiographic appearances and the bacterial content of the sputum are very crude indices of the patient's state Moreover, the patient's fate after discharge is probably determined much more by himself and his environment than by the treatment he has received in hospital

CHRISTOPHER BENNET [3] wrote in 1654

> " The manner of lying at Night and sleeping is by no means to be neglected Lying on the Left side is most hurtful to those who have the Lungs burdened by a thin Suffusion, and they who lie on their Backs are most incommoded if they are offended by a Distillation "

It seems that, although there may not nowadays be a " thin suffusion," lying on the left side can be harmful for patients with a tuberculous cavity on the right HELM [4] investigated the sleeping habits of a group of patients with unilateral cavities and found that spread to the other lung was commoner in those who habitually slept on the healthy side Sleeping on the side is thought to promote aspiration into the lower lung of infected material from a cavity in the upper Such aspiration spread is probably a common mode of progression, and recently SCHWARTZ [5] has claimed that another common route is by the bronchial lymphatics The infection passes along the chain of lymph-nodes and may reach the opposite side by the mediastinal lymphatic communications, segmental tuberculous pneumonia follows from rupture of a node into the bronchus and aspiration of the caseous contents It seems that posture in bed may also affect the size of cavities Over thirty-five years ago WEBB et al [6] [7] in the U S A advised that patients should be nursed on their affected side, and recorded many good results from this simple postural treatment Little more was heard of it until 1948, when DILLWYN THOMAS [8] reported that it was useful for some patients with large cavities who were being prepared for thoracoplasty Since then several others [9–12] have written favourably of this treatment, which has been variously termed reversed postural drainage, postural retention, or postural reduction The benefit from it has been ascribed to decrease in the volume of the dependent lung and changes in its blood-flow, lessened respiratory movement, and retention of secretions within the cavities or (by others) improved drainage of cavities

BENNET sought to explain his observations in the idiom of his time by means of " distillations," " fizzy serum," and " acrid humours " In his day he can have seen few cures, and he himself died of consumption a year after his book was published It is interesting to recall his long-forgotten advice, for the manner of lying is by no means neglected in the modern treatment of pulmonary tuberculosis by rest in bed

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[1] Mitchell R S *Amer Rev Tuberc* 1953, 67 401
[2] Mitchell, R S *Ibid* p 421
[3] Bennet C The Nature and Cure of Consumptions London, 1720
[4] Helm W H *Thorax* 1951 6 417
[5] Schwartz, P *Amer Rev Tuberc* 1953, 67 440
[6] Webb G B Forster, A M Houck, F M *J Amer med Ass* 1916 67 1422
[7] Webb G B Forster A M Burton, G G *Ibid* 1921, 76 846
[8] Thomas D *Tubercle* 1948 29 216
[9] Dormer B A. Greathead, E, Pirrie G, Smit, P, Randall T, Van Rensberg, M *Dis Chest* 1951, 20 407
[10] Deshmukh, M D Williams E H *Tubercle*, 1951, 32, 240
[11] Aslett, E, Erin L *Ibid*, 1952 33 206
[12] Lyons, J P *Ibid* 1953 34, 87

Recent results with aureomycin (Church 1950, Lynas 1950, Khayat and Jacoby 1950, Robinson 1951) have been more hopeful, and the course of the disease has apparently been shortened. In a case reported by Orme (1952), neither penicillin nor aureomycin appeared to have any effect, and the patient died.

In my view many features of the syndrome suggest an allergic basis, and in the case reported here it was decided to try the effect of adrenocorticotropic hormone (A.C.T.H.). So far only four previous reports of the use of A.C.T.H in this condition have been noted (Wammock et al. 1951, Agostas et al. 1951, Orme 1952, Steigman and Kelly 1952). It seems important to record the following case because of the dramatic response to A.C.T.H., and because the rarity of the disease makes it unlikely that a large series of cases can be studied in one centre.

CASE-RECORD

An obese woman, aged 54, was admitted to hospital on Oct. 17, 1951. She was first seen in the medical outpatient department one month previously, when she was found to be suffering from myxœdema, for which thyroid was given. One week before admission she developed dysuria and frequency which was treated with sulphadimidine and potassium citrate for four days. Both drugs were then stopped because tonsillitis, stomatitis, and an extensive generalised rash developed on the fourth day of treatment. Anti-histamine cream was prescribed before admission, but it did not seem to help the condition. Bilateral conjunctivitis was noted twenty-four hours before admission. There was no history of previous allergy or the taking of any drug before the onset of the dysuria, apart from small doses of thyroid extract. She had suffered from rheumatic fever in childhood. There was no significant family history.

On admission she was very ill with an axillary temperature of 101°F and a pulse-rate of 100 per minute. The stomatitis was so severe that she had great difficulty in swallowing and she had taken no fluids for at least twelve hours. There was swelling and blistering of the lips and buccal mucosa, and several sloughing erosions on the buccal mucosa where large vesicles had broken down. She had definite halitosis.

The rash covered the face, the upper arms, the forearms, the dorsum of both hands, the front of both lower legs, and the buttocks. It consisted of macules, papules, and vesicles: the macules were purplish-red, and over the forearms and legs they had the typical iris configuration seen in erythema multiforme. There were papules and vesicles on both labia majora and labia minora. Several of the vesicles had ruptured leaving sloughing erosions. The inflammation had extended to the urethra, thus accounting for the dysuria. The palpebral and scleral conjunctivæ on both sides were very injected. A diagnosis of Stevens-Johnson syndrome was made.

She also had aortic stenosis, with grade II apical and aortic systolic murmurs. The rhythm was regular and the blood-pressure was 100/70 mm. Hg. The electrocardiographic tracings were normal. No abnormalities were found in the respiratory system or abdomen, and a radiograph of the chest was normal. The lymphatic glands and nervous system were also normal.

Investigations.—Hb 92%; white-cell count showed a mild polymorphonuclear leucocytosis (87% polymorphs in a total count of 11,100); W.R. negative. Apart from a small amount of protein present on admission, which cleared completely within four days, the urine was normal.

Progress and Treatment.—On the day of admission 0·5 ml. of 1 in 1000 adrenaline was given by injection with a little relief, and she was able to swallow slightly more easily. This was followed by 5 ml. (50 mg.) of 'Benadryl' intravenously. The dysphagia recurred, and twenty-four hours later these drugs were repeated but with little benefit. There was no improvement in the skin condition.

Two days after admission, in view of the lack of response to the anti-histamines, it was decided to try A.C.T.H. She received 25 mg. intramuscularly every six hours for four days. The dose was reduced to 20 mg. eight-hourly for a further three days and on the eighth day 10 mg. was given eight-hourly. The drug was then stopped. Improvement was noticeable within twelve hours. After twenty-four hours swallowing was easier, but the patient had a sharp attack of diarrhœa and vomiting which cleared up in twelve hours. After three days on A.C.T.H. improvement was considerable; swallowing was normal, the rash was rapidly fading, the erosions in the mouth and vulva were healing, and dysuria had ceased. Conjunctivitis was still present but minimal. Ten days after admission tests of sensitivity to sulphadimidine were carried out, both as a patch test and intradermally. Both tests were negative.

The patient was discharged twelve days after admission, when the rash had almost disappeared. Three weeks later no signs of the disease remained.

DISCUSSION

The cause of this disease is still obscure. Stevens and Johnson (1922) thought that infective factors were important, and a virus infection has been suggested (Patz 1947, Finland et al. 1948, Anderson et al. 1949). Klauder (1937) and Fitzgerald (1947) pointed out the resemblance between this disease and human foot-and-mouth disease. There is justification therefore in the use of aureomycin. But the negative pathological findings emphasised by many authors (Murphy 1944, Erger 1944, Khayat and Jacoby 1950, Thomas 1950, Wammock et al. 1951) are more in favour of an allergic origin. Drug allergy has been noted as a cause, and cases described by Greenberg and Messer (1943) and Dardinski (1945) ended fatally after sulphadiazine therapy.

Sulphadimidine was not used in the case described here until after the onset of dysuria, which was taken as the first sign of the disease. The beneficial effects of A.C.T.H. in certain types of allergy are well known, and have been recently stressed by Simpson (1952), and Pickering (1952), and it was therefore decided to use A.C.T.H. Although the patient was very ill on admission, she had made an impressive recovery after only three days' treatment, and she was completely cured after ten days on A.C.T.H. The effect was so rapid that dangerous complications had no chance to develop; this applies especially to affections of the eye. There has been no recurrence so far. Recurrences have been reported (Thomas 1950, Robinson 1951, Orme 1952), and they are thought to be a feature of the disease. The few cases of Stevens-Johnson syndrome in which the use of A.C.T.H. has been reported have all responded favourably. The evidence seems to justify the trial of A.C.T.H. in more cases of this syndrome.

SUMMARY

Stevens-Johnson syndrome in a woman of 54 responded dramatically to A.C.T.H. The use of A.C.T.H. in more cases of this syndrome would give a clearer picture of its value. The dramatic response supports the suggestion that this is an allergic condition.

My thanks are due to Dr. Kenneth Robertson for permission to publish this case and for many helpful suggestions.

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Treatment of Hepatic Coma

In hepatic disease coma is a serious complication associated with a high mortality Fortunately this complication is uncommon, but because of its very uncommonness the value of any new form of treatment cannot easily be assessed Furthermore, until the cause of the coma is better understood, treatment will continue to be empirical

In some patients with severe hepatic disease coma may be precipitated by therapeutically induced changes in their blood electrolytes Large doses of glucose intravenously may result in severe hypopotassæmia, and severe salt restriction, especially if associated with paracentesis and administration of mercury diuretics, may lead to the low-salt syndrome With either of these states, there may be drowsiness and stupor, which is rapidly dispelled when the electrolyte imbalance is corrected and some of the successes claimed for various therapeutic regimes are probably attributable to this mechanism The prognosis also depends partly on the underlying hepatic lesion Coma supervening, for example in a case of Laennec's cirrhosis almost invariably heralds the closing stages of the disease, whereas recovery from coma associated with liver-cell necrosis is by no means rare The high mortality with coma in Laennec's cirrhosis is illustrated by KARL and his colleagues [1] Of their series of 58 patients, all but 1 died, and as two-thirds of the patients were in hospital when coma developed, the high mortality cannot be attributed to lack of opportunity for proper treatment KARL et al rely on tube feeding with an adequate high-protein, low-salt diet, with which intravenous infusion of glucose should be unnecessary Vitamin supplements are also recommended together with crude liver intravenously There is nothing really new in this treatment, and no reason to expect that it will yield significantly better results than its predecessors In the treatment of coma associated with acute hepatic necrosis the situation is somewhat different LATNER [2] has done well to emphasise that most patients can recover from this condition, owing to the survival of considerable numbers of liver cells and their extraordinary regenerative capacity In Laennec's cirrhosis, even where the patient is comatose, necrosis of parenchymal cells is usually insignificant but their impaired capacity for regeneration is well established In acute necrosis the failure of hepatic function that manifests itself in coma is presumably caused by some acute noxa that does not persist, with the removal or neutralisation of this agent the surviving liver cells re-establish adequate hepatic function In Laennec's cirrhosis however coma arises in the presence of what appears to be a numerically adequate number of liver cells, although in some such cases a hepatotoxin may be incriminated, usually the deterioration into coma is gradual and not attributable to any particular adverse event The production of hepatic coma in dogs, by gradually increasing hepatic ischæmia,[3] raises the possibility that in the cirrhotic liver decreasing intrahepatic circulation is similarly responsible for the loss of hepatic function here the ischæmia is progressive and irreversible, and the lack of response to treatment may thus be understandable

A comparison of LATNER's results in cases of "acute yellow atrophy" with those of KARL et al makes clear this distinction Of LATNER's 5 cases 4 recovered completely, the 5th regained consciousness but died from intercurrent cellulitis In the series of KARL et al, on the other hand, of 58 patients only 1 survived The only noteworthy difference between the therapeutic regimes in these two series is the administration by LATNER of tocopherol 300 mg intramuscularly each day This was given mainly because of its action in preventing dietary liver necrosis in rats, and it is extremely unlikely to account for the great contrast in the results Dr WALSHE last week described a more promising method of treating the cirrhotic patient in coma [4] Earlier,[5] as a result of paper-chromatographic studies of blood, urine, and cerebrospinal fluid (C S F) of patients in this state, he had obtained evidence of profound disturbance of amino acid metabolism, the most striking change was an increase of glutamine in the C S F, which was sometimes accompanied by an increase of glutamic acid On the basis of these findings, WALSHE suggested tentatively "that changes in the amino-acid pattern of the body fluids are capable of producing varying neurological syndromes," including that of hepatic coma We[6] remarked that "it is difficult to understand why a moderate increase" in the concentration of glutamine and glutamic acid in plasma and C S F "should so profoundly disturb the cerebral functions" It would now appear that the metabolic fault is not an excess, but rather a deficiency, of glutamic acid This substance is necessary for removing the highly toxic ammonium radicle, produced as a normal cerebral katabolite, which combines with glutamic acid to form the amide glutamine WALSHE has obtained striking results by giving large doses of sodium glutamate intravenously

WALSHE's findings of increased glutamine, and occasionally of increased glutamic acid, in the C S F in cases of hepatic coma, could, however, be interpreted as evidence, not of disturbed metabolism of amino-acids, but of increased cerebral ammonia formation This is further supported by the finding in hepatectomised dogs of a fivefold increase of glutamine among the free amino acids of the brain [7] If this interpretation is correct we are still far from comprehending the mechanism by which hepatic insufficiency affects cerebral metabolism, but it would enable us to understand the beneficial effect of glutamic acid

The Nurse's Responsibility

WHAT with techniques multiplying and housemen scarce it is becoming harder and harder to get through the daily work of the wards in the twenty four hours supplied by the solar system One solution of such problems is to depute the work to other people, and the doctor giving, say, a course of intravenous injections must often be tempted to say to a bright and handy sister "You could do these just as well as I can suppose you take them over If she is young and fired by the opportunity she may agree and in most cases all will go well she enjoys gaining an extra skill the doctor is relieved of a tie,

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[1] Karl M F Howell R A Hutchinson J H Catanzaro F G Arch intern Med 1953 91 1[illegible]9

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Poliomyelitis

In 1947 poliomyelitis appeared in this country for the first time on a large scale, with 7766 notified cases and 707 deaths in England and Wales. Since then the annual incidence and deaths have been much higher than before the late war, and in 1949 and 1950 they were about the same as in 1947. Intensive research into poliomyelitis has been proceeding for many years in America, where vast experience of epidemics and vast resources devoted to their study have yielded most of our knowledge of the virology, pathology, and treatment of the disease. One of the latest triumphs of American workers has been to grow the virus by means of tissue culture.[1] This technique may soon be adapted as a relatively cheap laboratory method of diagnosis; and it may lead in due course to an attenuated-virus vaccine for active immunisation. American workers have also shown[2] that in epidemics injection of gamma-globulin may help to prevent poliomyelitis, and that if it has been injected in the week before the onset of the disease it may modify the paralysis. In Britain RITCHIE RUSSELL[3,4] made a valuable contribution by showing that fatiguing physical activity in the preparalytic stage, and especially after the onset of meningeal signs, was definitely related to the severity of the ensuing paralysis. Now complete rest is enforced whenever the preparalytic stage is diagnosed or suspected. In a brief illustrated monograph[5] RITCHIE RUSSELL outlines his views on the nature of the disease, its clinical features, predisposing factors, the management of spinal, bulbar, and respiratory involvements, and reablement. On some of these aspects there are considerable differences of opinion among physicians, orthopædic surgeons, specialists in physical medicine, and physiotherapists, which lead to confusion in the management of patients, particularly during reablement.

The early stage of meningeal symptoms is critical; for 1–12 days the patient may hover between complete recovery and disastrous paralysis. Within a few hours the fate of tens of thousands of motor nerve cells may be decided by some stimulus to rapid multiplication of the virus. The factors which influence the vulnerability of nerve cells include: (1) physical activity between the minor illness (general symptoms) and the major illness (meningeal and paralytic symptoms), and especially after onset of the meningeal stage[3,6]; (2) local trauma, tonsillectomy, and parenteral injections; (3) transport in the acute stage over long distances[7,8]; (4) possibly pregnancy and menstruation[9]; and (5) upper respiratory infections.[10] Once the process of destruction has started it is quickly completed, and in cases of severe paralysis 60–90% of the motor neurones may disappear within a few days. All the other anterior horn cells, though showing chromatolysis in the acute stage of the disease, appear normal within 4–5 weeks, and wallerian degeneration does not occur in their axons.[11] Thus it is useless to base treatment on a policy of waiting for regeneration of nerves. Recovery of function over, say, 18 months, is due simply to hypertrophy of non-paralysed muscle and enlargement of the surviving neurone cells and fibres.[12]

In the care of muscles and joints no rigid splinting, plaster casts, or orthopædic frames should be applied even in the acute stage when paralysis is developing. Pain should be relieved with analgesics, and gentle passive movements of the joints through their full range should be practised from the first day. In some cases with asymmetrical paralysis muscle spasm or "protective fixation" in the acute stage may lead to contracture deformity if left untreated. Passive movements and maintenance of a neutral position by simple means, such as sandbags, footboards, and pillows, are the best remedies. Spasm should have disappeared about a month from onset. Some form of heat may be helpful for pain and muscle spasm, but hot packs are unnecessary: "There is no reason to suppose that the life of a single nerve cell has ever been saved by the use of hot packs." Muscle shortening is best countered by gentle passive movements and frequent changes of position. The main benefit from the Kenny treatment has been to counter the suggestion that paralysed or paretic limbs should be rigidly splinted. Physiotherapists must learn to start active movements after the first two weeks of the disease, and to introduce without delay active vigorous exercises to the point of fatigue. This will give maximal muscle recovery in a matter of weeks rather than months or years.[13] RITCHIE RUSSELL has failed to confirm that deliberately induced fatigue harms paretic muscles in the recovery stage. On the contrary, it gradually induces hypertrophy and greatly speeds reablement. After 2½ months the patient should be spending most of the day exercising the weak muscles and not the strong, so as to attain the best possible function with the least deformity. Limbs and trunk may be supported against gravity by suspension with slings and springs, in a water bath, or by other means. Trick movements which offend the

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[13] Mead, S. *J. Amer. med. Ass.* 1950, 144, 458.

"well-trained" physiotherapist should not be discouraged. **Ritchie Russell** holds that the patient should find his own way of executing movements so long as a watchful eye is kept on any developing deformity. Deformity may be countered by alternate active movement and rest in the prone position for an hour or two, three times a day. Even the severely paralysed should be walking or in a wheeled chair and ready to go home 5–8 months from onset. Long periods of hospital treatment are psychologically and physically undesirable, and plans for the future should be discussed as soon as the likely permanent disability can be assessed.

Ritchie Russell remarks that mobile teams are needed to deal with sharp outbreaks in small communities. Denmark's experience last year, however, when there was a very severe outbreak with much respiratory paralysis which soon exhausted the usual mechanical resources, suggests that such teams should be organised on a European rather than a national level, and possibly the European Office of W.H.O. might give thought to this. Denmark's adversity, however, has yielded valuable lessons, for, as Professor **Lassen**[14] reported last week, the death-rate from respiratory insufficiency was reduced by half when early tracheotomy with insertion of a tightly fitting rubber cuff tube was combined with bag ventilation, repeated aspiration and bronchoscopy, postural drainage, and the use of a stomach-tube.

Marasmus Today

Medical progress has made such terms as "marasmus," "athrepsia," and "congenital debility" almost obsolete, but the names remind us of the diagnostic difficulties of our predecessors, who, lacking the tools of modern medicine and the means of biochemical analysis, were denied the opportunities for accurate differential diagnosis which modern pædiatricians enjoy. The term "marasmus" was applied to a great many serious disorders which could not be differentiated, and in which gross emaciation was common. It is now clear that the bulk of these children were suffering from malnutrition due to underfeeding, from pyloric stenosis, nervous regurgitation, or pancreatic fibrosis, or from infections, such as gastro-enteritis, in which no known pathogens could be isolated, or from metabolic disorders such as idiopathic renal acidosis, hypervitaminosis D, cystinuria, and hypertrophy of the adrenal cortex. In the past most children who failed to thrive in infancy were vaguely said to have some digestive disorder, and many elaborate feeding formulæ were advised, usually without benefit, but we now know that many of these infants were either grossly underfed or suffering from a low-grade gastro-enteritis caused by coliform organisms, notably certain types of *Bacterium coli*, which tend to be pathogenic in infancy.[15] The era of strict theoretical feeding of infants has passed and the pendulum has swung back to the physiological custom of feeding to repletion, for infants know when they have had enough, and there is little danger of overfeeding. Often, atypical *Bact. coli* are not sought in routine bacteriological examinations, so a search should be specifically requested in infants who are suspected of having gastro-enteritis. Fortunately, certain of the newer antibiotics, particularly chloramphenicol, are often capable of curing the infection and restoring health and a rapid gain in weight. It is important to bear in mind that although these children often pass more stools than usual, the stools may look normal. A more general appreciation that underfeeding and coliform gastro-enteritis are common causes of failure to thrive (and even of marasmus) in infancy, has, more than anything else, put a stop to unnecessarily elaborate feeding methods, and it has led to the routine use of simple formulæ such as fresh boiled milk, water, and sugar, or National Dried Milk, water, and sugar. Indeed, there are relatively few conditions in which the infant fails to thrive where special modification of the diet is necessary—pancreatic fibrosis is one.

Idiopathic renal acidosis of infants, first described by **Lightwood**[16] in 1935 as "nephrocalcinosis infantum," is one of the most interesting causes of failure to thrive in infancy. The term "renal acidosis" was introduced in 1939 by **Hartmann**,[17] who was the first to attribute this disease to renal dysfunction. This curious biochemical disorder has been closely studied in the last few years, and the increasing number of cases now being identified shows that it is by no means uncommon. **Doxiadis**[18] has lately discussed the subject, and contributed 9 cases of his own. The infants were usually normal for the first one to six months of life, after which anorexia, vomiting, and constipation began. Progressive listlessness and an ashen-grey colour developed, and they no longer gained weight satisfactorily. The disease fluctuated sharply with periods of clinical improvement and deterioration. Urinary tract infection was a common feature. The main diagnostic finding was the pronounced discrepancy between the persistent acidosis in the blood and the alkalinity of the urine. Occasionally the urine was slightly acid, but the pH was never below 6.0. Indeed, the inability of the kidney to form a sufficiently acid urine, and so to maintain the normal blood pH and prevent acidosis, is the fundamental fault in this disease. **Latner** and **Burnard**[19] demonstrated that the essential defect is a lowering of the renal threshold for bicarbonate, caused by the inability of the proximal tubules to reabsorb it. **Doxiadis** believes that nephrocalcinosis, which has been regarded by some as synonymous with idiopathic renal acidosis of infancy, is not one of the main features of the disease, but tends to develop when renal acidosis is allowed to continue untreated for many months. The manifestations of a distal tubular lesion—thirst, polyuria, and urine of low specific gravity—which are the result of nephrocalcinosis, did not develop in **Doxiadis**'s patients who were adequately treated. They were given large amounts of alkali to counteract the acidosis: the dose was usually 5–10 g. of sodium and potassium citrate daily, with a sodium/potassium ratio of 2 to 1, until the infants had been well and gained weight for two to four months. Fortunately, the defect in the proximal renal tubule, the cause of which is unknown, is self-limiting, and if urinary or intercurrent infection or permanent damage from nephrocalcinosis and the patient is satisfied. But the experienced senior sister is apt to receive such invitations with reserve; for she knows there are occasions when even the simplest technique goes wrong and the patient demands redress. Who is then to take the blame, the nurse or the doctor? Moreover, such disasters are not necessarily trivial: in a case reported in the press [1] last November a patient lost her life.

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[14] Lassen, H. C. A. *Lancet*, Jan. 3, 1953, p. 37.

[15] See leading article, *Ibid*, 1952, ii, 323.

[16] Lightwood, R. *Arch. Dis. Childh.* 1935, 10, 205.

[17] Hartmann, A. F. *Ann. intern. Med.* 1939, 13, 940.

[18] Doxiadis, S. A. *Arch. Dis. Childh.* 1952, 27, 409.

[19] Latner, A. L., Burnard, F. D. *Quart. J. Med.* 1950, 19, 285.

> A doctor left a nurse in charge of a patient who was receiving a blood-transfusion. He told the nurse to take the blood-pressure at a given time, and if the systolic pressure was below 90 mm. Hg to connect and give another bottle of blood. The nurse took the blood-pressure at the time appointed, got a reading of less than 80 mm. Hg, noted this on the chart, and sent for another bottle of group-O blood. The bottle had to be obtained from a refrigerator in a neighbouring hospital, and, owing to some mistake in the transmission of messages, blood of group A was supplied. Transfusion with this blood was begun, and after the patient had received 3 oz. or less she died. At the inquest a doctor giving evidence said that responsibility for making sure that blood of the correct group is transfused rests on the person who attaches the bottle to the apparatus.

Most of us will agree that it is not part of a nurse's functions to take the blood-pressure, or to act on such a blood-pressure reading, or to give a blood-transfusion. This particular nurse seems to have obeyed instructions exactly; and the fact that she gave the wrong blood was no fault of hers. It was not her duty to check the accuracy of the label on the bottle sent from the dispensary. Nevertheless the mistake was made, and in the anxiety to apportion blame correctly it was naturally asked whether the extra bottle of blood had perhaps been given unnecessarily. The nurse was thus subjected to examination and criticism to which she should never have been exposed.

The Royal College of Nursing are rightly concerned about the whole question of delegation of the doctor's duties to the nurse; for if she accepts such assignments she lays herself open to claims on the ground of professional negligence (even though the thing done is outside her proper field). In a memorandum [2] circulated to the regional hospital boards and boards of governors of teaching hospitals the council of the college affirm that the syllabus of the General Nursing Council must be regarded as indicating the normal range of the State-registered nurse's duties; and though any nurse must expect, in emergency, to undertake duties outside this range, she should not undertake the day-to-day practice of procedures normally belonging to the doctor. Estimation of blood-pressure, withdrawal of blood from veins, and intravenous injection all fall outside the syllabus. The council propose that, unless gross negligence on the nurse's part is proved, the hospital authorities should definitely assume responsibility for any act she may undertake beyond the nursing duties. The council also make a second important point—that a nurse who is attending to her own work has no time to deputise for the doctor. A doctor who uses his nurses freely for such purposes is depriving the patients of nursing care to a greater extent than perhaps he recognises. Senior nurses say that if a trained nurse in hospital accepts the full implications of nursing, and does not have to spend her time in extraneous duties—either filling in domestic gaps at one end of the scale, or concentrating on quasimedical techniques at the other—she should have more than enough to do in caring for her patients, teaching, supervising students, and administering her ward. Undue responsibility is placed on the nurse, again, the council point out, when she is asked to get the patient's signature to the new "consent to operation" form now in use in many hospitals. This states that the patient has received an explanation of the nature of the operation he is to undergo, and the effect to be hoped from it. Though it is certainly a doctor's task to give him this explanation, it is sometimes delegated to a nurse, who is not always in the surgeon's confidence about what he intends to do, and in any case has not had the appropriate training for giving such an explanation. We agree with the council that every patient should be told plainly, by a doctor, to what he is agreeing.

There is every reason to treat nurses as colleagues: that is the proper relationship for professional people engaged in a joint enterprise. But we must not forget that nursing and medicine are two different disciplines, both requiring long training, and that proficiency in one does not ensure proficiency in the other, as a doctor's bandaging too often reveals. We should see quite clearly what we are doing when we delegate one of our own tasks to a nurse: we are putting her in a false and dangerous position which may result in damage to her professional reputation, and we may be hindering her in her duty to her patients.

The Coronation Honours

THE three new knighthoods for members of the medical profession in this country are conferred on the president of the General Medical Council, the president of the Royal Society of Medicine, and the director-general of the medical services of the Royal Air Force. Prof. David Campbell, in his sometimes forbidding office, has shown a wisdom and humanity that have strengthened the respect and affection in which he is held; Dr. F. M. R. Walshe, with his intellect and spirit, has long been the most valuably unrepresentative of our representatives; while Air Marshal Kilpatrick is a man whom all his associates, inside his service and outside it, will be glad to see honoured. The K.C.M.G. bestowed on Sir Bennett Hance is given for the important work he has done for the Commonwealth since he ceased to have charge of the Indian Medical Service. Among the administrators of the National Health Service, knighthoods are conferred on Mr. Frederick Messer, chairman of the Central Health Services Council, and on Mr. J. W. Bowen, chairman of the North-East Metropolitan Regional Hospital Board, while the Hon. A. J. P. Howard, chairman of St. Thomas's Hospital, is created K.B.E., and Miss E. M. R. Russell-Smith, an under-secretary of the Ministry of Health, D.B.E. Mr. J. E. Pater, the under-secretary especially concerned with hospitals, is appointed C.B., and Mr. W. G. Senior, principal dental officer of the Ministry, is promoted C.B.E. Mr. H. N. Linstead, M.P., secretary of the Pharmaceutical Society, receives a knighthood, and Miss D. M. Smith, matron of Guy's and chairman of the General Nursing Council, becomes C.B.E. The medical list which we print on p. 1149 takes account of distinguished work of many different kinds done in many different parts of the Commonwealth. The recognition given will be welcomed most by the colleagues who know how well it has been earned.

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1. *Daily Telegraph*, Nov. 11, 1952.
2. Memorandum on the legal position of the nurse who undertakes procedures outside her professional scope. London: Royal College of Nursing. 1953. 2*d*.

TABLE II—PRINCIPAL CAUSES OF DEATHS IN CEYLON AND WESTERN COUNTRIES

Causes	Per 1000 deaths				
	Ceylon		Eire	U S A	England and Wales
	1945	1948	1947	1947	1947
Bowel infection and infestations	118	114	19	6	12
Tuberculosis in all forms	26	43	66	34	49
Malaria and pyrexia	167	82	—	—	—
Cancer and other tumours	6	10	90	132	155
Diseases of the heart circulation and intracranial vascular lesions	57	72	366	688	474
Pneumonia and bronchopneumonia	85	86	42	38	64
Maternal deaths	58	25	3	4	2
Infantile deaths	128	154	57	46	30

these two trends will determine whether the Ceylon death-rate will remain stable at the new low level (table II)

Comparison with Eire

Cardiovascular Diseases

In Western countries diseases of the cardiovascular system (with the accompanying or attendant dangers of vascular intracranial lesions and possibly nephritis) account for 1 in 3 or 1 in 2 of all deaths (Ceylon 1 in 14) As they are diseases of the middle and later years of life they may be more prevalent in Western countries because people live longer there Age-specific deaths from diseases of the circulatory system are not available in Ceylon, but even supposing that all such deaths in Ceylon occur from 55 years and upwards, the death-rates per 1000 in Ceylon are less than those in Eire (Ceylon males 6 9, females 5 5 in 1949, Eire, males 31 4, females 31 7 in 1947)

Cancer

Similarly cancer, another hazard of the later years of life which accounts for 9–15% of all deaths in Western countries, produces less than 1% of deaths in Ceylon The age-specific mortality-rates show that for all age-groups the rates are lower in Ceylon than in Eire (table III) Part of this difference may be due to inaccurate diagnosis, although even among the better-educated classes in Colombo, where good medical facilities are available, the incidence of cancer is still low by Western standards

The death-rate from cancer has not varied significantly over the past twelve years, although the number of deaths recorded has been rising steadily The most common sites for cancer in Ceylon are the buccal cavity (42% of deaths from cancer in males and 23% in females), the digestive tract (25% in males), the uterus (23% in females) In Eire cancer of the digestive tract (especially cancer of the stomach and rectum) is the main cause of death from malignant disease Thus the distribution of cancer does not seem to be the same in Ceylon and Eire But it may be more accurate to say that, since cancer of the buccal cavity is an easily recognisable condition, more deaths in Ceylon are registered as due to this cause than to any other malignant growth

TABLE III—DEATH-RATES PER 100,000 OF THE POPULATION IN CEYLON AND EIRE

Causes of death	Death-rate in Ceylon (1948)	Death-rate in Eire (1947)
Diseases of heart	39 1	374 1
Other diseases of circulatory system	7 7	30 1
Vascular intracranial lesions	29 5	101 7
Cancer and other tumours	13 0	133 3
Diseases peculiar to first year of life	203 1	84 4
Puerperal eclampsia	25 9	—
Puerperal septicæmia	15 2	1 1
Tuberculosis of respiratory system	53 2	95 3
Other forms of tuberculosis	4 2	29 2
Bronchitis—all types	16 6	44 3
Pneumonia—all types	114 3	62 8
Other respiratory diseases	27 0	20 9
Diarrhœa and enteritis	71 1	28 5
Peptic ulcer	0 6	8 6
Appendicitis	0 7	3 1

Infant and Maternity Mortality

In Ceylon, the dangers to life during the first post-natal year are 3 to 4 times greater than in Eire The causes of infant deaths in Ceylon differ from those of Western countries Most of the reported causes in Ceylon are vague and unsatisfactory Thus "convulsions," "congenital debility," "prematurity," and "rata" each account for about a fifth of the registered infantile deaths How accurately the differential diagnosis between congenital debility, prematurity, and rata can be made is difficult to say Together they probably reflect the poor nutrition of the population, and for this reason the differences between the causes of infantile deaths in Ceylon and in the British Isles are noteworthy Diarrhœa and enteritis are 3 to 4 times more common as a cause of these deaths in Britain than in Ceylon, respiratory diseases are at least twice as common, and injury at birth more than ten times as common Since 1946 the infant-mortality pattern has tended to become Westernised The proportion of deaths occurring during the first month of life has increased, because, although the mortality-rates at all age-periods have been reduced, the reduction has been proportionately greater in the 1–12 months period.

The maternal-mortality rates are also higher than in Western countries, and this is true for most of the principal causes of maternal mortality

In Eire, as in Ceylon, hæmorrhage causes more deaths during the puerperium than during pregnancy, while toxæmia is a commoner cause of death, in both countries, during pregnancy than it is during the puerperium Puerperal sepsis is a commoner cause of death in Ceylon than other infections, the reverse is true in Eire Puerperal convulsions are not given as a cause of death in Eire, but are the major registered cause of death in Ceylon

Tuberculosis

The morbidity and mortality rates from tuberculosis in Ceylon have remained fairly stable since 1941. The recorded mortality-rates compare favourably with those of European countries, but this may be due to the difference in the accuracy of diagnosis Lack of social responsibility about tuberculosis is linked with inadequate diagnostic and therapeutic services so that a true picture of the distribution of the disease in Ceylon cannot be given

The available figures show that tuberculosis of the respiratory system accounts for 93–94% of all deaths from tuberculosis, and the number of recorded deaths from this cause seems to be slowly increasing The recorded death-rate from tuberculosis in Ceylon is lower at all ages than the rate in Eire In England a far smaller proportion of deaths are recorded as due to tuberculosis in other parts of the body than the respiratory system

Respiratory Diseases

With the drop in the mortality from malaria since 1946, diseases of the respiratory system have become one of the major causes of death in Ceylon, being responsible for about 1 in 10 of all deaths Bronchitis is a commoner cause of death in Western countries, while pneumonia is a commoner cause in Ceylon

Digestive Diseases

Diseases of the digestive system account for about 1 in 14 deaths in Ceylon Since 1946 the total deaths and the death-rates from these diseases have fallen owing to the decrease in deaths from diarrhœa and enteritis These diseases account for 70–80% of all deaths from diseases of the digestive system in Ceylon In Eire the proportion of deaths from diarrhœa and enteritis is lower, and the proportion of deaths due to peptic ulceration, appendicitis, hernia, intestinal obstruction, and diseases of the gall-bladder, bile-ducts, and pancreas is correspondingly greater

In most countries male infants have a higher mortality than female infants, and in Ceylon, during 1937–45, 1144 male infants died to every 1000 deaths of female infants

Annotations

PUBLICITY

CLOSE readers of the newspapers will have observed a recent change of practice as regards reports on charges of unprofessional conduct against doctors. Before the Medical Act, 1950, came into force, such charges were heard by the General Medical Council as a whole, and the council instructed the press that they should not publish reports before a decision was reached. Under the new procedure the hearing is undertaken by the Medical Disciplinary Committee of the Council; evidence may be (and in practice is) taken on oath; and newspapers are at liberty to report the proceedings hour by hour, as they do in cases heard in ordinary law-courts. Though the first applications for restoration to the Medical Register were heard by the Medical Disciplinary Committee in camera, all subsequent applications have been heard in public. One curious result of the changes under the new Medical Act is that evidence which could not be reported when it was given in the divorce courts becomes reportable when repeated during the hearing of cases by the committee.

One of the cases heard at the last session[1] attracted much attention in the press. On the Wednesday evening it had been the subject of an application for an adjournment, but the newspaper reporters generally decided that no reference to it could be made at that stage because the charge had not yet been read. One reporter, however, observed that the committee's notice forbade mention of anything in the programme of business "unless and until the case has come before the committee"; and his newspaper took the view that, as an application for adjournment had been made, the case could now be said to have come before the committee. This newspaper had already secured some photographs, and on Thursday morning it was able to offer its readers what it regarded as a scoop. We may add that the likelihood of widespread publicity will increase rather than diminish; for cases heard by the Medical Disciplinary Committee are in future to be reported by the news agencies (though the reports will not necessarily be circulated) and will more easily find their way into the local press.

The attitude of the newspapers towards professional bodies, and of professional bodies towards the newspapers, provides some curious contrasts. The disciplinary proceedings of the General Nursing Council, for example, though open to the public, are rarely if ever reported: even the nursing press does not give details of cases, and nurses consequently do not know the circumstances in which their disciplinary body takes action. For our own part we regard it as an obligation to report medical disciplinary proceedings—usually as briefly as possible, but more fully where any question of principle seems to be at stake. Objectionable though publicity may be, it is one of the safeguards of justice, and we should be sorry to see our profession adopt the privacy of the Inns of Court or the Law Society, which announce only their decisions, and thus leave the public without means of knowing what the respondent found to say in his defence.

MERCURIALENTIS

THE accessibility of the transparent structures of the eye to biomicroscopy with the slit-lamp and the binocular microscope has enabled these tissues to be displayed and examined under conditions of critical illumination and with a magnification sufficient to show, for example, the minute structure of the crystalline lens and the cornea. Most lesions of these structures are of purely ophthalmological significance: but in an increasing number of cases ocular signs are providing accurate evidence of general metabolic disturbances or intoxications—for example, the Kayser-Fleischer ring of hepatolenticular degeneration, the characteristic opacities of endocrine cataract, and the corneal and lenticular changes of the various types of metallic poisoning. In this last group, Hunter and Lister[1] emphasise the value of ocular signs in the early detection of chronic mercury poisoning, in which there is a characteristic brownish discoloration of the anterior lens capsule—mercurialentis. This change appears some considerable time before the onset of visual deterioration or general signs of mercury poisoning. It has been seen in people who have been exposed to mercury for long periods, usually in some industrial process involving contact with the metal or its salts. Hatters, who employ solutions of mercury salts in felting processes, may have mercurialentis as the earliest sign of absorption of mercury[2]; and thermometer makers may be similarly affected, either by the inhalation of vaporised mercury[3] or by accidental impregnation.[1] The slit-lamp microscope signs of mercurialentis have also been seen in those who make or repair mercury switches.[4] Chronic poisoning from mercurial compounds used medicinally is nowadays rare; but long-continued use of the yellow oxide, readily accessible as the ubiquitous "golden eye ointment," can lead to permanent discoloration of the eyelids and conjunctiva, and mercurialentis from this cause has been described by Fisher[5] and by Abramowicz.[6]

Mercurialentis is clearly of importance to industrial medical officers who are on the lookout for mercury poisoning. Locket and Nazroo,[4] who found no relation between the general clinical evidence of mercury intoxication and the appearance of the ocular signs, made the helpful suggestion that these signs might be used to detect the early results of long-continued exposure to low concentrations of atmospheric mercury. As far as the eye ointment of mercuric oxide is concerned, there are now so many equally effective treatments available that it is doubtful whether we can justify its continued use, with the possibility of discoloration of the superficial ocular tissues and lens changes.

PROPHYLAXIS IN MEASLES CONTACTS

IT is now generally agreed that human gamma-globulin is a safe and adequate means of attenuating, or even preventing, measles in contacts, provided that it is given not later than the sixth to ninth day of the presumed incubation period, assuming the incubation period to begin on the date of contact. The difficulty generally lies in deciding to what extent it should be used. It has been said that 1 pint of blood is needed to produce 1 gramme of gamma-globulin, and during a measles epidemic the number of contacts is so enormous that routine administration is impossible. It is generally restricted, therefore, to young children who are already suffering from an acute disease, such as whooping-cough or pneumonia, who are debilitated in some way, or who are inpatients in children's wards where the infection must be controlled if the work of the hospital is to continue.

An entirely different situation arose in the 1951 Greenland epidemic[7] in virgin soil when 99·8% of the population were affected. It was found possible to give one rather small dose of gamma-globulin to 520 people immediately after the first case of measles appeared in a certain district. This protection was given to children under 2 and people over 60, to pregnant women, and

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[1] *Lancet*, May 30, 1953, p. 1094.

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1. Hunter, D., Lister, A. *Brit. J. Ophthal.* 1953, 37, 234.
2. Rosen, E. *Amer. J. Ophthal.* 1950, 33, 797.
3. Atkinson, W. S. *Ibid*, 1943, 26, 685.
4. Locket, S., Nazroo, I. A. *Lancet*, 1952, i, 528.
5. Fisher, F. P. *Ophthalmologica, Basel*, 1946, 112, 170.
6. Abramowicz. *Pol. med. Wkly*, 1943, 21, 685.
7. Christensen, P. E., Schmidt, H. *Acta med. scand.* 1953, 145, 126.

In most countries in the West this higher male death-rate persists through life, but in Ceylon females have a consistently greater death-rate after the first year of life The reduction in the death-rate since 1946 has been proportionately similar for males and for females in all age-groups The absolute reductions for females have been greater than those for males, and, if this continues, the proportion of females to males in the population may be increased in the future At all ages and for both sexes, however, the mortality-rates for Ceylon are higher than for Britain so that, even with present medical knowledge and techniques, there is still hope for improvement in Ceylon

An American Comparison

Though Ceylon and Eire have similar crude total death-rates, the relative importance of the different causes of death varies greatly Presumably the mortality experience reflects the morbidity experience It is difficult to obtain reliable information on morbidity, but some comparisons are possible, since similar surveys of disabling illness have been made in Ceylon in 1950 and in the United States in 1949 (U S Public Health Service 1950)

In each survey the same concept of disability was used—viz, if a person was unable to do his regular work because of illness, he was said to be disabled Such a definition could be objectively applied to only the working population, and the surveys of disabling illness related only to the 14–64 age-group Only people unable to work on the day of the investigation were considered, and the unemployed were not included unless they were too ill to have worked Regular work was taken to include household duties by the women of the family and could be full-time or part-time

Neither survey sampled the inmates of such institutions as prisons, mental hospitals, and orphanages, nor the military population, nor transients with no fixed abode Each study was based on door-to-door interviews—17,946 households (1 in 80 of the total population) in Ceylon, and 25,000 households in the U S A

PREVALENCE OF "DISABILITY"

The Ceylon survey showed that, on an average week-day, the percentage of people aged 15–64 years in the civilian non-institutional population who were unable to work because of illness was 5 32 ± 0 096 (U S A 4 72) The average number of days of disability which might be expected in a year for each person in the sample group was 19 4 days (U S A 17 2 days)

These rates and durations are not strictly comparable since the two sample populations had different age and sex proportions The American sample, being composed of more middle aged people, would be more likely to suffer from the chronic, disabling illnesses of middle and later life A more accurate comparison can be made by applying the age specific disability-rates found for Ceylon to the American population Such a calculation indicates that, if the population of Ceylon had the same age-composition as that of America, then the disability rate in Ceylon would be 5 90% Similarly the average number of days of disability that might be expected in a year for each person would be 21 5 days (17 2 days in America)

In the Ceylon sample the prevalence of disabling illness increased with advancing age until, from 55 years onwards, 1 in about every 9 persons was disabled (In the U S A people aged 25–34 years had a lower prevalence of disabling illness than people in the other working age groups) The prevalence of disabling illness among men was lower than among women in the age group 15–54 years, the female prevalence in the U S A was only higher in the age-group 20–44 years These differences are comparable with the different sex mortality ratios in the two countries Of the disabled, over 34% in Ceylon had been disabled for three months or longer (in the U,S A 53%)

The types of diseases which caused disability in the Ceylon inquiry are set out in table IV

TABLE IV—PREVALENCE OF DISABLING ILLNESSES EXPRESSED AS A PERCENTAGE OF ALL CAUSES

Illness	Males %	Females %	Total %
Infective and parasitic diseases	32 7	30 2	31 1
Diseases of the blood	6 6	2 5	4 6
Diseases of the nervous system	10 0	7 6	8 8
Diseases of the circulatory system	1 8	0 9	1 3
Diseases of the respiratory system	6 5	8 0	7 3
Diseases of the digestive system	5 8	6 1	5 9
Diseases of the genito urinary system	1 2	1 9	1 6
Pregnancy childbirth, and puerperium	—	10 3	5 2
Cancer and tumours	0 4	0 3	0 3
Rheumatic diseases	13 8	14 4	14 1
Diseases of the skin	7 7	4 7	6 2
Diseases of the bones and joints	0 4	0 1	0 2
Diseases of the eye	2 1	0 9	1 5
Accidents	6 4	1 9	4 1

Physiological Characteristics

The morbidity and mortality patterns in Ceylon differ from those of the United Kingdom or U S A The differences are associated with, though not necessarily related to, differences in diet (Cullumbine 1951), in physique (Cullumbine 1949b), and in many physiological measurements The latter is not surprising, for some physiological characteristics have been related to the physical proportions of the body—e g, the surface area of the body has been correlated with the rate of basal metabolism, the blood volume, the vital capacity, &c If the body surface area varies, these physiological factors may well vary too

TABLE V—BODY COMPOSITION OF 50 CEYLONESE MALE STUDENTS AGED 21–25

Component	Mean	% of total body weight	% composition for British subjects (McCance and Widdowson 1951)
Weight (kg)	49 8	—	—
Height (m)	159 2	—	—
Plasma volume (c cm)	2510	—	—
Plasma volume (c cm /kg)	50 2	—	—
Extracellular fluid (1)	13 630	27 4	17 2–25 5
Fat (kg)	2 59	5 2	7 2–22 4
Cell mass (kg)	33 58	67 4	54 2–62 0

In fact the smaller, more ectomorphic, Ceylonese have lower resting systolic and diastolic blood pressures (Cullumbine 1949a), faster resting pulse rates, lower basal-metabolic rates (Cullumbine 1950), lower vital capacities, lower maximum breathing capacities, smaller residual air volumes (Cullumbine 1949c) than occidental peoples The Ceylonese values are typical of a person with a linear body build—i e, the ectomorph Some of their other physiological characteristics are also those of the thin man For example, their body composition—plasma volume (given by T 1824 dye), extracellular fluid (thiocyanate), fat content, cellular mass (determined by the method of McCance and Widdowson 1951)—is similar to that of the active thin man in the Western hemisphere (table V)

The absolute values of the mean extracellular fluid volume and the plasma volume are lower than those for average British or American subjects—3 13 litres plasma volume, 17 13 litres extracellular fluid volume (Henschel et al 1947)—but they form higher proportions of the body weight Similarly their fat content is low and their cellular mass relatively high The fat content of the body is low in undernourished or starved people (McCance and Widdowson 1951), who also have low blood pressures (Brozek et al 1948) an increased proportion of extracellular fluid (Henschel et al 1947), to tuberculous patients. In many of these cases the prophylactic could not exert its full effect, because measles was not always contracted at the first exposure but later when the effect of the gamma-globulin had partially or completely worn off. Yet even under these difficult conditions the measure was amply justified. There was obvious attenuation in many of the inoculated patients, even in adults, and there was no such attenuation in those who had not been inoculated. In an attenuated attack the prodromal stage was shortened, the rash was much less profuse, and there were fewer days of fever. Complications in those under 55 who were inoculated were less common than in the controls. The death-rate was also lower among those inoculated, when the deaths of tuberculous patients and premature infants were discounted. It was concluded that limitation of the spread of measles under such conditions by specific prophylaxis was impracticable, but that it was well worth trying to protect children under the age of 2, pregnant women, and old people. And in tuberculosis, gamma-globulin should be given first to those who have a real chance of recovery, and the dosage in such adults should be 2 to 3 g., which is 8–12 times the amount usually given to children under 2. Where exposure to infection persists, this dose should be repeated after an interval of two to three weeks.

PRESERVATION OF THE FAMILY

"THE family is tough, resilient, and adaptable," said the Bishop of Sheffield on May 20. "Human folly cannot destroy it, but it can hurt, corrupt, and weaken it." He was inviting the House of Lords to consider the effects of recent legislation and other influences on the well-being of the family; and it soon appeared from the debate that the Lords are as likely as the rest of us to form constellations of ideas, beliefs, and prejudices, and what one person sees as an evil for the family another may see as a good. Nevertheless there are some fixed stars in this zodiac which all can steer by; and one of these is that family well-being cannot exist apart from the family. Any measures which help to keep the family together, then, are worth pursuing; and the speakers had this well in mind. The Bishop of Sheffield suggested that nowadays, when the country is impoverished, and families are too small to keep mothers fully occupied, those with children over three years of age should be free to go to work, if they wish; it would therefore be an ill-chosen economy, he thought, to close nursery schools and classes or reduce the number of school-dinners. But though a good nursery school or class, open for a few hours in the morning and afternoon, benefits the child and refreshes the mother, it does not free her for full-time work in industry. Only a day-nursery can do this, and then only at the cost of keeping the child from his mother from early morning until, tired by a factory working-day, she fetches him at night. The three-year-old, or even the four- or five-year-old, is none the better for this kind of deprivation, and we believe that there is a strong case for not encouraging mothers of young children to do more than part-time work in industry. The Marquess of Salisbury would prefer to see them doing none at all, for, as he said, the basis of education, and especially of religious education, used to be the teaching given by mothers to their children in the homes; and no school syllabus, however admirable, can take the place of it. Since family life can only be conducted in a family home, he was anxious to see more houses built.

On a long view, it is in the interests of the family, the Bishop of Sheffield argued, that the principle of equal pay for equal work should go with family allowances. He noted, as many have done,[1] the temptation to solve the problem-family problem by dissolving the family—often by putting the children into an expensive institution, and the mother or father into an expensive prison. Our best resource for problem families has so far proved to be the family service unit, and he asked whether enough thought is being given to training people for this sort of work. Families often disrupt themselves, however, without any interference from a benignly intending State; and indeed, the growing divorce lists indicate that there are many more broken homes in England today than in the past. Lord Pakenham urged the need for the best marriage guidance or other advice we can give to help husbands and wives to make a greater success of their marriages—a need underlined by the Earl of Selkirk, who said that free legal aid is available to dissolve marriage but only very modest help is given to the bodies which work to maintain the married state.

Lord Beveridge, thinking of the physical health of the family, discussed the cost of social insurance, and said there were strong arguments for getting more of the money needed by taxation, and a great need to stabilise prices. In so far as we are treating people inadequately under National Insurance, he said, we are treating most inadequately those with large families.

The impulse to hold together, the binding centripetal force, is inherent in the family; for after all, in spite of disruptive forces, most families still keep their integrity. Large families, perhaps, generate more of this force: at all events, they do not seem to have flown apart as readily as modern small families. Perhaps, too, it takes more rugged selfishness to desert a large number of children than to desert one or two. But the damage done to the individual child by breaking up the family does not vary with family size; and an understanding of this fact should help parents to recover that principle of dedication to a common purpose which our times have undermined.

PLACENTAL BLOOD-FLOW

THE fœtus depends for its livelihood entirely on the exchanges in the placenta. The rate of maternal blood-flow in that organ is, therefore, of fundamental importance. Until now only indirect information has been available for the human species; and Browne and Veall[1] are to be congratulated on the technique they have evolved for direct studies. The first step is to localise the placenta; and this is done by injecting intravenously a small amount of radioactive sodium.[2] Only cases in which the placenta is on the anterior uterine wall are suitable for the blood-flow studies. Three days are allowed to elapse in order to reduce residual radioactivity to a negligible amount. The technique depends on the injection into the choriodecidual space of 10 μC of radioactive sodium in about 1 ml. of saline, and the subsequent recording of counts over the injection site. The disappearance-rate of the Na^{24} can thus be plotted, and the resultant curves in successful cases are of exponential form. The technical difficulty lies in finding the choriodecidual space. When the needle point is in the space blood flows freely into the syringe; and with experience Browne and Veall found that they could appreciate the various layers through which the needle point was passing. The nature of the curve of the disappearance-rate also confirms that the correct layer has been reached. In eight normal cases studied between the 38th and 40th weeks, the mean half-period was 21 seconds with a range of 13–30 seconds. In seven patients at the same gestation period, but with pregnancies complicated by pre-eclampsia or hypertension, the mean half-period was 65 seconds with a range of 47–102. There was no significant difference in results between the patients with pre-eclampsia and those with chronic hypertension. Browne and Veall admit that and a change of somatotype to that of ectomorph (Lasker 1947)

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[1] See *Lancet*, May 16, 1953, p. 983.

[1] Browne, J. C. McC., Veall, N. *J. Obstet. Gynæc.* 1953, 60, 141.
[2] Browne, J. C. McC., Veall, N. *Ibid*, 1950, 57, 566.

Our Ceylonese subjects came from well to-do families, so presumably they were eating sufficient food. Moreover they differed from undernourished people who show an increase in the actual volume of extracellular fluid and also a reduction in cell-mass The body composition of the Ceylonese probably represents an adaptation to their environment They need only a minimal body-fat content, and their small body-weight is partially due to this Chapman et al (1950) have found that on rice fruit diet American subjects reduce their body fat total body-weight, thiocyanate space, and blood-pressure

One importance of the physiological characteristics and the anthropometric characters of the Ceylonese people lies in their relation to dynamic fitness (Cullumbine 1949d) Thus the resting pulse-rate is correlated negatively with the ability to perform moderate effort, and the Ceylonese, who have a relatively fast pulse-rate, will be handicapped in this respect compared with Western people The resting systolic blood pressure is correlated positively with the ability to run with speed with strength, and with the ability to sustain moderate muscular effort to exhaustion All these aspects of dynamic fitness will probably, therefore, be better performed by Western races than by the Ceylonese, who have a relatively lower resting systolic blood-pressure Similarly speed, strength, and the performing of moderate exercise to exhaustion demand a stocky physique and are positively correlated with body-weight, so that the slimmer and lighter Ceylonese will be further handicapped compared with Western people On the other hand the performance of rapid and severe effort to exhaustion is best done by subjects with a slim physique, a body type more characteristic of the Ceylonese than the British Conversely, the ability to perform rapid and severe effort to exhaustion is positively correlated with the vital capacity, and the Ceylonese have a relatively small vital capacity

The people of Ceylon, therefore, have, on an average, different physical and physiological proportions, different functional potentials, and different morbidity and mortality experiences from the people of Britain To what extent these differences are related to the varying environments—climatic, social, economic bacteriological, parasitological—is still doubtful

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Occasional Survey

CHRONIC BULLOUS DISEASES

THE diagnosis of chronic bullous eruptions has always been difficult and sometimes impossible The more cynical have said "Wait and see If the patient dies, it is pemphigus, if not, it is dermatitis herpetiformis or erythema multiforme" Recent histopathological work by Civatte and others, cytological studies by Tzanck, and fresh knowledge of the biochemistry of blister fluids, have all helped to clarify the problem and to give the physician more confidence in deciding on the prognosis In addition, corticotrophin (A C T H) and cortisone have proved effective weapons in the control of these previously uncontrollable conditions

Lever,[1] who has reviewed present knowledge of pemphigus, believes that there are two sorts of malignant pemphigus, each with its own variants Thus pemphigus vulgaris has as a variant pemphigus vegetans in which there is more tissue response than in pemphigus vulgaris Pemphigus vegetans itself may be malign (Neumann type) or relatively benign (Hallopeau type, *pyodermite vegetante*), though this may terminate in the malignant form The other sort of malign pemphigus is pemphigus foliaceus, with a relatively benign variant, pemphigus erythematodes (Senear-Usher syndrome)

The clinical differentiation of all these types of pemphigus from the straightforward case of dermatitis herpetiformis or erythema multiforme is easy, but there are other relatively benign bullous dermatoses that may easily be confused with pemphigus There is, first, bullous pemphigoid, called by some bullous or senile dermatitis herpetiformis, and secondly there is benign mucous-membrane pemphigoid, also known as conjunctival or ocular pemphigus All these maladies can be differentiated today with some confidence by clinical observation combined with histopathological, cytological, and biochemical techniques

PEMPHIGUS VULGARIS

In pemphigus vulgaris the flaccid bullæ usually arise on normal-looking skin, rupture easily, and tend spontaneously to increase in size The denuded areas left by ruptured bullæ extend peripherally and show a collar of detached epidermis Nikolsky's sign is positive, pressure with the finger causing the epidermis to slide off even in areas where the skin appears normal (This sign may also be positive in pemphigus foliaceus, bullous pemphigoid, epidermolysis bullosa, and Ritter's disease [dermatitis exfoliativa neonatorum], and so is far from pathognomonic It is, however, negative in dermatitis herpetiformis, erythema multiforme bullosa, and other bullous conditions)

Pemphigus vulgaris nearly always involves the oral mucosæ, often extensively, and especially the vermilion border of the lips The bulla is seen on section to be epidermal and situated just above the basal layer In the bullous pool and bordering on it, are the acantholytic cells (epidermal cells devoid of intercellular bridges) described by Civatte Tzanck s smear test from the base of a bulla also shows acantholytic epidermal cells In pemphigus vulgaris electrophoretic examination of the bullous fluid, as of the serum, shows a steady decrease in albumin, which with globulin is lost from the denuded areas but unlike globulin is not rapidly regenerated Sodium and chloride are also reduced in proportion to the amount of skin involved The serum-calcium is lowered, but as this involves only the protein-bound fraction, the ionised fraction being unchanged, tetany does not develop A secondary anæmia develops in proportion to the severity of the pemphigus

In pemphigus vegetans, as in pemphigus vulgaris, the initial lesions are flaccid bullæ, but the denuded areas develop hypertrophic granulations—so-called "vegetations"—which extend peripherally These lesions are also sometimes seen in the flexures in cases designated pemphigus vulgaris The mucous membranes are involved in a fashion similar to that in pemphigus vulgaris

In the more benign variant, *pyodermite vegetante*, the primary lesion is a pustule In both forms of pemphigus the difference in disappearance-rates between the normotensive and hypertensive groups could be caused by differences in the placental-pool volume; but as there is no evidence of any difference in volume of maternal blood in the placentæ of normal and of hypertensive patients it seems reasonable to presume that the difference in disappearance-rates of Na^{24} is due to alterations in the rate of placental blood-flow.

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[1] Lever, W F *Medicine, Baltimore* 1953 32 1

This important technique may have perhaps two principal applications. First, it may throw some light on the problem of postmaturity by means of placental blood-flow studies in successive weeks after full term. Secondly, it may help to answer a question concerning the ætiology of pre-eclampsia. It was Young[3] who first suggested that the placental infarct might be concerned in the ætiology of pre-eclampsia rather than result from it. More recently Bastiaanse and Mastboom,[4] Beker,[5] and others have reported evidence that placental ischæmia may precipitate pre-eclampsia. Zeck and Assali[6] have confirmed that infarcts are significantly commoner with toxæmia than in normal pregnancies, and have shown that acute atherosis of the decidual vessels is commonly associated with toxæmia but is otherwise rare. It would appear, therefore, that the diminished placental blood-flow is due to narrowing of the decidual vessels; but, as Browne and Veall point out, the fact that placental ischæmia was of the same order in their chronic hypertensive patients as in those with pre-eclampsia suggests that the placental ischæmia is the result, rather than the cause, of the hypertension. Theobald[7] has reported successful results from surgical or chemical denervation of the internal iliac arteries as a means of improving the blood-supply to the uterus in cases of recurrent severe pre-eclampsia.

The origin of pre-eclampsia is still unknown; but fundamental research such as that by Browne and Veall will ultimately solve this difficult problem.

BACTEROIDES INFECTIONS

THE bacteroides are anaerobic, gram-negative, non-motile, non-sporing, often pleomorphic bacilli. They comprise a rather heterogeneous group, difficult to classify, and many are more commonly included in the genus fusiformis.[8] They are obligatory parasites which may be found both in disease processes and in the healthy mouth and intestinal tract of man and animals. In the human lower intestine organisms of this group are said to outnumber *Bacterium coli* by a hundredfold or more. Although they occur with such frequency they are seldom isolated in routine bacteriological examinations, for they can grow only with difficulty on artificial media. Brewer's thioglycollate medium is one of the most satisfactory, both for primary isolation and for subsequent subcultures.

Many examples of infections by these organisms have been reported.[9–11] The series described by Fisher and McKusick,[12] however, is of special interest, for it illustrates the value of the newer antibiotics in the treatment of these infections. The 14 cases described give a reasonable cross-section of the types of disease reported by other workers. An empyema developed in 7 cases, lung abscess in 5, liver abscess in 4, abdominal abscesses in 3, brain abscess in 1, mastoiditis in 1, other localised suppurations in 5, and subacute bacterial endocarditis in 2. The infections were often multiple, and in only 5 cases could a specific name be given to the bacteroides isolated. This organism was *Bact. funduliformis* (*Fusiformis necrophorus*) in each instance. An anaerobic streptococcus was found in association with the bacteroides in 5 cases.

The most striking clinical features were the extreme gravity of the illness and the foul-smelling pus in the abscesses. Large numbers of gram-negative bacilli could be seen in the pus, cultures of which became positive only after several days' anaerobic incubation. The white-cell counts were usually raised to about 20,000 per c.mm. and there was a tendency for high counts to persist for some weeks after the infection had been eradicated. The 2 patients who had endocarditis were the only ones in this series who died. The death of one was the result of heart-failure six months after the bacteroides infection had been eliminated by penicillin. Suitable combinations of surgery and antibiotics produced complete cures in all the other patients. The sensitivity of the organisms to antibiotics varied widely; most strains were highly sensitive to aureomycin, rather less so to chloramphenicol, and highly resistant to streptomycin. Susceptibility to penicillin showed the greatest variation, and strains sensitive to concentrations ranging from 0·056 units per ml. to 50 units per ml. were encountered.

THE CONCENTRATION CAMPS

"MILLIONS were killed by direct extermination, but millions more died of famine disease and its complications. Without taking direct murder into account, the average duration of survival in these camps was little over six months." These are the words of a group of Danish doctors,[1] some of whom were among the 6000 people taken from Denmark to concentration camps in Germany during the late war. These doctors now try to describe the social and hygenic conditions in these camps, the famine diseases, and the special difficulties that beset the survivors who returned to Denmark. Every attempt has been made to give factual information about the fate of the Danish inmates and the diseases from which they suffered. The report includes 117 tables, analysing the sufferings of the prisoners; but, as the authors remark, "statistics do not bleed," and so they set out the terrible details.

Tragedy gives men and women an opportunity to bring out their best, and many frightful stories are brightened by heroic efforts in the face of disaster. It was a peculiar evil bent of those who were responsible for organising the concentration camps that they succeeded in making heroism impossible. By mixing up prisoners of every class and nationality and by employing criminals and psychopaths as foremen prisoners, they ensured that lawlessness ruled behind the wires, and they broke up any solidarity among the prisoners. "The shortage of everything, especially food, resulted in an attitude of each one for himself and devil take the hindmost. To this would be added pocket-picking, violence and robbery, all of which were frequent and daily occurrences. Nobody felt safe, everyone being exposed to the danger of assault, particularly during the sparse and badly needed hours of sleep."

The clinical descriptions of the famine diseases are admirable: there are full pictures of hunger cachexia, hunger œdema, and hunger diarrhœa, and these conditions are discussed in the light of the reports of other observers and laboratory workers. Those already familiar with the literature may find little that has not already been reported, except in the long section dealing with the problems that arose after repatriation. Tuberculosis was from five to twelve times as common in those that vegetans the prognosis before the introduction of corticotrophin was usually as bad as in pemphigus vulgaris

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Microscopically there are papillomatosis, intra-epidermal, mostly suprabasal, acantholytic bullæ, and intra-epidermal eosinophilic abscesses

The only condition which can give a microscopic appearance identical to pemphigus vulgaris or pemphigus vegetans is the benign familial pemphigus of Gougerot and Hailey-Hailey, believed by some to be a bullous variety of Darier's disease (dyskeratosis follicularis) because of the presence of dyskeratosis and "grains" due to shrinkage of acantholytic cells similar to those seen in Darier's disease The differentiation of this malady from malign pemphigus is usually easy from the family history and the clinical characteristics with predominant involvement of the collar-line, axillæ, groins, and other friction sites

The serum-protein changes are similar in pemphigus vegetans to those found in pemphigus vulgaris, but are less distinct, and the electrolytes are not significantly changed except in pemphigus vegetans malignus

PEMPHIGUS FOLIACEUS

In pemphigus foliaceus the flaccid bullæ are subcorneal and easily ruptured, leaving superficial erosions, with the result that they are rarely seen This malady, then, presents more as an erythematous, oozing, scaling, and crusting eruption, usually starting on the face and chest, and resembling a mildly infective dermatitis or even lupus erythematosus The lesions tend to have serpiginous borders, with very extensive involvement, exfoliative dermatitis is resembled, but in exfoliative dermatitis Nikolsky's sign is negative The scales may show "carpet-tacks" on their undersurfaces The mucosæ and conjunctivæ are rarely involved, and the course, though variable, is usually chronic and not associated with much impairment of the general health in the earlier stages, death, if it occurs, usually results from intercurrent infection

The exact status of pemphigus erythematosus is uncertain There are inconspicuous bullæ and features resembling seborrhœic dermatitis and lupus erythematosus, and an uncertain course which may remain benign or terminate fatally in pemphigus vulgaris or, more particularly, pemphigus foliaceus

BENIGN FORMS OF PEMPHIGUS

In addition to these malign forms of pemphigus there are two conditions, more benign, which have to be differentiated

The first is the condition called by some bullous pemphigoid and by others bullous or senile dermatitis herpetiformis This occurs usually in the elderly, and rarely in children, as itchy tense bullæ, arising either from normal-looking skin or from amongst areas of erythema If the bullæ become broken, the resulting denuded areas do not enlarge but may, on the contrary, tend to heal The bullæ are both small and large and affect in particular the flexor surfaces The erythematous areas are large and often polycyclic, and the whole picture may resemble erythema multiforme The mucosæ are rarely involved, and the vermilion surface of the lips escapes Changes in the serum chemistry resemble those in pemphigus but are slighter The histological features are, however, quite different from true pemphigus, the bullæ being subepidermal and rounded at their edges There is no acantholysis, the epidermal cells being stretched over the bullæ and sometimes undergoing œdema and necrosis above the bulla Nikolsky's sign is positive, but the Tzanck test is negative for acantholytic cells though it shows many inflammatory cells and a few normal looking epithelial cells Bullæ of this kind are also found in dermatitis herpetiformis, herpes gestationis, erythema multiforme, and epidermolysis bullosa The course of this malady is relatively benign except in the very old, in whom it may end fatally Remissions may occur

In benign mucous membrane pemphigoid (pemphigus conjunctivæ, ocular pemphigus) the special features are a predilection for the oral mucosæ and conjunctivæ and a pronounced tendency to scarring, the bullæ being subepidermal and associated with a great deal of inflammatory reaction Scarring of the palpebral fissures or of the mouth may occur, and adhesions between the eyeball and the lids may limit movements of the eye Xerosis, corneal ulceration, or the development of an opaque horny membrane over the cornea may lead to blindness The disease may be confined to the mouth for a considerable time before other areas are affected, and scarring is much less pronounced here than on the eyes About half the patients have skin lesions—either recurrent bullæ, healing without atrophy, or red areas with flaccid bullæ going on to denudation and smooth atrophic scarring The course is usually benign, apart from the serious ocular damage

TREATMENT

Among hypotheses on the causation of these mysterious maladies, that most favoured today is interference with some enzyme activity in the skin A viral or bacterial cause has not been substantiated

Despite ignorance about the nature of pemphigus and pemphigoid eruptions, one thing is clear their control has been revolutionised by the introduction of corticotrophin In the past, arsenic, suramin, and vitamin D were used, with uncertain effect, and blood transfusions have been given in an attempt to bring about a remission Antibiotic drugs, particularly aureomycin and chloramphenicol, have been reported to cause remissions in a proportion of cases when first used, but not subsequently

In 1940, Talbott et al [2] reported the value of adrenal cortical extract in the control of pemphigus All types of pemphigus and pemphigoid respond well to corticotrophin or cortisone provided the dosage is adequate, but the beneficial effect is temporary, and if relapse is to be prevented the drugs must be given either continuously with a maintenance dose or in repeated courses

Against continuous treatment are the many unpleasant side effects of corticotrophin—in particular, fluid retention leading to cardiac decompensation, low potassium alkalosis, reactivation of old pulmonary tuberculosis or of a peptic ulcer, psychoses, and severe infections To avert some of these possible side effects, a low sodium chloride intake, prophylactic potassium chloride 2–6 g daily, and the administration of an antibiotic are indicated

With regard to dosage, Lever believes that this should be adjusted according to the clinical response, and that eosinophil-counts and 17-ketosteroid estimations are of secondary importance

The usual initial dose of corticotrophin is up to 40 mg intravenously, given over an 8 hour period, the amount depending on the severity of the case, 40 mg intravenously is equivalent to 280 mg of corticotrophin, or to 700 mg of cortisone, intramuscularly

A reduced daily dose of 20 mg should be maintained for several weeks after the lesions have healed Then follows the difficult decision whether to adopt continuous or intermittent dosage, and whether to give corticotrophin or cortisone Cortisone, when it can be more readily produced, should prove the drug of choice for ambulant patients once the condition has been brought under control returned as in the corresponding age-groups of the male population of Copenhagen at that time. In addition to the great risk of infection in the camps, evidence shows that the low calorie-intake itself probably impaired the processes of immunity. No special form of "concentration-camp tuberculosis" was found, but the prognosis for the repatriated prisoners seemed to be better than might have been expected. On the other hand, psychological reablement was often slow. Restlessness and an inability to concentrate retarded the return to normal social life and working activities. The dissatisfaction of the active members of the resistance movement with the subsequent political developments may have contributed to the persistence of these symptoms.

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The Danes remark that they had been singularly ill-equipped by their medical education to deal with famine diseases. We may fairly hope that the evils of the concentration camps will never come again; but, in the present state of world agricultural and food economy, it is certain, even in the most optimistic outlook, that many of the world's doctors will have to deal with hunger cachexia, œdema, and diarrhœa. Among their many commitments medical teachers could usefully devote a little more time to these diseases, and this excellent Danish report would help them to do so.

AMŒBICIDES

In the last few years so many new amœbicides have appeared that their comparative evaluation has been somewhat difficult. Emetine, carbarsone, chiniofon, and di-iodohydroxyquinoline ('Diodoquin') have been followed in quick succession by chloroquine, bismuth glycolylarsanilate ('Milibis'), and the antibiotics—chloramphenicol, aureomycin, and terramycin (oxytetracycline). Normally it is difficult to get enough patients for the trial of a single amœbicide; and to keep them under observation long enough for repeated examinations of the stools, to see if relapse ensues after recovery from the acute condition, is even more difficult. An unusual opportunity to observe the response of acute amœbic dysentery to therapy with several of the new amœbicides arose recently in a United Nations prisoner-of-war camp in Korea, where Martin and his colleagues,[1] of the U.S. Medical Services, in collaboration with members of the U.S. Public Health Service, treated 644 cases. The criteria for diagnosis were diarrhœa, abdominal tenderness and pain, blood and mucus in the stools, lesions of the colon visible on sigmoidoscopy, and trophozoites of *Entamœba histolytica* in the stools. The number of cases sufficed for comparative trials of twelve drugs or combinations of drugs. Saline smears of stool specimens were examined for *E. histolytica* on the first, second, fourth, and sixth days and weekly thereafter for six weeks; sigmoidoscopy was done every week. The criteria of cure were disappearance of diarrhœa and exudate in the stools, absence of trophozoites or cysts of *E. histolytica*, normal sigmoidoscopic appearances, and freedom from symptoms. Vegas[2] carried out a similar study on civilians at Caracas, Venezuela. He treated, and followed up for six to twenty-four months, 264 patients with amœbic dysentery, which he estimates to be present in about 9% of the middle and upper classes in Caracas. With such a large number of patients Vegas was also able to compare the clinical effectiveness of a number of amœbicides.

Both Vegas and the North American workers failed to confirm the early enthusiastic reports on the value of aureomycin in amœbiasis; the initial results were good, but the relapse-rate was high. In fact none of the drugs given alone prevented relapse. Emetine, carbarsone, aureomycin, and chiniofon gave a reasonably good initial response, but there were many relapses. Chloramphenicol was disappointing in the hands of both groups of workers. Terramycin gave the best results of any one drug, but its side-effects after long use—diarrhœa, pruritus ani, and abdominal cramps—and its high cost were serious drawbacks. Vegas considers that bismuth glycolylarsanilate is one of the best amœbicides. Even so, over 50% of the patients he treated with this drug were passing cysts again one year after treatment.

Amœbiasis may not be a purely localised intestinal infection but a systemic disease as well. If this is so, a combination of a relatively insoluble amœbicide, acting only in the gut, with one that is readily absorbed might be expected to give the best results. In the hands of Vegas a combination of the non-absorbable arsenical, bismuth glycolylarsanilate, with the highly absorbable chloroquine proved more effective than any single amœbicide or combination of amœbicides. Martin and his colleagues observed a good initial response with a combination of bismuth glycolylarsanilate and chloroquine; but the relapse-rate was high. They obtained the best results with terramycin, which is absorbed, combined with any of the standard amœbicides, such as emetine, carbarsone, chiniofon, and chloroquine. Elsdon-Dew et al.[3] also obtained good results by combining an antibiotic with one of the established amœbicides. The antibiotics act not only on the amœbæ but on associated and probably symbiotic bacterial flora in the gut. Wilmot et al.[4] have shown that antibiotics have little or no effect on amœbic liver abscess, where there is no confusion between antibacterial and anti-amœbic effect. This suggests that in amœbic dysentery antibiotics act largely on the symbiotic bacteria rather than directly on the amœbæ. It therefore seems that in treating amœbic dysentery we should aim at killing one bird with two stones—that is, with an amœbicide and a drug acting on symbiotic organisms in the gut.

SINGLE VENTRICLE WITH PULMONARY STENOSIS

When the ventricular septum has failed to develop there is a single ventricular cavity into which the auriculoventricular valves open and from which the aorta and pulmonary artery, usually transposed, arise. The patient usually dies in infancy or childhood but may survive to middle age. Campbell et al.[5] describe six cases of single ventricle with pulmonary stenosis, and a seventh of single ventricle with pulmonary atresia; and they also review 85 reported cases of single ventricle.

Their cases were not diagnosed during life; and Campbell et al. show that such cases are liable to be mistaken for Fallot's tetrad. The structural defects in the two conditions are similar, the main difference being that in one the interventricular septum is incomplete and in the other absent. Likewise the symptoms and physical signs may be exactly the same in the two conditions. In all seven hearts there were other defects in the heart chambers, valves, and great vessels; anomalous pulmonary veins were common. The plain radiographic appearances were not diagnostic, but angiocardiography showed a rapid spread of dye to the left side of the heart, from which Campbell et al. think a diagnosis of common ventricle might be suspected. The electrocardiogram (E.C.G.) of these cases is of especial interest, as it is a problem where, in the absence of the interventricular septum, the conducting bundle and its branches lie. In each case the E.C.G. showed the pattern seen in left ventricular preponderance or hypertrophy; the auriculoventricular conduction-time, judged by the P–R interval, seems generally to have been within normal limits for the ages of the patients; but one E.C.G. seems

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1. Martin, G. A., Garfinkel, B. T., Brooke, M. M., Weinstein, P. P., Frye, W. W. *J. Amer. med. Ass.* 1953, 151, 1055.
2. Vegas, J. S. *Ibid*, p. 1059.
3. Elsdon-Dew, R., Armstrong, T. G., Wilmot, A. J. *Lancet*, 1952, ii, 104.
4. Wilmot, A. J., Armstrong, T. G., Elsdon-Dew, R. *Amer. J. trop. Med. Hyg.* 1952, 1, 429
5. Campbell, M., Reynolds, G., Trounce, J. R. *Guy's Hosp. Rep.* 1953, 102, 99.

Special Articles

CORONATION HONOURS

The list of honours published on June 1 contains the names of the following members of the medical profession

K C M G

Lieut General Sir **James Bennett Hance**, K C I E O B E, M D Camb, F.R C S E
Medical adviser to the Secretary of State for Commonwealth Relations, and President of the Medical Board, Commonwealth Relations Office

K B E (Military)

Air Marshal **James MacConnell Kilpatrick** C B, O B E, M B Belf, Q H P
Director general, R A F Medical Services

K.B E (Civil)

Francis Gordon Bell, M C, M D Edin, F R C S
Formerly professor of surgery, University of Otago

Knights Bachelor

The Hon **Nicholas Attygalle**, F R C S, F R C O G
President of the Senate of Ceylon
For services to medicine

David Campbell, M C, M D Glasg F R F P S
President of the General Medical Council, regius professor of materia medica and therapeutics, University of Aberdeen

Francis Martin Rouse Walshe, O B E, M D, D SC Lond, F R C P F R S
President of the Royal Society of Medicine, consulting physician, University College Hospital, and the National Hospital, Queen Square

C B (Military)

Major General **Joseph Clinton Collins**, C B E, M R C S, Q H S

Major General **Frederick Knowles Escritt**, O B E, M R C S, Q H S

C M G

Philip Stanley Foster, M B N Z, F R C S, F.R.A C S
Consulting surgeon, Christchurch Hospital, New Zealand, chairman, Medical Council of New Zealand

George Macdonald, M D Lpool, M R C P
Professor of tropical hygiene, University of London, and director of the Ross Institute of Tropical Hygiene

C V O

John Nigel Loring, M.R C S
Apothecary to Her Majesty's Household

C B E (Military)

Colonel **Kenneth Barron Fraser**, CH M Sydney, F.R A C S, R.A.A M C
Visiting senior surgeon, Children's Hospital, Brisbane

Air Commodore **Patrick Brunton Lee Potter**, O B E, M D Sheff, R.A F

Air Commodore **Frederick Elvy Lipscomb**, M R C S, Q H.P, R.A.F

Surgeon Captain **Samuel Gerald Weldon**, M B Dubl, R N

Colonel **Frederick William Whiteman**, O B E, M B Glasg, Pakistan Armed Forces Medical Services

C B E (Civil)

William George Barnard, F.R C.P
Professor of pathology in the University of London at St Thomas's Hospital

Gilbert Brown, M.B Lpool, F F.A R C S
Honorary consulting anæsthetist, Adelaide Hospital, South Australia

Thomas Morris Davies, M.R C S
Deputy director general of Medical Services, Ministry of Pensions

Alan Taylor Howell, M B Camb
Director of Medical Services, Tanganyika

William Leslie, M C, M B Lond
For political and public services in Cornwall

Archibald Daniel Marston, F R C S, F F A R C S
Lately dean of the Faculty of Anæsthetists, Royal College of Surgeons

Arnold Ashley Miles, M D Camb, F R C P
Director of the Lister Institute of Preventive Medicine

Gilbert Innes Strachan, M D Glasg, F R C P, F R C S, F R C O G
For political and public services, and for services as professor of obstetrics and gynæcology, University of Wales

Richard Robertson Trail, M C, M D Aberd, F R C P
Medical director, Papworth and Enham Alamein Village Settlements for the Tuberculous

M V O (4th class)

James Lawrence Bunting Ansell, M R C S
Surgeon Apothecary to the Household at Sandringham

O B E (Military)

Surgeon Commander **John Mansel Reese**, M R C S, R.N

O B E (Civil)

Francis Ward Allinson, M B Lond, F R C S
Professor of surgery, Medical College Hospital, Dacca, Bengal

Charles Anthony Boucher, D M Oxfd
Medical officer, Ministry of Health

Cecil Burnham, M B Edin, F.R.C S E
Lately commandant, Star and Garter Home for Disabled Soldiers, Sailors, and Airmen, Richmond, Surrey

William John Hughes Butterfield, M D Johns Hopkins, B M Oxfd, M R C.P
Member of the scientific staff of the Medical Research Council

Richard Alexander Seymour Cory, M B Brist
Senior medical officer, King George V Jubilee Memorial Sanatorium, Liguanea, Jamaica

Kenneth John Grant, M B Glasg
Medical officer of health, Great Yarmouth
For services during recent floods in the Eastern counties

Eben Stuart Burt Hamilton, M C, M B Edin., F R C S E
Commissioner, Duke of Lancaster's District, St John Ambulance Brigade

Albert Joseph Hawe M D Lpool, F R C.P
Senior specialist, Gold Coast

Gordon King, F R C S, F.R C O G
Professor of obstetrics and gynæcology, University of Hong-Kong

James Sanderson McGregor, M D Glasg
Medical superintendent, Saxondale Hospital, Radcliffe-on Trent, psychiatrist, Nottingham General Hospital

Colonel **William Joseph Moody**, M B Camb, F.R C S E, I M S retd
Lately medical adviser to the British Political Resident, and chief quarantine medical officer, Persian Gulf

George Rankine, M C, M.B Edin
General practitioner, Dundee

Sarah Anderson Jameson Rankine, M B Glasg
Medical officer in charge of St Margaret's Hospital, Poona, Bombay

Henry Richards, M B Lond
Assistant director (Public Health), Sudan Government

George Robertson Ross, M B, PH.D St And
A member of the Public Services Board, Southern Rhodesia

Emrys Cadwaladr Thomas, L.R C P E
Director, Victoria Hospital, Damascus

John Duncan White, M B Edin
Director, Radiodiagnostic Department, Hammersmith Hospital, London

Thomas Macfarlane Wilks, M B E, M R C S
Area commissioner, St John Ambulance Brigade, London.
For services during recent floods in the Eastern counties.

Donald Bagster Wilson, M D
Director, East Africa Malaria Unit

to show ventricular pre-excitation, and this and one other show what could be regarded as partial right bundle-branch block.

The diagnosis of single ventricle in life, apart from its academic interest, is important from the point of view of surgical treatment. The prognosis is said to be better when pulmonary stenosis is present, and therefore no attempt should be made to relieve this. On the other hand Campbell et al. recommend that subclavian-pulmonary anastomosis should be done when there is considerable cyanosis and disability, although they found that in their own proved cases this had not been beneficial.

BARBITURATES AND ALCOHOL

Two recent deaths from barbiturate poisoning have attracted considerable attention.[1] [2] In each instance the total quantity of the drug taken, as estimated by post-mortem examination, was scarcely more than the maximum therapeutic dose—it was certainly nowhere near the amount usually regarded as lethal. But, in both cases, a small quantity of alcohol had apparently been taken about the same time as the barbiturate, and this, above all, was regarded as the sinister complication. At one inquest the pathologist's view is said to have been that "even a minute quantity of alcohol would speed the action of the drug"; and at the other a psychiatrist is quoted as saying that "occurrences of this kind are constantly happening. There have been three or four accidental occurrences in the past ten days to my knowledge." In view of such statements the coroners concerned, quite naturally, issued stern warnings to doctors and to the public.

But if the danger is as great as this, it is strange that so little has been said about it in the past. It may be mentioned to students, but with no great emphasis, and there must be thousands of doctors in practice who know nothing of this possibility of the barbiturates. Moreover, considering that barbiturates are so freely dispensed under the National Health Service[3] and that most people in this country are not teetotallers, it is surprising that deaths from this cause have not been more numerous. In the U.S.A. alcohol and barbiturates are also consumed in large quantities, but again few deaths have been attributed to their combined action.

In 1943 Jetter and McLean[4] investigated this very question; for, as they observed, "the possibility of synergism between alcohol and a barbiturate is a matter of considerable practical as well as theoretic interest." In rats they demonstrated a definite synergism between the two drugs when given in sublethal doses. But even when both drugs were given together, each in half the maximum sublethal dose, only 1 out of 6 rats died. Clearly, there was a synergistic effect, but that is a very different matter from potentiation. Jetter and McLean also cited 3 examples of fatal poisoning in man; in these cases it was clear that one drug alone could not have caused death. But the total quantities involved were very great; and one victim "was addicted to both alcohol and barbital." Again, with mice and dogs, Ramsey and Haag[5] found further evidence of synergism, but none of potentiation; and the concentration reached in the body by the two drugs was no different whether they were given alone or together. Pharmacologically, both alcohol and the barbiturates are depressants of the central nervous system, so a synergistic action is not unlikely; but, as we have said, that is a far cry from the potentiation necessary to turn innocuous individual doses into a fatal combination.

The dangers of giving barbiturates to those who take alcohol have probably been overstated. On the other hand, of course, barbiturates are in themselves deadly drugs, which are perhaps used too lightly today. Moreover, their effects vary considerably from one person to another, not only in the amount needed for a given hypnotic effect, but also in the dose that proves fatal. And in those who regularly take barbiturates a further factor may have to be considered, for Brodie[6] has shown that the action of thiopentone becomes progressively longer with repeated doses, even though the dose remains the same. The drug, it seems, is taken up by the fatty tissues and later released into the body-fluids; and a similar thing is possible with the longer-acting barbiturates. If so, the cumulative effect may be serious and a disastrous combination with alcohol easier to explain. But the fact remains that thousands of people take barbiturates in the usual doses, even more drink alcohol in one form or another, and yet few deaths have been proved to be due to the two drugs in combination. To give an extreme example, patients with inoperable cancers are often given generous amounts of wines and spirits and large doses of barbiturates at the same time; but they seldom die of alcohol-barbiturate poisoning.

If the possibilities are really as serious as some of the evidence at these inquests suggests, then the matter demands urgent inquiry. But it may well be that these two tragedies are examples of particular idiosyncrasies, serious enough in themselves, but no basis for a general alarm.

VACCINATION AND ECZEMA

THE death of a doctor's 5-month-old baby from generalised vaccinia on the eczematous skin (eczema vaccinatum) in a district where virulent cases of smallpox had occurred,[7] emphasises the occasional tragedy which the practice of vaccination, like many other normally harmless medical procedures, entails.

It is not easy to present to a sedulously inquiring parent a balanced view of the substantial advantage likely to accrue to the child and the community from successful vaccination when the minute risk associated with the operation must be mentioned and accepted. But guiding rules are now fairly clear. Vaccination should preferably be performed in infancy during a stabilised period of good health, and should unhesitatingly be postponed if the child is ailing in any way, and especially if suffering from infantile eczema, tuberculous primary complex, syphilis, or any febrile attack or septic condition of the skin. Similarly, any infant with eczema should be rigidly isolated from any person recently vaccinated. The vaccination lesion should not be looked on as simply a localised sore, but rather as a local lesion accompanied by a viræmia which can set up metastases in any devitalised area of skin or elsewhere. Infantile eczema, even if mild at the time, is perhaps the most obvious contra-indication to vaccination in this country; for a large area of skin sown with numerous vaccinal lesions can be rapidly fatal unless, perhaps, the secondary septic intoxication is at once overcome by effective antibiotic treatment. This rule is generally valid even when there is smallpox in the district; for, with few exceptions, the risk of acquiring smallpox will be much less than the very substantial risk of developing dangerous eczema vaccinatum. In cases of infantile eczema, vaccination should preferably be postponed until the skin has been completely normal for at least a year. This generally means postponement to the pre-school age and a consequent slight increase of the minute risk of postvaccinal encephalitis. But this danger is so small as to be negligible compared with the hazards of eczema vaccinatum.

THE death was announced last week of Dr. H. M. LESTER, director of medical services in Malaya.

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4. Jetter, W. W., McLean, R. *Arch. Path.* 1943, 36, 112.
5. Ramsey, H., Haag, H. B. *J. Pharmacol.* 1946, 88, 313.
6. Brodie, B. B. *Fed. Proc.* 1952, 11, 632.
7. *Yorkshire Post*, May 26, 1953.

M B E (Military)

Lieutenant JOHN WILLIS COOMBE, R A A M C
Major DESMOND KEITH TUCKER, M R C S , R A M C
For gallant and distinguished services in Korea

M B E (Civil)

HENRY SIDNEY ATKINSON, B M Oxfd
Chairman of the committee of 135 (Reigate and Redhill) Squadron, Air Training Corps
DOROTHY DELBRIDGE, M B Brist
For medical services in Fiji
FRANCIS JOHN GRAHAM, L.R C P I
Medical practitioner of Sydney, New South Wales
GEOFFREY BUCKLAND ORBELL, M B
Of Invercargill, New Zealand
WILLIAM OLIVER PETRIE, M B Edin
Medical officer, Nyasaland
RONALD REES POWELL, M R C S
Chairman, Reigate Unit Committee, and Southern Area representative, Sea Cadet Council
SOO HOY MUN, M B
Honorary medical officer, Chinese Maternity Hospital, Federation of Malaya

PHYSICAL TREATMENT AT THE BRITISH SPAS

AT the suggestion and under the direction of the medical committee of the British Spas Federation, an investigation of the effect of physical treatment, including hydrotherapy, on rheumatic cases at a number of centres has been carried out The following information has been supplied to us by Lord Horder and Dr G D Kersley, respectively chairman and secretary of the committee

It was realised from the start that a completely controlled therapeutic trial was not possible, because it was impossible to rule out psychological influences Such factors must, however, play their part in the effect of therapy, and every effort has been made to give genuine clinical assessments Only typical cases of rheumatoid arthritis, osteo-arthritis, and fibrositis were investigated, and no parenteral therapy was used during the period of observation Cases were assessed before treatment, directly after treatment—i e , in three to six weeks—and again three months later

128 cases of rheumatoid arthritis, 227 of osteo arthritis, and 112 of fibrositis were followed up in this way, and the results were statistically analysed by Mr E Lewis Faning, D SC , of Cardiff University Degree of pain on movement or at rest, swelling, tenderness, and range of movement were numerically recorded, together with age and sex, on a special pro forma drawn up for the purpose No points of especial interest were forthcoming from analysis of age and sex groups, but the general effect of treatment, both immediate and after three months, is of importance and accords well with clinical impressions

In the rheumatoid arthritis group of 128 patients approximately half, it is stated, appeared to derive significant immediate benefit, and a slightly larger number were definitely improved on a three months' review This applied both to a more "active" and to a more "quiescent" subgroup In the former 68% showed decrease in tenderness and 54% in swelling of the worst affected joint, but only 36% had reduction of pain at rest Only 1 patient appeared to be worse

In the group of 227 osteo arthritics, approximately two thirds stated that they had less pain and half had increase in range of movement After three months the result was slightly less good, with 62% stating that they had less pain than before treatment

In the group of 112 "fibrositis," again two thirds claimed improvement, and the result of assessment three months later showed neither increase nor decrease in this benefit figure

In England Now

A Running Commentary by Peripatetic Correspondents

Westminster Abbey But an Abbey transformed into a theatre—and this word is entirely appropriate, since the part of the Abbey where the Coronation ceremonies take place is termed the theatre, and the seating of the whole building has been redesigned so that all present may see some part of the service with their own eyes, though many will have seen less than those who watched through the eyes of the television cameras What then did we who were there see ? We saw the colours , the blue of the carpet in the nave repeated in the hangings in front of the lower tiers of seats and again in front of the gallery, and, filling the seats like a human flower garden, the scarlet of the robes of the aldermen of the City of London, the scarlets, blues, and golds of the full-dress uniforms and the decorated greens golds, and blues of costumes from the far East And beneath the gilded hanging chandeliers and the floodlights which diffused a sunny radiance from the ceiling glowed the robes of the peers and peeresses, the copes of the clergy, and the cassocks of the choirboys , and the standards carried by the standard-bearers , and the diamonds in the tiaras and the sceptre and the Imperial Crown itself shone and glittered

And we saw the Queen, not through some mechanical medium but face to face , and for at least one spectator the most moving moment was not the crowning itself but her first appearance, when after all the processional panoply she entered through the west door and moved slowly up the nave, her hands clasped with palms upwards before her, and her face that of one dedicated

But we in the Abbey saw also the unseen "Here's an acre sown indeed with the richest, royal'st seed,' wrote Beaumont *On the Tombs in Westminster Abbey*, and, though he went on to moralise in conventional fashion on the mortality of kings, his insight as a poet served him better perhaps than he knew For the history enshrined in the Abbey is indeed the seed from which our present greatness has sprung Its roots are in the past, and from these it must draw its nourishment, but its leaves spread in the sunshine of today, and if the present lives upon the past it is equally true that the past derives its vitality from the present Orders of knighthood and the heraldry which emblazons their pomp would soon become an empty show if the chivalry which gave them birth could find no expression in the England of today and feel no challenge in the quests of the modern world So a Coronation is a rebirth, a new life growing from the 'acre sown indeed with the richest royal'st seed"

And the life of the nation thus renewed comprehends far more than merely government, administration, and defence Prominent though these features were in the processions, it was the whole nation which was represented in the Abbey, and represented not only by living men and women but also by an unseen cloud of witnesses from the past and by that simple representative of the common people, the Unknown Warrior, whose tomb divided every procession entering and leaving the Abbey

So the past and the present intermingled and not only were the living moved by the ceremony they witnessed but it seemed that the bones of that stout old monarchist, Samuel Johnson, and the dust that was once Thomas Hardy, ironical but compassionate commentator upon dynasts were fondly stirred by the fanfare of trumpets and the fresh boys' voices shouting *Vivat Regina, vivat Regina Elizabetha !*

* * *

The damp but enthusiastic crowds who waited on the stands and pavements outside the Abbey were rewarded by a magnificent military parade, but it was really the coaches that made it a royal occasion We all began by being indebted to the peers who bravely drove to Westminster in all the flunkeyed splendour of their family equipages The opening of the procession itself was entrusted to an experienced annual performer—the Lord Mayor's coach burnished and resplendent and guarded by pikemen The Speaker's coach accompanied by attendants in green velvet, rounded Parliament Square with a swinging motion which might well have

Before Our Time

RECORD OF THE CASE *

Sir JOHN CHARLES
M.D. Durh., F.R.C.P., D.P.H.
CHIEF MEDICAL OFFICER TO THE MINISTRY OF HEALTH

AT 8 o'clock on the evening of Thursday, October 24, 1867, Wagner scored the final bars of *Die Meistersinger*, inscribed the time and date, and laid down his pen.

Without any comparable marking of the chronology, but just as conclusively, a Theban scribe set aside his pen 3600 years ago, "in the middle of a line, in the middle of a sentence, in the middle of a word." His task had been the copying of an old surgical treatise, written in its primordial form at least a thousand years earlier.

Five hundred years before this scribe began his labours, a commentator had added to the original text an interpretation of some of its archaic words and phrases, and these glosses too were transcribed on to the roll of reed paper, which we know as the Edwin Smith Surgical Papyrus.

The treatise was in essence a catalogue of 48 surgical cases, all males, and many of them warriors. The descriptions of the surgical experiences of those patients are, in the conventional sense of the words, our earliest medical records. The grouping of the 48 cases suggests that they were part of a larger collection. Commencing with the head and skull, they next include the neck, clavicles, humerus, sternum, and spinal column—and then cease abruptly. The logic of the descriptive scheme envisages a commentary on the surgery of the thorax, abdomen, and lower members. But some event or person interrupted the work of the scribe. He evidently contemplated the resumption of his copying, for a stretch of 31 inches of virgin papyrus was left between his unfinished task and the engrossing of a collection of incantations and medicinal and cosmetic recipes.

Not only was there order and method in the planning of the treatise, but the presentation of each case conformed to a simple pattern. First there came an identification of the case; next a statement of the examination; then a diagnosis and a tentative prognosis in three ascending degrees of severity—an ailment that could be treated, an ailment that could be contended with, an ailment not suitable for treatment. Finally, the treatment was prescribed. Here is the record of a simple case—a broken nose.

> If thou examinest a man having a break in the column of his nose, his nose being disfigured, and a depression being in it, while the swelling that is on it protrudes, and he has discharged blood from both his nostrils—thou shouldst say concerning him "an ailment which I will treat."
>
> Thou shouldst cleanse it for him with two plugs of linen. Thou shouldst place two other plugs of linen saturated with grease inside of his two nostrils. Thou shouldst put him at his mooring stakes until the swelling is reduced. Thou shouldst apply for him stiff rolls of linen by which his nose is held fast. Thou shouldst treat him afterwards with grease, honey and lint every day until he recovers.

The hand of the gloss-writer has explained the unusual simile—"put him at his mooring stakes" means putting him on his customary diet, without administering a prescription.

Of the 48 cases described, no more than 15 were assigned to the category of the hopeless, and in 1 instance only did the practitioner substitute magic and incantations for surgery.

THE HIPPOCRATIC CORPUS

Twelve hundred years after the unfinished business of the Edwin Smith Surgical Papyrus, there was accumulated in Greece a very different collection of medical and epidemiological knowledge. This corpus of writings, a veritable library of treatises, aphorisms, case-histories, and the like, is associated with the name of Hippocrates. How much is attributable to Hippocrates himself one cannot now say, but the collection represents the thoughts and experiences of tough minds and keen observers.

Here again we have a group of medical records to study, and on this occasion surgery is joined by medicine and midwifery and the patients are freemen and slaves, men, women and children often identified by name or domicile. The celebrated clinical picture-gallery of the first and third books of *Epidemics* displays 42 cases, 25 of them fatal. They are preceded by brisk, critical commentaries, the so-called constitutions, which discuss in general terms the meteorological conditions of the respective seasons, the epidemic disorders which were prevalent, their trends and features. So we find it recorded that in the spring of some undatable year

> Many had swellings beside one ear, or both ears, in most cases unattended with fever, so that confinement to bed was unnecessary. In some cases there was slight heat, but in all the swellings subsided without causing harm. . . . This was the character of them—flabby, big, spreading with neither inflammation nor pain. . . . The sufferers were youths, young men, and men in their prime, usually those who frequented the wrestling school and gymnasia. Few women were attacked.

Then follow in no particular order and in varying detail the clinical histories and descriptions of the patients.

Lastly, as an appendix to the majority of cases in the third book of *Epidemics*, we encounter a sort of registrar's summary, a synoptic line of a few Greek capital letters, which gives the duration, outcome, and character—that is the operative word—of the disease. Seven such capitals epitomised the death from fever and diarrhœa of a woman who seven days previously had had a miscarriage.

The 42 case-histories of those two books of *Epidemics* have been described as the most remarkable product of Greek science. They differ markedly from the records of the Edwin Smith papyrus. Their breadth of clinical interest is greater; the presentation of the case is fuller; the statement of personal and social detail is more elaborate. But their outstanding distinction is to be seen in the cool day-by-day study of the progress of the pathological phenomena in the body of the patient. Often the phrases which record these changes have caught for all time the physiognomy of disease or the prolegomena of dissolution. Oddly enough, in comparison with Egyptian practice, there is a virtual omission of any reference to treatment.

That combination of calm observation and apparent implicit reliance on the curative powers of Nature has given rise to the suggestion that the Hippocratic case-book is little more than a "meditation upon death." Such comment is not altogether fair, because in another of the books of the corpus, the *Regimen in Acute Disease*, the cardinal remedies are adequately described.

Amongst the diseases met with are examples of those protean Mediterranean malarial fevers, of puerperal and wound infections, of the pneumonias and dysenteries, and of several strange delirious states which cannot be precisely identified. Here are two specimens of these records, as brief and succinct as any in the collection:

> (*a*) Crito, in Thasos, while walking about, was seized with a violent pain in the great toe. He took to bed the same day with shivering and nausea; regained a little warmth; at night was delirious.
>
> Second day. Swelling of the whole foot, which was rather red about the ankle, and distended; black blisters; acute fever; mad delirium. Alvine discharges unmixed, bilious and rather frequent. He died on the second day from the commencement.

> (*b*) Another woman, after a miscarriage about the fifth month, the wife of Hicetas, was seized with fever. At the beginning she had alternations of coma and sleeplessness; pain in the loins; heaviness in the head.

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* Opening address at the First International Congress on Medical Records. London, Sept. 8, 1952.

made a longer journey trying to its occupants. The Colonial rulers rode in open carriages which allowed us to admire the vivid and delicate colours of their robes and their strange and beautiful headdresses. Salote, the genial Queen of Tonga, in her petunia cloak was the crowd's favourite. The prime ministers and the princes and princesses of the blood royal were in closed but elegant carriages. The Queen Mother and Princess Margaret in the glass Irish Coach prepared us for the splendours of the State Coach itself carrying the Queen to her crowning with flowers on her lap and carrying her back to her people with the orb and the sceptre in her hands.

* * *

Well, of course, Selfridges have their horse, the crowns swing over The Mall, the emblematic guardsmen march down Whitehall, the pink roses of Regent Street have promoted as lively a discussion as the red and white ones, the City is tented in white streamers, the Strand has hopefully erected a maypole. All these in their way are part of the Coronation celebrations. But on none of them has more loving care been lavished than on those in our cul de-sac. These were put up on pre-Coronation Thursday by Mr Morganti, the greengrocer, Mr Pollak, the shoemaker, Mr Bernstein, the tailor, young Jack Morganti and a large Alsatian dog with the help of a ladder borrowed from the workmen who are demolishing a house on the bombed site at the corner. Mrs Morganti had run the Union Jack through some nice hot suds, and the colours had come up lovely, though perhaps it had shrunk a little. Anyhow it proved too small to stretch from the lamppost to the barber's shop. But Mr Bernstein resourcefully made a small seam along one edge through which he ran a piece of white tape. Thus informally suspended it has taken the wind to everybody's satisfaction. Surely it is quite a compliment to the Queen that all these Ruths, instead of moping about among alien corn, have been briskly nailing up bunting.

* * *

To the conscientious doctor there is always a snag about taking even a Coronation weekend off. We can take four weeks off at a stretch and the fates are with us. Our patients remain alive. They don't develop obscure surgical conditions, go into comas, have stillborn babies, or depart en bloc to the doctor across the road. They behave, in fact, as normal healthy human beings. But let me take a weekend off, or worse still Friday to Sunday night, and everything happens. Supposedly healthy patients choose that time for dying suddenly. They develop acute appendices, they have heart attacks, they gas themselves, they go into premature labour. But on Monday morning everything drops back to normal. It doesn't only happen to me. My partner complains bitterly that it happens to her too, and other colleagues say the same. It almost seems that it is against Nature for a G.P. to take a weekend off. If our patients really benefit by our taking long holidays and are worse when we take short ones, it certainly won't be too unpleasant to pander to their fads for once.

* * *

I was sitting by the window looking out on lovely country in blazing sunshine while the doctor examined my host's small son. Lazily I listened with half an ear to the list of symptoms: high temperature, a terrible cough, a flush, pain in the back of the neck but no stiffness. What would the diagnosis be, I wondered. "I suppose it's alotothis again," said the father. The doctor nodded, shook down his thermometer, and wrote out a prescription. Alotothis? I hastily repeated to myself cyanosis, halitosis and all the familiar words of that family, but I was still baffled. I did not like to betray my ignorance so I asked no questions. The child was better next day, but the infection went through the house with a 3-day interval between cases.

When I was back in town I developed the mysterious disease myself and called in a colleague. I told him my symptoms and then added with pride: "I can tell you what the diagnosis is." But he was not listening. "You know," he said, "there's a lot of this about."

Letters to the Editor

JUNIOR RESIDENT STAFF

SIR,—As long as the hospital administrator regards the junior resident staff as cheap labour, and no more, so long will the shortage in provincial hospitals continue. A resident may expect to receive as well as to give: married quarters and television sets are no substitute for supervision, instruction, and the opportunity for self-improvement. The shortage in the United States is at least as serious as it is here, and a committee of the American Medical Association has recently issued a report which deserves reading.[1] Probably the most important statement was a reaffirmation of one which is embodied in the association's "essentials of an approved internship": to be suitable for an internship a hospital must be one in which "the educational benefits to the intern are considered of paramount importance, with the service benefits to the hospital of secondary significance."

London W 1 FILIUS TERRÆ

SIR,—There are those who object to the National Health Service being termed an industry; but from the article by Mr Hurst and his colleagues (May 23) it would seem that the outlook on working hours and working conditions which pervades industry has now permeated that service.

Speaking of possible remedies to deal with the apparent shortage of junior doctors in hospitals the writers say: "It seems certain that doctors will not go back to the earlier unsatisfactory conditions of long working hours; nor should they be expected to do so." When I was a young houseman at Westminster Hospital I never knew that time existed. I was happy round the clock even if that meant little or no sleep, no leisure, and no recreation—which often was the case. My total remuneration was £1 a week and all found, including laundry, plus the odd theatre ticket from the matron's office.

Such phrases as 'working hours' and 'unsatisfactory conditions'' never entered our thoughts—still less our vocabulary. We were supremely happy to find ourselves on the threshold of our chosen career.

Public Health Department,
Cardiff J GREENWOOD WILSON

SIR,—I wonder whether Mr Hurst and his colleagues have inquired into the views of the junior medical staff. Their article (May 23) suggests lack of understanding of the doctor's side of the problem.

In the first place, few medical men who have competed for posts in the better-known hospitals or in general practice, would agree that there is a shortage of doctors.

In selecting a hospital post, two factors are usually considered: (1) the experience to be obtained or the value of the post as a background for obtaining further posts; and (2) the attractiveness of the hospital—its atmosphere, accommodation, food, &c. It is perhaps to be deplored that the posts offering the best experience often have the least "name value" in applications for further posts; but that is not the administrator's problem. What does concern him is the resentment felt by many residents at the petty restrictions, legislation, charges, economies, and so on, so often imposed upon them by the "nine-till-five" staff. The long hours and extra duties of the houseman are always taken for granted, and only rarely is anything done to cheer up his quarters or to improve his food. More often thanks for his twenty-four hours' service are expressed in the form of a bill for 2*d*. for a cup of coffee given to a friend.

From my own experience I should say that what is chiefly needed is a change in the attitude of the administrative staff towards residents.

EX-HOUSE-OFFICER

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[1] J. *Amer. med. Ass.* 1953, 151, 499.

Second day. Bowels disordered with scanty, thin stools, which at first were uncompounded.

Third day. Stools more copious and worse; no sleep at night.

Fourth day. Delirium; fears; depression. Squinting of the right eye; slight cold sweat about the head; extremities cold.

Fifth day. General exacerbation; much wandering, with rapid recovery of reason; no thirst; no sleep; stools copious and unfavourable throughout; urine scanty, thin and blackish; extremities cold and rather livid.

Sixth day. Same symptoms.

Seventh day. Death.

The shorthand epitome of this second case requires eight Greek capital letters.

These are crisp, comprehensive narratives, composed by an alert eye-witness. Medical literature, except in rare examples, shows nothing like them for the next 1700 years.

THE MIDDLE AGES

After them came that long dark vista of the earlier Middle Ages. Here and there in the ancient and medieval chronicles, amongst the "sad stories of the death of Kings," there are credible accounts of the last illnesses of the royal and the great, sufficient to provide the material for a diagnosis. Such descriptions, however, are too infrequent to be regarded as a fruitful source of information for our present purpose.

THE RENAISSANCE

Medical recording had to wait until 1507 for its renaissance. That year saw the publication of the posthumous masterpiece of the Florentine physician, Antonio Benivieni, *De abditis nonnullis ac mirandis morborum et sanatationum causis*. The discussions of the hidden causes drive from a study of 24 post-mortem examinations, and each individual finding is linked to a short description of the earlier clinical assessment of the patient.

In this simple form of correlation we can see the germ of the clinicopathological conference of today, and Benivieni as the precursor of the Cabots.

If royal mortality provided an indifferent field for research, there is, at any rate, one satisfactory piece of detailed medical history writing which leaves little unsaid about the health and habits of James I of England. The author was Theodore Turquet de Mayerne, a Swiss, who commenced practice in Paris, became physician-in-ordinary to the then King of France, Henry IV, and in 1611 was invited to England to take up the appointment of first physician to its monarch.

The memorandum "On the preservation of the King's health," a document of upwards of 4000 words, was written in December, 1623, two years before the King's death. It is as candid and thorough an appreciation of the psychology and pathology of a human being, albeit a King, as ever pen communicated to paper. For any historian of the troubles of the Stuart dynasty, this portrait is of ætiological significance, but, in this context, only a few of its passages need be quoted from Sir Norman Moore's translation. It commences thus:

> James the First, King of Great Britain, was born at Edinburgh in the year 1566, on June 19th, at half-past eleven in the morning, and is now aged over 57 years. He had a drunken wet-nurse and was suckled for about a year. He has a very steadfast brain, which was never disturbed by the sea, by drinking wine, or by driving in a coach.
>
> He is easily affected by cold and suffers in cold and damp weather. His chest is broad and well formed, and the vital parts contained therein have strong and lively warmth and never are afflicted unless as a result of morbid conditions elsewhere. The liver naturally good, large, of much blood, warm, liable to obstructions, and inclined to generate much bile. The spleen now easily heaps up melancholic juice, the presence of which is indicated by various symptoms. There is no swelling in either of these viscera and no hardness. Each hypochondrium is soft and never distended, except with wind. The stomach is always ready for the burden of a large quantity of food and is prompt to get rid of any hurtful excess, chiefly by the bowel.
>
> His legs seem not strong enough to sustain the weight of the body. His habit loose and of pervious texture, and he readily heats with dry heat. Skin thin and delicate, so that it itches easily. Fauces narrow, causing difficulty in swallowing, which defect is hereditary from his mother and grandfather James V of Scotland.
>
> *Air.*—His Majesty bears all changes of air fairly well; in damp weather with a south wind he is attacked by catarrh.
>
> *Food.*—As regards food he does not much amiss except that he eats no bread. He generally takes roast meats. Owing to want of teeth he does not chew his food but bolts it. Fruit he eats at all hours of day and night.
>
> *Drink.*—In drinks he errs as to quality, quantity, frequency, time, and order. He promiscuously drinks beer, ale, Spanish wine, sweet French wine, white wine (his normal drink), and Muscatelle wine (whence he has diarrhœa), and sometimes Alicant wine. Nevertheless, he does not mind whether wine be strong or no so it be sweet. He has the strongest antipathy to water and all watery drinks.
>
> *Affections of the mind.*—His mind is easily moved suddenly. He is very wrothful, but the fit soon passes off. Sometimes he is melancholy from the spleen in the left hypochondrium exciting disorders.
>
> *Excreta.*—He often blows his nose, sneezes very often. Does not spit much unless from catarrh. Stomach easily made sick if he retains undigested food or bile. Vomits with great effort, so that after being sick his face appears for a day or two spotted with red spots. Much wind. Vapours from his stomach precede illness. The alvine discharge is uncertain and depends on the nature of his food, which often produces morbid changes. A tendency to looseness gets rid of a burden produced by what he has eaten.
>
> *Former illnesses and present aptitude to various morbid dispositions.*—The King to the sixth year of his age was not able to walk, but was carried about, so weak was he from the bad milk of his drunken nurse. Between the second and fifth year he had smallpox and measles. In his fifth year for twenty-four hours he had suppression of urine, nevertheless no sand or slime was ejected.
>
> He is of extreme sensitiveness, most impatient of pains: and while they torture him with most violent movements his mind is tossed, and bile flows around his præcordia, whence the evil is not relieved, but made worse.
>
> He demands relief and freedom from pain, little considering about the causes of his illness.
>
> *As to remedies.*—The King laughs at medicine, and holds it so cheap that he declares physicians to be of very little use and hardly necessary. He asserts the art of medicine to be supported by mere conjectures, and useless because uncertain.

Mayerne, with his uncanny observation and assiduous *curatio*—he proposed a placebo for every trivial symptom—nevertheless paid tribute to ancient and medieval doctrines. For him catarrh descends from the brain to produce coryza, the humours boil in the stomach, and the spleen from its seat in the left hypochondrium excites disorders. More than seven years before Mayerne completed his memorandum, William Harvey had already proclaimed the circulation of the blood. And with its ultimate general acceptance physiology shook off the strings of Galen, and medicine began, however tentatively, to take its modern shape.

The experimental method established itself; logical reasoning replaced speculative opinion; cause and effect began to be bracketed together in the minds of the medical faculty.

MORGAGNI

Let us skip another century and take counsel of Giovanni Battista Morgagni, chief professor of anatomy at Padua and president of the university. He obtained his first appointment in Padua in 1712, and there remained for over fifty years, amassing reputation and honours as anatomist, pathologist, physician, man of affairs, and philosopher. He died in his ninetieth year in 1771, ten years after the publication of his monument, "more durable than brass," the great repository of medical and pathological experience entitled *De sedibus et causis*

TUBERCULOSIS IN GLASGOW

SIR,—I am sorry that in my letter of May 2 I stated there was no consultant in tuberculosis in the Western Region This is inaccurate, as pointed out by several of your correspondents I was thinking, when writing, of the clinic service and did not intend my statement to be inclusive of medical superintendents of sanatoria or orthopædic surgeons doing mainly tuberculosis Despite this, it is true that this Western Region is the most poorly staffed in the United Kingdom, although the problem is most acute here A statement from the Regional Board on the staffing of the chest clinics and associated beds would be most instructive to your readers The medical staff in these clinics has been pressing for improvement for many months The death-rate, as elsewhere, has shown a welcome fall The number of notifications of new cases and of children developing tuberculous meningitis leaves no room for complacency

The vituperative letter of the Medical Officer of Health obviously reflects his sense of frustration in the face of the hopeless housing situation This is understandable, for at present building rates it will take between forty and fifty years to supply the needed 150,000 houses This is the figure shown in 1945 to be essential to relieve overcrowding and to replace unfit and insanitary houses A prominent member of the housing committee stated in a public meeting recently that there were 161,000 families waiting to be rehoused These facts will enable your readers to appreciate the bare outline of the problem The instance I gave revealed just a little of the human misery hidden by such figures

Tuberculosis in Glasgow will not be eradicated until a fully staffed medical and nursing service is associated with a radical approach to rehousing The Regional Board and the Corporation of Glasgow are challenged by a situation unparalleled in the British Isles, and all resources should be mobilised to give them much-needed help

Central Middlesex Hospital,
London N W 10

HORACE JOULES

SIR,—By drawing attention in your columns to the deplorable position with respect to tuberculosis in the city of Glasgow, Dr Joules has done his Scottish colleagues a valuable service, and the substance of his comments is certainly accepted by the overwhelming majority of general practitioners in the area

One can only deplore that the Medical Officer of Health and the Senior Tuberculosis Officer consider it "impertinent for someone from the South of England to make comments on the situation" The tone and content of their reply confirms the strong suspicion existing in Glasgow that those concerned with the tuberculosis service are guilty of complacency, one instance of which is their quotation of improved mortality rates While such improvement is, of course, to be welcomed, it means nothing more than that more patients with tuberculosis are being cured, or are being kept alive longer, as a result of the surgical and chemotherapeutic innovations of the past decade But it does *not* mean that the tuberculosis endemic is under control, nor does it means that the rate of new notifications is falling *On the contrary* the following statistics for new notifications of pulmonary tuberculosis in Glasgow tell their own grim story

Year	*Cases*
1935	1757
1940	1908
1945	2641
1950	2446
1951	2207
1952	2235 (provisional)

If the 1952 figure is broken into the quarterly notifications there is a clear indication of a substantial deterioration, which has been accelerated in the first quarter of 1953

	1951	*1952*	*1953 (provisional)*
3rd quarter	514	519	—
4th quarter	496	564	—
1st quarter	—	547	622

Why does not the M O H, whose job I have always understood to be the prevention of disease, not quote these figures instead of the number of deaths ?

Is it not evidence of complacency when the Western Regional Hospital Board announces, as it recently did, that *after 3 years' consideration* work was now to begin on new chest clinics and advertisements were to be placed for new consultant posts ? Is this the realistic sense of urgency possessed by the board ? Dr Laidlaw and Dr Gemmill tell us how many tuberculosis consultants there are in Glasgow Perhaps they will now tell us how many, if any, are at work outside of hospitals, in the chest clinics

The Western Regional Board area has the lowest number of hospital beds, per annual new cases or per population, of any of the regions of Scotland, excepting the South-Eastern Yet nearly two-thirds of the new notifications in Scotland each year are in the Western Region Does not this suggest complacency ?

Dr Laidlaw and Dr Gemmill adduce historical reasons for Glasgow's specially bad housing record Instead of defending the status quo in housing, they should be using their influence to demand a special allocation to meet the city's crying need, as shown by the following comparison of percentages of population in 1951 living at a density of over 3 per room and of 2–3 per room

	Over 3 per room	*2–3 per room*
England and Wales	0 3	1 8
Glasgow	8 6	17 3

There are very nearly as many people living at more than 3 to a room in the Glasgow region alone as in the whole of England and Wales

Before throwing stones at Dr Joules, let Dr Laidlaw and Dr Gemmill put their own house in order When the Glasgow tuberculosis physicians and administrators achieve a speed of admission of new cases to hospital comparable to that in the area around Dr Joules's hospital, we will perhaps allow them their complacency

Glasgow

R LESTER BLACK

PNEUMONIA COMPLICATING CHICKENPOX

SIR,—In connection with your annotation of April 11, I should like to describe the following case

A woman, aged 21, was admitted to this hospital on Sept 28, 1952, with a diagnosis of chickenpox There was a typical, fairly profuse rash of characteristic distribution and appearance Temp 102°F, pulse rate 100 per min, respirations 22 per min Examination of the chest showed no definite physical signs, but the patient appeared slightly cyanosed

Routine treatment was started—namely, local application of dusting powder and oral hygiene Because it was judged that the rash, when fully developed, would be profuse penicillin was ordered, 250,000 units six hourly, in order to keep the rash "clean"

On Sept 29 the temperature was still high—103°F—and the patient had a slight cough, otherwise she was not complaining Over the left lower chest the percussion note was dull, and there were generalised fine crepitations in the lower half of the chest on both sides The respiration rate was still 22 per min

On Sept 30 the patient's cough was slightly troublesome and productive Radiography showed "gross mottling throughout the lung fields, which in the presence of a normal heart and obvious absence of industrial occupation is suggestive of Boeck's sarcoid or more probably a miliary type of pneumonia" Examination of the sputum showed no departure from the normal bacterial flora A blood count showed 11,000 white cells per c mm with no unusual differential count *morborum*. In that great work, clinical histories march side by side with the revelations of the post-mortem table, and wherever possible a correlation is established between them. "The Seats and Causes" is in construction a collection of 70 letters, each dealing with a separate subject or disorder. It runs to about a million and a half of words, mentions many hundreds of individual patients both "intra-vitam" and "post-mortem," and rejoices the heart of the reader by the provision of four comprehensive and associated indexes.

In the introduction Morgagni modestly introduces both himself and the original recipient of the letters:

> I have not dwelt long upon explications, and have taken care to intersperse other remarks relative to the practice of medicine, some of which relate to the history thereof, and some to the history of anatomy, and finally, many things which relate to the pursuits and studies of the young gentleman to whom I addressed the letters, and this with an intention to withdraw his imagination for a while, from the horrid and perpetual idea of diseases and dead bodies.

There is a Chaucerian flavour about the citizens of Morgagni's world. Little phrases etch and identify them. Here are some of the patients:

> A nobleman of Bologna; a woman of 40 years of age of a fleshy habit but a sallow colour, having eaten onions; an ostler, near sixty years of age, tall and fat, being used to eat much and drink very freely; a woman of Padua, by name Jacoba, the wife of Angelo Zanardi—finding 13 ribs on each side of her; a monk who was noble both in his birth and his manners; a woman of 75 years of age, of a manly aspect and very fat; a certain man skilled in the art of music, and the use of its instruments.

The first of the 70 letters is inscribed "Of Pain in the head." It parades before us "A boy of 13 years of age, of a ready wit, whose brother and sister had died of a consumption" followed by "a man about 40 years of age, (who) had been liable for many years to a pain in the right hypochondrium." "To those two histories," continues Morgagni, "give me leave to add a third, which though it does not relate to a man but a sheep is far from being unworthy of our notice."

Where there is such a wealth of material it is difficult to select. From over 700 necropsies, here are three histories, neither better recorded nor more brilliantly depicted than scores of others. Each is in its way notable. The first is probably the original picture of the Stokes-Adams syndrome; similarly, the second is an early, if not the earliest record of a patient in the grip of "angina pectoris"; the third vividly recounts the rupture of an aortic aneurysm.

I

> "A merchant at Padua of 64 years of age, of a square stature, and of a fat habit of body, but not to excess. He having been formerly subject to a rheumatism . . . had been cured by medicinal remedies: so that notwithstanding he was taken up with many and various businesses continually, he was, nevertheless, in good health; when of a sudden he was seized with very violent affections of the mind. . . .
>
> "A few days, after these commotions, a kind of vertigo coming on, he fell down—and on the day following he began to be troubled with convulsive motions, together with an attack similar to epilepsy. . . ."
>
> After several months during which the patient improved and then relapsed, Morgagni's services as a physician were asked for. He writes: "whom visiting by way of consultation I found with such a rarity of the pulse that within the sixtieth part of an hour the pulsations were only 22—and this rarenes which was perpetual . . . was perceived to be even more considerable, as often as even two (epileptic) attacks were at hand—so that the physicians were never deceived, if from the increase of the rareness they foretold a paroxysm to be coming on."

II

> "The mother of a family, who was two and forty years of age—had long been subject to a kind of paroxysm, which appeared in the following manner: on using pretty quick exercise of body, a kind of violent uneasiness came on, within the upper part of the thorax on the left side, joined with a difficulty of breathing, and a stupor of the left arm, all which symptoms soon remitted when those motions ceased. This woman then, having set out . . . from Venice to go up the continent in a wheeled carriage, and being cheerful in her mind, behold the same paroxysm returned, . . . and saying that she should die, she actually died on the spot."
>
> At the post mortem Morgagni found "the Aorta—not a little dilated at the curvature" with "compleat bony scales," of a small size; not to mention frequent marks of ossification being begun."

III

> "A man who had been too much given to the exercise of tennis and the abuse of wine, was . . . seized with a pain of the right arm, and soon after of the left joined with a fever. After these there appeared a tumour on the upper part of the sternum like a large boil; by which appearance some vulgar surgeons being deceived, and either not having at all observed, or having neglected the pulsation, applied such things as are generally used to bring these tumours to suppuration, and these applications were of the most violent kind. As the tumour still increased others applied emollient medicines from which it seemed to them to be diminished. But it not only soon recovered its former magnitude but was . . . seen to increase every day.
>
> "Wherefore, when the patient came into the Hospital of Incurables . . . it was equal in size to a quince and . . . began to exude blood in one place so that the man himself was very near having broken through the skin . . . when he began to pull off the bandages, for the sake of showing his disorder.
>
> "But . . . he was prevented going on, and ordered to keep himself still, and to think seriously and piously of his departure from this mortal life, which was very near at hand and inevitable. And this really happened on the day following from the vast profusion of blood that had been foretold, though not so soon expected by the patient. Nevertheless, he had the presence of mind immediately as he felt the blood gushing forth, not only to commend himself to God, but to take up with his own hands a basin that lay at his bed-side, and, as if he had been receiving the blood of another person, put it beneath the gaping tumour."

THE CABOT CASE-RECORDS

Our panoramic sweep covers another century and a half and crosses an ocean to New England. There, in Boston, at the Massachusetts General Hospital, April, 1914, saw the commencement of an enterprise in the Morgagni mode and tradition—the Cabot Case Records.

The primary imaginative inspiration came from the brothers Cabot—Richard the physician and Hugh the surgeon. But week by week since their day the ante-mortem and post-mortem records of the hospital have been used to provide the dialectical and demonstration material for an inquisition, known throughout the world as the clinicopathological exercise or conference.

Approximately 5000 cases have been carried to a complete conclusion and elucidation at these conferences, and recorded accordingly. Only rarely has the arbiter, the pathologist, had to say *causa mortis ignota*. This M.G.H. collection is a thing unique in the modern medical world.

The original conferences were the private and somewhat informal arena of the Cabots and their students. Later, the circle of disputants was enlarged, and now each Thursday-morning conference has its own pair of prima donnas, sometimes from the resident company, sometimes guest artistes.

Comparisons between 1914, or even 1924, and the present day mark the tremendous increase in the armamentarium of diagnosis, a change in the types of disease encountered, and the rising level of the age of patients.

Only on a few diseases can one reasonably contrast the showing of the old warriors and the new.

For those who delight in such comparison I would recommend a study of the differential diagnosis of miliary tuberculosis. They will find that, despite the greater refinement of X-ray technique and the evolution of laboratory procedures which have aggrandised the electrolytes, the mother wit and experience of the clinician

In view of the radiographic appearance and the fact that the chest condition had arisen in the acute stage, the patient was put on aureomycin 0 5 g six hourly

Within thirty six hours the temperature, pulse, and respiration were normal, and the patient made an uninterrupted complete recovery A further radiograph seven days after the first showed normal lung fields A specimen of blood taken on Oct 9 contained cold agglutinins 1 32, examination for M G streptococcal agglutinins was negative

Pneumonia during an attack of varicella is extremely uncommon [1,2] In the case described here, the patient's rapid improvement coinciding with the giving of aureomycin (she had previously had 1,500,000 units of penicillin) would suggest that this was a case of varicella complicated by virus pneumonia with secondary bacterial infection The fact that this pneumonia was present at the onset might suggest that it was due to the varicella virus That this virus does cause pneumonia has been shown by the finding of varicelliform lesions and characteristic bodies in the lungs post mortem

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IAN M McLACHLAN

HOSPITAL COSTING

SIR,—Dr Avery Jones's contention (May 16) that a general community hospital should have at least 90% bed occupancy, and that 93% bed-occupancy is perfectly feasible, should not pass unchallenged To allege that lower bed-occupancy figures are a "large scale extravagance" is an extraordinary statement from a clinician of Dr Avery Jones's standing and experience

Members of lay committees find it extremely difficult to appreciate the significance of percentage bed-occupancy figures and they are unlikely to be helped if doctors themselves do not understand them I would submit that *high* percentage occupancy figures may reflect an inflexible system of bed-allocation and may be a source of extravagance I would, however, first of all plead that we beware of paying too much attention to all these figures There are several points which need emphasis

1 Percentage bed occupancy approaches 100 in institutions for the chronic sick, and high figures are achieved in all hospitals or wards which have a waiting list and a slow turnover of long-stay cases

2 The monthly turnover of cases in a ward or hospital may be greatly increased without altering the percentage bed-occupancy—in fact, the latter almost invariably falls The quicker the turnover the more likely it is that beds will fall vacant unexpectedly, and the more difficult it is to fill them promptly

3 An increased turnover, despite the almost inevitable fall in percentage bed occupancy means greatly increased work for the medical and especially the nursing staff

4 Only those on the spot who have clinical responsibility for the patients can decide how best to use the available resources, and it is doubtful whether any figures, however detailed, can reflect the remarkable variations between one ward and another

5 It is usually unjustifiable to compare percentage occupancy figures for different hospitals

6 It is sometimes of value to compare the percentage bed occupancy figures for the same hospital at different times, *but only in conjunction with other essential data* However, only the grossest variations are likely to be of much significance, and considerable circumspection is necessary in their interpretation.

There has, of late, been an unhealthy preoccupation with "phoney" statistics of all kinds, and this has been encouraged by the ever-increasing flood of monthly and other returns demanded by the Ministry and the regional hospital boards Associated with this trend one has at times noted a regrettable lack of honesty and care in compiling these returns Nevertheless, however honest and careful we all are it is very doubtful whether the compilation of such figures is of any real value outside the hospital itself I entirely agree with Dr Avery Jones that a report on this subject by an independent medical foundation would be most opportune, and fortunately such a report is to be published by the Administrative Staff College of King Edward's Fund

It may be relevant to recall that at one large hospital at which I once worked my ward sisters regularly asked me to keep patients in at the end of each month "so that the bed returns don't look too bad" I ignored their pleas and pointed out that, although this might be to the detriment of their bed returns, it was to the advantage of the patients, the nursing staff, and the hospital finances Unoccupied hospital beds are surely less of an extravagance than unnecessarily occupied ones or ones kept deliberately filled by clinicians and administrators who are keen to make a good "score" in their bed returns

Real statistics can be of real value, but "phoney" figures are fallacious and mere humbug Fortunately most patients want to get out of hospital as soon as possible, and most doctors are only too anxious to maintain a rapid (sometimes too rapid) turnover The integrity of the individual doctor in the service of his patients is surely the only real safeguard against wastage of hospital beds All the figures in the world and all the Ministerial injunctions will never achieve so much as a contented hospital staff who are left to do their best for the community they serve

I am certain that the efficiency which Dr Avery Jones seeks is more likely to be achieved if the hospitals gain greater financial and administrative independence rather than by comparing figures in the annual reports of the Ministry of Health

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"HARLEQUIN" COLOUR CHANGE IN THE NEWBORN

SIR,—I read with interest the account of this condition by Dr Neligan and Dr Strang,[1] and would like to describe an example of it

Early in September, 1952, a 24 hour-old twin girl was noticed by the nursing staff to exhibit colour changes in the skin—"half of the body became a deeper red, may be left or right side" At 48 hours these changes in skin colour were striking The infant, lying on its back, showed on its right side a brilliant red with a sharp line of demarcation down the centre of the face and trunk The pupils were equal, and to the touch there was no obvious difference in skin temperature After a few minutes the left side began to flush and the right side slowly faded. For the next week these changes occurred up to 11 or 12 times daily, sometimes involving one side of the body and sometimes the other, and lasting 3–4 minutes on each side

At that time inquiry locally revealed no previous experience of this phenomenon. This infant, the first of twins in a primipara, had a birth weight of 5 lb $3^1/_2$ oz There had been a transverse arrest of the head, necessitating extraction with Kielland forceps, the head crowned in the left occipito-anterior position. It was thought that perhaps there had been some trauma to the sympathetic chain as a result of a difficult rotation However, the second child, also a girl, with a birth weight of 4 lb $13^1/_2$ oz, had been delivered easily but at 36 hours exhibited similar colour changes The attacks were not so pronounced and were less frequent They ceased on the 5th day Attempts to photograph these changes were unsuccessful

Following this the nursing staff kept a closer watch on all babies having incubator care, and further examples were observed.

Our observations are essentially similar to those described by Neligan and Strang in that if the infant is lying on its side the lowermost half of the body is the brighter red, changing the position of the infant will reverse these changes If left undisturbed the changes

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1 Waring J J Neubuerger K. T Geever, E F *Arch intern Med* 1942, 69 384

2 Claudy W D *Ibid* 1947 80, 185

[1] Neligan, G A, Strang L B *Lancet*, 1952, ii, 1005

are often the deciding factors. And over the years the personal honours are evenly divided.

THE ESSENTIALS

It is time to gather together the lessons of our circumspection in time and place. Nearly 5000 years come within our compass, for the earliest Egyptian record precedes the Edwin Smith papyrus by a millennium. From their primitive salves, linen rolls, and incantations to our antibiotics and radioactive isotopes is a gigantic stride. Yet we still use salves and bandages, we still place men at their mooring stakes. Now as always observation and experience are the foundation upon which diagnosis, treatment, and prognosis are built. Individual men and women are no less prone to error, and that fallibility is another of the companionable common factors which help to bridge the ages.

From the point of view of the student of records, those treasures which he rescues from the archives can never be better than the best of the efforts of the best of the contemporary clinicians and scientists.

One does not expect Mayerne to anticipate and outdo Morgagni. The trouble arises when the physician of the day falls short of the Hippocratic standards, and uses the cant phrases of the moment instead of his mother wits.

Let us see if we can distinguish some of the essentials of good record-keeping as we have already observed them.

Above all comes the scheduling of the facts, and the little verse of Kipling mentions most of them.

> " I keep six honest serving-men, (they taught me all I knew)
> Their names are What and Why and When, and How and Where and Who."

But in our studies we have been given more than facts. The best records have been pictures, and the attributes of those pictures have been these—at least as I see them.

Order has been a characteristic throughout. What more orderly than the presentation of that Egyptian warrior's broken nose, or the recital of the pathology of the living as seen in James I.

Accuracy.—Here we have no yardsticks except we regard as such our ability, despite the efflux of time, and the difficulties of definitions and translations, to recognise the descriptions and the diagnoses as comparable to something within our knowledge and experience.

Brevity.—Except Mayerne, the writers of all our texts are masters of concise expression. Morgagni is discursive at times, but that is when he is bent on instructing his young friend. When he wills it, no-one can epitomise more pertinently or more epigrammatically. Then other less important virtues have been disclosed—*Balance* in the presentation of a mass of information; and *Saliency*, the gift of emphasising the outstanding features.

Finally, we come to *Selectivity*. Except for Mayerne—and his essay was on a special theme—all our teachers have been selective in the information they have laid before us. They have not invited us to study everything, but only certain examples from their several collections.

Hippocrates, in writing the Constitutions, obviously draws upon more clinical material than he leaves with us in the individual cases of the books of *Epidemics*. Morgagni, also, tells us that, if he were to write all that he knows about aneurysms, it would fill a volume in itself.

It seems impossible to contemplate the holding of a grand clinicopathological conference on every inguinal hernia or tonsillectomy. The essential facts must be recorded. The six honest serving-men must make their mark.

Thereafter, as with our predecessors, a wise discretion will determine what shall be set out in detail, and what omitted, for the guidance, instruction, and charitable consideration of posterity.

Bibliography at foot of next column

The Wider World

THE HEALTH OF A TROPICAL PEOPLE

A Survey in Ceylon

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II. ENVIRONMENT, HEALTH, AND PHYSIQUE

THE difference in the incidence of infective and parasitic diseases in tropical and in temperate countries is well known, but owing to incomplete and inaccurate registration of deaths precise comparisons are difficult. Ceylon has probably the most comprehensive system of registration in all Asia, and the mortality figures can be compared with those of Western countries. Such a comparison has been made between Eire and Ceylon, which resemble each other in that they are of much the same size, have predominantly agricultural economies, and have only one large city.

Since 1946 the crude death-rate in Ceylon has dropped suddenly to about the same level as in Western countries. This can be attributed to the near eradication of malaria by the use of D.D.T. as a control measure for mosquitoes. The fall in the incidence of malaria has been accompanied by a big reduction in infant mortality, maternal mortality, and in some of the other major causes of death (table I).

TABLE I—DECREASE IN DEATHS BETWEEN 1946 AND 1949

Cause	Decrease	
	No. of deaths	% of total decrease
All causes	44,018	100
Malaria and pyrexia ..	16,459	37·4
Pneumonia	3193	7·2
Influenza	588	1·3
Infant deaths	10,755	24·4
Puerperal deaths	2081	4·7
Dysentery	1116	2·5
Diarrhœa and enteritis ..	1913	4·3

Some of these reductions can be attributed to the destruction by D.D.T. of vectors of disease other than the mosquito, but not all can be so explained. It could be claimed that the lowering of the malaria morbidity has increased the general resistance of the population. We might then have expected an interval between malaria eradication and the evidence of increased resistance to other diseases, but all the mortality reductions occurred together and suddenly.

In one year the general death-rate fell from a level typical of Asian or backward countries to one comparable to that of the more prosperous and advanced countries. At the same time the mortality pattern has changed. Although 1 in every 9 deaths is still due to parasitic and infective diseases and only 1 in 14 to renal-cardiovascular diseases, there are definite signs that the mortality picture is becoming "Westernised." The proportion of deaths due to diseases of the middle and later years of life is gradually rising and that due to infective diseases is falling. The relative rapidity of

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last up to 25 minutes In 1 case the changes included the tongue No pupillary changes were noted The attacks appear to have no pathological significance, as infants seen to be affected have thrived

These observations have so far been confined to infants in incubators This includes all premature infants and those in whom perhaps there has been some difficulty in establishing respiration The remainder of the babies born in this 100-bed maternity unit are dressed and placed in ordinary nurseries, where such changes would not be so easily observed So far the highest birth weight among infants in whom such changes have been observed was 7 lb 6 oz The attacks may start from the *1st day of life and up to 71 attacks in one child* have been seen Attacks seem to be commonest soon after feeding In one premature infant with a birth weight of 2 lb 12½ oz no attacks were observed until the 21st day, at which time the weight was 3 lb 6½ oz

It was the impression of those who witnessed these *attacks initially that* one side actually "flushed" indeed the staff referred to "blushing babies" We are still not convinced that there is pallor of one side as opposed to flushing of the other, and in only 1 case did we feel that one side became paler than normal One infant who showed colour changes was cyanosed This infant had been delivered normally at full term (birth weight 7 lb 6 oz) On the same day the nurse's notes recorded "sudden colour change, blue on left side, right side quite pink, duration 2–3 minutes"

After six months in a unit in which 133 babies have been nursed, these changes have been observed in 9 cases We have no better explanation than that put forward by Neligan and Strang

Acknowledgment is made to Dr H Medovy and the staff of the Winnipeg General Hospital for their help

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MYSOLINE IN THE TREATMENT OF EPILEPSY

SIR,—Dr Butter, in his article of May 23, makes his report on sane male patients Since 'Mysoline' became available last year it has been used at Long Grove Hospital for some of the patients in the wards containing mostly epileptics In addition to their epilepsy all the patients have some mental disorder

Disregarding the effect on the frequency of convulsions, which has always been equal to, and in many cases better than, that of phenytoin and phenobarbitone, the change in patients' behaviour is of special interest Some patients improved dramatically in behaviour and sociability They showed more readiness to accept treatment and to cooperate in ward routine These were recognised as cases in which the mental disorder was more one of affect than of personality Among these was a case with psychomotor attacks in which, as in Dr Butter's case of the same kind, great improvement was seen

A larger number of patients derived little appreciable benefit, and it has become clear that the more psychotic the patient's thoughts and behaviour the less benefit he is likely to obtain from this drug Such symptoms are frequently false beliefs of persecution or other ideas of reference, and these appear to mask any change of mood, so deeply are they rooted in the patient's mind Patients with obvious mental deficiency also appear to show little social improvement with mysoline

A report on mysoline in mental disorders was given at the meeting of the Royal Medico Psychological Association at Warley Hospital, Brentwood, Essex, on April 21, 1953, and the views expressed there are borne out by our experience at Long Grove Hospital

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KWASHIORKOR

SIR,—Kahn[1] has good cause to complain of the arbitrary and unpractical definition of kwashiorkor by Brock and Audret[2] in their W H O publication

The Ga, reported by Williams[3] to use the word, came to the Gold Coast as refugees from the slaughter at Benin by the Eyo or Yoruba at the end of the 16th century They borrowed religion, customs, and many words from their Akan neighbours[4, 5] *Kwashiorkor* is an Akan word

To compress 2500 years of Akan history into a paragraph has proved as difficult as getting the dormouse into the teapot[6–10] Behind the religions, Egyptian, Sabean, Libyan, and Numidian, with which the Akan have been in contact during this long period, lies the ancient philosophy of Babylon In this struggle between Good and Evil, misfortune to the individual that could not be accounted as the inevitable sequence of transgression of the Law was attributed to the Devil, his minions the Influences, or his friends and followers the Sorcerers

Nathaniel Uring,[11] on the Gold Coast in 1710, noted "The Natives have no Knowledge of Letters, but have a Notion of God which they call John Company (*Onyankopon*), they say he is a good Being, and hurts no Man, and therefore pay Adoration to the Devil (who they call Bone Sam (*Sasabonsam*)) to pacify him that he may do them no Harm" Rattray[12, 13] describes Sasabonsam as red in colour, and the wizards and witches as having red auræ All are very greedy

Sir A B Ellis[14] pointed out that the Akan (Gold Coast) Ewe (Dahomey), and Yoruba (Nigeria) all came from the interior, and had much in common in religion, customs, and language He did not see *Kwashiorkor* on the Gold Coast, but described *Abiku* (destined for death) the Demons who seized the bodies of Yoruba children up to the age of 12 He is quoted by Sir J G Frazer[15] "On the Slave Coast when a mother sees her child gradually wasting away, she concludes that a demon has entered into her child and takes her measures accordingly To lure the demon out of the body of her offspring she offers a sacrifice of food, and while the devil is bolting it, she attaches iron rings and small bells to her child's ankles, and hangs iron chains round his neck The jangling of the iron and the tinkling of the bells are supposed to prevent the demon, when he has concluded his repast, from entering again into the body of the little sufferer" The late Marshall Findlay and I exhibited a collection of these anklets and bells among other phylacteries in 1951[16]

In the traditional customs of marriage in Britain the bride puts on something old and something new, something borrowed, and something blue,' and this is stated vaguely to be for luck The old and the new are proved defences against the Devil[17], the borrowed is a disguise[18], and the blue is the antithesis of red, the Devil's own colour The bauchles tied to the back of the carriage are a further prophylactic use of the old The ringing of the church bells, and the music and noisy merriment that follow, are the driving off of the Devil by noise[18] The wedding feast is an appeasement of any possible ill wishers These indeed are precautions against *Kwashiorkor*, the Gudeman, or his friends, interfering with the fruits of matrimony, the children

As Kahn has pointed out, malnutrition due to pap feeding has been and still is world-wide That is to say, pap has been, and still is, considered, by some, an adequate substitute for mothers' milk It is homœo avoided, complete recovery takes place in three to twelve months. Doxiadis has shown that the prognosis is good when the condition is satisfactorily treated from a fairly early stage, but that otherwise permanent renal damage is likely. The relation of the disease to nephrocalcinosis of adults remains uncertain.

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[1] Kahn E *Lancet* March 7, 1953 p 496
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[3] Williams C D *Lancet* 1935 ii 1151
[4] Quartey Papafio A B *J Afr Soc* 1914 13 167
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[17] Hoernes M Primitive Man London 1900
[18] Frazer J G Folklore in the Old Testament London 1918

Recently Lightwood and Payne[20] described a group of infants with the same gross clinical features as those of idiopathic renal acidosis—anorexia, vomiting, constipation, and loss of weight—but in whom there was no acidosis and the urine was normally acid. There was, however, hypercalcæmia with a blood-calcium level of 12–15 mg. per 100 ml., and the blood-urea and plasma-protein levels were also raised. After an illness lasting from five to fifteen months or more, slow spontaneous recovery took place. Lightwood and Payne described 10 cases of this syndrome which they called "idiopathic hypercalcæmia of infants." The cause is unknown.

Action of Parathyroid Hormone

Primary disturbance of the function of the parathyroid glands is rare. The symptoms of hyperparathyroidism are so varied that the condition may long remain unrecognised; it may be diagnosed only after renal stones have been removed, or after bone thought to be involved by tumour has been resected and been found to be affected by osteitis fibrosa. Murphy et al.[21] remark that the manifestations of hyperparathyroidism include, as well as bone deformities and loss of stature, weakness, fatiguability, mental changes, weight loss, bone and muscle pains, gastro-intestinal symptoms, polydipsia, and renal colic. Hypoparathyroidism is hardly less versatile in its manifestations,[22] which range from tetany, paræsthesiæ, cramps, and laryngeal stridor to gastro-intestinal disturbances, mental derangement or retardation, cataracts, ectodermal lesions, and poor dentition.

Collip,[23] who first prepared parathyroid hormone (P.T.H.), showed that his extract could raise the serum-calcium level in normal and parathyroidectomised dogs, but it was not clear whether this was secondary to a primary action on the bones or on the kidneys. The main exponents of the bone theory [24–26] suggest that P.T.H. stimulates osteoclastic resorption of bone with consequent reparative activity by osteoblasts, and that the changes in blood and urine levels of calcium and phosphorus are natural sequelæ of this primary action on bone. There can be little doubt that P.T.H. does affect bone directly, as Barnicot[27] showed in rats by parathyroid intracerebral grafts; bone was eroded only in close proximity to the parathyroid tissue. Ingalls et al.[28] also found histological evidence of osteoclastic resorption in nephrectomised animals treated with parathyroid extract. Moreover the time relations of the bone changes after administration of P.T.H. fit quite well with the observed changes in blood and urine levels of calcium and phosphorus.[26] The bone theory has, however, one obvious weakness; for, since both calcium and phosphorus are resorbed, hyperphosphatæmia as well as hypercalcæmia would be expected, whereas in fact hypophosphatæmia develops in uncomplicated hyperparathyroidism.

Albright[29] is the main advocate of the kidney theory of the primary action of P.T.H. He believes in the following sequence of events: (1) increased renal excretion of phosphorus; (2) lowered serum-phosphorus; (3) resorption of calcium and phosphorus from bone owing to a decrease in the saturation of the body-fluids with calcium and phosphorus; (4) increase in serum-calcium; (5) increase in urinary calcium; (6) further resorption of bone unless dietary calcium is adequately increased; (7) weak bones; (8) osteoblast stimulation, and therefore increase in both resorption and formation of bone. In this theory the basic assumption is the original renal tubular incompetence to reabsorb phosphorus; and Albright cites the observation that after an injection of P.T.H. the increase in urinary phosphorus precedes that of urinary calcium. Milne[30] exposed a fallacy in this reasoning when he administered calcium and phosphate separately but simultaneously into opposite arm veins, or gave preformed colloidal calcium phosphate; in each case the time relations in the excretion of phosphorus and calcium were the same as after injection of P.T.H. Milne has also pointed out that the increased urinary loss of phosphorus after administration of P.T.H. is insufficient to account for the observed lowering of the serum-phosphorus; for this is in dynamic equilibrium with the much larger phosphorus content of the extracellular fluid.[31] Thus there is still doubt as to the distribution of the phosphorus that disappears from the blood. Tweedy and Campbell[32] have provided clues by their radiophosphorus studies, in which they showed that the accumulation of labelled phosphorus reached values 20% higher in the liver and 18·5% higher in the kidneys in rats receiving parathyroid extract than in controls. Whether or not this effect is primary, Tweedy and Campbell established that P.T.H. increases the phosphorus clearance by the kidney. This has been confirmed by Milne,[10] who pointed out that the low phosphorus clearance in hypoparathyroidism is much more dramatically increased by P.T.H. than the relatively high phosphorus clearance of normals. Some of the clinical effects of hyperparathyroidism appear, on the other hand, to be caused chiefly by the direct effect of P.T.H. on bone resorption. Stewart and Bowen[33] have reported further data on the relative importance of the renal and osseous actions of P.T.H. They showed that in nephrectomised dogs intravenous administration of parathyroid extract immediately after operation produced within 8 hours the normal response of hypercalcæmia. They also developed the ingenious oxalate-tolerance test of parathyroid function, described earlier by Patt and Luckhardt.[34] In normal dogs intravenous administration of sodium oxalate

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produced a precipitous drop in the serum-calcium, followed by a gradual return toward normal levels within 6 hours, but when the animals had *previously* had the thyroid and parathyroid glands removed there was no appreciable return of the serum-calcium towards pre-injection levels The recovery phase of the oxalate-tolerance curve in nephrectomised dogs was, however, found to be the same as that in normal animals, so **Stewart** and **Bowen** concluded that *the parathyroid gland exerts a control over serum-calcium that is primarily independent of the kidneys* Much other evidence [35] suggests, however, that the ability of P T H to raise the serum-calcium is greatly impaired in the absence of the kidneys, although the animal is then usually *in a far from physiological state*

Dent [36] has recently driven further nails into the coffin of the Albright theory as the sole explanation of parathyroid action He confirmed that in normal men any phosphorus diuresis after injections of P T H was only slight, and he found *that the serum-calcium* rose, whereas the serum-phosphorus tended to fall only if it was originally high (as it was in the hypoparathyroid cases studied by **Albright**) Artificial lowering of the serum-phosphorus did not lead to a rise in serum-calcium to maintain the solubility product, and hyperparathyroidism with renal failure and raised serum-phosphorus may be followed by the typical bone changes of von Recklinghausen's disease If **Albright**'s suggested sequence of changes were correct, one would expect osteomalacia and not osteitis fibrosa to result Very recently **Stewart** and **Bowen** [37] have shown that preparations of P T H inactivated by formaldehyde with respect to their power to raise the serum-calcium still increase the urinary phosphorus output in dogs That this phosphorus diuresis is an artefact is suggested by the similar results when extracts of spleen and thymus are administered **Dent** [36] has further drawn attention to the apparently irrational dissociation of the bone changes in hyperparathyroidism from the changes in the blood-electrolyte levels, and has suggested (as did **L'Heureux** et al [38] on the basis of electrophoretic studies) that there may be more than one parathyroid hormone, and these may differ in the locus of their actions

It seems clear that parathyroid extracts can act directly on bone and on kidney, and perhaps too much attention has been focused on which of these actions is primary, for the work of **Martin** and **Perkins** [39] suggests that P T H may have a quite different primary action **Martin** [40] has obtained data which seem to show that in some cases of hyperparathyroidism the calcium binding power of the serum-albumin is more significantly and consistently increased than in other cases which in turn significantly exceed normal values After surgical treatment of the hyperparathyroidism the calcium binding power of the serum-albumin usually returns to normal in cases without demonstrable persisting renal damage Perhaps such changes in the calcium-binding power of the body-proteins may explain the metabolic actions of P T H

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Annotations

THE COURT EXPERT

If two doctors were to disagree *about a diagnosis,* it would be patently absurd to call in a layman to settle the issue between them Yet, as we suggested a year or two ago,[1] something hardly less peculiar happens in *legal proceedings* whenever irreconcilable opinions are expressed by *medical experts* engaged by the opposing sides Sometimes, it is true, both parties may accept a written report prepared by a member of the medical profession, but in many important trials whose outcome largely depends on scientific evidence, there is a hiatus in specialist opinion which has to be bridged by judge and/or jury finding their own solution of a technical problem

Medicine being an applied science, it seldom deals *with facts* from which only one inference is possible Moreover, medical evidence can seldom be visibly and *conclusively demonstrated to the court* This is true not only where sanity *or mental disturbance* is in question, but *in almost every case where a medical* opinion involves forecasts or is the result of laboratory *investigation* which *goes beyond simple* observations Being unable *to verify* his statements, judge and jury *must rely on the intelligence and professional* conscientiousness of the expert witness Accordingly the *court has to concentrate on testing his impartiality* and *competence*

Much interest therefore attaches to an American experiment in which the Supreme Court of New York will appoint court experts other than those chosen by the contesting parties [2] For some time past, United States courts, in dealing with medical expert evidence have had difficulties similar to those encountered in Great Britain but perhaps even more sharply focused In the United States almost all the testifying is done by *a very small proportion of the doctors,* and the fees asked sometimes depend on the expert's rhetorical gifts as much as on his professional skill and eminence The preparation of experts' reports for each party, moreover, is one of the principal causes of delay in the disposal of cases where a personal injury has been sustained and where it is necessary to estimate future incapacity In these circumstances, the plan to be tried for a year in New York aims at "better and quicker justice" for *the solution of conflicting medical claims, by avoiding* the former system under which "*a plaintiff's* doctor may tend to describe his patient as just about killed while the defendant produces a doctor who hardly finds scratches" The leading professional State organisations, the New York Academy of Medicine and the New York County Medical Society, have agreed to appoint a panel of about sixty experts of the highest standing in the various branches of their profession, including orthopædics, neurosurgery, neurology, and psychiatry, on whose knowledge and aid the courts can call whenever the need arises If in the preparation of the trial it is found that the medical claims of the two parties differ widely, the judge will, on his own initiative, assign an expert from the panel to examine the plaintiff and to provide a written report which will be available both to the court and to the two parties This expert is not a referee such as we have in this country under the Workmen's Compensation Acts His report is not binding on the court, nor are the parties precluded from cross-examining the expert in person at the trial or from calling in other experts of their own choosing, though it is expected that the court expert's report will often be accepted by all concerned, since it offers from the outset high guarantee of impartiality and competence Finally, it is hoped that the new system will have "the

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1 *Lancet* 1951 ii 453
2 New York *Times*, Nov 24, 1952

plasic, the child appears to like it, and when sick prefers it to milk. Not until the end of last century did the medical profession realise that it was inadequate. The pining and death of infants weaned on to pap were, therefore, in olden times, unaccountable—i.e., the work of the Devil. The fiend who stole the bodies and souls of children, mentioned by Sir Walter Scott,[19] was *Kwashiorkor*, a particular manifestation of the protean gentleman who was "going to and fro in the earth, and walking up and down in it."

The merits of *kwashiorkor* as a name for infantile malnutrition due to the protein deficiency of a pap diet are:

1. It indicates a widespread belief as to its ætiology which goes back to the Neolithic philosophers of pre-Adamic times.[20]
2. It is kenspeckle—i.e., outstanding and remarkable.
3. It is simple of pronunciation, and like Lawrence's *ruelli*, you can spell it almost anyway you choose, which cannot, I fear, be done with *Mehlnährschaden*, *hypothrepsia*, and other suggested descriptive alternatives reminiscent of the "Great text in Galatians."

Edinburgh, 3. A. MacPherson.

SPHAGNUM MOSS

Sir,—Your annotation (May 23) regarding the use of sphagnum moss for urinary incontinence recalls to my mind that prior to the first world war, when employed as a surgical dresser at a large provincial hospital, I had to see that the automatic pump, of the Sprengel type, draining the bladder in cases of suprapubic prostatectomy was working satisfactorily. Not infrequently they ceased to function (invariably owing to interference by the patient); so, to absorb the resulting overflow of urine, several muslin bags filled with sphagnum moss were packed round the patient. These kept him comparatively dry and comfortable; the bags swelled up in a most astonishing way to many times their original size.

Royal Scottish National
Institution, Larbert,
Stirlingshire.

C. A. E. Innes Brownlee.

ERYTHEMA MULTIFORME AND A.C.T.H.

Sir,—The exact ætiology of erythema multiforme still appears to be rather obscure. If the syndrome is caused by a single agent, it is probably due to a virus.[21] In support of this theory, keratoconjunctivitis was reproduced in rabbits' eyes from fluid taken from bullæ, and cytoplasmic inclusion bodies were demonstrated.[22] A virus has been sought in laboratory animals but without success. Steigman and Kelly,[23] reporting on a case treated with A.C.T.H., state that the ætiology of erythema multiforme may be multiple, sensitisation playing an important part.

On Sept. 15, 1952, a 9-year-old boy was admitted to hospital with erythema multiforme. There was a diffuse maculopapular rash covering the limbs, back, buttocks, and face. The lesions on the arms were surmounted by urticarial weals, several hæmorrhagic in character. A.C.T.H. was given, and there was a remarkable improvement within 48 hours, followed by a rapid recovery.

The rash developed whilst the child was on a hop-picking holiday. He became lethargic and feverish, and had conjunctivitis, chemosis, balanitis, and generalised pharyngeal injection. On Sept. 18 vesicular lesions appeared on the buccal mucosa, the chemosis increased, and photophobia developed. A chest radiograph showed no focal lesion. The highest white-cell count was 17,900 per c.mm., with only 2% eosinophils. A heavy growth of non-pathogenic hæmolytic streptococci was isolated from a throat swab. The urine was normal. The Mantoux reaction was negative to 1/100. The erythrocyte-sedimentation rate was 33 mm. in the first hour. On Sept. 21 A.C.T.H. was given (15 mg. six-hourly). Within forty-eight hours the rash and oral lesions had begun to subside. On Sept. 24 the dosage was reduced to 10 mg. six-hourly. Further bacteriological examination of the blood and urine was negative. On Sept. 30 A.C.T.H. was stopped. A follow-up in the outpatient department showed that he was quite fit and gaining weight, with no recurrence.

Whittington Hospital,
London, N.19.

Derek H. Clark.

OPHTHALMIA NEONATORUM

Sir,—As you say in your leading article (May 16), gonococcal ophthalmia neonatorum, which was common towards the end of the last century, has now almost entirely disappeared. However, minor infections of the eyes in infants must still be one of the most common forms of neonatal infection, and the 1935 cases notified in 1950 must represent a very small proportion of those actually occurring. These infections seldom cause any permanent damage to the eyes, and it is surely high time that ophthalmia neonatorum ceased to be a notifiable disease.

I note that you recommend penicillin as by far the most effective form of treatment. I believe this to be untrue. In many maternity units a penicillin-resistant *Staphylococcus aureus* seems to be almost endemic, and in my experience about 80% of the cases of ophthalmia encountered are caused by this organism. Penicillin in these cases is of course useless. Sulphacetamide 30% or propamidine isethionate 0·1% drops are usually effective, and would appear to be the treatment of choice until the sensitivity of the infecting organism to various antibiotics has been determined.

Southampton
Children's Hospital.

D. A. J. Williamson
Pædiatrician.

TREATMENT OF ADVANCED MALIGNANT DISEASE

Sir,—Mr. W. G. MacGregor and Dr. C. L. Lewis (April 4) describe their experience with administration of A.C.T.H. and aureomycin in advanced neoplastic disease, as used by McGuire and McElhone.[1] About the time that method was introduced we had under scrutiny about fifty patients with inoperable neoplastic disease who happened to be on a similar schedule and had been maintained in comfort for a considerably longer time than we had believed possible with "orthodox" modes of cancer therapy. Against criticism of McGuire and McElhone's schedule[2] we could cite two reports[3 4] offering them indirect support. We doubt the correctness of their premise that "cancer" is a virus disease and hence amenable to antibiotic therapy, but we think that certain items in their schedule did have the effect of prolonging the comfortable life-span of their patients.

Two years ago, one of us reviewed the reasons why he gave an antibiotic-containing "animal protein factor" (A.P.F.) to patients with leukæmia and other cachectic diseases.[5] Not only was the expected anabolic effect forthcoming, but surprising hæmatological improvement as well. It now turns out that those patients who received A.P.F. were actually getting a combination of mycin antibiotic and a steroid, the latter having a pronounced eosinopenic action in laboratory animals. Furthermore, like McGuire and McElhone's, our patients were receiving plenty of milk and large doses of potassium. We used the milk to reduce intestinal proteolysis, and the potassium because in patients with severe adaptation

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[19] Scott, W. Introduction to the Tale of Tamlane. Minstrelsy of the Scottish Border. London, 1931.
[20] Lane, E. Manners and Customs of the Modern Egyptians. London, 1908.
[21] Ashby, D. W., Lazar, T. *Lancet*, 1951, i, 1091.
[22] Anderson, J. A., Bolin, V., Sutow, W. W., Kitto, W. *Arch. Derm. Syph., Chicago*, 1949, 59, 251.
[23] Steigman, A. J., Kelly, J. J. *Lancet*, 1952, i, 875.

[1] McGuire, F. A., McElhone, M. *Med. J. Aust.* 1951, ii, 769.
[2] Lucraft, F. *Ibid*, 1952, i, 92.
[3] Barnard, R. D. *Hawaii med. J.* 1952, 11, 57.
[4] Barnard, R. D., Orens, L. R. *N.Y. St. J. Med.* 1951, 51, 2797.
[5] Barnard, R. D. *Lancet*, 1951, i, 1157.

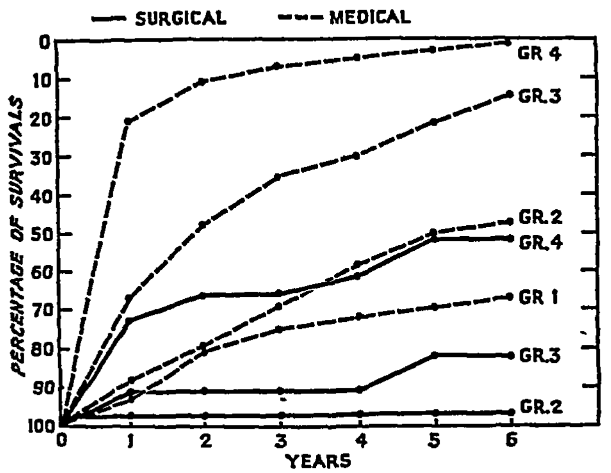

Fig 1—Survival rates in 30 cases of hypertension according to retinal grading

Present Series

At the Westminster Hospital we have, from the very first case, acted with a physician, and by far the greater number of the cases reported here were sent to us for operation by a medical colleague, who has borne the brunt of the work involved in following them up In every case we have also had the cooperation of the ophthalmic surgeon, the pathologist, and the biochemist

Bilateral lumbodorsal sympathectomy has been performed in 106 personal cases, 102 of which were done at the Westminster In addition there were 3 cases in which only one side was operated on in 2 of these death took place from cerebral hæmorrhage before the second stage, and in the 3rd (an experimental case over the age-limit) headache was relieved and the patient does not wish for, or in my opinion need, a second operation

Mortality

The Westminster patients have all been followed up The operative mortality was 5

(1) As already mentioned, 2 patients died of *cerebral hæmorrhage* in the second week after the first stage of the operation

(2) 2 other patients died of *local hæmorrhage* These were, on looking back, avoidable deaths In those days post operative hypotension was considered to be a common cause of death, but with the new drugs any dangerous fall of blood-pressure after operation can be counteracted. In our early cases we did not drain the wound, and at necropsy on these 2 patients a hæmatoma was found in the paravertebral space opened up by the operation A drain is now left in as a routine and a transfusion is given if a large loss occurs, but this has almost never been necessary, perhaps because of improved technique

(3) There was 1 case of *prolonged hypotension* following the use of the new methonium compounds as an anæsthetic

TABLE I—NUMERICAL VALUES OF CLINICAL FINDINGS (Smithwick 1951)

Factor	Numerical value
Cerebrovascular accident with or without minor residue	1
Abnormal electrocardiogram	1
Enlarged heart	1
Impending heart-failure	1
Phenolsulphonephthalein excretion less than 25% in 15 min. or less than 60% in 2 hr	1
Age 50 or more	1
Mild angina	1
Cerebrovascular accident with residue (cerebral deterioration or definite involvement of arm and/or leg)	2
Frank congestive heart-failure moderate angina	2
Phenolsulphonephthalein excretion less than 20% in 15 min.	2
Unsatisfactory response to sedation	2
Phenolsulphonephthalein excretion less than 15% in 15 min	3
Nitrogen retention	4

All our efforts to raise the blood-pressure failed No other cause of death was found post mortem

Classification

The cases have been graded according to the retinal changes, using the following classification

Grade 1—Mild narrowing or sclerosis

Grade 2—Moderate to marked sclerosis characterised by exaggeration of the arterial reflex and arteriovenous compression

Grade 3—Angiospastic retinitis characterised by œdema, cotton wool exudates, and hæmorrhages superimposed on a combination of spastic and sclerotic changes in the arteries

Grade 4—As for grade 3, but in addition measurable œdema of the optic discs

On this grading there were 31 cases of malignant hypertension with papillœdema (grade 4), 39 cases of angiospastic retinitis with hæmorrhages and exudates (grade 3), and 24 cases with grade-1 and grade-2 retinal changes

Results

All these cases have been carefully followed, and the 30 which were operated on five or more years ago have been analysed to give the survival-rates shown in fig 1 In this chart the figures for medically treated cases reported by Keith, Wagener, and Barker (1939) have been superimposed for comparison, and our results bear out the conclusions reached by Smithwick (1951) on the value of surgical treatment These first 30 patients include 1 in grade 4, who cannot be traced for the last two years and is regarded as having died

TABLE II—METHOD OF DETERMINING NUMERICAL GRADE OF HYPERTENSION

Factor	Numerical value
Example I	
Abnormal electrocardiogram	1
Cerebrovascular accident without residue	1
Phenolsulphonephthalein excretion 20% in 15 min	1
Total	3 = Numerical grade
Example II	
Abnormal electrocardiogram	1
Enlarged heart	1
Phenosulphonephthalein excretion 10% in 15 min	3
Total	5 = Numerical grade

In the grade-4 cases there is a five-year mortality-rate of nearly 50% and at first sight it seems impossible to predict which patients in this group will benefit most More help, however, is given by a new method of classification devised by Smithwick (1951) which is not based solely on the retinal changes

Smithwick's New Classification

A numerical value is assigned to each of a number of significant factors that may be found in these cases (table I) and the patient's numerical grade is the sum of the numerical values of the factors found in his case, as shown in table II By this new system, taking account of factors other than retinal changes, Smithwick classifies his cases in four groups, as shown in table III

For assessing the prognosis in any particular case, we have found this system far more satisfactory than grading by retinal appearances alone It resembles a method of grading suggested by Northfield (1948)

In our comparatively small number of cases (a hundred-odd against nearly six hundred of Smithwick) we have observed that papillœdema is not necessarily the worst prognostic sign, and, when they were reviewed on Smithwick's classification, it was found that his group 4 was a far more accurate indication of prognosis than the retinal grade 4 For example, in our cases 65% of retinal grade 4 and 90% of retinal grade 3 were alive three years after operation, whereas on Smithwick's grading the figures would have been 45% of group 4 and 80%

disease ingestion of antibiotics has an adrenocorticomimetic effect,[6] part of which is mineralocorticoid [7] and may cause severe electrolyte imbalance. During the past four years we have refined our antibiotic ingestion schedule, and we would suggest that Mr. MacGregor and Dr. Lewis, or anyone intending to employ any modification of the McGuire-McElhone method, should consider the schedule we have particularly applied to inoperable neoplastic disease.[8]

1. *Type and Dose of Antibiotic.*—McGuire and McElhone use aureomycin hydrochloride in conventional doses. We never use the mycin hydrochlorides, because we too originally encountered severe gastro-intestinal upset with them. We employ either terramycin *base* or streptomycin cobaltochlorophyllinate, neither of which markedly affects intestinal-tract pH. Since our purpose is to reduce intestinal bacterial proteolysis, our dose seldom exceeds 100 mg. daily.

2. *Choice and Dose of Corticotherapeutic Agent.*—A pronounced corticomimetic effect will follow antibiotic administration in any subject with adaptation disease, whose adrenals still respond to stimulation. Where this effect is predominantly mineralocorticoid (deoxycortone-like) cortisone is given in small dosage (12·5 to 50 mg. daily) until the mineralocorticoid preponderance subsides. We never employ A.C.T.H., because all available preparations of it unduly stimulate production of mineralocorticoid.

3. *Treatment of the Patient.*—Treatment cannot be rigidly formalised, and our "schedule" [8] is only useful in that it illustrates the complications likely to arise from exhibition of antibiotics in adaptation disease and how these are to be circumvented. It points out that transfusion of packed red cells will be better borne by these subjects than will transfusion of whole blood, and why. It stipulates avoidance, if possible, of opiates or barbiturates. This does not mean that we permit cancer patients to remain in pain, either physical or mental. The former is immediately brought under control by appropriate nerve-block or—where no other alternative presents—by chordotomy or leucotomy. The latter merits special mention because in any adaptation disease part of the stress is often emotional. Having seen acute leukæmic children doomed by the atmosphere of death around them, we have applied what was learnt in that connection to the management of the cancer patient, of his family, and—sometimes more important—of his attending physician. We refuse to acknowledge to any of these that there is such a thing as a "hopeless" or "terminal" cancer case, and instead we take a positive attitude of hopefulness. The greater part of treatment effort is spent convincing the patient that he will soon be back at work and continue there during a normal life-span. And primarily because of this, he not infrequently does return to work.

The tone of editorial comment on cancer research in this country begins to show a discreet modulation of the brass section that has been blaring out the virtues of "cytotoxic" therapies, including irrational radiotherapy and extensively destructive surgery. The departures suggested by McGuire and McElhone's report may thus get a more impartial hearing. There is nothing new about palliative or sustentive régimes for the cancer patient, and in the light of present knowledge there is reason to believe that results claimed by the Freund-Kaminer school,[9] first in Austria and later at the Pearson Research Institute in England, as well as the Revici group [10] now in the United States, were genuine. These workers approached the cancer patient as a subject of what we would now call a disease of adaptation. In their employment of what was to them available as antibiotic or adrenocorticomimetic agents, they appear refreshingly modern. Anyone interested in the patient with cancer might learn something from them, as we have done.

Hewlett,
Long Island, U.S.A.

ROBERT D. BARNARD
LEON N. KESSLER.

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6. Barnard, R. D. *N.Y. St. J. Med.* 1950, 50, 1852.
7. Barnard, R. D. *Ibid*, 1951, 51, 534.
8. Barnard, R. D. *Ibid*, 1953, 53, 93.
9. Freund, E. Cancer. London, 1946.
10. Revici, E. *Pasteur*. 1943, 2, 121.

THE TREASURES OF BARTS

SIR,—Your annotation of May 23 suggests that the renterer of Barts, who between 1420 and 1460 copied the deeds of the hospital, would have valued the "indenture signed and sealed by Henry VIII giving the hospital to the Mayor and Commonalty and Citisens of London." I doubt it.

Up to 1535 there were in London four hospitals, all of them well endowed. Soon all four were emptied; the staff turned out; the endowments taken away. So the poor and the sick had no hospitals. Henry gave back one of the hospitals, St. Bartholomew, but retained the endowments. On his deathbed he regranted the hospital buildings and most (not all) of the endowments; he became the "Founder." This is stated in R. W. Chamber's *Thomas Moore*; he cites in support Norman Moore's *History of St. Bartholomew's Hospital*, vol. II, p. 126.

Amsterdam. TH. H. SCHLICHLING.

BLOOD-GROUPS AND REPRODUCTION

SIR,—Further evidence in support of the suggestion that the blood-groups A and O are less unlike than A and B in reproductive characteristics has come to light from the data of Bryce et al.[1] and Boorman.[2] Boorman's data are drawn from 2000 mother-infant combinations, and Kirk et al.[3] have pointed out that, in this sample, mothers whose latest infant was A-incompatible show, on the average, a steady and substantial fall in fertility with increasing age relative to mothers whose latest infant was compatible (mostly mothers of O infants); they are much more fertile than the mothers of compatible infants below the age of 20, and much less fertile than them above the age of 40.

TABLE I—AVERAGE PARITY OF MOTHERS OF ABO-INCOMPATIBLE INFANTS (BOORMAN)

Over-all average parity	Group of latest infant	Age-group of mothers whose latest infant was ABO-incompatible				
		14–19	20–29	30–34	35–39	40–49
1·92	B	1·00	1·41	2·36	3·00	5·00
1·77	A	1·43	1·37	2·14	2·75	2·91

But the data also show that this age-difference is even greater between mothers of A-incompatible infants and mothers of B-incompatible infants; the details of these two types of mother are given in table I. If this were confirmed it would indicate changes with age in the relative fertility of B, O, and A fathers as well as mothers.

TABLE II—RATIO OF OBSERVED TO EXPECTED MOTHERS

Mothers of the same group as their latest infant				Mothers of a different group from their latest infant				
Data of Bryce et al.		Data of Boorman				Data of Bryce et al.		
Group	Observed/expected	Group	Observed/expected		Group	Observed/expected	Group	
AB	1·17	O	1·01	1·08	B	1·06	B	
O	1·02	A	1·01	1·05	AB	0·99	AB	
A	0·99	AB	0·93	0·92	A	0·99	A	
B	0·96	B	0·85	0·92	O	0·97	O	

The over-all ratio of observed to expected mothers in Boorman's sample is 1·03 for AB mothers, 1·00 for O mothers, 1·00 for A mothers, and 0·99 for B mothers, while in Bryce et al.'s sample of 7856 mother-infant combinations the ratio is 1·02 for AB mothers, 1·01 for B mothers, 1·00 for O, mothers and 0·99 for A mothers, the average parity being 2·43. But

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1. Bryce, L. M., Jakobowicz, R., MacArthur, N., Penrose, L. S. *Ann. Eugen., Lond.* 1950, 15, 271.
2. Boorman, K. E. *Ibid*, p. 120.
3. Kirk, R. L., Kirk, M., Stenhouse, N. S. *Brit. J. prev. soc. Med.* 1953, 7, 1.

of group 3 Using Smithwick's classification 26 of our cases qualify for group 4 as opposed to 31 placed in retinal grade 4

The excretion of phenosulphonephthalein (P S P) has not been estimated hitherto in our cases, and we have adopted equivalents of renal function as estimated by urea excretion tests as follows

P S P excretion less than 25% in 15 min = 83% normal renal function

P S P excretion less than 20% in 15 min = 66 6% normal renal function

P S P excretion less than 15% in 15 min = less than 50% renal function

Smithwick's own results are shown in fig 3, which compares survivals after dorso-lumbar sympathectomy with survivals in cases treated medically (Keith et al 1939)

The Operation

In all our cases the surgical technique was based on that of Smithwick (1940) This involves section of the diaphragm and removal of the sympathetic chain from D8 or D9 down to below L3, with all the splanchnic nerves, and a careful dissection and removal of the cœliac ganglion As complete an ablation of this ganglion and its many filaments to the adrenals as possible is considered to be an important part of the operation, producing the effects of a partial bilateral adrenalectomy (fig 2) To test this we have on several occasions combined bilateral partial adrenalectomy with the procedure described above, but it is too early to reach any conclusions about the value or otherwise of this step

TABLE III—CLASSIFICATION OF HYPERTENSION

Group	Numerical grade	—
1	Less than 4	Eyegrounds grade 0 or 1
2	Less than 4	Eyegrounds grade 0 or 1 with changes in cerebral cardiac, and/or renal areas, eyegrounds grade 2 3, or 4, with or without *changes in cerebral, cardiac, and/or renal areas*
3	4 or more	Resting diastolic blood pressure less than 140 mm Hg, changes present in cerebral cardiac and/or renal areas but do not include (1) cerebrovascular accident with severe residue (2) frank congestive heart failure, or (3) phenolsulphonephthalein excretion less than 15% in 15 min associated with poor response to sedation
4	4 or more	(1) Resting diastolic blood pressure less than 140 mm Hg, combined with one or more of the following (1) cerebrovascular accident with severe residue (2) frank congestive *heart failure, or (3) phenolsulphonephthalein excretion* less than 15% in 15 min associated with poor response to sedation (2) Resting diastolic blood pressure 140 mm Hg or more

Anatomical studies of the innervation of the kidney and adrenal glands show that their nerves pass from the cœliac ganglion and the upper two lumbar ganglia, hence, removal of the splanchnic nerves and the sympathetic chain from D9 or D10 to L2 should effectively denervate the kidneys and adrenals

Great care is taken to avoid opening the pleura There is no doubt that morbidity is lessened by this precaution No attempt is made to attain high levels of section in the thorax Any arteriolar release achieved in the thorax is slight compared with that produced in the splanchnic, lumbar, and leg areas, and the only real advantage of Smithwick's over Adson's sub diaphragmatic approach is, I believe, that all the splanchnic nerves can be easily identified This is particularly important where the greater splanchnic nerve is hidden in the adventitia of the aorta and only emerges for a short distance to end in the cœliac ganglion Postoperative complications are now uncommon The only severe one, a persistent neuralgic pain extending down to the iliac fossæ, is avoided by sharp section and removal of an adequate length of the subcostal nerve to ensure its not being involved in scar tissue

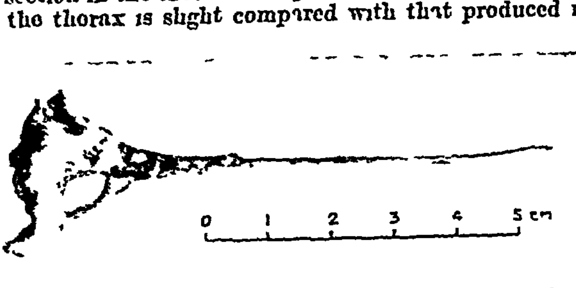

Fig 2—Ablated left cœliac ganglion with its filaments to adrenals.

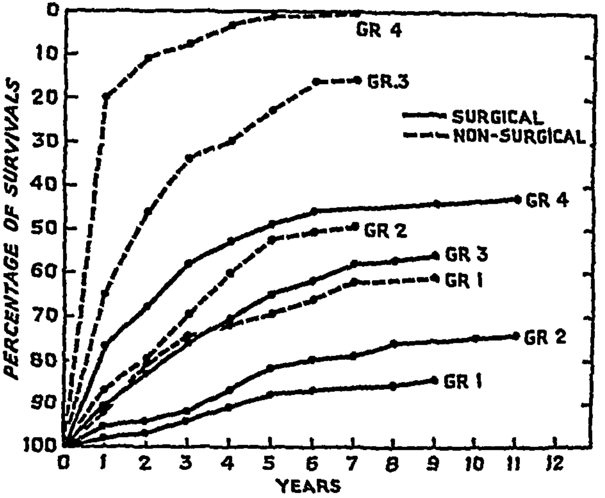

Fig 3—Smithwick s series Comparison of results in 538 cases treated surgically with results in 411 cases treated medically (Keith et al 1939, Smithwick 1951)

Hypertension and Pregnancy

It has always been taken for granted that pregnancy in severe hypertension is a great danger, and early termination is usually advised In dealing with diseases we do not completely understand it is, however, sometimes useful to question time honoured opinions based only on general grounds and the 3 cases described below may be a pointer to new ideas on hypertension

Case 1 —Mrs A , aged 30, was admitted in June, 1947, with a blood pressure of 230/155 mm Hg, severe grade 3 hypertensive retinitis, and some enlargement of the left ventricle but with a good renal function She presented with blurring of vision She underwent bilateral lumbodorsal *sympathectomy and was discharged on July 28, 1947*, with a blood pressure of 145/110 Fig 4 shows her retinal appearances before and after operation

A year later, 1948, she married and at follow up was found to have no symptoms and to have good eyesight and retinæ normal except for slight arteriosclerosis Her blood pressure had, however, risen to 195/125 In 1949 she became pregnant Her blood pressure decreased during early pregnancy, and she had a normal delivery on Feb 28, 1950, of a healthy female child, who is now aged 3 The patient attended recently, when her blood pressure was 190/130, and her retinæ were unchanged more than five years since her operation

Case 2 —Mrs B , aged 34, was admitted in April, 1951, with a blood pressure of 190/135 mm Hg, grade 3 retinitis, and an enlarged heart, which showed electrocardiographically abnormal hypertensive changes Her renal function was normal She complained of headaches during the past three years and of steadily progressive deterioration of vision She had been married several years and had been anxious to have a child Bilateral lumbodorsal sympathectomy was done in two stages in April The blood pressure decreased to 140/100 in June, and the retinæ cleared She became pregnant for the first time at the end of 1951 Fig 5 shows her progress recorded by the sphygmomanometer Labour was induced by the obstetrical department by rupturing the membranes, and she was delivered of a normal female child on Aug 15 last year She has no symptoms and says she has never felt better

TABLE III—RATIO OF OBSERVED TO EXPECTED MOTHER-INFANT COMBINATIONS (BRYCE ET AL.)

Infants ex mothers	Observed/expected	Infants ex mothers	Observed/expected	Infants ex mothers	Observed/expected
—	—	A ex B	1·23	—	—
O ex B	1·08	B ex A	1·20	A ex AB	1·04
B ex O	1·04	AB ex AB	1·17	B ex AB	0·93
O ex A	1·00	O ex O	1·02	AB ex B	0·84
A ex O	0·95	A ex A	0·99	AB ex A	0·78
—	—	B ex B	0·96	—	—

in both samples, as is seen in table II, the descending order of the ratios of observed to expected mothers is O-A-B when the mother and her latest infant are of the same group, and the reverse when the mother and her latest infant are of different groups. In three of the four divisions of table II the difference between the B and A mothers is greater than the difference between the A and O mothers; and that this is not due to the smallness of the number of group-B mothers is suggested by the fact that in the same three divisions the ratio of observed to expected AB mothers—an even smaller number—lies between that of B and A mothers.

Bryce et al. reckoned the amount of variation within their sample (it is greater than that found in Boorman's sample) to be statistically significant. They also pointed out that their excess of A infants of B mothers and of B infants of A mothers, and their shortage of AB infants of A and B mothers, is repeated in Boorman's sample; their own excess of A infants of B mothers, and their shortage of AB infants of A mothers, were so large as to be significant in themselves, and their excess of B infants of A mothers was very nearly so. But the similarity of the samples is even more striking when one compares their 14 individual classes of mother-infant combination, and it is convenient, and also genetically legitimate, to divide these into the groups shown in table III. This gives the ratios of observed to expected mother-infant combinations in the sample of Bryce et al., and the descending orders of ratios seen here are repeated in Boorman's very much smaller sample with two exceptions—transposition of B ex O and A ex O and the placing of AB ex AB between A ex A and B ex B.

TABLE IV—RATIO OF ABORTIONS TO STILLBIRTHS (KIRK ET AL.)

Over-all abortion-stillbirth ratio	Group of mothers	Age-group of mothers of abortions and stillbirths					
		Up to 20	21–25	26–30	31–35	36–40	Over 40
2·66	O	2·10	3·09	4·00	1·85	2·75	1·30
2·38	A	1·40	2·48	3·92	1·78	1·47	1·80

But perhaps the most notable feature of the sample of Bryce et al. is that the highest of the ratios of observed to expected mother-infant combinations are found in the only three classes consisting of heterozygous infants of heterozygous mothers, the over-all ratio for these three classes being 1·21 and for the other classes 0·99, while the corresponding ratios for Boorman's sample are 1·24 and 0·99. Should the same result appear in further samples it might then be worth while considering whether the high frequency of these three classes was due to their heterozygosity giving rise to heterosis or hybrid vigour. In this connection Haldane[4] had said: "It is true that, in the case of (ABO) incompatibility between mother and fœtus, heterozygotes are less fit than homozygotes, but it is unlikely that this influence is enough to counteract the general disadvantage of homozygosis." If this were confirmed it would be interesting to see if the disadvantage of homozygosis was related, in part, to sex.

Boorman's sample unavoidably excluded many abortions and also many normal multiparæ, and that this may be important is suggested by the data of Kirk et al. on 3750 Rh-positive O and A mothers. In this sample, as is seen in table IV, the ratio of abortions to stillbirths is higher for O mothers than for A mothers in every five-year age-group up to the age of 40; and if the same result appeared in further samples greater differences might be found between A and B mothers, and the possible effect of the mothers' Rh group would need to be considered. Moreover, Kirk et al. pointed out that their ratio of O to A primiparæ is significantly higher than their ratio of O to A multiparæ, there being a marked excess of group O primiparæ in every five-year age-group, except 31–35; and here again A and B mothers might show greater differences than would A and O mothers. The sample of Bryce et al. may well have been affected in similar ways.

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University of Aberdeen.

T. M. ALLAN.

AN UNUSUAL TYPE OF HERNIA

SIR,—It would seem that an uncommon type of direct inguinal hernia was known to Mr. Hamilton Russell,[1] for he wrote in 1922:

> "There are two kinds of direct inguinal hernia, one of which is caused by a small congenital sac that usually comes straight through the conjoined tendon to project at the external ring. The other form, which is seen with great frequency, consists of a bulging directly through the posterior wall of the inguinal canal internal to the epigastric vessels."

I operated upon my first case on Jan. 7, 1935, and like others have had several examples.

London, W.1.

CAMERON MACLEOD.

THE ILLEGIBLE CANDIDATE

SIR,—The proposal to penalise illegible candidates is a generation too late; in fact, speaking as one who has to contend continuously with illegibility among those who have qualified, I feel that the deducting of marks is not sufficiently severe and only the extreme penalty of failure would have been adequate. However much a doctor may be satisfied with his own bad writing, there appear to be at least two aspects of it which never occur to him. First, it is expensive. If he intends his script to convey information, then the person receiving it has to spend a considerable time in deciphering it and the few seconds (if any) saved to the writer by writing badly involve the reader in maybe as much as half an hour's struggling before any sense can be made of the illegible script. It is the recipient who pays for this, not the writer. In the second place, it is a discourtesy. It never seems to occur to the bad writer that he has the obligation to make his script legible to the person to whom he sends it, and one can only regard bad writing in communications as no less ill-mannered than paying an ordinary social call ill-dressed, unwashed, and with muddy boots.

West Park Hospital, Epsom, Surrey.

W. W. KAY.

A PHILOSOPHY OF MEDICINE

SIR,—Sir Russell Brain's oration to the Medical Society of London, which you published on May 16, is in essence a plea for the outlook which he has summed up in the statement: "Medicine is a branch of biology, and I believe that the philosophy should be based upon a re-examination of the conception of the living organism as a whole." Sir Russell Brain in this statement gives point to the fact, too readily overlooked by investigators, that the human creature developed in its growth and behaviour before the coming of medicine, and that it is in the growth and behaviour of the creature that we must seek for that integrative working principle which, to quote Sir Russell Brain, operates as "a dynamic transaction which itself integrates the activities of the organs."

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[4] Haldane, J. B. S. *Ann. Eugen., Lond.* 1950, 15, 15.

[1] *Brit. J. Surg.* 1921–22, 9, 502.

Case 3.—Mrs O., aged 42, was admitted in July, 1948, with a blood pressure of 250/145 mm. Hg and a grade 3 retinitis. She also had been anxious to have a baby but had been sterile. Her sympathectomy was done in two stages at the end of July and the beginning of August, 1948, after which her blood-pressure fell and her retinæ cleared.

Fig. 6 shows her blood pressure over the years since operation and since reporting on Sept. 15, 1952, three months' pregnant. She said she felt better than at any time since the operation. Termination of pregnancy was advised at first by the physicians, but in view of cases 1 and 2 it was agreed to observe her progress and allow her to continue.

Owing to a slight rise in the blood pressure cæsarean section was performed, and she was delivered of a healthy female infant on Feb. 17. She left hospital with a blood pressure of 170/110.

Another patient who underwent sympathectomy elsewhere, is at present under the care of the obstetrical department, which has kindly sent the following notes.

Case 4.—Mrs R., aged 29, in her second pregnancy, expected delivery on Feb. 17, 1953. In December, 1948, she underwent lower segment cæsarean section at thirty weeks for severe pre-eclamptic toxæmia (blood pressure 206/140 mm. Hg, œdema, and ? albuminuria) after failed bougie induction. The baby weighed 2 lb. and lived only forty-eight hours. On the patient's discharge from hospital her blood-pressure was 150/110. On April 9, 1951, she was referred to the Royal Infirmary, Derby, with blood pressure 150/110 and a trace of albuminuria. There was a slight response to 'Sodium amytal.' There was good concentration of the urine. The eyegrounds showed early grade-1 hypertensive fundi. An intravenous pyelogram was normal.

On May 1, 1951, a right lumbodorsal sympathectomy (T4–L3) was done. On July 2, 1951, the blood-pressure was 180/114. On July 3, 1951, a left lumbodorsal sympathectomy was done. The blood pressure level following this operation was not recorded. At the first visit to the Westminster Hospital in July, 1952, when the patient was eight weeks' pregnant, her blood-pressure was 140/110 settling to 130/100 on rest. On Jan. 23, 1953, when she was eight months' pregnant her blood pressure was 120/90 when she was sitting, 110/70 when she was standing, and 150/110 when she was lying down. There was considerable tachycardia, no œdema, and no albuminuria.

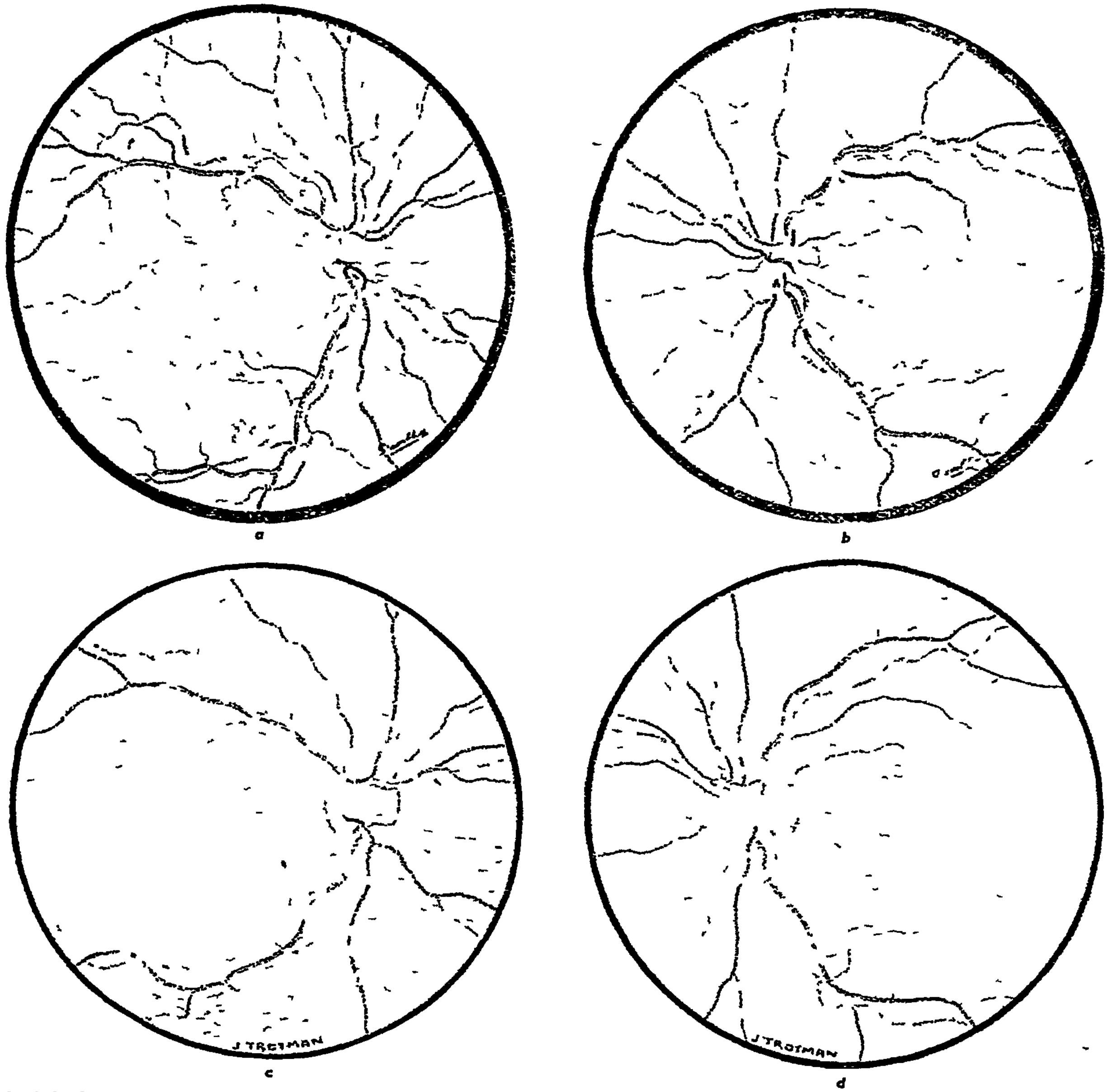

Fig. 4—Retinal appearances in case 1: a, right eye before operation; b, left eye before operation; c, right eye after operation; d, left eye after operation.

The method which enabled Mr. F. Matthias Alexander to discover a directive influence capable of guiding and controlling the living self, so that it operated as an integrated whole and thus as a mechanism working under the influence of what might be called a "dynamic transaction," was the direct experimental observation of the whole living man working as a mechanism in his everyday environment. It is an indication of the limiting influence of specialisation and professionalism that the essential appropriateness of Mr. Alexander's method still awaits recognition by those very persons who profess that what they most desire for men's use and profit are just those very consequences which followed from Mr. Alexander's experiments.

Bolton, Lancs. MUNGO DOUGLAS.

Diary of the Week

JUNE 7 TO 13

Monday, 8th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. A. L. Cochrane: Medical Field Work.
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, W.1
7.30 P.M. Dr. E. Gurney-Clark (New York): Natural History of Acquired Syphilis and its Relationship to Preventive Medicine.

Tuesday, 9th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. H. L. Jaffe (New York): Giant Cell Tumour (Osteoclastoma) of Bone. (Moynihan lecture.)
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital, W.2
5 P.M. Prof. J. R. Squire: Hypersensitivity and Disease. (Almroth Wright lecture.)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Prof. C. A. Keele: Hyperidrosis.

Wednesday, 10th

ROYAL COLLEGE OF SURGEONS
5 P.M. Prof. Milroy Paul: Surgery of Congenital Anomalies of Midline Ventral Abdominal Wall. (Hunterian lecture.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. R. E. O. Williams: Control of Airborne Infection.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. W. Riddell: Pathogenesis of Tinea Capitis.
MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (*Royal College of* Surgeons, 18, Nicolson Street, Edinburgh.) Dr. T. N. MacGregor: Sex Hormones and their Impact on Medical and Surgical Practice.

Thursday, 11th

ROYAL COLLEGE OF SURGEONS
5 P.M. *Sir James Paterson Ross*: Unsolved Problems in Surgery of Sympathetic Nervous System. (Bradshaw lecture.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. B. Ackner: Depression. (Second of three lectures.)
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Riddell: Superficial Fungus Infections of Skin.
WEST LONDON HOSPITAL MEDICAL SCHOOL
4.30 P.M. (11, Chandos Street, W.1.) *Sir Clement* Price Thomas: Benign Tumours of Lung. (Alex Simpson Smith lecture.)
NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Dr. Jaffe: Solitary Fibro-osseous Lesions of Bone and their Relation to Fibrous Dysplasia.
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. J. A. Tulloch: Prognosis after Myocardial Infarction.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Medical School, Small's Wynd, Dundee.) Prof. David Campbell: Function of General Medical Council and its Influence on Medical Education and Ethics.

Friday, 12th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr. H. Osmond-Clarke: Modern Management of Skeletal Tuberculosis.
4 P.M. Dr. C. L. Cope: Adrenal Cortical Function.
INSTITUTE OF CARDIOLOGY
5 P.M. (1, Wimpole Street, W.1.) Prof. John McMichael: Right Ventricular Failure. (St. Cyres lecture.)
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. F. R. Bettley: Clinical Demonstration.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. Aleck Bourne: Delay in Labour.
UNIVERSITY OF LEEDS
8.15 P.M. (*General Infirmary, Leeds.*) Prof. Sydney Sunderland (Melbourne): Applied Anatomy of Peripheral Nerve Trunks.

Saturday, 13th

ASSOCIATION OF CLINICAL BIOCHEMISTS—SOUTHERN ENGLAND AND SOUTH WALES
1.30 P.M. (Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, W.1.) Regional Meeting.

Notes and News

WORLD HEALTH ASSEMBLY

AT the closing session of the sixth World Health Assembly in Geneva on May 22, the retiring director-general, Dr. Brock Chisholm, in a farewell address, reviewed the achievements of W.H.O. since the idea of an international plan for health was first put into practice in 1946. But, he said, we were only at the very beginning of a long and challenging endeavour. Whether the promise of W.H.O. could be fulfilled depended, for one thing, on the participation of *all* nations: health, like peace and security, was indivisible, and the fight against disease could only be won through the concerted effort of all. Five years ago, we had hoped that W.H.O., as a non-political body, could be spared the frustrating effects of a politically *and psychologically* divided world; but it had not been so. And Dr. Chisholm hoped that the universal solidarity which had prevailed at the birth of the organisation would return. Turning to financial handicaps, he said that what W.H.O. was spending on the world's health was no more than the sum laid out by many a large city on its own municipal sanitary arrangements. The organisation's budgets had been and were ridiculously small; and if we were to close the gap which now separated a healthy minority from a majority which continued to live in bondage to disease and misery, then W.H.O. must be given more money with which to play its part.

In carrying out the specialised work of the organisation, there was, Dr. Chisholm thought, a danger of losing sight of the paramount aim for which W.H.O. was created—*namely*, to lay the economic and social foundations for a lasting peace. Clearly, successful health campaigns alone could not promote social progress, for the physically reabled people might merely swell the ranks of the unemployed, dissatisfied, or hungry. The extra labour gained by these campaigns would mean progress only if the people freed from disease were assured of capital investment for production and stabilised markets for distribution, and if they were *guaranteed* sufficient work and adequate educational and cultural facilities for themselves and their children.

Looking at the world scene today, Dr. Chisholm said that man must now learn to live with himself and to reshape his entire pattern of thinking and behaviour in order to build a completely new system of human relationships, adjusted to a changed world. He must realise that ruthless competition, the old rule of survival, had at this stage of scientific and technological development become synonomous with suicide for all of us, and that it had to be replaced by coöperation based on mutual understanding, compromise, and agreement. Dr. Chisholm concluded: "For this generation there is no sane alternative but to accept with courage and determination the realities of a new era. The time for courage, determination, and action, even it may be for martyrdom, is *now*; the place is *here*, wherever we may be and whatever *our responsibilities at the moment*. Every action, every word, works for, or against, the great ideal of peace on earth. We, the peoples of the world, not only in the councils of the nations, but, far more importantly, in our daily living, will decide whether we and our children will live and die in misery and fear far worse than anything we have known, or whether we and they can construct and enjoy a happy and peaceful world community."

THE GENERAL PRACTITIONER

THE Coronation number of the *Practitioner*[1] contains, besides an attractive "pictorial record" of British Medicine, a symposium on General Practice Today and Tomorrow, introduced by Mr. Iain Macleod, the Minister of Health.

The status of the general practitioner, Mr. Macleod says, depends essentially on three things—the trust of his patients, the respect of his colleagues, and the means to do his job adequately. In the last resort all these depend on himself, but there is much that others can do to help him. First, he has a right to be treated by hospital doctors as a colleague and an equal, an essential member of the team.

> "He should have direct access to X-ray and pathological services for his patients, he should receive *prompt* information when his patients leave hospital and, when he refers patients for consultation, he should be sent the mature and considered opinion of a senior

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[1] June, 1953. Published at 5, Bentinck Street, London, W.1. 7s.

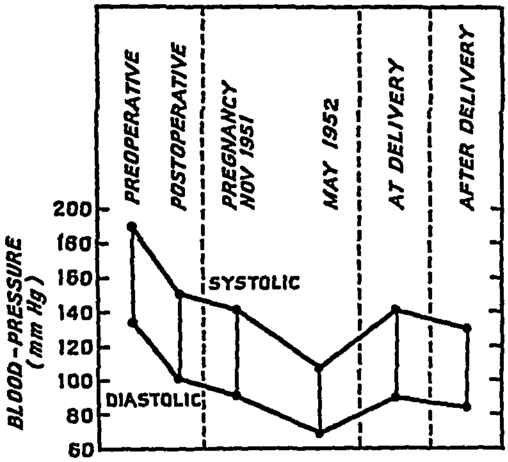

Fig 5—Blood pressure in case 2

On Feb 12 she was delivered of a healthy male child by cæsarean section, and her blood pressure on discharge from hospital was 130/90

The benefit of pregnancy in these cases may be explained either by the circulation of fœtal hormones or by the increase of pelvic circulation due to the arteriovenous shunt in the uterus

Obstetricians say that hypertensives very rarely become pregnant, and this has been regarded as Nature's safeguard in these women against the harmful effects of a pregnancy Without in any way advocating this operation for the cure of sterility, I must point to the fact that pregnancy occurred in 2 of these cases after a long period of infertility, and this may be an indication of the removal of another of the abnormalities produced by the disease

Discussion

Like other stress diseases hypertension is almost certainly on the increase In 1937 the Metropolitan Life Insurance Company of New York stated that half a million deaths took place annually in the United States from hypertension, and that after the age of 45 the death-rate was four times that of cancer and twenty times that of diabetes or of tuberculosis

Thirteen years later Master, Dublin, and Marks (1950) in a report from the statistical bureau of the same life assurance company, made a belated attempt to lift the gloom these figures must have cast by telling us that blood-pressures usually considered above normal were found in about a fifth of the men in their 20s reviewed by them, and that after the age of 45 they are more common than the so called normal blood-pressures These findings do not lessen the seriousness of the figures cited in 1937,

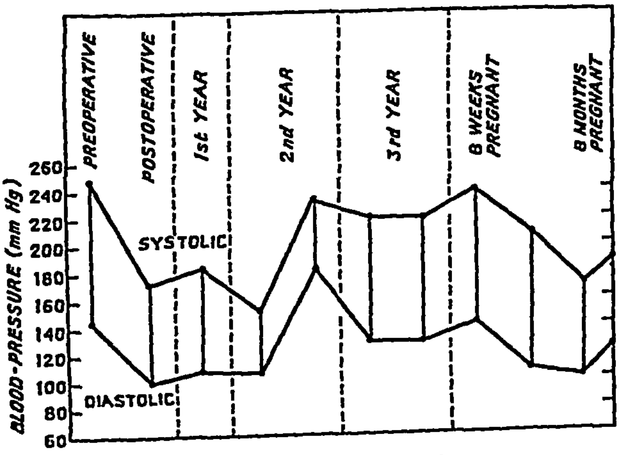

Fig 6—Blood pressure in case 3

but do make it clear that a rise in blood-pressure is not in itself of great importance This is not new in 1925 Sir James Mackenzie said

> "There has been so much nonsense talked and written about high blood pressure that I am constrained to draw attention to our extreme ignorance of the cause and consequence of raised blood pressure That we are totally ignorant of the cause does not prevent many people adopting heroic measures for reducing it, without even considering the wisdom or necessity of so doing That it may be a physiological process for the benefit of the organism is seldom considered It would not be exaggerating to say that the present state of our knowledge of this subject is so wanting in trustworthy data as to warrant neither a sound prognosis nor a rational therapy In some cases it is associated with manifest disease of the arteries or the kidneys, and here a grave prognosis can safely be ventured, but the high blood pressure forms but one datum, and the older physicians could have given as sound a prognosis before the invention of the instrument for estimating the blood pressure"

It is well known that many hypertensives, especially women, tolerate a high blood-pressure without symptoms up to, and beyond, their allotted span However, among these people are those—and we know them to be a very large number—who will die well before their time after severe suffering

There are, it seems to me, three ways of explaining these latter

(1) At some stage the organism begins to deteriorate from the sustained rise in blood pressure, although such deterioration does not seem to be in exact relation to the figure

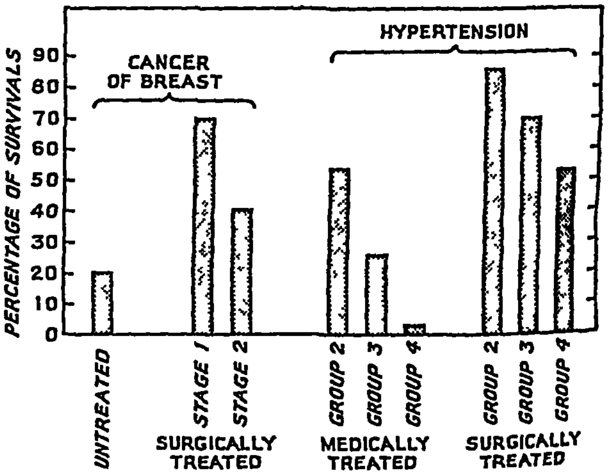

Fig 7—Five-year survival rates in hypertension and in cancer of breast.

obtained—a malignant hypertensive may have lower sphygmomanometer readings than those obtained over several years in benign cases

(2) All the severe cases with a bad prognosis may belong to a separate disease entity—another form of secondary hypertension such as Cushing's syndrome and adrenal *tumour*—but one whose original cause is still unknown

(3) All the patients may be benign hypertensives in whom a new factor has been added to make a relatively normal condition into a fatal one

At present we can only recognise these cases by the damage produced by this new factor, such as retinal, renal, cardiac, and cerebral damage, and their symptoms of headache, disturbance of vision, breathlessness, encephalopathy, or threatened heart failure These are the cases which must be treated with all the resources at our command, whether we choose medicine or surgery

It is wrong and foolish to raise bogies and to spread alarm needlessly, but it is just as reprehensible to ignore dangers and to take no steps to find out the best method of meeting them The insidious threat—what one might call "the underground" in disease—must be attacked just as energetically as the cancerous lump For the member of the staff, not a brief account of findings by a house officer. He should also be made welcome in the hospital if he cares to accompany or visit his patient or to come on a consultant's round. All these requirements are common practice in many parts of the country but there are still hospitals where they are not—to the great detriment of hospital and patient."

The public-health service, too, has a part to play.

> "Just as the consultant has his team of nurses, almoners and medical auxiliaries, so the general practitioner can now have *his* team, organized and made available by the medical officer of health. The district nurse is an old friend and ally, so in many areas is the midwife; but the value of the health visitor has not yet been fully recognized by the general practitioner and her place in his team has still to be worked out."

The general practitioner, for his part, must see to it that he keeps well informed, whether by reading or by post-graduate courses. He must also see to it that the environment in which he sees his patients is such as to inspire respect and confidence. He must reciprocate the coöperation of his colleagues.

> "If these requirements are met, we shall hear less of patients demanding to be sent to hospital because they think that only there can they get the best treatment. We must at all costs break down this attitude for there are many patients for whom hospital care is wrong and that of their own doctor right. This will enable the elaborate and expensive panoply of the hospital to be reserved for those who really need it."

The main subject of the symposium is the means whereby the practitioner can do his job adequately—including his house, his professional premises, his equipment, his dispensary, and his secretarial arrangements.

UP THE REBELS

FROM time to time in every age the image of the noble savage running in wild woods attracts admiring glances. Dr. Robert Lindner is chief consultant to the Board of Correction of the State of Maryland; and his latest book [1] is devoted to proving the necessity for modern man to strive to transcend the limitations of the "triad" consisting of his physical environment, his bodily and mental equipment, and his life-span. According to him, all current institutions, philosophies, and religions direct their efforts to producing adjustment and conformity, and he sees in this the danger that mankind will be reduced to a race of robots, "Mass Man," whose ultimate revolt will be primitive and anarchic and lead to chaos and destruction. He criticises the teachings of many eminent modern American psycho-analysts who in different ways recommend to their patients a passive and resigned attitude: Franz Alexander's concept of the neurosis as a "failure in domestication" of man's hostile impulses, Erich Fromm's and Harry Stack Sullivan's emphasis upon social and cultural factors rather than upon instinctual trends in the genesis of neurosis, and above all Karen Horney's interpretation of neurotic illness in terms of maladjustment to the social environment, come in for some searching criticism.

The individual's dragooning into adjustment begins with the parents encroaching upon his instinctual urges in early infancy in the two important spheres of eating and elimination, and control or suppression of overt sexual behaviour is the next sphere in which the child is made to feel that instinctual life is "bad" if it does not conform to adult requirements. Dr. Lindner feels that most psychologists and psychiatrists, flattered and supported by the seductive approval of the influential section of the community (whose good favour they have so hardly won), unconsciously tend to support its claim that the individual must conform to its mores. Many of the methods of present-day psychiatry—confinement in State hospitals, electro-shock, and, above all, lobotomy—may then be regarded as punitive measures against the "rebel."

Dr. Lindner gives an interesting account of human history in terms of psycho-analysis. He sees the expanding society as one where the frontier serves not only as a zone to which the bad and lawless elements resort, but also as a growing-point. When the frontier becomes rigid, both these types of "rebel" return to the centre of the society and a process of decline sets in. This is controlled at first by an oligarchy, which encourages the proletarianisation of the deprived classes and buys their support with bread and circuses; but sooner or later both the rulers and the masses turn to the Great Man, the symbol of their unconscious desires for primitive and lawless modes of behaviour.

His final chapters offer a prescription which is not easy to follow. He seems to advise that we should educate our children more in accordance with the knowledge we have already gained about man's instinctual endowments; and that psychologists and psycho-analysts should encourage their patients to become "rebels" in an enlightened sense. He is careful to point out that the "rebel" will promote not only his own welfare but that of the community in which he lives; but he seems curiously unaware that it is precisely because man is so uncertain of what his hostile and antisocial impulses might compass that he has, from time immemorial, subjected himself to cultural confines.

WAKLEY AND BARTS

ROUND about St. Bartholomew's Hospital, as a contemporary notes,[1] lie Rahere Street, Paget Street, and Gee Street—all likely enough names for the hospital governors to choose when houses were being built on hospital property. But what, he asks, of Wakley Street, which lies so close beside them? For Thomas Wakley, founder and first editor of THE LANCET, was the avowed enemy of that great Dr. John Abernethy whose forcible character has survived in many a good story, so that it can almost be counted as one of the Barts treasures in itself.[2] Abernethy obtained an injunction against Wakley in the Court of Chancery, for publishing his course of surgical lectures without permission. Surely, the editorial paragraph suggests, the governors would not have named a street after *him*.

That depends, it seems to us, on when the street was built; for the stormy passages between Wakley and Abernethy, that clash of giants, blew up out of a relatively clear sky. When Wakley published his first issue of THE LANCET on Oct. 5, 1823, it was with the open intention of conveying "to the Public, and to distant Practitioners as well as to Students in Medicine and Surgery, reports of the Metropolitan Hospital Lectures"; and he began, in the very first issue, with one of Sir Astley Cooper's lectures. It was an honourable purpose, with a good deal more in it than met the eye, for at that time, as Sir Squire Sprigge, a later LANCET editor, described in his *Life and Times of Thomas Wakley*, a few teachers held a monopoly of students' fees for attendance at lectures, and provincial doctors had no access to what was being taught in London. Moreover though some among the few holders of the rich teaching posts were great figures, some had gained their positions by interest or purchase. Astley Cooper never objected to the publication of his lectures in THE LANCET: he recognised the importance of disseminating medical knowledge and experience, and only stipulated that his name should not be printed. Abernethy was a good deal less dignified in his style than Cooper, peppering his racy lectures with: "I'll be hanged. . . ." "Egad. . . ." and the like; and he was irritated to find these mannerisms faithfully reported. Moreover, like Wakley he was a natural fighter, and willingly took the lead on behalf of smaller men whom Wakley had alarmed by his accurate reporting. The harmonious relations established between THE LANCET and the teachers by the liberal views of Cooper were thus transformed to a battle royal, with Abernethy as champion of the teachers and Wakley as champion of the profession at large; and the first ten years of our now relatively sedate journal were enlivened by ten court actions. Nevertheless when the battle-cries died down, it may well be that the governors of Barts conceded that Wakley deserved a street beside Paget, Gee, and even Rahere himself; and smiling named one for him.

University of Oxford

In a congregation held on May 26 a statute was promulgated giving effect to the decision reached on March 10 (see *Lancet*, March 21, 1953, p. 605) to raise the retiring age of holders of academic posts from 65 to 67. Holders of administrative posts will not be included in the new scheme.

International Congress for Physical Therapy

The first congress of the World Confederation for Physical Therapy is to be held in London from Sept. 7 to 12. Mr. Iain Macleod, the Minister of Health, will open the congress, and the speakers will include Mr. Herbert Seddon, Dr. Herman Kabat (California), Dr. Hugh Burt, Dr. Wallace Graham (Toronto), Sir Clement Price Thomas, Mr. L. W. Plewes, and Dr. F. S. Cooksey. Further particulars may be had from the secretary of the Chartered Society of Physiotherapy, Tavistock House (South), Tavistock Square, W.C.1.

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[1] Prescription for Rebellion: Some Methods of Psychoanalysis Attacked by a Psychoanalyst. London: Gollancz. 1953. Pp. 305. 16s.

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[1] *St. Bart's Hosp. J.* May, 1953, p. 99.
[2] *Lancet*, May 23, 1953, p. 1035.

latter there are accepted surgical treatments which are by no means necessarily a cure, or even the ultimate best method, but they are the best at our disposal They prolong life and alleviate suffering

Hypertension is more prevalent and more fatal than many forms of cancer, and a standardised treatment is long overdue Whether this should be by drugs or by surgery cannot yet be finally decided, there being no five year figures for the treatment with methonium compounds as there are for lumbodorsal sympathectomy, but I contend that, if the same approach were made to hypertension as is made to cancer, the evidence we have at present would establish surgery to be as obligatory in the severe cases as a radical mastectomy is for early carcinoma of the breast

It is instructive to compare the severe form of hypertension with that of cancer of the breast In both conditions the ultimate outcome of untreated cases can be predicted with reasonable certainty In cancer of the breast there are universally established methods of treatment which are not condemned because in many cases they do not cure the patient Their value lies in the proof of five-year or ten-year cures and the removal of a lump which, if untreated, would cause much suffering

Fig 7 shows the five-year survival-rates for untreated and surgically treated cancer of the breast compared with the five-year results in medically and surgically treated hypertension The figure for untreated carcinoma of the breast is the mean of the upper and lower figures given by Shimkin (1951) The figure for the results of surgical treatment is based on the recent review of cases at the Cancer Hospital by Professor Smithers (1952) and is the average survival-rate for all grades of malignancy in stages 1 and 2 of breast cancer The figures for hypertension are taken: (*a*) for the non-surgical cases, from Keith et al.'s (1939) cases added to Smithwick's (1951) cases who refused surgery, and (*b*) for those treated surgically, from Smithwick's (1951) figures Assuming that Smithwick's figures are correct, it is obvious that if the condition under consideration were some form of cancer instead of hypertension, the need for surgery would be generally accepted Smithwick has shown quite clearly, in a series far larger than any reported in this country, that the prognosis for patients with hypertensive cardiovascular disease, ranging from slight to severe, is significantly improved by sympathectomy.

Surgical treatment of hypertension cannot be condemned because it does not guarantee a permanent cure Yet it *is* commonly condemned because the blood-pressure often returns to its preoperative level, even though symptoms remain in abeyance and more certain evidence of improvement is visible in the fundi and in the size of the heart (Harland and d'Abreu 1949) Physicians, I venture, tend to become the slaves of their sphygmomanometers The relief of crippling headaches and the restoration of normal sight to one going blind cannot be dismissed as mere relief of symptoms and as no indication that the progress of the disease has been decreased or even halted

Conclusion

A raised blood-pressure is a common finding in many normal healthy people and in itself may be unimportant If it is accompanied by evidence of damage to the cardiovascular system or to the renal system it becomes a disease with a high and early mortality Such cases should be treated with the best resources at our command.

On present evidence surgery offers the best chance of prolongation of life Moreover it removes very serious and crippling symptoms and allows the patient to return to work—a very important point in the type of person commonly afflicted. The old-fashioned methods of complete rest alone may, by their frustrating effects, accelerate the fatal course of the disease, whose progress should be judged not by the sphygmomanometer but by the information provided by cardiac efficiency, the retinae, and renal function Judgment of the new methonium compounds must await five-year results in each group to compare with those of surgery

The object of this article is to survey those cases with evidence of damage indicating a poor prognosis which have undergone operation, and to put forward our findings on the assessment of these cases and the effects of surgical treatment Their analysis bears out the findings of Smithwick and emboldens one to say that, in the present state of our knowledge, we are as justified in counselling lumbodorsal sympathectomy in a case of severe hypertension which has not progressed to a hopeless stage and is not over the age-limit as we are in advising radical mastectomy in a case of stage-1 or stage 2 cancer of the breast

I acknowledge gratefully the great help given me in providing material for this paper by the physicians of the Westminster Hospital, particularly Dr C Gavey, and the ophthalmic surgeons and the obstetrical and pathological departments I also wish to thank my surgical registrar, Mr. David Woodhead, F.R.C.S., who has compiled all the follow up findings and helped me in many other ways

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DETECTION OF WEAK Rh ANTIBODIES IN MATERNAL ANTENATAL SERA

THE VALUE OF ENZYME-TREATED TEST CELLS

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ANTENATAL Rh typing is performed on a large scale in this country and abroad, and, now that effective methods of treatment are available for hæmolytic disease of the newborn, it is important to know during the antenatal period whether the maternal serum contains Rh antibodies

The majority of mothers whose babies are affected with hæmolytic disease are Rh-negative, and their sera contain Rh antibodies, anti-C + D, and anti-D, or occasionally anti-D + E Rh-positive women may rarely give birth to children affected with hæmolytic disease, in these cases the commonest antibodies are anti-E and anti-c, in that order

In most laboratories the search for Rh antibodies is confined to the sera of mothers who are known to be Rh negative—i e, D-negative In the case of Rh-positive mothers the sera are examined only where the history suggests hæmolytic disease of the newborn

The presence of a Rh antibody in the maternal serum should be considered to be pathological In this Transfusion Service Rh antibodies from about 950 cases have been examined, and in only 1 instance does the evidence suggest that the antibody may be of natural occurrence, there being no evidence of immunisation

It is customary to examine the maternal serum upon the mother's first or second visit to the antenatal clinic

University of London

The degree of D.SC. has been conferred on A. D. M. Greenfield and C. L. Oakley.

The following have passed the final examination for the degrees of M.B., B.S.:

Honours.—J. H. Bulmer, R. Y. Calne, A. F. Champion, M. L. Crosfill, M. J. Hodgson, Homi Feroze Jeejeebhoy, B. S. Jones, Peter Knipe, Caroline S. Koblenzer, Paul Mestitz (university medal), J. L. Turk, T. H. M. Warburton, R. S. Williams, D. A. H. Yates.

Pass.—Jessamine M. Akhurst, D. P. Adamson, B. L. Anderson, Margaret L. Arden, Janet E. Arnott, J. F. Arthur, K. J. Atkins, Bridget K. Attlee, N. J. Badham, Jean F. Baker, Patricia M. Banks, A. R. Barber, C. J. Barlow, M. J. Barnard, Joyce Barnett, A. F. Barrett, B. A. J. Barrow, J. L. Barton, D. A. V. Bearblock, A. R. Bearn, D. P. Beck, Yvonne G. Beeching, Mary A. M. Beeney, J. S. Bennett, F. E. Bennetts, Roy Benson, E. G. A. Bernez, P. B. Biddell, G. C. Bird, I. C. Black, N. A. Black, A. G. Boag, Anne Booth, R. T. Booth, P. D. Bowen, W. M. S. Boyd, Ann N. Bradford, J. J. Bradley, Margaret H. Bradshaw, Cynthia I. Breillat, Eileen M. Briant, E. R. Briant, B. J. Brook, E. F. Brooks, Irene P. Brown, Jean Brown, Joan T. Bruce, Barbara J. Bruce Low, Jennifer T. Bryant, E. A. C. Buckell, J. S. Bunting, Vivien Burn, J. D. Bury, Katharine M. Cadbury, Ailleen M. Caldwell, C. D. Campbell, Pamela F. Carter Braine, Elizabeth O. Castell, R. A. Cawson, D. R. Chase, Chia Ah Kwan, R. G. Chitham, Gillian M. Churcher, D. L. Clarke, D. J. A. Clarke, Percy Cliffe, Mary Clothier, Peter Cook, D. C. Cornish, Kathleen D. F. Corti, Violet G. Cousins, Gerda J. Crow, Gordon Currie, Agnes M. S. Curry, P. J. Dally, B. L. P. Dalton, Robert Danbury, Helen M. Danziger, Shirley F. Dauncey, A. P. Davies, F. Ll. Davies, Gaius Davies, D. A. de Renzy-Martin, A. G. F. Dominick, F. de S. Donnan, B. W. Duck, D. V. Duckworth, G. W. Duckworth, P. G. Dunbar, G. T. Dunger, Sylvia Dunn, J. V. Dyer, L. W. Eldon, Lindsay M. Elliott, Mary A. Elsdale, Jean A. Evans, J. Ll. Evans, Jean A. Fairhurst, J. K. Fanning, R. H. Farrell, C. P. Farthing, P. L. Fieldus, John Fisher, Margaret Fisher, Alan Fletcher, Sheila M. Forbes, W. A. Forrest, Bernard Fox, Phillida M. Frost, I. C. Fuller, Gillian Gandy, D. C. Gardner, A. P. Garland, Katharine R. Garrett, R. E. M. Geldart, K. W. Giles, M. C. Glassett, R. B. Glover, D. H. Glyn, R. M. Goddard, H. R. Gomp[illegible], Daphne F. Grainger, V. A. Grantham, J.[illegible]berg, A. H. Gretton, A. J. G. Griffin, T. P.[illegible] W. L. Griffiths, Valérie A. E. Guex, J. A.[illegible] J. M. S. Hague, M. I. Hale, Judith M. H[illegible] V. T. Hammond, Dorothy E. Harris, Derek Harvey, S. K. Heywood, J. B. Hickling, D. A. Hill, G. G. Hill, M. C. Hill, Donald Hines, Natalie J. Holloway, G. W. Holmes, E. T. R. Holt, Blanche M. Hooper, J. S. Hopkins, E. C. Howarth, Moinuddin Mohiyuddin Husainee, D. S. Hutton, J. R. F. Ingall, H. P. H. Ivens, Richard James, J. C. Jelleyman, J. A. Jemson, A. H. John, Martin Johnstone, Vivian K. Jones, Nancy Kaan, C. G. Keith, Kevin Kelly, A. B. Kennard, P. A. H. King, Sheila M. King, P. J. W. Knell, S. M. Lacey, Laurence Langdon-Herring, P. T. Lascelles, J. O. N. Lawson, Lesley P. Leader, Michael Leahy, Phillip Lebon, Lee Lian-Hong, John Le Gassicke, E. R. Lester, Barbara Lewis, E. C. Lewis, Agnes D. F. Lodhi-Hyder, T. A. E. C. Lorenzen, Peter Los, R. E. Lovelace, Margaret F. Lowe, M. M. Lubin, D. F. Lunn, A. G. McCallum, Margaret P. McDonald, Patricia McDonald, E. N. McKenzie, M. B. McK[illegible], Dorothy M. McWhirter, D. H. Marjot, Geoffrey Matthews, David Mattingly, P. G. Mellett, M. H. Mercer, D. G. Mitchell, J. S. Miller, D. B. Moffat, Mary Moffatt, G. L. Money, I. A. M[illegible], [illegible] Moore, P. B. Moorhead, D. T. G. Morgan, Patricia L. Mortimer, R. F. Morton, R. J. Mules, L. R. Mundy, Lilias M. A. Munro, M. A. Ness, R. G. D. Newill, C. G. H. Newman, Jack Nickson, Norma H. W. Noakes, J. S. Noaks, J. S. Norell, Jean M. North, M. P. O'Dwyer, J. S. Ogilvie, Gillian Oliver, L. C. Oliver, P. J. Olney, Elizabeth S. Ordish, Pamela M. Ordish, C. S. Osen, Nancy M. Page, R. B. Parker, D. F. Parkin, J. J. Parry, Helen L. M. Partridge, I. S. Paterson, Iris O. Peachey, D. E. Pearsons, C. M. H. Pedler, Elizabeth L. M. Perkins, J. F. Perren, B. Ll. C. Phillips, R. M. Phillips, L. A. Pike, E. M. Pilkington, R. G. Pledger, R. W. Plowright, P. B. Poole, C. J. Porteous, M. F. Porter, O. H. D. Portsmouth, Rosemary D. Prior, J. D. Pryce, M. A. Pugh, A. I. Rae, P. J. Rawlinson, R. D. H. Reddy, P. I. Reed, N. D. Reis, C. H. J. Rey, J. W. Richardson, Donald Ricketts, C. C. Riley, Brenda K. Rimmer, G. D. Ripley, T. M. F. Roberts, O. W. Robinson, S. B. Rosalki, Vera Rose, Annette B. Rosenkranz, R. G. Rowe, A. D. Rowlands, J. A. C. Rozario, Aileen M. Ryan, H. S. S. Ryan, N. R. Sales, Dorothy Sanderson, E. C. Scanlon, J. A. Scanlon, Kenneth Scott, S. C. C. Scott, F. G. M. Seager, Muriel J. Seaman, Patricia M. Searle, P. H. Setna, R. J. Sharland, Joan P. V. Shaw, C. S. Sheldon, Stanley Shere, Rhiannon Shorter, Elkan Silverstone, Elizabeth A. Smith, Mary N. Smith, M. G. Smith, Sylvia F. R. Smith, J. T. Smyth, B. A. Southgate, P. E. Spalding, F. G. H. Spice[illegible] Mary K. Stedman, T. B. Stephen, J. W.[illegible] Stevens, Phyllis A. Stevens, V. W. Steward[illegible] Storey, Roy Stowe, M. K. Strelling, David Stuart, B. D. Thomas, D. H. C. Thomas, D. K. MacM. Thomas, Douglas Thomas, H. M. Thomas, Patricia I. Thomas, Heather B. Thompson, Diana J. Thuell, Janet C. Tonge, A. H. Tooley, J. B. Tucker, B. A. Tudgay, Lesley P. D. Tunnadine, Margaret I. Upton, P. J. Verrill, G. R. Vesey, C. M. Vickery, C. T. Vincent, G. D. Vinden, M. T. Wade, G. S. Wakefield, Maire P. Wallington, Patricia G. Wallis, Margaret P. Watson, H. R. Watson-Baker, Adrian N. E. Watt, Marjorie E. Watts, J. L. Weeks, P. K. Wheatley, Elizabeth P. Wheaton, B. R. Whittard, Jean B. Wickings, J. J. Williams, Margaret S. I. Williams, Myrtle L. Williams, T. C. G. Williams, M. S. Wilson, Shelagh R. Winhurst, A. G. Winfield, A. R. Winrow, Rosemary J. Wisdom, A. E. Wood, Cynthia Wright, H. A. Yerbury, J. R. Young, K. J. Zilkha.

Royal Society of Arts

The gold Albert medal of the society for 1953 has been awarded to Dr. E. D. Adrian, O.M., P.R.S., for his contributions to neurophysiology.

Linnean Society of London

The Linnean gold medal has been awarded to Prof. P. A. Buxton, F.R.S.

Oliver Award

The committee of the Oliver Memorial Fund intend making a sixth award (£50) to a British subject for original work or services in connection with blood-transfusion. The committee will welcome applications and communications drawing their attention to suitable candidates. Applications must be sent before Aug. 31 to the hon. treasurer, Mr. F. W. Mills, c/o National Provincial Bank Ltd., Holborn Circus, London, E.C.1.

Children and Dangerous Drugs

Branch representatives of the Pharmaceutical Society have asked the Ministry of Health to publicise the importance of tablets and other medicines being kept out of reach of children. They also suggest that, in addition to publishing advertisements, the Ministry should approach the B.B.C.; the television authorities might be asked to produce a documentary illustrating the potency of many of the medicines now being dispensed.

Rodents and Rodent Control

By arrangement with the United States Public Health Service, a series of films illustrating the habits of rodents and the latest methods of rodent control in the United States will be shown at the Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W.1, on Thursday June 11, at 2.30 P.M. Applications for tickets should be sent to the secretary of the institute as soon as possible.

CORRIGENDA: *Accidents at Home.*—The numbers of deaths from accidents in the home (60,000) and from accidents on the roads (48,000), which we gave on May 30 (p. 1107), were the totals for the period 1940–49 and not the yearly averages.

Cerebral Angiography.—Our leading article of May 16 says that the first carotid angiography in this country was done in 1932 at the National Hospital, Queen Square. We are informed that a case investigated by carotid angiography at Edinburgh in 1929 is illustrated in H.M. Traquair's *Introduction to Clinical Perimetry* (London, 1938; p. 252).

Angiocardiography.—In our leading article of May 30, where we quote the views of Goodwin et al. on the use of angiocardiography in congenital heart-disease, our reference should be to their recent paper on this subject in the *British Journal of Radiology* (Goodwin, J. F., Steiner, R. E., Mounsey, J. P. D., MacGregor, A. G., Wayne, E. J. *Brit. J. Radiol.* 1953, 26, 161).

Appointments

BARNS, T. E. C., M.A., B.M. Oxfd, M.R.C.O.G.: obstetrical specialist, Colonial Medical Service, Malaya.

FARQUHAR, J. B., M.B. Birm., F.R.C.S., M.R.C.O.G.: consultant surgeon (part-time) in obstetrics and gynæcology to the United Leeds Hospitals and to other Leeds hospitals under the Leeds R.H.B.

WATKIN, JAMES, H.C., M.B. Lond.: part-time asst. (S.H.M.O.), department of psychiatry, St. George's Hospital, London.

WHEILDON, ALICE, M.B. Melb., M.R.C.O.G.: asst. M.O., Finchley and Hendon area.

Manchester Regional Hospital Board:

CAPPER, J. I., M.B. Leeds: tuberculosis physician and M.O., mass miniature radiography unit, Preston.

DIXON, R. I., M.R.C.S., D.A.: consultant anæsthetist, Barrow and Furness hospital centre.

KARFOOT, A. K., M.B. Manc., D.A.: consultant anæsthetist, Barrow and Furness hospital centre.

SLATER, H. B., M.B. Manc.: tuberculosis physician, Oldham and Ashton hospital centres.

North East Metropolitan Regional Hospital Board:

AMULREE, Lord, M.A., M.D. Camb., F.R.C.P.: part-time geriatrician (consultant), St. Matthew's Hospital, London.

FRANCE, N. E., M.B. Wales: full-time pathologist (consultant), Queen Elizabeth Hospital for Children, London.

TUCK, IVY, M.B. Lond.: full-time pathologist (consultant), St. Margaret's Hospital, Epping.

South Western Regional Hospital Board:

FINN, DENIS, M.B. Lpool: asst. psychiatrist, Horton Road and Coney Hill hospitals, Gloucester.

GALLA, THOMAS, M.B. Edin.: registrar in psychiatry, S.W. region.

HUNTER, R. M. M., M.B., B.SC. Edin., M.R.C.P., D.P.H., D.P.M.: consultant psychiatrist, N. Gloucestershire clinical area.

LINTON, C. D., M.B. Brist., D.OBST.: anæsthetic registrar, Southmead Hospital, Bristol.

SCHWARTZ, SAMUEL, M.B. Cape Town, F.R.C.S.E.: orthopædic registrar, Winford Orthopædic Hospital, near Bristol.

WALKER, W. L., M.B. Aberd., D.P.H., D.P.M.: senior registrar in mental deficiency and child psychiatry, Bristol clinical area.

and, if no antibodies are found, to repeat the test during the seventh or eighth month of pregnancy In some instances Rh antibodies are very weak and difficult to detect, especially during the first three months of pregnancy but also in some sera on the second examination during the later months of pregnancy Rh-positive children born to mothers whose sera contain such Rh antibodies are often mildly affected, for example, the only evidence of abnormality may be a positive Coombs test on the cord-blood or, coupled with this, hæmatological changes but no clinical sign of hæmolytic disease Nevertheless this is not invariably so, and mothers whose sera contain such weak antibodies may give birth to children who are severely affected with the disease Weak Rh antibodies present during the early antenatal period may increase in strength during the later months The danger here is that only a single sample of blood, obtained early in pregnancy, is available for testing Owing to the inadequacy of the tests or the manner in which they are performed, these weak Rh antibodies may, at this stage, go undetected and the mother be delivered at home, hence, there may be delay in diagnosis and treatment prejudicial to the child's complete recovery

Exchange transfusion is now carried out at birth, in certain circumstances, as the treatment of choice in hæmolytic disease Diamond et al (1951) and Mollison (1951) have laid down the conditions under which exchange transfusion should be done It has also been shown that exchange transfusion is an effective method of treatment in these conditions and diminishes or abolishes the chances of kernicterus

If Rh antibodies are present in the maternal serum, the mother's pregnancy and delivery should be observed and hæmatological and serological observations should be made on the cord-blood at the time of birth in case there should be the need for an exchange transfusion If no indications for treatment are present, the child should be observed both clinically and hæmatologically during the ensuing weeks, so that treatment may be instituted before a desperate or dangerous situation develops

It is therefore of considerable importance to know in advance whether the maternal serum contains Rh antibodies, even though these may be weak

I report here the results obtained in 200 cases recently studied in which Rh antibodies were detected, and describe the value of the slide technique with enzyme-treated test cells as a screening method for the detection of these antibodies, especially the very weak Rh antibodies

Technical Methods

There are four main tests for detecting the presence of Rh antibodies in sera

1 Agglutination test in saline
2 Agglutination test in albumin.
3 Antiglobulin, or Coombs test
4 Enzyme treated cell test

In these tests the serum is examined with Rh-positive cells used as test cells I shall not give technical details of the first three of these tests, because they have been described by Mollison et al (1952) In all these methods suitable control tests are necessary, especially in the antiglobulin or Coombs test In my laboratory this test is done on microscope slides, a reading being made and recorded at 2 4, and 6 minutes If the test is negative Rh sensitised cells are added to the slide to make sure that the Coombs reagent is active

PREPARATION AND USE OF ENZYME-TREATED CELLS

Group O Rh positive cells of type $R_1 \left(\begin{smallmatrix}CDe/CDe\\CDe/cde\end{smallmatrix}\right)$ and $R_2 \left(\begin{smallmatrix}cDE/cDE\\cDE/cde\end{smallmatrix}\right)$ are collected in acid citrate dextrose (A C D) mixture, four volumes of whole blood to one volume of A C.D mixture—i e, similar to the proportions of anticoagulant and blood in a 500-ml bottle These cells are washed three times in physiological saline solution, and one volume of washed packed red cells is mixed with one volume of papain buffer mixture consisting of equal parts of papain and buffer solution, and with one volume of activator The mixture is incubated in a water bath for 10 minutes at 37°C The cells are spun down, and the supernatant fluid is removed, the cells are then washed once in physiological saline When the cells are being washed, violent shaking should be avoided These cells are referred to as papainised cells 1–2 ml of washed packed cells is normally prepared

The papainised cells are freshly prepared on alternate days, although they can be stored for 1 or 2 days in saline solution in the refrigerator Experiments with methods for prolonging the preservation of papainised cells in the refrigerator and with the preservation of them frozen solid in glycerol have given encouraging results and will be reported elsewhere

The papain buffer and activator solutions are prepared as follows

Papain —Papain (dry powder, B D H) 1 g, saline solution 100 ml

Buffer —Disodium hydrogen phosphate 12 H_2O 3 6 g, water 100 ml

Activator —L cysteine hydrochloride 0 2 g, saline solution 100 ml

The papain solution is best preserved frozen solid The activator solution is freshly prepared The solutions are kept separately, and the buffer is mixed with the papain, and one volume of this is added to one v ume of activator and one volume of packed cells incubation in the water-bath

The test is performed on a microscope sli temperature One volume of a 10% sus papainised cells in saline solution is mixe volume of the serum under test, the latter with physiological saline, making the final the serum 1 4 Alternatively, a volume o *serum and a volume of saline solution* can together, and two volumes of cell suspensi The slides are gently rocked for seven min results may be read under the lower power of scope but are clearly visible through a hand cavity plastic tile can be used instead of a gl *scope slide, but it is a less sensitive* met results of the test are scored as follows

+ + + + − = Massi no free cel
+ + + + = Very with a few
+ + − = Many with mo
clearly visible
+ − = Multiple clumps of 6–8 cells with man
just visible to the naked eye
+ = Small clumps of cells with many free
through a hand lens

The patients' sera were usually 24 hours old whe

With each batch of tests controls are put up c of a mixture of papainised cells and normal ser a group-AB donor and diluted 1 2 in saline This is to ascertain that the cells are not spon agglutinable

Each batch of papainised cells is tested wit selected incomplete Rh antibody to see that t equally strongly treated on each occasion of this standard antibody by various meth R_1R_2 (CDe/cDE) test cells are shown in table I particular Rh antibody, in a dilution of 1 100, result visible to the naked eye should be obtaine strength of the agglutination will depend on the sc of the test cells and varies from + − to + + +

Rh antibodies are demonstrable at 37°C as at room temperature, but a number of positive appear at room-temperature which are not pr 37°C, although occasionally false positive res

ACETYLCHOLINE AND THE HEART BEAT*

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IN considering the relation of acetylcholine to the heart beat we think first of all of the action of the vagus nerve. When stimulated, the vagus liberates acetylcholine, and this diminishes the rate and force of the beat. Since cardiac muscle resembles skeletal muscle in being striated muscle, the action of acetylcholine on cardiac muscle is anomalous, for acetylcholine stimulates skeletal muscle, and it might therefore be expected to stimulate cardiac muscle also. Why then does it inhibit cardiac muscle?

The action of quinidine on cardiac muscle raises the same question. Quinidine is used to restore the normal sinus rhythm in auricular fibrillation. According to Prinzmetal et al. (1952) auricular fibrillation is due to the discharge of impulses at a very high rate from an ectopic focus, and the effect of quinidine is to diminish the rate of discharge to such a point that the sinus node resumes its function as pacemaker. Now quinidine, like procaine and quinine, is a substance which has been shown to antagonise the action of acetylcholine in all forms of muscle (Dawes 1946). Thus in the presence of quinidine a given concentration of acetylcholine has much less effect in stimulating both the frog rectus muscle and the rabbit intestine and in inhibiting the heart. Quinidine thus raises the threshold for acetylcholine. The action of quinidine in diminishing the rate of discharge of an ectopic focus in fibrillation would be explained if the discharge was actually initiated by acetylcholine. Thus we come back to the question why acetylcholine, so far from initiating a discharge of impulses, normally has the opposite effect and inhibits the rate and force of the beat.

The suggestion had already been made, briefly, by Koshtojanz (1938) but notably by Abdon (1945), that acetylcholine plays a part in the contraction of cardiac muscle. Neither of these workers was able to demonstrate that acetylcholine stimulated the heart to beat; and, so long as the only known action of acetylcholine was to inhibit the heart, it did not seem that serious attention could be given to this view. Attempts were therefore made by us to discover conditions in which acetylcholine stimulated cardiac muscle.

Experiments

ACTION OF PROGUANIL ON THE HEART

Many of our observations were made on the auricles of the rabbit heart. When the heart is excised, the auricles can be dissected from other tissue and suspended in a well-oxygenated bath of Locke's solution at 29°C. They beat spontaneously, and the contractions can be recorded on a drum by a light lever. The rate of beating varies from 80 to 150 per minute.

During a study of the pharmacological action of the antimalarial substance proguanil ('Paludrine') the observation was made that, when added to the bath containing the beating auricles, proguanil in a concentration of 10^{-4} (1 g. in 10,000 ml., or 1 mg. in 10 ml.) gradually reduced the amplitude of the contractions and after 30–40 minutes caused the contractions to stop. The beat was not resumed during the next 30–40 minutes. If, however, acetylcholine was added to the bath in a concentration of 10^{-6}, the beat began again and continued until the acetylcholine was removed, when it stopped once more. When acetylcholine restarted the beat, further additions of acetylcholine augmented the amplitude (Burn and Vane 1949).

ACTION OF ACETYLCHOLINE ON STOPPED AURICLES

The significance of these observations was not clear, since the changes in cardiac tissue caused by proguanil were unknown. The question arose of demonstrating a stimulant action of acetylcholine without proguanil. My colleague, Dr. Edith Bülbring, was able to to this by allowing the auricles to beat in the bath for 24–30 hours, during which time the contractions became feebler and stopped spontaneously. She found that the addition of acetylcholine in concentrations of 10^{-7}–10^{-6} caused the beat to begin again and to become fairly vigorous in 15–30 minutes. The beat then continued for some time after the acetylcholine was removed. This demonstration clearly established that acetylcholine had two actions, one the stimulation of the exhausted auricles, and the other the well-known inhibition of the auricles when set up fresh in the bath. Moreover, both actions were observed in the same preparation: the first addition of acetylcholine caused the beat to begin again; the next addition increased both the amplitude and the rate; and a further addition then caused inhibition. The demonstration that in certain circumstances acetylcholine stimulated the auricles made the hypothesis seem much more likely that a local production of acetylcholine caused the heart beat.

It may be noted at this point that the concentrations of acetylcholine used to start the beat of the stopped auricles were low—much lower than those found by Hoffmann et al. (1945) to stimulate the heart after treatment with atropine. This is a different action of acetylcholine which, when studied in the auricles, has been found by Kottegoda (1953) to be exerted only by concentrations of acetylcholine as high as 10^{-5}–10^{-4} and to be prevented by hexamethonium. Thus it appears to be a ganglionic action, distinct from the action of acetylcholine in starting the beat of stopped auricles which is effected in concentrations of 10^{-7}–10^{-6} and which appears to be exerted on the cardiac tissue itself.

THE CHOLINE-ACETYLASE SYSTEM

If the contractions of auricles are maintained by the synthesis of acetylcholine, we might expect in the first place to find acetylcholine present in the auricles. Recent determinations in the Oxford laboratory by Briscoe and Trendelenburg gave a mean result of 4·8 µg. of acetylcholine per gramme of fresh tissue.

The synthesis of acetylcholine is effected by choline acetylase, and Comline (1946) found this enzyme present in rabbit auricles. This enzyme converts the inactive substance choline to acetylcholine, energy being provided by adenosine triphosphate, and acetyl groups coming from citrate. We determined the activity in freshly excised auricles (Bülbring and Burn 1949) by preparing an acetone-dried powder, which was incubated according to the procedure of Feldberg and Mann (1946). At the end of incubation acetylcholine was found to be present and was estimated on the frog rectus muscle by comparison with a solution of acetylcholine of known strength. The amount of acetylcholine formed was expressed per gramme of acetone powder per 75 minutes, which was the time of incubation. Having made observations on freshly excised auricles, we made other observations on auricles which had ceased to beat after being suspended in the isolated organ bath for 24–30 hours, and finally we made observations on auricles which, having ceased to beat, were stimulated by acetylcholine to resume the beat. The results of this investigation are given in table I and show that the choline-acetylase activity of the auricles which had ceased to beat was much lower than that of fresh auricles.

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* A lecture given in the University of Oslo on March 25, 1953.

TABLE I—TITRES OF STANDARD ANTIBODY IN VARIOUS TESTS

Test	Dilutions of standard anti Rh serum									
	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512	Control
Albumin agglutination	+++++	+++++	+++	+	−	−	−	−	−	Neg
Coombs	+++++	+++++	+++++	+++++	+++	++	−	−	−	Neg
Papainised-cell	+++++	+++++	+++++	++++	++++	+++	++	+	−	Neg

appear at 37°C If a positive reaction is obtained at room-temperature, the test should be repeated at 37°C by placing the freshly prepared cell serum-saline mixture in a capillary slant either in a water-bath or in an incubator at 37°C or on a warm viewing-box If agglutination is still present at 37°C, the serum should be examined to confirm that a Rh antibody is present This is done by testing it with its own cells and with Rh-positive and Rh-negative cells, the latter selected to contain all other blood-group antigens

Occasionally antibodies are detected at 37°C with papainised cells, which are auto antibodies These will react with the patient's own papainised cells and with Rh-negative papainised cells, they are therefore usually readily identifiable as such If it is thought that Rh antibodies are occurring together with auto-antibodies, which is extremely rare, the serum should be absorbed with the patient's own papainised cells and re examined

Results

The results of testing 200 Rh antibodies from D-negative mothers are shown in table II The results are those obtained in testing the first sample of maternal serum received in that particular case The results of testing, of course, may alter during pregnancy, but, since second samples may not be available, it is important to consider the results obtained with the first sample received This table is compiled on the assumption that the Coombs or antiglobulin test is used in combination with the saline agglutination test If these two tests are used together, only a very small proportion of antibodies (about 1%) will remain undetected This variety of antibody is very uncommon, and in the two cases referred to in table II second samples obtained at a later date gave a positive Coombs test If the albumin test is used alone on the first sample received, 7% of antibodies will remain undetected, if more than one examination of the maternal serum is undertaken, it is probable that, even so, about 5% of antibodies would be missed if this method alone were used All the sera tested by the papainised-cell technique described above gave a positive result This applied to those sera which gave results by only one of the other methods described (classes III and IV)

The frequency of false positive results with the papainised cell technique was determined by the examination of sera from Rh-positive persons 1264 sera, obtained from the blood of Rh-positive healthy donors of all ABO groups, were tested with Rh-positive papainised cells on microscope slides at room-temperature, 28 positive results were found 16 out of the 28 were visible only on microscopy, and only 3 of these 28 were still active at 37°C with the papainised test cells when tested in capillary slants These 3 sera were also active with Rh negative papainised cells and with their own papainised cells at 37°C, no Rh antibodies were detected If microscopy of the test is used, therefore, the number of false positive results will be about 2%, but, if a hand lens is used, this would not amount to more than 1% In the technique used it is recommended that all positive results should be repeated at 37°C in capillary slants, and, when this was done, only 3 of 1264 sera showed false positive results, about 0 25% Moreover these can readily be distinguished from true anti-D antibodies

Comments

It is useful to consider whether there are any general technical details which will assist in the detection of weak Rh antibodies Firstly, the specimen from the patient should be freshly collected and free from antiseptics Sometimes it is advantageous, especially with the saline agglutination test, to inactivate the serum at 56°C for 25 minutes before use Secondly, the selection of sensitive test cells is most important All Rh-positive cells are not equally sensitive when used for the detection of anti-D antibodies, and it has usually been found that Rh-positive cells of type R_2r (cDE/cde) or R_2R_2 (cDE/cDE) are more sensitive than cells selected from most other genotypes This will be seen, for example, in table III, and, although the antiserum may react more strongly with cells of these types, or with cells of type R_1R_2 (CDe/cDE), or weakly or negatively with cells of type R_1R_1 (CDe/CDe), the serum does not contain an anti-E antibody, indeed such sera gave negative results with $R''r$ (cdE/cde) cells In preparing enzyme-treated cells and in selecting cells for doing other Rh tests,

TABLE II—RESULTS OF TESTING 200 Rh ANTIBODIES FROM D NEGATIVE MOTHERS

Class	Tests		No tested
I	Saline agglutination	+	121 (*60 5%*)
	Albumin agglutination	+	
	Coombs test	+	
	Papainised cell test	+	
II	Saline agglutination	−	
	Albumin agglutination	+	63 (*31 5%*)
	Coombs test	+	
	Papainised-cell test	+	
III	Saline agglutination	−	14 (*7%*)
	Albumin agglutination	−	
	Coombs test	+	
	Papainised-cell test	+	
IV	Saline agglutination	−	2 (*1%*)
	Albumin agglutination	+	
	Coombs test	−	
	Papainised cell test	+	
	Total		200

TABLE III—TESTS OF SERUM DI—, WHICH CONTAINS WEAK Rh ANTIBODIES

Saline agglutination	Albumin agglutination	Routine Coombs test with mixed group-O Rh positive cells	Special Coombs tests with selected cells										Papainised Rh-positive cells
			R_2r cDE/cde	R_2R_2 cDE/cDE	R_1r CDe/cde	R_1R_1 CDe/CDe	R_1R_2 CDe/cDE	R_2r cDE/cde	R_1r CDe/cde	$R''r$ cdE/cde	rr* cde/cde	rr* cde/cde	
Neg	Neg	Negative	+	++	+	Neg	Neg	+	+	Neg	Neg	Neg	+++

* Normally 4 Rh negative cells are used containing all the other antigens

TABLE I—SYNTHESIS OF ACETYLCHOLINE BY RABBIT AURICLES

	Acetylcholine (µg. per g. of auricle powder per hr.)		
	Fresh auricle	Stopped auricle	Restarted auricle
—	48	0	..
	33	8	..
	30	5	..
	75	0	40
	40	8	35
	55	5	32
	40	12	40
	47	18	38
Mean	46	7	37

While this result was not surprising, the much higher values for auricles which had begun to beat again when stimulated by acetylcholine showed that the choline-acetylase activity was related to the rhythmic contractions. The results in table I provided direct evidence for the view that acetylcholine is synthesised in the auricles, and that, when a threshold concentration is reached the acetylcholine initiates the wave of contraction perhaps in the same way as in skeletal muscle; in so doing the acetylcholine is destroyed and the building up of the concentration begins again.

THE ACTION OF THE VAGUS

When acetylcholine is added to the bath containing the contracting auricles, the amplitude of the contractions is decreased and the rate of beating is slowed. It occurred to us that this inhibitory action might be due to a depression of the synthesis. We therefore tested the effect of adding acetylcholine to the tube in which the acetone-dried powder prepared from the auricles was incubated in the course of determining the choline-acetylase activity. In carrying out these experiments we mixed powder prepared from four or five auricles and distributed portions weighing 50 mg. in a series of tubes. One of these was incubated in the usual way as a control tube, and to the others acetylcholine was added in amounts corresponding to 5, 10, 20, 40, and 80 µg. per gramme of powder before incubation. In all, 17 experiments were made, and each experiment showed that the presence of acetylcholine partially inhibited the action of choline acetylase. When the values in each experiment were expressed as a percentage of the synthesis in the control tube, mean values could be calculated (table II). These results indicate that the action of acetylcholine in slowing the rate and decreasing the force of the beat is accompanied by and may in part be due to the depression of the synthesis of acetylcholine.

THE ACTION OF ESERINE

The destruction of acetylcholine is due to the action of cholinesterase. Ord and Thompson (1950) have found that in the auricles of the rat both true and pseudo-cholinesterase are present, the proportion of the latter being greater than that of the former. An investigation of the action of eserine, which inhibits the action of cholinesterase, was therefore undertaken (Burn and Kottegoda 1953). Concentrations varying from 10^{-8} to 10^{-3} of eserine sulphate were tested, the effect being observed for 30 minutes. Even the lowest concentration affected both rate and amplitude, the rate being usually decreased and the amplitude always increased. When higher concentrations were used, the effects were greater though in the same direction, until the auricles were exposed to a concentration of 10^{-3}. This depressed the amplitude and after a few minutes arrested the contractions (see fig. 1). The mean effects of different concentrations are shown in table III.

TABLE II—INHIBITORY ACTION OF ACETYLCHOLINE ON SYNTHESIS OF ACETYLCHOLINE BY RABBIT AURICLES
Mean of 17 experiments

—	Amount of acetylcholine added (µg. per g. of auricle powder)				
	5	10	20	40	80
Percentage of control synthesis	71	70	55	54	30

These results of the effect of eserine on the auricles are by themselves strong evidence that the rhythmic contractions are maintained by the formation of acetylcholine within the auricular tissue. The evidence that a low concentration of eserine modified the contractions clearly indicates that the cholinesterase present in the auricles exercises a control of the rhythmic activity, for eserine in a concentration of 10^{-8} presumably acts only by inhibiting cholinesterase—i.e., by reducing the rate of destruction of acetylcholine. The increase in amplitude caused by concentrations from 10^{-8} to 10^{-4} therefore showed that, by progressively reducing the rate of destruction of acetylcholine, the force of the contraction was steadily increased. When, however, the rate of destruction was slowed still further by a concentration of 10^{-3}, the force of contraction was reduced, with the result that at this point the concentration of acetylcholine appeared to be in excess of the optimal concentration for the force of contraction.

While eserine thus augmented the amplitude in low concentration and depressed it in high concentration, the mean effect on the rate was depression with all concentrations. A double effect on the rate was, however, seen in several preparations, the lowest concentrations increasing the rate and higher ones decreasing it. Moreover, in a series of perfused frog hearts it was observed that the usual effect of eserine in concentrations of 10^{-7} and 10^{-6} was to increase the rate. Thus the observations showed that eserine could increase the rate of contraction just as it increased the force of contraction, though the point at which a further increase of concentration decreased the rate occurred much sooner. Thus the evidence indicated that the optimal concentration of acetylcholine for the highest rate of beat was not related to the optimal concentration for the greatest force of beat.

TABLE III—EFFECT OF ESERINE SULPHATE APPLIED FOR 30 MINUTES ON RABBIT AURICLES

Concentration of eserine (g. per ml.)	No. of experiments	Percentage change	
		Rate	Amplitude
10^{-8}	6	−6	+12
10^{-7}	6	−10	+27
10^{-6}	9	−22	+16
10^{-5}	11	−18	+40
10^{-4}	14	−32	+58
10^{-3}	7	Arrest	−57

ARREST OF THE BEAT

In a concentration of 10^{-3} eserine arrested the beat in a few minutes; the beat recommenced when the fluid in the bath was changed. Since the concentration was so high, this effect of eserine might have been due to some other action than that of an anticholinesterase. We found, however, that, when auricles had been beating in a bath overnight, the effect of lower concentrations of eserine, such as 10^{-5}, was much greater. Whereas this concentration depressed the rate of a group of seven fresh auricles by a mean figure of −7%, it depressed the rate of a group of five auricles beating from 20 to 24 hours by −58%. My colleagues E. Bülbring, H. J. Shelley, and S. R. Kottegoda have found that when auricles have been beating in Locke's solution for this length of time they lose pseudocholinesterase without any loss of "true" cholinesterase. Thus the effect of a therefore, it is an advantage to select at least some of the cells from group R_2r (cDE/cde) or R_2R_2 (cDE/cDE), but even within this group not all cells are equally sensitive

The period of pregnancy during which the sample of serum is obtained is important Many sera obtained early in pregnancy contain weak Rh antibodies only, and these may be stronger in later months, although this is not invariably so Several cases have been seen, however, in which the antibodies did not appear until the end of the seventh or during the eighth month of pregnancy It seems advisable, therefore, if the maternal serum does not contain antibodies at the beginning of a pregnancy, for it to be re examined a second time not earlier than the eighth month

Many methods have been described using enzyme treated cells for detecting Rh antibodies (Morton and Pickles 1951, Rosenfield and Vogel 1951, Wiener and Katz 1951), but they involve a technique done at 37°C The advantage of the present method is that it permits the test to be done rapidly on microscope slides at room-temperature

I shall not discuss here the effect of pH on the papainisation of red cells or the various activators that could be used in their preparation, or the fact that the difference in the manner in which the blood is collected affects the degree of papainisation of the red cells (Stratton 1953)

The papainised-cell technique is valuable in that unlike the saline and albumin agglutination and Coombs tests, it can be used alone and, so far as can be ascertained from the results detailed above, will detect all types of Rh antibody Investigation of sera containing Rh antibodies which gave a weakly positive result with the Coombs test alone (table II, class III) showed that good positive results were obtained with the papainised-cell slide technique, and this method appears to be as sensitive as the Coombs test Occasionally a positive papainised cell test has been obtained where the routine Coombs test was negative, however, if the Coombs test was repeated with single group O Rh-positive cells of specially selected genotypes, in contradistinction to the routine test in which mixed group-O Rh-positive cells of unknown genotypes are used, positive results were obtained (table III) In certain other cases (Stratton and Stone 1953) sera were found which gave a positive papainised-cell test before the Coombs test was positive

One of the disadvantages of any technique using enzyme-treated cells is that there is a tendency for false positive results to be obtained, particularly if the test is done at room-temperature This is partly due to the presence of naturally occurring and other specific antibodies in the sera and to the occurrence in certain sera of an auto antibody to enzyme-treated cells (see below) It is to be noted that the phenomenon of Rosenthal and Schwartz (1951) obtained when trypsinised cells are used does not always occur when papainised cells are used The papainised-cell slide test is very sensitive and gives few false positive results, even though done at room temperature This is attributable to the high degree of enzyme treatment given to the cells, making them very sensitive (which is achieved by the use of the enzyme activator), coupled with the dilution of the maternal serum 1 2 before the test

Occasionally auto agglutinins to enzyme-treated cells are present in normal sera The circumstance of a combination of Rh antibody and auto agglutinin present in the same serum has not been met so far in testing Such a combination of antibodies might be suspected if the results of testing with Rh positive papainised cells are much stronger than similarly treated Rh negative ones The rouleau-forming property of certain antenatal sera has not caused difficulties in this test, but, if sera are tested which have very strong rouleau-forming properties, aggregation of enzyme treated cells will take place Since the test is done in a saline medium, microscopy might suggest or confirm the presence of the rouleau formation In a recent case, in which the serum showed very strong rouleau-forming properties, aggregation did take place with enzyme treated cells, when the serum was diluted 1 3 instead of 1 2 and the papainised cells were added, the rouleau formation was abolished The test is so sensitive that it is very doubtful whether, if a Rh antibody were present together with this severe rouleau formation, its detection would be prevented by a serum dilution of 1 3

This enzyme cell slide technique is designed especially for the purpose of detecting Rh antibodies and is intended to be used as a screening test Certain specific antibodies may give a positive result at room-temperature with this technique, although rarely at 37°C, for example, anti P and anti Lewis are detected at room-temperature, but these antibodies usually do not give positive results in capillaries at 37°C, anti Kell antibodies may give a positive result in capillaries at 37°C As stated already, therefore, it is important that the nature of the antibody should be confirmed The term "false positive" result is used here for the sake of simplicity and is intended to mean a positive result which does not indicate the presence of a Rh antibody at 37°C The incidence of these is about 2% at room temperature, but they are of rare occurrence at 37°C

Summary

The importance of weak Rh antibodies is considered, and various factors concerned in their detection are described and discussed

A slide technique using papainised cells for the detection *of Rh antibodies is described*

This slide technique is shown to be sensitive, and suitable for use as a screening test

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URETERIC TRANSPLANTATION INTO AN ISOLATED LENGTH OF ILEUM

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With an increasing awareness of the consequences of ureterocolic anastomosis there has arisen a dissatisfaction with the results of this operation Serious renal complications have developed not only as immediate sequelæ but also months or years after an apparently successful transplantation Attacks of pyelonephritis are common, and, together with dilatation of the kidney pelvis and of the ureters, they are associated with various degrees of renal damage Recent investigations have shown that these complications are frequent and figure prominently among the causes of death following this operation It has also been shown that, after ureterocolostomy, serious biochemical disturbances may arise, of which hyperchloræmic acidosis and uræmia are the most likely

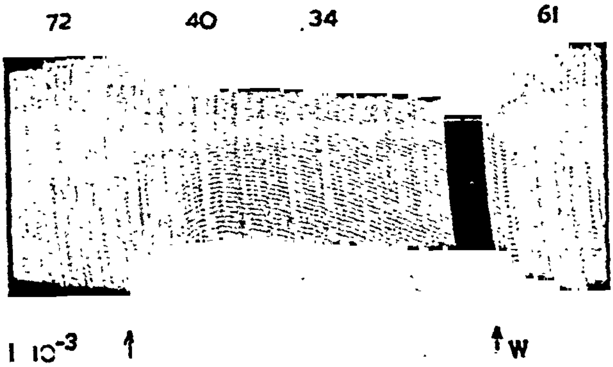

Fig. 1—Record of spontaneous contractions of isolated rabbit auricles in Locke's solution. Rate 72 per minute at 29°C. Addition of eserine to bath to make a concentration of 1 mg. per ml. (E10^{-3}) slowed rate to 40 after 2 minutes and to 34 in 5 minutes. Contractions stopped after 8 minutes. Beat started again when eserine was washed out (W).

given concentration of eserine on the rate of auricular contractions depends on the amount of pseudocholinesterase present, and the evidence points to the conclusion that concentrations as high as 10^{-3} cause the arrest of fresh auricles simply by inhibition of cholinesterase. The substance di-*iso*propylfluorophosphonate affects the rate of beating in the same way as does eserine, causing arrest of the beat in concentrations from 10^{-3} to 5×10^{-3} Molar.

ACTION OF ESERINE IN HEART-LUNG PREPARATION

Dr. J. M. Walker and I have recently studied the action of eserine in the heart-lung preparation of the dog prepared by Starling's method. The medullary centres are excluded from the circulation, and the vagi are cut; so that there is no central control of the heart-rate, which depends on the impulses from the sinus node. The addition of eserine to the reservoir of blood (0·6 mg. in 600 ml.) to make a concentration of 10^{-6} caused the rate to fall. This fall was, in one experiment, from 122 per minute to 64 per minute in 10 minutes, at which lower level it remained (see fig. 2). The injection of 10 µg. of atropine sulphate restored the rate to its original level.

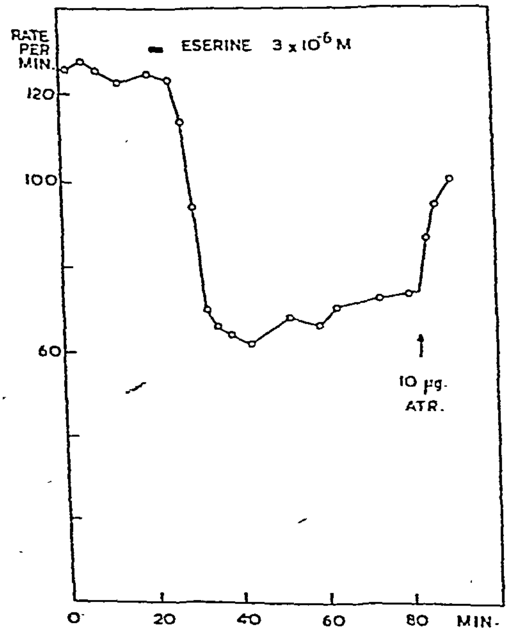

Fig. 2—Heart-rate in dog heart-lung preparation. 600 ml. of blood was in system. When eserine 0·6 mg. was added to the venous reservoir, the rate fell from 124 to 60 per minute. Rate rose when atropine 10 µg. was injected.

To make certain that this effect of eserine was not due to the presence of the vagal nerve-endings from which it was conceivable that some acetylcholine might still be liberated, we tested the effect of eserine in preparations made from dogs in which the vagi had been cut four days previously. Though larger amounts of eserine were necessary, the same decrease in the rate was observed when eserine was added to the blood, and the rate was again restored by atropine. Thus, when the cholinesterase in the heart was inhibited, the rate slowed. The only deduction which can be made from this observation is that the rate is governed by the production of acetylcholine which in the presence of eserine accumulates. Since the effect was seen 96 hours after section of the vagus nerves, the acetylcholine cannot have been liberated at the vagus endings.

IRREGULARITIES OF BEAT

The evidence thus far obtained indicated that there were conditions in which acetylcholine stimulated the rate and force of the beat and also conditions in which it depressed the rate and force of the beat. Eserine also exerted the same dual action. These observations are consistent with the view that the initiation of the beat is due to the formation of acetylcholine, which fires the conducted disturbance when its concentration reaches a certain threshold. On this view irregularities of the beat would be likely to be associated with irregularities of acetylcholine formation and would be modified by the application of acetylcholine or of eserine.

A systematic study of irregularity has not been made, because we do not know how to produce it at will. The effect of eserine was, however, observed in the isolated auricles, some preparations of which beat irregularly. In a concentration of 10^{-5} or 10^{-4} eserine was observed to convert an irregular beat to a regular beat. This change was observed sometimes without and sometimes with an accompanying change in amplitude. The change was sometimes accompanied by a slowing of the rate and sometimes by a quickening of the rate (see Burn and Kottegoda 1953). These results suggest that the irregularity was due to an irregular production of acetylcholine, so that sometimes a longer interval and sometimes a shorter interval was required to reach a concentration sufficient to set up the contraction wave. We may suppose that in the presence of eserine the destruction of acetylcholine was slower, and therefore the threshold concentration for the initiation of the contraction wave was always reached in a given time.

In the heart-lung preparation the injection of acetylcholine was found to correct and also to cause irregularity. Thus in a preparation freshly set up a 2 to 1 block persisted for 15 minutes, the auricles beating 152 a minute, and the ventricles beating 76 a minute. Injection of acetylcholine 4 µg. caused the block to disappear. On the other hand, in another preparation, in which eserine had been added to the blood so that the concentration was $1{\cdot}3 \times 10^{-6}$ g. per ml., the injections of 0·1 µg. and of 0·2 µg. of acetylcholine caused not only slowing but also irregularities of the beat.

Discussion

The evidence supports the theory that in the auricles of the heart acetylcholine is produced locally by choline acetylase and initiates a contraction when its concentration reaches a threshold value. The acetylcholine is then destroyed by cholinesterase, and the rate and force of the beat seem to be dependent on the balance between these two enzymes.

When Grey Turner (1929) reported the results of this operation in a detailed account of the progress of his patients he showed that many of them had unpleasant and serious complications He said that he was convinced that most of his patients developed some degree of ascending infection, and in the two necropsies that were performed there was definite and gross evidence of its existence, although neither patient had had symptoms indicating its presence He emphasised, however, his belief that a moderate degree of renal infection is not incompatible with average good health

It is plain from the reports of cases of long survival that the operation can yield good results there are instances of patients who have lived many years after transplantation of the ureters into the colon Nevertheless analyses of large series of cases, especially the comprehensive investigation made for the British Association of Urological Surgeons by Jacobs and Stirling (1952) clearly indicate that in general the long-term results are by no means satisfactory, at least half the patients have attacks of pyelonephritis, many have evidence of renal damage, and fully 80% show biochemical abnormalities Acidosis, demonstrated by an alkali reserve below the limit of the normal range, is found in 80–85% of patients A much smaller group show clinical evidence of acidosis that may end in coma and death

Because of the dissatisfaction felt with the standard operations of Stiles (1911) and Coffey (1911) there have recently been attempts to prevent stenosis at the ureterocolic junction (Nesbit 1949, Cordonnier 1949, Leadbetter 1951), but it is becoming plain that these have neither materially affected the incidence of ascending infection in the kidneys nor reduced the number of deaths from renal causes

Apart from recurrence of the disease for which the ureterocolic anastomosis is done, three factors seem responsible for many of the unhappy results

(1) Ascending infection with recurring attacks of pyelonephritis, ureteritis, and secondary stricture formation

(2) Primary stenosis at the site of the ureterocolic anastomosis, with hydronephrosis and renal destruction

(3) Biochemical disturbances probably caused by the absorption of urinary waste products from the large bowel, in association with renal damage

Each of these is a direct consequence of the implantation of the ureters into the large bowel

Cutaneous ureterostomy has been done successfully for many years, but the difficulty of collecting urine from two small stomata has led to its being little used Schnagel and Sewell (1948) have described the creation of spout ureterostomies in an effort to overcome this difficulty, but there has been no wide application of this method

After some experimental work in dogs (Annis 1952), in which it was shown that the small bowel could be used quite satisfactorily to take the place of, and act as, a ureter, we used a length of ileum, isolated from the intestinal tract, to collect urine from the ureters and to carry it to the skin-surface, where it drained into an ileostomy bag This operation was performed in patients who otherwise would have had a ureterocolic anastomosis The proximal end of this isolated length of ileum was closed, and the ureters were implanted into it The distal end protruded through a stab incision, and a Rutzen-type adhesive ileostomy bag was fitted We find that Bricker (1950) described a similar operation, but it was done as an alternative to a wet colostomy in patients in whom both the bladder and the rectum were excised He said that the patients were better able to manage a simple colostomy and an "ileostomy" that drained clear urine Our experience with the wet colostomy confirms this, but it has been our impression that biochemical changes occur less often in the patients who have a wet colostomy than after the usual ureterosigmoid anastomosis Perhaps this is because there is less pressure within the colon, and less delay in the expulsion of urine from it Bricker (1950) reported good results in 10 cases done since 1946 the patients were in good health, there was no azotæmia, and the intravenous pyelograms were normal He concluded that there was no justification for attempts to make an artificial bladder after pelvic evisceration when an adhesive bag could be quite manageable and satisfactory

It is too early to assess fully the results in our four cases, but they are encouraging

CASE-RECORDS

Case 1 —A man had a papilliferous tumour completely occupying the bladder

Operation (Professor Wells) —On Jan 4, 1952, the bladder was removed, a length of about 8 in. of ileum was mobilised, and the continuity of the small intestine was restored by end to end anastomosis The upper end of the isolated intestine was closed, and into it each ureter was implanted by direct mucosa to mucosa anastomosis The lower end of the isolated ileum was implanted into the side of the pelvic colon A valve was made at the ileocolic anastomosis in the hope of preventing reflux

Postoperatively the patient was discharged on Jan 28, passing urine from the rectum and feeling very well When he was seen a month later all seemed satisfactory The blood urea level was 33 mg per 100 ml, and the other biochemical factors studied were normal On intravenous pyelography both kidneys appeared normal The side limb of small intestine seemed to be effectively preventing regurgitation from the large bowel into the ureters, but in the course of the next three months the patient developed attacks of pyelitis Although he was in no worse condition than many patients who have had the conventional ureterocolic anastomosis, it became plain that this operation had not prevented ascending renal infection

Second Operation —On June 3 the loop of small intestine was detached from the pelvic colon and brought out as an ileostomy draining urine Since that time there have been no further attacks of pyelitis and the man feels well When seen recently he was having some difficulty in collecting urine from the ileostomy He is quite dry during the day, but there is some leakage at night The ileum was brought out through the lower end of the abdominal incision, and the bag does not fit closely to the skin In the other patients the ileum has been brought out through a separate stab incision, and this difficulty has not been encountered

Case 2 —A man, aged 38, was first seen by us in February, 1952 In 1942 he began to have attacks of frequency and scalding, which continued until, in 1945, he had a left epididymectomy and right nephro ureterectomy for tuberculosis After this operation he developed urinary fistulæ from the nephrectomy scar and a watering can perineum For seven years he had worn napkins to collect the urine and had passed none normally

On examination he was rather thin and pale On the perineum were four or five small openings, all leaking urine Intravenous pyelography showed a distended left ureter which appeared to be obstructed near the bladder, and the left kidney showed pelvic and caliceal hydronephrosis There was a thimble bladder The blood urea level was 26 mg per 100 ml, and a radiograph of the chest was normal No specimen of urine was examined for tubercle bacilli, because it could not be properly collected

Operation (W R Hunter) —On Feb 26, 1952, a low left abdominal incision was made in the shape of an inverted Y, the flap being turned down for the ileostomy A grossly dilated ureter was exposed and divided and about 9 in of the lower ileum 1 ft from the ileocæcal valve was isolated and mobilised with its blood supply intact (fig 1) The bowel was reconstituted by end to-end anastomosis The isolated loop of bowel was sutured end-to end with the ureter in an isoperistaltic fashion (fig 2) The anastomosis was laid on

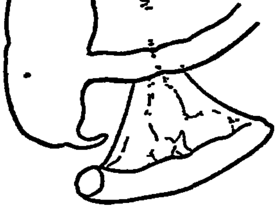

Fig 1.—Isolation of ileal segment

The theory depends in the first place on the demonstration that acetylcholine has more than one action, and that its effect is not merely to diminish the rate and force of the beat as when the vagus is stimulated. Acetylcholine will start the beat of the auricles when it has stopped, and increase the rate and amplitude. Moreover eserine, which inhibits the action of cholinesterase, will increase the rate of the perfused frog heart, and the rate of some preparations of the rabbit auricles. Eserine also increases the force of contraction of rabbit auricles proportionally to its concentration in the range 10^{-8}–10^{-4}. All these observations indicate that acetylcholine can initiate the beat and increase its rate and force.

The usual effect of acetylcholine in depressing the beat appears to be explained by the theory that there is an optimal concentration (or range of concentration) of acetylcholine both for the rate of beat and for the force of the beat. Acetylcholine in excess of this optimal concentration depresses both the rate and the force of the beat, in part by depressing its own synthesis. So far as the rabbit auricles are concerned when isolated and beating in a bath, the optimal concentration of acetylcholine for the most rapid rate of beat is different from that for the greatest force of beat.

The theory agrees well with what is known of the action of quinidine on the heart. This substance is used to restore a normal rhythm in auricular fibrillation. According to Prinzmetal et al. (1952) auricular fibrillation is due to the discharge of impulses at a high rate from an ectopic focus. Quinidine reduces the rate of discharge to such a point that it is less than the rate at which impulses leave the sinus node and the sinus node therefore resumes its normal function. Now quinidine is an antagonist of acetylcholine—i.e., it raises the threshold at which acetylcholine is effective. Its action in reducing the rate of discharge from an ectopic focus is precisely the action to be expected if the discharge is due to the initiation of impulses by the formation of acetylcholine at the ectopic focus. In the presence of quinidine the time taken for acetylcholine to be formed in sufficient concentration to discharge a contraction wave would be prolonged, and so the rate of discharge would fall.

It is probable that acetylcholine is concerned not only with the initiation of the rhythmic contractions but also with the conduction of the impulse and with the force of the contraction. Evidence concerning conduction is provided by the fact that quinidine decreases the rate of conduction, and also by the observations of Prinzmetal and his colleagues that the infusion of acetylcholine into the dog prevents the failure of conduction which otherwise occurs when the heart is driven electrically at very high rates. Evidence concerning the force of the beat is provided by our own observations on the action of eserine in increasing the amplitude of the contractions of the auricles. Further investigation on these points is obviously required.

The formation of acetylcholine in the auricles may take place either in nervous tissue or in non-nervous tissue. In 1924 Gray pointed out how close was the parallelism between the activity of cilia and of the sinus region of the excised frog heart. We have recently shown (Bülbring et al. 1953) that the ciliary movement in the nerve-free gill-plates of the sea-mussel mytilus is controlled by the local production of acetylcholine. The parallelism observed by Gray, then, suggests that in the heart the acetylcholine may also be produced in tissue which is not nervous.

Summary

Evidence is described which shows that the rhythmic contractions of the heart are due to the local production of acetylcholine. This is synthesised by choline acetylase, and when the concentration rises to a threshold value the wave of contraction is initiated. The acetylcholine is then destroyed by cholinesterase.

There appears to be an optimal concentration of acetylcholine for the maintenance of the beat, and amounts in excess of this optimum depress the rate and force of the contraction. This is the effect seen when the vagus nerve is stimulated.

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SURGERY IN SEVERE HYPERTENSION

A SURVEY OF RESULTS

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THE surgical treatment of hypertension demands careful collaboration with a physician, and our experience at the Westminster Hospital shows that, as regards the advisability of operation, physicians and surgeons are not always ranged in opposing camps. Nevertheless surgery has in late years had a bad press in Britain from physicians, as may be seen from the following opinions:

(1) "There is no doubt that sympathectomy sometimes leads to an improvement in the retinæ, renal function, and the electrocardiogram in patients with malignant hypertension, and it is possible that surgery is justified in these patients until medicine has something more satisfactory to offer. However, the overall results in hypertensive disease are disappointing and have been overestimated. This operation should not be advised for the treatment of hypertension other than in its severe and malignant stages" (Brigden 1952).

(2) "If we could only select with certainty those few cases which do respond we should be very pleased to continue recommending sympathectomy, but unfortunately all the preoperative tests to improve selection which have been tried seem to have failed utterly. We must reluctantly admit that a large number of quite useless operations have been performed and that there is very little prospect of any satisfactory improvement in surgical technique or selection in the near future" (McMichael 1952).

(3) "The results of sympathectomy may be briefly summarised by saying that in a very small group of cases the operation will produce results which cannot be obtained by any other means at the present time. It is still extremely difficult to predict the case in which the benefits will be worth while" (Platt 1950).

Against these we have the surgical opinion of Smithwick (1951):

"The evidence available at present indicates quite clearly that the prognosis for patients with hypertensive cardiovascular disease ranging from slight to marked is significantly improved by thoracolumbar splanchnicectomy."

And lastly what we may take to be a neutral opinion in the *British Medical Journal* (1952):

"There is now little doubt that surgical treatment has materially lowered the fatality-rate of hypertension."

the pelvic wall and covered with peritoneum, and the intestine was sutured along the left wall of the pelvis and brought out through the abdominal incision, being sutured to the parietal peritoneum along its length The right hand free edge of the mesentery of the isolated loop was sutured to the anterior abdominal wall A spout ileostomy was made, the skin pedicle being used on the under surface and a split skin graft on the upper surface This is not the ideal arrangement, but, had the incision been made to cover the upper surface with the skin pedicle, the epididymectomy scar would have transected the skin flap The wound was closed snugly round the isolated loop of intestine A rubber catheter was tied into the ileostomy Urine began to collect immediately

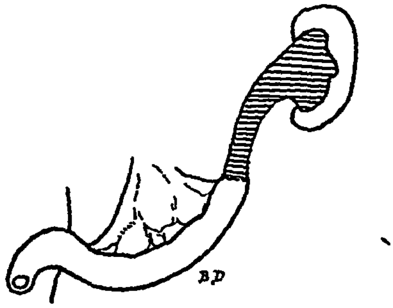

Fig 2—Implantation of single dilated ureter into ileal segment

Result—Convalescence was smooth, and he was discharged from hospital on May 11, after completing a course of streptomycin and *p* aminosalicylic acid All his sinuses were then dry He has remained well and put on 15 lb in weight in nine months All his fistulæ are dry, and urine collects satisfactorily in an ileostomy bag The CO_2 combining power and plasma chloride, plasma sodium, plasma potassium, and blood urea levels are all normal

Case 3—A woman, aged 71, had a papilliferous tumour involving the length of the right ureter and the bladder

Operation (Professor Wells)—On April 1, 1952, the right kidney and ureter and the bladder were removed About 12 in of ileum was isolated with its blood supply intact, and the intestinal continuity was restored by end to end anastomosis The proximal end of the isolated segment was closed and the distal end brought out to the skin surface The remaining ureter was implanted by a direct mucosa to mucosa technique into the upper end of this isolated length of terminal ileum Urine drained from the ileostomy immediately

Result—She made an uninterrupted recovery An adhesive Rutzen type ileostomy bag was applied, and urine collects in it freely When seen six months after the operation, she was very well and active The blood urea level was 32 mg per 100 ml, and the CO_2 combining-power and serum sodium, serum chloride and serum potassium levels were normal An intravenous pyelogram was normal and showed no hydronephrosis (fig 3) Mr H N Daniel, of Lancaster, writes "She is quite happy, comfortable, and doing house work and enjoying her life, and gets about and visits her friends The skin around the ileostomy is healthy and does not appear in any way soggy or excoriated She has a copious flow of clear urine from the ileostomy"

Case 4—A man, aged 44, complained of frequency and lower abdominal pain with hæmaturia for about three months Intravenous pyelography showed good concentration on both sides, with some right hydronephrosis and hydro ureter due to obstruction in its intramural portion There was a filling defect (fig 4) due to a papilliferous neoplasm, occupying the greater part of the bladder Cystoscopy confirmed this, and there were several other small papillomata on the posterior wall and another large one on the left lateral wall Biopsies showed no definite evidence of malignancy, Bimanual examination revealed a mass palpable in the bladder It was decided that nothing short of total cystectomy would be of any avail.

Operation (W R Hunter)—On Oct 23, 1952, through a midline infra umbilical incision a large mass was palpable in the right side of the bladder, but there were no palpable glands in the pelvis and no evidence of extravesical spread About 10 in of the lower ileum, about 1 ft from the ileo cæcal valve, was isolated, and the bowel was reconstructed by end to end anastomosis The proximal end of the isolated loop was closed The distal end was temporarily closed to prevent soiling the wound and was later used for the ileostomy opening The left ureter was isolated and was passed through the pelvic mesocolon and implanted into the isolated segment of small bowel by a modified tunnel procedure The isolated segment of bowel was now sutured along the brim of the pelvis from left to right until the right iliac fossa was reached The right ureter was isolated and was similarly implanted (fig 5) A U shaped incision was made in the right iliac fossa and a skin flap turned up, and after the muscles had been split the distal end of the isolated segment was delivered through the wound With several interrupted sutures the isolated segment of bowel was made to lie snugly in the right iliac fossa The several raw areas on the peritoneal surface were then reperitonealised The loop of ileum outside the abdomen was covered with the skin fashioned from the incision, and split skin grafts were applied to its under surface A catheter was tied into the segment of bowel to drain away urine Total cystectomy was done

Result—The patient's convalescence was smooth and he was discharged from hospital three weeks after the operation He wears an appliance to fit a spout ileostomy Intravenous pyelography five weeks after operation (fig 6) showed both kidneys to be working normally with still a little hydro ureter

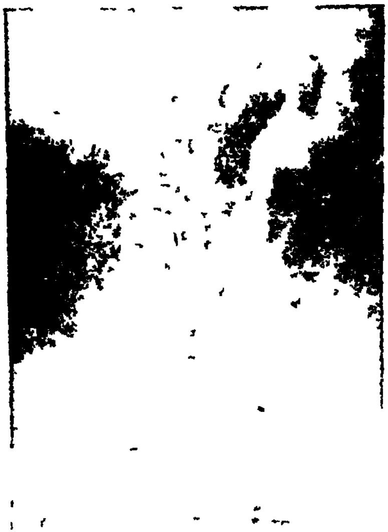

Fig 3—Intravenous pyelogram six months after ablation of right kidney, right ureter and bladder and implantation of left ureter into ileal segment (case 3) Arrow points to ileal segment

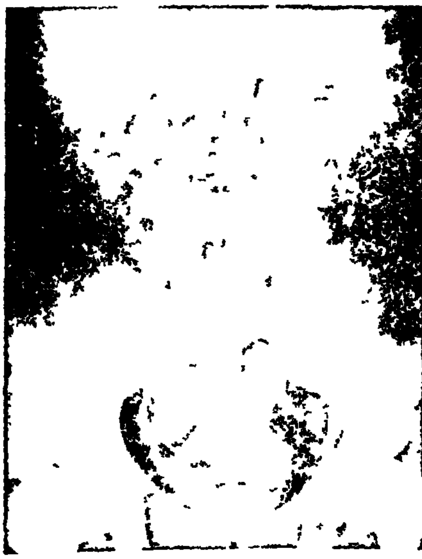

Fig 4—Intravenous pyelogram showing right hydro-ureter due to obstruction by vesical neoplasm (case 4)

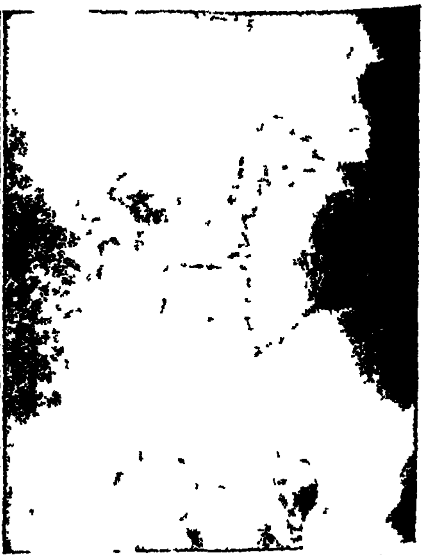

Fig 6—Intravenous pyelogram five weeks after operation (case 4)

ychological and prophylactic effect" of inducing dical experts on both sides to be careful in their sertions and claims, because these might always be viewed by an outstanding authority in their own ld.

For some years the State of Massachusetts has provided, civil proceedings, pre-trial examination of psychiatric ses by impartial medical specialists, and this arrangeent is said to be working well. The result of the ew and far wider experiment in New York may well fluence the development of practice in this country. ndeed, no legislative innovation would be required to troduce a parallel working system here, for under the ules of the Supreme Court (R.S.C. 0·37A, r.1) the court r a judge may already "in his discretion at any time n the application of any party appoint an independent xpert (to be called "the court expert") to enquire and eport upon any question of fact or of opinion not nvolving questions of law or construction." Unfortunately, applications under this rule have been but few nd far between, and it would perhaps be well if judges were given power to call in court experts from an ppropriately prepared list even where no such express equest is forthcoming from the parties.

TREATMENT OF BARBITURATE POISONING

SUICIDAL poisoning with barbiturate drugs is becoming increasingly common,[1] and the mortality may be high even in those who come under medical care. Nilsson in Sweden has shown the value of good medical treatment without convulsant drugs,[2] and Locket and Angus in this country have had similar results.[3] In their series of 84 patients who were not given convulsant drugs there were only 2 deaths. Analeptics are not a treatment for anoxia or asphyxia, and their value is obviously difficult to assess when survival may depend on the skill of the nurse and the doctor in managing an unconscious patient. Nevertheless it has become the practice to give analeptics for barbiturate poisoning because they reduce the mortality in poisoned animals; but then experimental animals do not enjoy the nursing attention that is the patient's right.

In comparing different analeptics the effect of chance on mortality-rates cannot be gauged when deaths are numbered in single figures. Mortality-rates depend on age, individual idiosyncrasy, and the condition of the liver and kidneys, as well as on more obvious factors such as the dose and type of the drug and the amount vomited. Hence little is to be gained from comparing the results of different workers, as Koppanyi and Fazekas[4] have done. They conclude in the end, largely from their own experience, that the best initial treatment is to give 5 ml. of a 10% solution of leptazol. If there is a response to this "orientation dose" they continue with the same dose given every 10 or 15 minutes. Otherwise they give picrotoxin 25 mg. followed by 15 mg. every 15 minutes, provided of course that convulsions are avoided. In general leptazol is more likely to be effective against the rapidly acting barbiturates, and picrotoxin against the slowly acting ones. Koppanyi and Fazekas do not recommend caffeine or nikethamide. Dick[5] discusses 160 reported cases and 11 of his own, all treated with amphetamine; and he favours this analeptic, if only because it is relatively safe. The Council on Pharmacy and Chemistry of the American Medical Association[6] point out that there are deficiencies in investigations of analeptics. Indeed, the evidence for giving picrotoxin at all must be judged inadequate by modern standards; and the cumulative effect of successive doses often means that too much is given, for it has a latent period of up to 30 minutes. On the other hand, leptazol acts quickly and for a short time, and it is often given in inadequate doses.

The use of ultraviolet absorption spectrophotometry has lately provided a satisfactory method of measuring the concentration of barbiturates in body-fluids. Apart from giving much-needed data on the distribution and excretion of barbiturates, this method may facilitate both treatment and diagnosis. By providing a measure of the severity of poisoning, it should make the comparison of the results of different treatments an easier matter.[7] Alwall et al.[8] in Lund have used the method to study means of increasing the elimination of barbiturates. The rapidly acting barbiturates are of course largely destroyed in the healthy liver, but the more slowly acting ones are mainly excreted in the urine. Alwall et al. were remarkably successful in speeding the elimination of phenobarbitone in poisoned rabbits by exchange ultrafiltration and by dialysis. Forced polyuria was less effective. They applied dialysis successfully in two patients, but the full details have not yet been given. Barbiturates are distributed throughout the body-water,[9] and it is unlikely that exchange transfusion[4] can aid elimination effectively; on the other hand where dialysis with an artificial kidney is practicable recovery may probably be hastened in patients poisoned with the longer-acting members of the group. But whether the mortality-rates can be improved with dialysis or with analeptics will remain in doubt until controlled clinical trials have been carried out.

RACIAL PREJUDICE

RACIAL prejudice is a powerful disruptive social force breeding violence and harming every community it touches: and its influence is becoming increasingly apparent in many parts of the world. There is every need therefore to understand its origins, to prevent its spread, and to control its manifestations. Unesco, as the international organisation charged with the spread of peace and goodwill through education, is trying to play its part by calling together a number of sociologists, anthropologists, and geneticists to prepare joint statements on the subject of race, setting out the scientific aspects,[10] and by publishing popular booklets to carry the facts to lay discussion-groups, school-children, and others who may benefit from this information. The latest publication is *What is Race?*[11] which explains the elements of genetics, with a wealth of attractive diagrams, and scientifically refutes some popular ideas of inheritance and the belief in a purer race. The scientists answer the three basic questions—Is there a pure race? Is there a superior race? and are there unchangeable race differences?—with a definite No. The word "race" is used here in the general sense of a group of human beings [illegible] with physically inherited characteristics differentiating [illegible] them from other human beings. But in everyday usage [illegible] race means a good deal more: it means, for instance, the classification of man by nationality, culture, [illegible] which colour [illegible] of his skin; and the class[illegible] may have little to do with his ancestry. [illegible] their own use and [illegible] another word for [illegible] different meaning.

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[illegible] *Fed. Proc.* 1950, [illegible] 65, [illegible] 112.

[illegible] Department [illegible] 1952. Organisation [illegible] produced a precipitous drop in the serum-calcium, followed by a gradual return toward normal levels within 6 hours, but when the animals had previously had the thyroid and parathyroid glands removed there was no appreciable return of the serum-calcium towards pre-injection levels The recovery phase of the oxalate-tolerance curve in nephrectomised dogs was, however, found to be the same as that in normal animals, so STEWART and BOWEN concluded that the parathyroid gland exerts a control over serum-calcium that is primarily independent of the kidneys Much other evidence [35] suggests, however, that the ability of P T H to raise the serum-calcium is greatly impaired in the absence of the kidneys, although the animal is then usually in a far from physiological state

DENT [36] has recently driven further nails into the coffin of the Albright theory as the sole explanation of parathyroid action He confirmed that in normal men any phosphorus diuresis after injections of P T H was only slight, and he found that the serum-calcium rose, whereas the serum-phosphorus tended to fall only if it was originally high (as it was in the hypoparathyroid cases studied by ALBRIGHT) Artificial lowering of the serum-phosphorus did not lead to a rise in serum-calcium to maintain the solubility product, and hyperparathyroidism with renal failure and raised serum-phosphorus may be followed by the typical bone changes of von Recklinghausen's disease If ALBRIGHT's suggested sequence of changes were correct, one would expect osteomalacia and not osteitis fibrosa to result Very recently STEWART and BOWEN [37] have shown that preparations of P T H inactivated by formaldehyde with respect to their power to raise the serum calcium still increase the urinary phosphorus output in dogs That this phosphorus diuresis is an artefact is suggested by the similar results when extracts of spleen and thymus are administered DENT [36] has further drawn attention to the apparently irrational dissociation of the bone changes in hyperparathyroidism from the changes in the blood-electrolyte levels, and has suggested (as did L'HEUREUX et al [38] on the basis of electrophoretic studies) that there may be more than one parathyroid hormone, and these may differ in the locus of their actions

It seems clear that parathyroid extracts can act directly on bone and on kidney, and perhaps too much attention has been focused on which of these actions is primary, for the work of MARTIN and PERKINS [39] suggests that P T H may have a quite different primary action MARTIN [40] has obtained data which seem to show that in some cases of hyperparathyroidism the calcium binding power of the serum-albumin is more significantly and consistently increased than in other cases which in turn significantly exceed normal values After surgical treatment of the hyperparathyroidism the calcium-binding power of the serum-albumin usually returns to normal in cases without demonstrable persisting renal damage Perhaps such changes in the calcium-binding power of the body-proteins may explain the metabolic actions of P T H

Annotations

THE COURT EXPERT

IF two doctors were to disagree about a diagnosis, it would be patently absurd to call in a layman to settle the issue between them Yet, as we suggested a year or two ago,[1] something hardly less peculiar happens in legal proceedings whenever irreconcilable opinions are expressed by medical experts engaged by the opposing sides Sometimes, it is true, both parties may accept a written report prepared by a member of the medical profession, but in many important trials whose outcome largely depends on scientific evidence, there is a hiatus in specialist opinion which has to be bridged by judge and/or jury finding their own solution of a technical problem

Medicine being an applied science, it seldom deals with facts from which only one inference is possible Moreover, medical evidence can seldom be visibly and conclusively demonstrated to the court This is true not only where sanity or mental disturbance is in question, but in almost every case where a medical opinion involves forecasts or is the result of laboratory investigation which goes beyond simple observations Being unable to verify his statements, judge and jury must rely on the intelligence and professional conscientiousness of the expert witness Accordingly the court has to concentrate on testing his impartiality and competence

Much interest therefore attaches to an American experiment in which the Supreme Court of New York will appoint court experts other than those chosen by the contesting parties [2] For some time past, United States courts, in dealing with medical expert evidence, have had difficulties similar to those encountered in Great Britain but perhaps even more sharply focused In the United States almost all the testifying is done by a very small proportion of the doctors, and the fees asked sometimes depend on the expert's rhetorical gifts as much as on his professional skill and eminence The preparation of experts' reports for each party, moreover, is one of the principal causes of delay in the disposal of cases where a personal injury has been sustained and where it is necessary to estimate future incapacity In these circumstances, the plan to be tried for a year in New York aims at "better and quicker justice" for the solution of conflicting medical claims, by avoiding the former system under which "a plaintiff's doctor may tend to describe his patient as just about killed while the defendant produces a doctor who hardly finds scratches" The leading professional State organisations the New York Academy of Medicine and the New York County Medical Society, have agreed to appoint a panel of about sixty experts of the highest standing in the various branches of their profession, including orthopedics, neurosurgery, neurology, and psychiatry, on whose knowledge and aid the courts can call whenever the need arises If in the preparation of the trial it is found that the medical claims of the two parties differ widely, the judge will, on his own initiative, assign an expert from the panel to examine the plaintiff and to provide a written report which will be available both to the court and to the two parties This expert is not a referee such as we have in this country under the Workmen's Compensation Acts His report is not binding on the court, nor are the parties precluded from cross-examining the expert in person at the trial or from calling in other experts of their own choosing, though it is expected that the court expert's report will often be accepted by all concerned, since it offers from the outset high guarantee of impartiality and competence Finally it is hoped that the new system will have "the

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[1] *Lancet* 1951 ii 481
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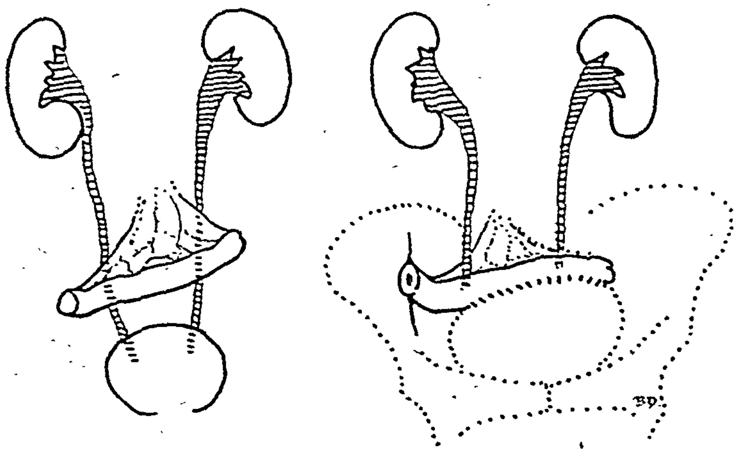

Fig. 5—Implantation of both ureters into isolated ileal segment (case 4).

on the right side. The patient is now well and his blood-urea is 36 mg. per 100 ml.

DISCUSSION

We have treated four patients by this method. In case 1 pyelitis had developed after an isolated segment of ileum was used as a conduit between the ureters and the colon. Once the distal end of the ileum was separated from the colon and drained externally the pyelitis quickly cleared, and the patient has remained well. We feel this can be accepted as positive proof that the colon is the exciting cause of the infection. In this case the external ileostomy provided drainage good enough to allow the infection to clear. So far there have been no recurrent attacks.

In case 2 a solitary left-sided hydronephrosis with gross hydro-ureter followed removal of the other kidney for tuberculosis. It is generally agreed that the transplanting of a grossly dilated ureter into the large bowel is unsatisfactory. If one of the tunnel methods is used, the technical difficulties of getting the whole of the cut end of the ureter into the bowel are almost insurmountable. If an end-to-side anastomosis after the Nesbit operation is done the operation is less difficult, but the chance of an ascending infection is very high. In the present case the ureter was dilated to about 1 in. in diameter, and from earlier notes we found that a hydro-ureter had been present for at least five years. A direct end-to-end anastomosis between the cut end of the ureter and the proximal end of the isolated segment of bowel was the method adopted in this case (fig. 2). It seems that this method of dealing with hydro-ureter and hydronephrosis of the solitary kidney in tuberculosis offers better prospects than any method of implantation into the large bowel. There is certainly less risk of infection, and even when only a small segment of ureter remains above ureteric strictures the method can still be used.

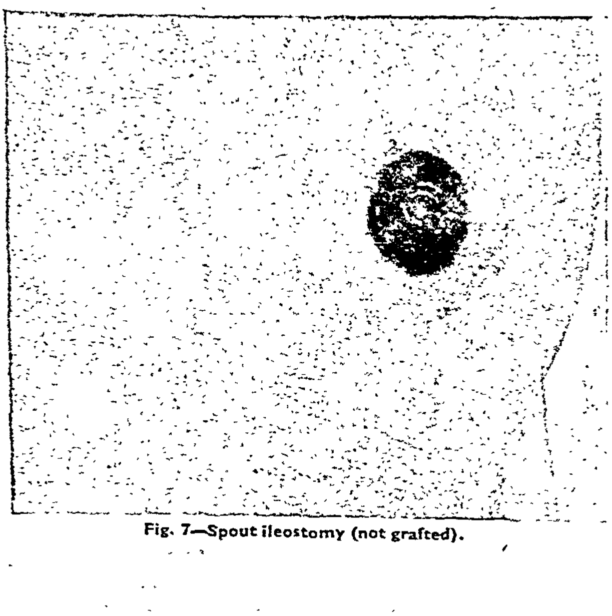

Fig. 7—Spout ileostomy (not grafted).

In cases 3 and 4 transplantation was done for bladder growths.

Preoperative preparation has been with succinyl sulphathiazole and streptomycin by mouth. In all the cases a segment of lower ileum was used and the bowel continuity was restored by end-to-end anastomosis (fig. 1). The length of the isolated segment was estimated by previously applying it along the path in which it would finally lie.

The method of implanting the ureter into the bowel can be either of the mucosa-to-mucosa type, especially if the ureter is slightly dilated, or, as in case 4, a tunnel procedure. Since the risk of reflux is very small a valve is not needed, and the formal anastomosis is probably the better since it is very unlikely to lead to stricture and allows immediate free drainage.

The management of the isolated loop in the peritoneal cavity has varied. In some instances it has been allowed to lie free, but in the later cases it has been closely sutured to the pelvic brim and the iliac fossa on the side on which the ileostomy was to be made (fig. 5). This method has worked satisfactorily and has left no foramina through which gut might herniate. Some of the terminal ileostomies have been made with a small mucosal spout (fig. 7) and others have had a spout covered with skin. It is advisable to have the covered spout about 2 in. long, with its upper surface covered by full-thickness skin with the immediate split-skin graft applied to the under surface. If this technique is adopted the inevitable slight contraction of the graft tends to make the spout turn downwards and fit nicely into the urinal (Wells 1952). These patients have remained dry and comfortable with a close-fitting ileostomy bag (fig. 8). With the flush ileostomies an adhesive bag has been used.

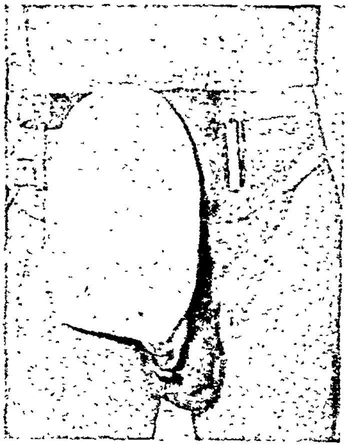

Fig. 8—Ileostomy bag.

After operation urine has flowed freely in $^1/_2$–1 hour. Urine drips constantly; and every few minutes, with contraction of the intestine, it spurts out.

Technically the operation is not difficult; but, compared with ureterocolic anastomosis, more care is needed to secure hæmostasis when dealing with the implant into the small intestine. Unlike the colon, which is relatively avascular, the small intestine bleeds freely.

Although in cases 3 and 4 the implantation and cystectomy were done in one operation, there is no reason why the cystectomy should not be done later. If this were decided, it would be better to bring out the ileostomy in the right or left iliac fossa.

After the operation no patient has shown clinical evidence of pyelonephritis or of renal destruction; all have intravenous pyelograms similar to the preoperative pictures; none have shown any of the biochemical

THE LANCET

LONDON SATURDAY, JUNE 13, 1953

Cation-exchange Resins

A CATION-EXCHANGE resin is formed by the condensation of many molecules of either carboxylic or sulphonic acids to form a high-molecular-weight polymer This is insoluble in water and has many free valency bonds, about half are linked to water, but the rest are available to combine rather loosely with different cations, including hydrogen When a column of resin charged with one cation, such as sodium, is exposed to a solution of the salt of another cation, such as potassium, the sodium and potassium will "exchange,' leaving the resin charged with potassium, if enough potassium-containing solution has been used to perfuse the resin column If instead of using a large quantity of potassium-salt solution, the sodium-charged resin is merely immersed in a solution of potassium salt, an equilibrium will be attained which will depend on the concentration of potassium in the solution, and on the "affinity" of the resin for the different cations In general, resins have most affinity for divalent cations, such as calcium and magnesium, and, among monovalent cations, for potassium, sodium, ammonium, and hydrogen in that order In-vitro experiments indicate that some resins may combine with 5 m eq of cation per g of resin, but when resins are ingested by patients, their power to combine with cations is of the order of 2 m eq per g of resin[1]

Three years ago we noted that, among other applications of exchange resins to medicine, they could be used to withdraw sodium from the diet, and so to permit a more liberal and varied regimen for patients undergoing salt restriction[2]—an application first suggested by DOCK[3] on the basis of experimental work In 1950 suitable resins were becoming available for medical use in this country, but few accounts of their use had been published This deficiency has now been repaired almost to the point of embarrassment, the metabolic effects of exchange resins have been intensively studied,[1 4 5] the clinical indications have been more closely defined,[6–8] and certain hazards of long-continued administration have become apparent[9] Most of the patients studied have been in cardiac failure with œdema,[10] or have had massive œdema due to primary renal disease[11] The resin has been used in conjunction with a low-salt diet, and earlier balance studies[12] suggested that it simply prevented absorption of sodium from the diet but other work has shown at times a fæcal excretion of sodium greater than the dietary sodium[8] The main action of the resin is however, in preventing absorption of sodium, and actual depletion of body sodium takes place mainly by urinary excretion There is some evidence that such excretion may be enhanced in resin-treated patients, and in some cases which have become resistant to mercurial diuretics, resins may restore excretion of sodium after injection of such a diuretic Most of the resins used are in the hydrogen or ammonium cycle, and so have an acidifying effect, they may thus counteract the alkalosis that arises during prolonged mercurial treatment, which is strictly chloruretic rather than natriuretic, simple correction of alkalosis has been observed to restore the diuretic response to mercurials[13] Thus, summing up the credit side of the therapeutic use of resins, it would seem that they are useful adjuvants to a low-sodium diet, and they may restore the diuretic response to mercurials in patients with alkalosis

On the debit side, the original hydrogen-loaded resins caused buccopharyngeal irritation, but this has been controlled by the use of resins in the ammonium cycle Potassium depletion has been observed after some months of treatment with resins,[9] but this can be prevented by giving part of the resin in the potassium cycle A much more serious danger of long-continued resin treatment, when combined with mercurial diuretics, is the production of the "low-salt' syndrome, first described by SCHROEDER,[14] in which, although œdema persists, the actual circulating plasma becomes depleted of salt, this "central salt depletion' exerts its usual unfavourable effects on cardiac output and renal function Patients with this syndrome may occasionally respond to infusion of hypertonic saline[15] or potassium[16], but generally its onset indicates that biochemical tinkering can no longer delay the progress of cardiac failure From their experience of prolonged treatment with resins of patients with congestive heart-failure, GREENMAN et al[9] suggest that for about six months these provide a relatively safe supplement to the basic therapy, but that thereafter "hyponatræmia, hypopotassæmia, and hypocalcæmia are frequently observed"

A less usual, but much more decisive, application of cation-exchange resins in medicine is for the treatment or prevention of potassium intoxication in patients with anuria or severe oliguria ELKINTON et al[17] showed that resin given in a dose of 50 g. per day in the ammonium cycle lowered the serum-potassium, it was best given orally, but some effect could be obtained by rectal administration Here again, resin treatment is not a substitute for the very effective protein-free and electrolyte-free diet of BULL et al[18], but it is a useful addition to their regime when the serum-potassium increases dangerously changes that are associated so often with ureterocolic anastomosis.

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SUMMARY

Each of four patients has had the ureters implanted into an isolated length of ileum, through which urine was brought to the abdominal wall to collect in an ileostomy bag.

In two patients the operation was done in association with total cystectomy for carcinoma of the bladder.

In a third it was done after nephro-uretero-cystectomy for diffuse papillomatosis; and in a fourth it was done for multiple urinary fistulæ following nephrectomy for tuberculosis.

All the patients are happy and well; and except in case 1, in which the technique was faulty, there has been no difficulty in keeping dry and in collecting urine in the ileostomy bag.

No patient has shown evidence of the many complications that are known to follow ureterocolic anastomosis.

This method has given us fresh confidence in approaching the operation of total cystectomy and the other procedures where urinary deviation is necessary.

ADDENDUM

Since this article was submitted for publication the operation has been carried out in five other patients.

We wish to thank Miss Barbara Duckworth for the line drawings and Mr. Wilfred Lee, of the University Central Medical Photographic Department, for the reproduction of the radiographs.

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AN ARTIFICIAL BLADDER

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BILATERAL cutaneous ureterostomy has been proved by general experience to be very unsatisfactory. The mechanical difficulty of collecting the urine from both sides and keeping the patient dry, and the frequent stenosis of the orifices and attacks of ascending renal infection, render subsequent existence often short and always irksome and unpleasant. When, therefore, the bladder is removed by operation, or put out of action by disease, the orthodox procedure is to transplant both ureters into the sigmoid colon. Such patients can lead normal and comfortable lives and die many years later from unrelated diseases, as did one of my patients from coronary thrombosis fourteen years after total cystectomy for carcinoma of the bladder. In these cases the colon has really been reverted to an early developmental stage of a cloaca containing both fæces and urine. It is surprising, however, how many of these patients learn to know when they are going to pass flatus, urine, or fæces. The use of antibiotics has rendered the old danger of attacks of ascending renal infection much less of a menace than formerly.

Because in some cases of extensive pelvic malignant disease it is necessary to remove the lower bowel in addition to the bladder, the formation of some type of artificial bladder had been contemplated. Much experimental work on this subject has been reported from America (Bisgard 1943, Bisgard and Kerr 1949, Rubin 1948, Bricker 1950). Glaser (1952) in this country has recently reviewed the subject. Very few clinical successes have been reported and, so far as I am aware, none have been reported in this country.

METHODS

The following methods are available:

(1) *With preservation of urethral sphincter control.*—In this method the ureters are transplanted into an isolated loop of sigmoid colon, of which the upper end is closed and the lower end is anastomosed to the urethra or to the bladder neck. The continuity of the colon is, of course, restored. So far as I know, this method has only been practised on animals.

(2) *With preservation of anal sphincter control of rectal artificial bladder and establishment of terminal colostomy.*—Some urologists in this country regularly practise this method with total cystectomy. The sigmoid colon is divided and a terminal colostomy fashioned. The ureters are transplanted into the lower part of the colon, of which the upper end is closed. Those who use this method believe that a terminal colostomy is a small price to pay for a smaller risk of ascending pyelonephritis than after orthodox bilateral uretero-sigmoidostomy.

(3) *Skin stoma only of artificial bladder with no sphincter control.*—Here the ureters are transplanted into an isolated loop of small or large bowel, of which one end is closed and the other brought out on the surface of the abdomen. Such patients, of course, have no control over the urinary discharge and must always wear a bag. By making the superficial end of the bowel project a little distance beyond the skin, and by grafting its surface, a Rutzen bag can be made to fit well and to be far less trouble than might be expected.

(4) *Skin stoma only of artificial bladder with sphincter control of ileocæcal valve.*—In this method the ureters are transplanted into the isolated right colon, the right end of the divided transverse colon is closed, bowel continuity is restored by ileo-transverse colostomy, and the distal end of the divided ileum is brought out on the skin-surface as a terminal ileostomy. *Continence depends on the competence of the ileocæcal valve.* In the case reported below this procedure was very satisfactory, the valve being very competent. However, I believe from experience of cases of large-bowel obstruction that the ileocæcal valve is competent only in about 50% of people. It might be worth while, therefore, to prove the competence of the ileocæcal valve by barium enema in every case in which the formation of an artificial bladder from the right colon is contemplated.

INDICATION

The indication for the operation is an extensive malignant pelvic disease in which any chance of cure entails removal of all the pelvic viscera. Though this extensive operation at present is only done in the advanced and hopeless cases, it is likely that by performing it in borderline cases of carcinoma of the rectum, bladder, or uterus, long-term cures would become more common. Perhaps also in cases of urinary fistulæ following malignant infiltration and radiation therapy the formation of an artificial bladder would render life at least tolerable. Occasionally also when the central nervous control of the bladder and rectum has been destroyed, and the resultant sepsis has reduced the capacity of the bladder to that of a mere thimble, as in the case described below, the formation of an artificial bladder could be the bridge from chronic invalidism to an active and useful life.

CASE-RECORD

Miss A, aged 26, was first seen by me at the urological clinic of the Manchester Royal Infirmary in January, 1950, complaining of frequency and precipitancy of micturition for a month. She could not hold the urine for more than thirty minutes during the day and she had to get up many times at night.

She was referred by Dr. Fergus Ferguson, under whose care she was first admitted to the Manchester Royal Infirmary in December, 1945, having had sudden onset of weakness of

Ureteric Transplantation

In the past few years surgeons have been expressing increasing dissatisfaction with the present operations for transplanting the ureters into the large bowel Last year we drew attention to the electrolyte disturbances which may follow the operation[1] the early reports of Ferris and Odel[2] have been repeatedly confirmed, and the recent survey by the British Association of Urological Surgeons of the late results of ureterocolic anastomosis has revealed that, of the cases suitable for analysis, nearly 80% showed some degree of acidosis following operation[3] Many patients with electrolyte disturbances do not show any overt symptoms or signs, but occasionally very serious or even fatal consequences may arise Even in the absence of obvious sequelæ a chronic state of acidosis cannot be regarded with complacency, especially in young children in whom there may be long-term effects on skeletal growth[4 5] The cause of the electrolyte disturbance is still disputed Whilst reabsorption from the bowel is the most widely accepted explanation, many workers[6 7] contend that renal tubular damage resulting from ascending infection plays an equally important rôle Wilkinson[8] has suggested that the primary defect is excessive loss of potassium from the bowel, owing to increased colonic secretion in response to the presence of excessive fluid In addition to the electrolyte disturbances, many other complications may follow the operation Last year's survey[3] showed that complications occurred in 41 4% of the 1673 cases reviewed, 12 6% were the complications of any major operation, whilst the remainder were particularly related to this type of operation and included such conditions as urinary fistula and pyelonephritis The over-all postoperative mortality in the 1673 patients was 21 1%, but, excluding operations for carcinoma, the mortality was 11 5% The mortality figures were not significantly affected by the particular technique of anastomosis, although it was thought that the newer methods of direct anastomosis[9 10] showed promise of being free from many of the defects of the earlier procedures of Coffey[11] and Stiles[12]

With so many hazards it is not surprising that surgeons have been exploring other methods of diverting the urinary stream from the bladder Direct cutaneous ureterostomy is dangerous and unpleasant, making life a burden for the patient Construction of an artificial bladder from a segment of the bowel is, in theory, an attractive solution, but it presents many technical difficulties The earliest experiment on the formation of an artificial bladder was that of Tizzoni and Foggi[13] in 1888, and the operation was first performed on man by Verhoogen[14] in 1908, using a segment of ileum as a bladder and draining it through an appendicostomy The patient died shortly afterwards Other attempts have since been made, but with little success With the increasing scope o cancer surgery, operations for pelvic evisceration hav become increasingly common The "wet colostom which is produced when ureteric transplantation i combined with a colostomy following excision of th lower bowel and the bladder is difficult to manag with comfort, and Bricker[15] therefore revived a early operation and did a ureteric transplant int an isolated loop of ileum, which drained through a ileostomy, together with a separate "dry" colostom He found that patients managed better with tw separate artificial orifices than with a combined one they remained in good health, and up to four year after operation there was no evidence of hydro nephrosis Glaser[16] has recently reviewed the subjec of the artificial bladder and described two main group of procedures By one urethral function is preserved a length of bowel being substituted for the bladde and anastomosed to the ureters above and to th urethra below This operation has been done only o animals[17 18], it is technically difficult, and th indications for it would be very few The other grou or procedures involve substituting for the bladder a length of bowel draining through a skin stoma Th artificial bladder could be fashioned from the ileum from the ileocæcal region, or from a portion of colo alone The indications for this operation would b mainly extensive pelvic cancer or, occasionally intractable vesicovaginal fistula The advantage claimed for the separation of the urinary and fæca streams are that the danger of ascending infection i diminished, the area of mucosa exposed to urine i very much reduced and therefore electrolyte reabsorp tion will be lessened, and the pressure built up insid the artificial bladder will be much less than that which develops in the colon, especially during defæca tion, and so there will be much less risk of regurgitation up the ureters As Annis[19] points out, the indications for establishing a substitute for a ureter alone ar very few, but occasionally it may be possible to preserve a fairly healthy kidney by excising a diseased ureter and replacing it with a length of bowel Davids and Lesnick[20] report successful experimental ureteric substitution in dogs, and suggest that this technique may prove useful in conditions such as penetrating injuries of the ureter, surgical injuries, ureteric tumours, either primary or due to extension from other organs, and ureteric stenosis following healing of a tuberculous ureteritis

This week we publish four papers dealing with the application of these techniques to man Dr Foret and Dr Heuschen report a case in which both ureters were partly replaced by a single isolated loop of ileum Their technique differed from the experimental ones of Annis and Davids and Lesnick in that the base of the intestinal loop was anastomosed to the bladder apparently leaving a free communica tion between the two ureters Their patient survived operation and was in normal health a year later The other three papers all deal with the construction of an artificial bladder Mr Annis and his colleagues did the operation in 9 cases as an alternative to ureteric transplantation The ureters were anastomosed to an

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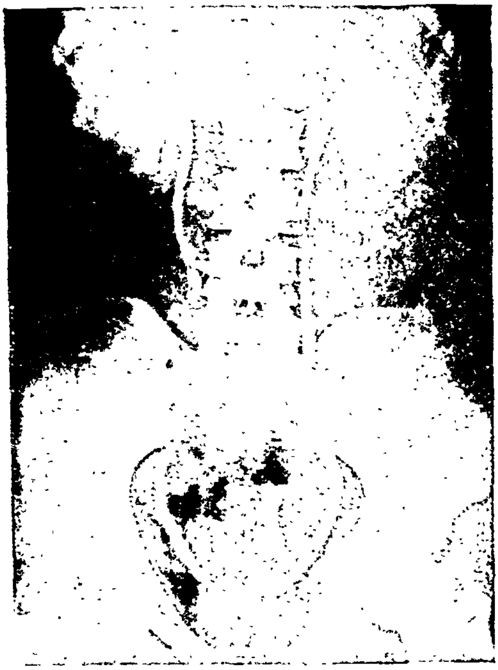

Fig. 1—Intravenous urogram showing gross dilatation of ureters, pelves, and calices on both sides, and a tiny contracted bladder.

the legs and disturbance of bladder function. She was then found to have transverse myelitis at the level of D10, and she was in hospital and a convalescent home until November, 1946. On discharge she had bilateral spastic paraparesis and pes cavus but could walk fairly well with a stick, and, though normal bladder sensation was absent, she had sufficient awareness of the desire to void to be socially normal and to carry on her occupation as a cashier. She was kept under regular observation by the neurological department of the Manchester Royal Infirmary and seen at short intervals. The improvement in her condition was maintained. During 1947 she had trophic ulceration of both feet, but this healed with simple treatment. In 1948 she had intermittent cramps in the legs and for some time received weekly injections of curarine, with considerable improvement. In December, 1948, she underwent an operation for lengthening the right tendo Achillis. After this she continued work without interruption until January, 1950, when she was readmitted under Dr. Fergus Ferguson because of great deterioration in her urinary condition.

Investigations

On examination I found her in good general condition, with clean and moist tongue and no obvious abnormality of the alimentary, respiratory, cardiovascular, or urinary systems.

Her urine was normal on microscopy and on culture. Her blood-urea level was 40 mg. per 100 ml., and urea clearance was 76% of average normal. On cystometrography the pressure rose to 50 cm. of water with less than 1 oz. of fluid in the bladder. The fluid then began to leak along the side of the catheter. Cystoscopy showed a small bladder containing less than 2 oz. of urine. The mucosa showed diffuse areas of erythema. Both ureteric orifices were normal. No trabeculation was seen. There was no relaxation of the bladder neck. The external urethral sphincter was lax, and the patient had no urethral or bladder sensation. During the cystoscopy the bladder capacity could be increased to 8 oz. by hydrostatic pressure. Ordinary radiography and intravenous urography showed good function of both kidneys but considerable ureteric, pelvic, and caliceal dilatation. The cystogram showed that the bladder was of very small capacity (fig. 1).

It was decided to test the capacity of the rectum to act as an artificial bladder, and many tests were made. The rectal sphincter had fair tone, but the anal canal had no sensation. On many occasions, about 10 oz. of fluid was instilled into the rectum, but the patient had no power to hold it at all. In an attempt to keep the patient dry an inlying urethral catheter was used for several weeks, but urine often leaked alongside it. The patient was eventually transferred to the Withington Hospital under my care on Sept. 7, 1950, when further investigations were made. A blood-count showed 4,630,000 red cells per c.mm., Hb 81%, and white cells 5000 per c.mm. The urine contained a moderate number of red cells and white cells, and on culture gave *Bact. coli*. The blood-urea level was 44 mg. per 100 ml. Cystometrography showed a very hypertonic bladder which would hardly hold any fluid without emptying alongside the catheter. There seemed to be complete absence of bladder sensation.

Progress

About this time the patient had a severe attack of ascending pyelonephritis, due to *Bact. coli*, which responded to sulphonamides. Further tests of the rectal continence showed that ureteric transplantation would be of no avail.

Suprapubic cystostomy.—After a consultation with Dr. Ferguson, although it did not seem likely that a suprapubic cystostomy could be of much benefit to the patient, it was decided to give it a trial. The operation was done on Sept. 20, 1950, under general anæsthesia. The patient made good progress and was discharged on Nov. 11, 1950, having been fitted with a Millin suprapubic bag. For a short time she appeared to be much more comfortable but then urethral leakage started again.

Millin sling operation.—On readmission on Dec. 13, 1950, retrograde cystography showed a very tiny bladder with reflux up both ureters. As ureteric transplantation was fraught with the danger of rectal incontinence; and there was the secondary possibility of ascending renal infection, it was decided to try and tighten the urethra. Riches has sometimes done this in cases of neurogenic bladder with a very lax urethra (Riches 1951). On Feb. 26, 1951, I did a Millin sling operation on the urethra through a transverse lower abdominal incision under general anæsthesia. The patient made good progress after this and was discharged on April 4, 1951. She had had no incontinence since the operation, and abdominal exercises had improved the tone of her muscles very much indeed. She went back to work and was fairly comfortable.

Obliteration of urethra.—Readmitted on Oct. 3, 1951, because of further urethral leakage, she pleaded that the urethra should be obliterated. I was not very keen to do this, because it meant that the suprapubic cystostomy would definitely be permanent, and I always lived in the false hope that the nervous disease might recover. However, on Oct. 11, 1951, I exposed the urethra from below under general anæsthesia, ligatured it, and sutured the superficial tissues together over it. The patient was very well afterwards but started to leak again on Nov. 3. Further attempts to obliterate the urethra were made on Nov. 15 and Dec. 6, and again were unsuccessful.

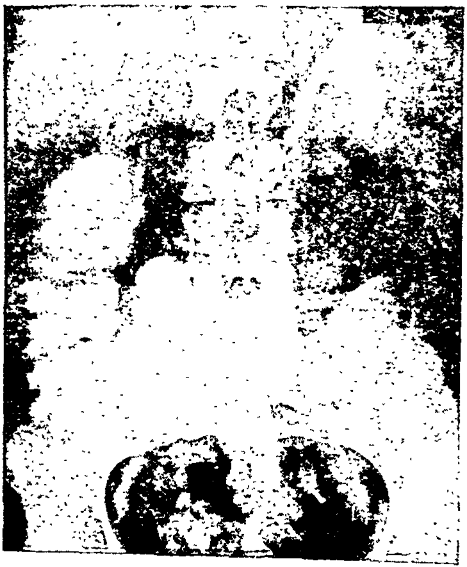

Fig. 2—Intravenous urogram with retrograde cystogram of artificial bladder showing good function of both kidneys. Right kidney has returned nearly to normal; left kidney is still considerably dilated.

isolated loop of ileum. This was brought to the surface as a flush ileostomy, or else a spout was fashioned; in either case it was possible to fit a satisfactory ileostomy bag. All of these cases have been free from trouble up to the time of reporting. In the 1st case a *transplantation operation was done at first, using a* loop of ileum as a bridge between the colon and the ureters. It was hoped by this means to prevent regurgitation from the bowel up the ureter, but, although there was no radiographic evidence of such regurgitation, the patient developed attacks of pyelitis. After the ileal loop was separated and brought to the surface, there were no further attacks. Mr. MOORE had the difficult problem of treating a contracted paralytic bladder in a patient who had had transverse myelitis and who was unable to hold even a small volume of fluid in her rectum. He constructed from the ascending colon an artificial bladder draining through an ileostomy. As the ileocæcal valve was competent his patient was able to hold urine in her bladder for two hours. Her progress was very satisfactory up to the time of reporting five months later. BRICKER[21] failed to produce a continent intra-abdominal urinary pouch and has now abandoned the attempt. He prefers to use a short ileal loop as a conduit rather than a storage receptacle, since this lessens the risk of a stagnant pool of urine becoming infected and also reduces both the area of mucosa available for reabsorption and the length of time that urine is exposed. The last paper, by Dr. WILSON, is a careful study of a single patient who developed a temporary electrolyte disturbance after transplantation of the ureters into an isolated loop of ileum. EISEMAN and BRICKER[22] have studied the absorption of electrolytes from isolated ileal loops before and after implantation of the ureters. Urea and chloride were both absorbed, although the absorption was relatively slow; and they pointed out that, provided the loop is fairly short, the quantities absorbed would not be enough to produce any distinct changes in the serum chemistry. The fact that the changes in Mr. MOORE's patient were only temporary would suggest that some other factor than simple reabsorption of electrolytes was the main cause. Whether this factor was impairment of renal function or, as he suggests, some change in the function of the ileal mucosa cannot be decided with certainty.

As yet few patients have had this type of operation and the period of observation has been too short for proper assessment. HIGGINS[23] found in dogs that when the isolated lower segment of the rectosigmoid was used as an artificial bladder it contracted down after two years so that its capacity was practically nil. So far there have been no reports of late contractions of the artificial bladder in man, but careful follow-up studies will be needed to clarify this point. MITCHELL and VALK[24] declare that "diversion of the urine to the bowel is much too valuable a procedure to be abandoned because of a resulting abnormality in the body chemistry"; but this is only one of the many troubles that may follow ureteric transplantation into the colon, and there is a clear need for further investigation, both clinical and experimental, of alternative procedures.

Annotations

THE DENTISTS AND THE MINISTRY OF HEALTH

THE decline in demand for treatment following the imposition of charges in the National Health Service cannot yet be said to have had a decisive effect upon the recruitment of dental officers to the school dental service, whose staffs were so seriously depleted in the early years of the N.H.S. Though the number of school dentists in England, Wales, and Scotland has risen from the equivalent of 817 full-time officers in January, 1952, to 998, this trend cannot be expected to continue long enough to bring substantial relief to a service nominally responsible for the dental care of $5^1/_2$–6 million children. The ground lost since 1947 has not yet been recovered, and, as the numbers of newly qualified dentists will soon be insufficient to replace those retiring from practice each year, it cannot be hoped that the service will ever have enough members to provide comprehensive dental care for all the children of the country.

An anomalous position has arisen in which, for the first time for several years, many dental practitioners are not fully occupied and would be willing to accept more children as patients in their practices under the N.H.S., while the school dental service remains seriously understaffed and unable to fulfil its responsibilities. The British Dental Association contends that this anomaly could be abolished to the benefit of all parties by a simple administrative procedure by which the school dental service would arrange with practitioners to treat in their surgeries, those children who cannot through pressure of numbers be given treatment in the school clinics. For some months the association has been trying to persuade the Government to accept this suggestion; but the recent publication of its correspondence with the Minister of Health shows that little progress has been made. In a letter dated March 30, 1953, the association refers to the "very large measure of agreement" between the parties on the subject of the dental treatment of children. The two sides agreed that the best method of providing necessary treatment was by means of full-time salaried dental officers in the school dental service, and that their recruitment should proceed as quickly as possible. Meanwhile the service should be supplemented by general practitioners working in local-authority *clinics as part-time officers on a sessional basis*; but for some years to come there would inevitably remain in certain areas a considerable number of children unable to obtain necessary treatment through the school dental service. The association proposed that these children should most appropriately obtain treatment through part IV of the National Health Service Act, 1946, and "that it was highly desirable that the parents of these children should be encouraged to take them for treatment to a practitioner in the general dental service." The Minister of Health's reply of May 2 defines the main point at issue between the parties as the association's suggestion that the dental services of local authorities should take the initiative in referring children for treatment to dentists willing to provide it under the general dental service, and considers this proposal "would have an adverse effect on recruitment and thus could not fail to hinder the development of a service for children." The local dental executive committees were the bodies designed to give this kind of help and advice to the public. The letter records the Minister's appreciation of the way in which dentists are coming forward with offers of help as part-time officers in the school clinics, and considers that this help is largely responsible for the improved staffing of the school service.

The Government evidently think the British Dental Association's scheme would be too costly, and by dividing the treatment of school children between two distinct

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The Artificial Bladder

We then decided that the only possible course was to form an artificial bladder. Repeated investigations had confirmed that the bladder was very small and contracted, and the upper urinary tract much dilated, and from time to time the patient had had severe attacks of ascending pyelonephritis.

Operation.—On May 1, 1952, under general anæsthesia, the transverse colon was divided, through a right paramedian incision, near its right end, and its proximal end was closed. The ileum was divided across in its last 6 inches, and an ileo-transverse colostomy was made. The lower end of the ileum was brought out through the middle of the wound. The patient was very ill after this operation, largely owing to the weak abdominal muscles which made respiration difficult, but she gradually improved on careful treatment and got up and about again. We were interested to know how much absorption would take place from the isolated right colon, and many tests were made, 10 oz. of physiological saline solution being run into it and drained off again after two hours. During this time about 40% of the fluid content and 52% of the chloride were absorbed.

The second stage of the operation was performed on July 14, under general anæsthesia, through a transverse lower abdominal incision dividing both rectus muscles. The left ureter was transplanted into the left side of the cæcum, which was mobile and could be brought over to it and sutured to the incision in the parietal peritoneum so that the anastomosis was extraperitoneal. The right ureter was transplanted into the right of the cæcum by a similar method. In both cases direct union by mucosal sutures was made. The appendix was removed. A Foley catheter was left in the cæcum through the terminal ileum.

Postoperatively the patient made very satisfactory progress. A careful check was kept on the blood chemistry, which remained normal throughout. The patient was eventually discharged on Oct. 8, when she was very well, could hold her urine in the artificial bladder for two hours and, by catheterising herself during the day, remain dry and comfortable. During the night a catheter was passed into the cæcum and left there and allowed to drain. This routine was adopted because of the great danger of absorption from the artificial bladder if it was allowed to contain urine all night.

Follow-up.—The patient was last seen on Jan. 21, 1953, when she was very well in herself ("better than she has been for years") and even walking much better. The artificial bladder was no trouble. She was emptying it every two hours during the day and leaving a catheter in all night. She was on a salt-free diet and taking an alkaline mixture by mouth. Her blood-urea level was 24 mg. per 100 ml. Detailed chemical investigations of the blood showed that the content of calcium, sodium, potassium, phosphate, and chloride and the alkaline reserve were normal. Intravenous urography (fig. 2) showed excellent function of both kidneys. Practically all the dilatation of the right ureter, pelvis, and calices had disappeared, but that on the left side, although much better, was still considerable. Since discharge the patient had continued her occupation as a cashier and had lost no time from work.

SUMMARY

Infection and contraction of the bladder following transverse myelitis, caused total urinary incontinence.

This was treated by the formation of an artificial bladder from the right colon. The result was excellent, and the patient has returned to her normal occupation.

The possible uses of an artificial bladder in surgical treatment are briefly reviewed.

That a successful result was eventually obtained was in a large part due to the devoted attention of Sister Townes and her nurses at the Withington Hospital, the many anæsthetists who from time to time administered to the patient, my successive registrars and house-surgeons, and not least to the patient's own great moral courage and unshakable confidence.

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HYPERCHLORÆMIC ACIDOSIS FOLLOWING IMPLANTATION OF THE URETERS INTO AN ISOLATED LOOP OF ILEUM

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ELECTROLYTE imbalance in surgical patients has been extensively studied during the past decade, and particular attention has been directed recently to the problems of electrolyte imbalance following implantation of the ureters into the sigmoid colon. So far as is known hyperchloræmic acidosis following ureteric implantation into an isolated loop of ileum has been described in only one patient (Bricker 1952, Eiseman and Bricker 1952). Substitution of a short isolated loop of terminal ileum for the bladder, with end-to-end restoration of ileal continuity, first reported by Bricker (1950), does not yet seem to have been extensively practised.

CASE-RECORD

A 74-year-old man in good general condition was admitted to hospital on Jan. 2, 1952, with a history of loss of weight and vague abdominal pain during the preceding month. Rectal examination showed a moderately enlarged prostate. Occult blood was present in the stool, and a preliminary laparotomy on Jan. 29 showed a carcinoma of the recto-sigmoid. A left iliac colostomy was made. Because the tumour had invaded the bladder, it was necessary at the operation on March 3 to carry out pelvic evisceration with transplantation of the ureters into an isolated 6-inch loop of *terminal ileum.*

Preoperative excretion pyelograms showed poor concentration of the dye on both sides at ten and twenty minutes. The preoperative blood-urea level was 24 mg. per 100 ml.

Postoperative Progress

During the first two weeks convalescence was satisfactory, apart from a mild chest complication. The urine output on the day of operation was 300 ml., on the next day 635 ml., and thereafter averaged 1520 ml. per day during the remainder of the period of investigation. On March 18, *fifteen* days after operation, the patient was obviously unwell and was very drowsy, but no gross abnormality could be found on clinical examination. The blood chemistry was:

Urea	74	mg. per *100 ml.*
Sodium	134·5	m.eq. per litre
Potassium	5·0	m.eq. ,, ,,
CO_2-combining-power	12·5	m.eq. ,, ,,
Chloride	107·5	m.eq. ,, ,,

To correct the acidosis, sodium citrate was given by mouth (2 g. t.d.s.) *from* March 19 for thirteen days. On March 20 the blood chemistry was:

Urea	84	mg. per 100 ml.
CO_2-combining-power	12·5	m.eq. per litre
Chloride	99·1	m.eq. ,, ,,

To determine whether some obstruction had developed at the uretero-ileal *anastomoses, indigo-carmine* (5 *ml.*) was injected intravenously, and appeared at the "ileostomy" *fourteen minutes after injection.*

By March 28 his general condition had improved greatly: he had become completely alert and was feeling very well. The acidosis had been largely corrected, and the blood chemistry was:

Urea	40	mg. per 100 ml.
Sodium	142 0	m.eq. per litre
CO_2-combining-power	20·0	m.eq. ,, ,,
Chloride	97·7	m.eq. ,, ,,

On April 4 blood examination showed:

Urea	29	mg. per 100 ml.
Sodium	148·0	m.eq. per litre
Potassium	4·6	m.eq. ,, ,,
CO_2-combining-power	25·3	m.eq. ,, ,,
Chloride	101·7	m.eq. ,, ,,

A second injection of indigo-carmine on April 5 was *followed* by the appearance of the dye at the "ileostomy" in twelve minutes. An excretion pyelogram on April 7 showed good excretion on both sides at five minutes.

Since discharge from hospital on April 9 he has remained well. No sodium citrate was taken *after* April 9. On Oct. 8 a further excretion pyelogram was considered to be *normal.*

services—the National Health Service and the local-authority school service—would threaten the future development of the latter It would certainly be hard to predict the consequences of having part of the work paid for by fees per item of service while the rest was performed by dentists receiving a salary which is at present below the average for N H S general dental practitioners But the essential argument against the association's plan is surely that it offers a short term palliative rather than a solution to the problem It seems a pity that some means cannot be found to make greater use of the help offered by the dental profession, but the million half hour appointments which the association believes that private practitioners would set aside each year for child patients could affect only about 250,000 additional children Only so many would be able to receive reasonably full dental care, and the vast majority of the young would still only be able to obtain emergency treatment for relief of pain On the other hand, the Minister of Health would be rash to assume that prolongation of the present depressed state of general dental practice is going to abolish the staffing difficulties of the public services, or that it could be the basis of a sound school service

Discussions will remain unrealistic until both sides recognise that the dental profession is too small to fulfil all its tasks, and will soon be growing smaller The present slacking in demand for adult treatment does not indicate that the community has suddenly ceased to need dental care it is simply a measure of the public's indifference to, and ignorance of, the importance of dental health It would be unfair to consider either the Minister of Health or the British Dental Association guilty of complacency about this, though their exchange of letters does not suggest that either has given much thought to its significance

CORTISONE IN BELL'S PALSY

MANY different pathological processes can give rise to paralysis of the facial muscles, but in most cases the cause is an apparently intrinsic peripheral lesion of the facial nerve It is to this type that the name Bell's palsy has been given, and, as Kettel[1] points out, this title covers all cases of facial paralysis in which no clear local cause is evident Speculation about the origin of this condition has resolved itself into two main channels Kettel[1] and Hall,[2] among others, believe that the prime cause is local ischæmia, whilst Morris[3] holds that it is an inflammatory process in the nerve and its sheath Most workers agree, however, that the nerve is compressed within the fallopian canal, and that this compression contributes to the impairment of neural function It was to alleviate the long term effects of such compression that Ballance and Duel[4] devised their operation of decompression of the nerve, their technique has been employed by the protagonists of both schools, each school very reasonably supporting this practice by its own theory of the lesion Most cases of Bell's palsy recover spontaneously, usually recovery begins after about three or four weeks, and usually this recovery is complete Those who consider doing decompressive operations are guided both by the persistence of the paralysis beyond the first four weeks and by the absence of response to faradism The operation tends, therefore, to be done some time between the sixth and tenth weeks

This latent period—the natural consequence of therapeutic prudence—is undesirable if the enduring and disfiguring paralysis seen in certain cases is really due to the compressive effect of inflammatory œdema A report by Rothendler[5] is therefore of special interest both for its therapeutic and for its ætiological implications Believing that the palsy is due to a non-specific acute inflammatory reaction, Rothendler decided to try the effects of cortisone He treated 5 cases within five days of onset, 1 at nine days, and another at ten days The cortisone dosage varied, but the course amounted to about 3 g given orally or intramuscularly over a twelve day period In 6 of the cases recovery began in the first week and was complete at the end of the second In the 7th case, in which the treatment was unsuccessful the paralysis was very severe and had already been present for ten days when treatment began In the first 6 cases the rapid and complete recovery was clearly not spontaneous Rothendler expresses the view that cortisone relieves the acute œdema and inflammatory reaction in the nerve and its sheath, and indeed the success of this treatment constitutes prima-facie support for the inflammatory hypothesis of causation It may well be that the old name "rheumatic facial paralysis" deserves more respect than has been accorded to it by modern authorities

Cortisone is still difficult to obtain in this country, and its administration is associated with certain hazards Nevertheless, the striking benefit from so short a course of treatment, and the implied avoidance of the danger of permanent disfiguration, certainly justifies an extended trial of this drug in Bell's palsy—always provided, of course, that it is given in the first few days after the onset of the disease

CONTINUOUS OR DISCONTINUOUS PENICILLIN

WE have lately drawn attention to the desirability of basing the dosage of antibiotics on the in-vitro sensitivity of the infecting organisms[6] The work of Gould et al[7] has shown that the logical interpretation of laboratory tests can lead to successful treatment with doses very much less than the "standard" ones, at any rate in urinary tract infections Undesirable side effects are diminished or eliminated by this means, and the danger of producing resistant strains of bacteria seems to be much less than might have been expected Gould and his colleagues gave the drugs at 6 hourly intervals, and a report by Eagle et al[8] now suggests that attention to the spacing of doses may still further increase the efficiency of treatment They investigated the relation between the dosage, the interval between injections, and the therapeutic efficiency in streptococcal infections of mice

Chain and Duthie[9] demonstrated that penicillin exerted its greatest bactericidal action on organisms in the logarithmic phase of growth This indicated that the efficiency of therapy might be increased if the interval between two injections was such that dormant organisms had begun to multiply by the time of the second injection Eagle et al, however, conclude that the greatest efficiency is achieved when the penicillin concentration at the site of the infection is continuously maintained at the level which exerts the maximal bactericidal action in vitro They found that a penicillin free interval between injections prolonged the total duration of treatment necessary for cure They injected large numbers of mice intramuscularly with a highly virulent strain of group A streptococcus, and penicillin was then given to these mice according to a number of different treatment schedules The intervals between injections were $^{3}/_{4}$, $1^{1}/_{2}$, 3, 6, 12 and 24 hours and the number of injections varied from one to sixteen On each schedule mice

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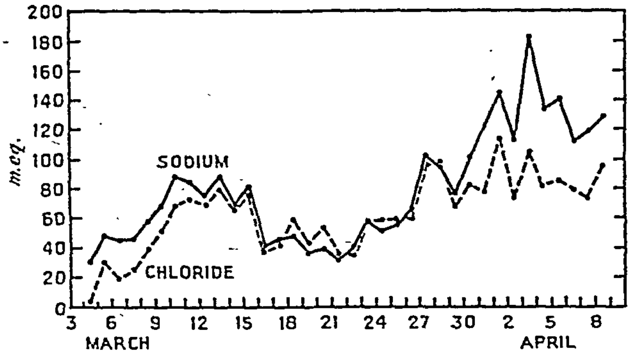

Fig. 1—Daily output of sodium and chloride during the period of study.

SPECIAL STUDIES

Methods.—Collection of urine began on the day after operation. The urine was collected into a Rutzen bag applied to the "ileostomy" and determinations were made on twenty-four-hour samples from 8 A.M. to 8 A.M.

Sodium was measured by an internal standard flame photometer, chloride by Sendroy's method (modified by van Slyke and Hiller 1947), and urea by the hypobromite method.

Sodium citrate administration began on March 19, (2 g. t.d.s.). During the last eight days of the period of study the amount was varied, being increased to 3 g. t.d.s. for four days, and then reduced to 1 g. t.d.s. for the last four days.

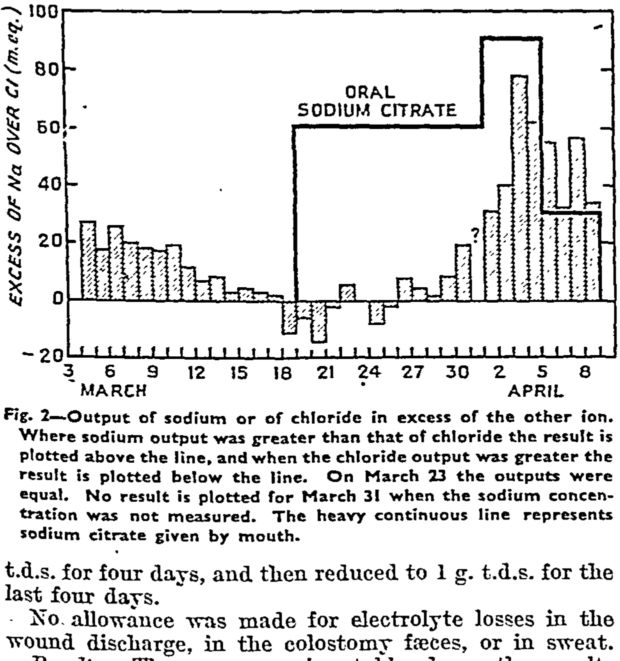

Fig. 2—Output of sodium or of chloride in excess of the other ion. Where sodium output was greater than that of chloride the result is plotted above the line, and when the chloride output was greater the result is plotted below the line. On March 23 the outputs were equal. No result is plotted for March 31 when the sodium concentration was not measured. The heavy continuous line represents sodium citrate given by mouth.

No allowance was made for electrolyte losses in the wound discharge, in the colostomy fæces, or in sweat.

Results.—The accompanying table shows the results of the urine analysis. Up to the fourteenth day after the implantation operation the patient made satisfactory progress, but next day he was in a state of moderately severe acidosis, the CO_2-combining-power of the plasma was 12·5 m.eq. per litre and the chloride concentration was just above the upper limit of normal. By the same date the blood-urea level had risen from a preoperative figure of 24 mg. per 100 ml. to 74 mg. Treatment with sodium citrate began on the sixteenth postoperative day, and was followed first by a fall in the chloride concentration and later by a correction of the low CO_2-combining-power. The blood chemistry was normal on the thirty-second day after operation.

Except on the first two days after operation, the urine volume was adequate, averaging 1520 ml. a day. The urea concentration in the urine showed little variation from day to day, but tended to fall from March 26 onwards. Sodium and chloride excretion ran more or less parallel during the first four weeks after operation (fig. 1). The outputs of each were low at first, but rose during the first week after operation, and remained fairly constant for six days. There was an appreciable fall in the daily outputs of sodium and chloride in the third week after operation, but this was followed by a rise in the amounts excreted during the fourth week.

At first the excretion of sodium exceeded that of chloride, although there was a gradual decrease in the amount by which the sodium excretion exceeded chloride excretion during the first two weeks after operation (fig. 2). During the third and fourth postoperative weeks the sodium output bore an inconstant relationship to the chloride output, while in the fifth week the excretion of sodium gradually increased until it exceeded that of chloride by an amount which approximated closely to the amount of sodium administered as sodium citrate.

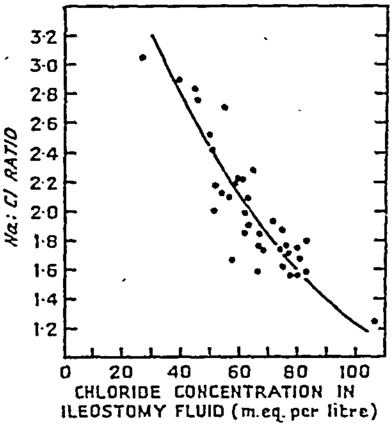

Fig. 3—The relation between the Na : Cl ratio and the chloride concentration in 37 samples of normal ileostomy fluid.

DISCUSSION

The interpretation of the blood and urine changes in this case is difficult. The five weeks of this study may arbitrarily be divided into three periods, the first lasting for eleven days from the day of operation until March 14, the second for fourteen days from March 14 to March 28, and the third from March 28 onwards.

In the first postoperative period of eleven days 180 m.eq. of sodium was excreted in the urine in excess of chloride. Assuming that in the diet taken by the patient during this period the Na/Cl ratio was approximately 1, it is surprising that the urinary loss of sodium was so much in excess of chloride, especially when there was a considerable serous discharge from the pelvic wound, presumably with a sodium concentration greater than its chloride concentration. Extrarenal loss of sodium in excess of chloride is usually associated with the excretion of a urine in which the Na/Cl ratio is considerably less than 1 (Denton et al. 1951, Wilson 1952). "Post-renal" modification of the urine by the ileal mucosa may have counteracted any renal response which there may have been to the developing sodium depletion and acidosis.

In an attempt to elucidate the problem of the development of a state of hyperchloræmic acidosis in this patient, a parallel study was made of the sodium and chloride content of normal ileostomy fluid. The sodium concentration of this fluid is greater than that of chloride (fig. 3).

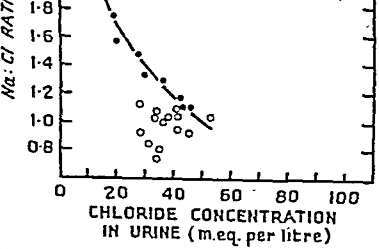

Fig. 4—The Na : Cl ratio in the urine of the present case has been plotted against the chloride concentration. Each dot or circle represents one day

were injected at each of seven dosage levels (0 05, 0 2, 0 8, 3 2 12 5 50, and 200 mg per kg body-weight) The 50% survival rate of each group was then determined The full mathematical analysis of the series was complicated, but the authors selected for detailed comment those aspects directly connected with the problem under investigation For example, six to eight injections, each of 3 2 mg of penicillin per kg body-weight, given at intervals of $^{3}/_{4}$ hour, were needed for a 50% survival in one group of mice If injections of the same dose were given three hourly, only two or three injections gave the same survival-rate Increasing the intervals to 12 hours, however, necessitated three or four injections Comparable results were found with all other doses investigated It is clear that if the intervals were too short, penicillin was still present in effective concentration at the time of each injection, so that the full benefit of the preceding injection was lost If the intervals between injections were too long, then the organism multiplied and longer treatment was necessary The total treatment time required for mice injected every $^{3}/_{4}$ hour was $4^{1}/_{2}$ to 6 hours with 3-hourly injections it was 6 to 9 hours, and with 12 hourly injections 36 to 48 hours The interval between injections also had a pronounced effect on the total dose of penicillin required to effect a cure For example, when four injections were given at intervals of $^{3}/_{4}$ hour, a total dose of 68 mg per kg was needed When the four injections were given at 3 hourly intervals, however, the total dose needed was only 3 mg per kg, while for four 12-hourly injections the total dose for cure was 7 6 mg per kg

The streptococcus used by Eagle et al was killed at a maximum rate in vitro by 0 024 µg of penicillin per ml Approximately half of the penicillin in the blood-stream is bound to serum-protein, so that a serum concentration of about 0 05 µg per ml would be needed to provide maximum bactericidal action in tissue fluids Eagle and his colleagues have determined the total time for which the serum-penicillin level was at or above this critical level in groups of mice treated by various schedules until they were cured They call this the " aggregate penicillin time " The number of injections varied from one to twelve, and the intervals between injections from $^{3}/_{4}$ hour to 12 hours, but the aggregate penicillin time remained remarkably constant at about 4 hours throughout the series Increasing the interval between injections to 24 hours, however, caused a sharp rise in the penicillin time necessary for cure, apparently because of bacterial multiplication between injections These results indicate that the efficacy of penicillin treatment is determined primarily by the total time for which the drug remains at effective levels at the site of infection, provided that the interval between injections is not long enough to allow bacterial multiplication

It is a far cry from mice to men, but in this instance the same factors are likely to govern the response of both species The work of Eagle et al suggests that penicillin should be given to man in a way that ensures that the concentration at the site of infection remains continuously in excess of that necessary to kill the infecting organism in vitro The exact timing of the injections would depend upon the preparation and dose of penicillin used, but the most economical régime, and the one which would produce the most rapid cure, would be that in which each injection was given when the penicillin concentration at the site of infection had fallen to the in-vitro bactericidal concentration for the organism concerned Knowledge of the concentrations of antibiotics that can be attained in the tissues is at present scanty, but advances in this direction, combined with rational interpretation of bacterial sensitivity tests, should clearly lead to a reduction in the massive doses of antibiotics at present given, and therefore to less side-effects and unnecessary expense

TREATMENT OF COUGH

It is not always easy to decide when to interfere with a cough—particularly a postoperative one Even when the decision to treat it has been made, the choice of remedies is enormous, though the really effective drugs are few A conference [1] at Cornell University has lately debated these questions

The majority of the drugs which are said to stimulate the respiratory secretions are emetic when given in large enough doses, but it is extremely doubtful whether they have any real effect in the doses usually given Boyd et al [2–5] have shown that in lightly anæsthetised cats ammonium chloride and carbonate, ipecacuanha, tinct camph co, potassium iodide, creosote, and several of the essential oils will all increase the volume of fluid secreted by the respiratory tract In man, however, there is no such evidence Both Alstead [6] and Howell,[7] who have made long and painstaking studies of the volume of the sputum secreted by chronic bronchitics, failed to show that it was influenced at all by any of a large number of expectorants used in conventional doses But Herxheimer and McAllen [8] have recently suggested a method of using potassium iodide intermittently in doses of gr 15–25 which they claim does produce a real increase in respiratory secretion Probably one of the best expectorants is a hot drink, many a chronic bronchitic and sanatorium patient will testify to the value of his early morning cup of tea as a loosener of phlegm This probably explains the popularity of the celebrated hot-water mixture (mist sod chlor *N F*)

Of the opiates and their derivatives and the few other drugs, such as methadone, which depress the cough reflex, linctus diamorphinæ is incomparably the most effective, but the danger of addiction means that it must be kept strictly in reserve and used only when all safer drugs have failed One speaker at the Cornell conference advocated the wider use of small doses of morphine, but, for the same reason, few would agree with him The main discussion concerned the dosage of codeine The preparations normally used in this country contain quite small doses For example, the ordinary linctus codeinæ *N.F* contains gr $^{1}/_{8}$ to the drachm and the strong linctus gr $^{1}/_{4}$ Many people, including Alstead, have recommended larger doses—e g, gr 1 four-hourly On the other hand, Muschenheim, at the Cornell conference, made a plea for smaller doses at shorter intervals He cited an experiment carried out before the war in an American sanatorium by Davenport,[9] who found that out of 475 patients with troublesome cough only 21 required more than gr $^{1}/_{6}$ of codeine to control it—only one-third of the traditional dose formerly given in this institution But Hillis [10] found no evidence that the action of codeine, even in large doses of up to gr 3, was any greater than could be explained by the factor of suggestion In experimentally produced cough in man he was impressed by the importance of the psychological factor in contributing to the success of various drugs—which may well account for the divergent views on the optimum dosage of codeine

The dry hacking cough of tracheitis and acute bronchitis is helped by warm moist air, and the Americans favour continuous treatment with a steam kettle rather than the intermittent treatment with jug and towel, which is perhaps more popular in this country The wheezing cough is helped by antispasmodics, and one

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The fact that the Na/Cl ratio varies with the chloride *concentration suggests that the rates of absorption* by the bowel of sodium and chloride are neither equal nor proportional to the concentrations of the two ions. At any particular chloride concentration the sodium concentration is, within limits, a certain function of the chloride concentration. The curve in fig. 3 bears a striking resemblance to that in fig. 4, which was obtained by plotting the Na/Cl ratio against the chloride content of the urine during the first postoperative period in this patient with ureteric transplantation into the ileum. It is therefore suggested that during the first eleven-day period the mucosa of the ileal loop was functioning more or less normally, attempting to produce a fluid in which the sodium and chloride concentrations bore some predetermined relation to each other. During the second period of fourteen days this early correlation between sodium and chloride concentration disappeared (fig. 4).

The patient had become clearly unwell about the middle of the second period, by which time a severe acidosis was present. The urine Na/Cl ratio fluctuated appreciably during this second period, and the disappearance of the previous relationship between sodium and chloride output suggests that the activity of the ileal mucosa had now become modified. Also, during this fourteen-day period the excretion of sodium and of chloride decreased. Such a decrease might be anticipated if, in the presence of a more or less constant intake and normal renal function, a deficit of these ions had developed. A state of sodium deficiency in fact developed during the first period of eleven days, to which the excess of urinary sodium over chloride contributed. Furthermore, during this first period the daily output of sodium and of chloride had risen rapidly, more rapidly in fact than would be expected after a major operation (Wilkinson et al. 1949). Absence of the usual postoperative period of chloride retention in this case may have been associated with some degree of chloride deficit. The fact that during the second period of fourteen days the daily outputs of both sodium and chloride fell, sodium more than chloride, is further evidence that the initial activity of the ileal mucosa had become modified, and that normal renal responses to states of sodium and chloride deficit were becoming manifest.

POSTOPERATIVE CHANGES IN URINE

Date	Urine volume (*ml.*)	Concentration			Daily output			Na/Cl ratio	Oral sodium citrate (m.eq.)
		Na (m.eq. per l.)	Cl (m.eq. per l.)	Urea (g. per 100 ml.)	Na (m.eq.)	Cl (m.eq.)	Urea (g.)		
March 4	635	48·9	5·5	1·2	31·1	3·5	7·6	8·9	. . .
„ 5	1475	32·4	20·5	1·2	47·8	30·2	17·7	1·6	. .
„ 6	1315	33·9	14·5	1·3	44·6	19·1	17·2	2·3	. .
„ 7	1355	33·9	19·3	1·5	46·0	26·2	20·4	1·75	. .
„ 8	1425	39·8	27·7	1·4	57·7	39·5	20 0	1·45	. .
„ 9	1700	40·3	30·0	1·3	68·5	51·0	22·1	1·35	. .
„ 10	1880	46·6	36·5	1·5	87·6	68·6	28·2	1·3	. .
„ 11	1705	49·8	43·0	1·3	85·0	73·4	22·2	1·15	. .
„ 12	1530	50·0	45·3	1 3	76·5	69 3	19·9	1·1	. .
„ 13	1845	47·3	43·0	1·4	87·4	79·4	25·8	1·1	. .
„ 14	1600	43 2	41·2	1·4	69·1	66·0	22·4	1·05	. .
„ 15	2010	40·2	38·4	1·3	81·0	77·2	26·1	1·05	. .
„ 16	1080	37·4	34·7	1 3	40·4	37·5	14·0	1·1	. .
„ 17	1295	35·2	33·8	1·4	45·6	43·8	18·1	1·05	. .
„ 18	1650	28·7	35·2	1·4	47·4	58·1	23·1	0·8	. .
„ 19	1395	26·5	31·3	1·4	37·0	43·7	19·5	0·85	61
„ 20	1550	24·9	34·2	1·4	38·7	53·1	21·8	0·73	61
„ 21	1185	27·3	29 0	1·5	32·4	31·4	17·8	0·94	61
„ 22	1200	33·5	29·3	1·5	40·3	35·2	18·0	1·14	61
„ 23	1615	35 5	35·4	1·4	57·4	57·2	22·6	1·0	61
„ 24	1430	39·4	41·5	1·3	51·3	59·3	18·5	0·95	61
„ 25	1300	42·6	45·5	1·2	55·4	59·2	15·6	0·94	61
„ 26	1440	46·3	41·6	1 0	66·6	59·9	14·4	1·1	61
„ 27	1740	58·3	56·0	1·0	101·5	97·5	17·4	1·04	61
„ 28	1530	62·5	63·5	1 0	95·5	97·1	15·3	1·0	61
„ 29	1335	57 2	51·5	1·1	76 5	68·8	14·7	1·1	61
„ 30	1655	60·9	49·4	1·0	100·9	81·8	16·6	1·2	61
„ 31	1495	?	52 0	?	?	77·8	?	?	61
April 1	1930	75·0	58·7	0·9	145·0	113·3	17·4	1·28	92
„ 2	1332	84 7	55·0	1·1	113·0	73·3	14·7	1·54	92
„ 3	1705	107 0	61·1	0·8	182·5	101·2	13·6	1·75	92
„ 4	1675	79·5	48·6	0·9	133·0	81·3	15·1	1·63	92
„ 5	1575	89·1	51·2	0·9	140·0	85·3	14·2	1·64	31
„ 6	1400	78 8	56 4	0·8	111·0	79·0	11·2	1·4	31
„ 7	1410	84 2	52·1	1·1	119·0	73·5	15·5	1·62	31
„ 8	1345	95 2	70·1	0·9	128·0	94·3	12·1	1·4	31

During the second period treatment with sodium citrate was started, and between March 19 and March 28 550 m.eq. of sodium was given. Despite this, the excretion of sodium in the urine was still less than, or only just in excess of, that of chloride. It seems probable therefore that the sodium deficit had only just been made good by the end of the second period.

Only during the last six days of the study did the output of sodium in the urine exceed that of chloride by approximately that amount of sodium given as citrate. This might be expected if renal function, with regard to sodium deficit or excess, were normal, and if the urine passed at the "ileostomy" was not modified by the ileal mucosa.

In spite of the excretion of apparently adequate amounts of urea (see table) the blood-urea level rose from 24 mg. per 100 ml. preoperatively to 84 mg. on March 20. Eiseman and Bricker (1952) investigated the absorption of urea from an ileal loop isolated from both urinary and fæcal streams, and they showed that after the urine had been in the ileum for about two hours there was no further appreciable fall in the concentration of non-protein nitrogen, which was between 500 and 700 mg. per 100 ml. This concentration of non-protein nitrogen is comparable to the urea concentration observed in the present case. The mechanism of the fall in blood urea between March 20 and April 4 is obscure, for it is unlikely that the permeability of the ileal mucosa decreased with a reduction in activity of the mucosa. It is possible, however, that the uptake of urea from the ileum is an active process and is related to the general activity of the mucosa.

There is another possible explanation of some of the observations made in this case. Before operation the intravenous pyelogram showed poor renal concentration of the contrast medium although the blood-urea level was normal. The prostate was moderately enlarged, but the patient gave no history of chronic urinary obstruction. Unfortunately the complete blood chemistry was not investigated before operation. It has been pointed out that hyperchloræmic acidosis may develop in cases of chronic prostatic obstruction, the blood chemistry returning to normal after relief of the obstruction (Shackman 1952). A restoration of certain aspects of renal function has also been observed by Lich (1942) and Hughes (1946). It could be argued that in the present case there was some reversible impairment of renal function due to mild prostatic obstruction, which was relieved by transplantation of the ureters into the ileal loop, or that mild obstruction developed following operation. The first possibility is supported by the postoperative improvement of the intravenous pyelogram, but it does not explain the development of acidosis *after relief of the obstruction.* The speed with which the indigo-carmine appeared at the "ileostomy" is against the second possibility. The fact that the patient remained well after discharge from hospital, even without oral sodium citrate, supports the supposition that the mechanism responsible for the acidosis had then ceased to operate.

SUMMARY

A man of 74, with carcinoma of the pelvic colon, had hyperchloræmic acidosis following pelvic evisceration and transplantation of both ureters into an isolated loop of terminal ileum.

The function of the ileal mucosa in the early postoperative period may have contributed to the sodium deficiency which developed, and it may have counteracted the normal renal responses to this deficiency. The activity of the mucosa subsequently changed, with *reduction in, and finally cessation of,* "post-renal" modification of the urine by the bowel.

References at foot of next column

of the Cornell speakers emphasised the value of intravenous aminophylline in the treatment of cough associated with an asthmatic attack The productive coughs of bronchiectasis and chronic bronchitis can be greatly assisted by intelligent postural drainage The patient will soon learn that his comfort can be much increased by clearing the chest at certain strategic times—for example, before meals, before bed and before the day's work The troublesome exacerbations of infection, which are a feature of chronic bronchitis, may be shortened by continuous postural drainage, such as is commonly used in the treatment of lung abscess Unfortunately this method is no good for those patients whose condition has deteriorated to the point of heart-failure, it is really they who need it most, but they must be nursed sitting up Of course, a stubborn nocturnal cough may be an early sign of cardiac failure from other causes, and for these patients an extra pillow, digitalis, and a mercurial diuretic will be more effective than any cough mixture

BRUCELLOSIS

THE exact prevalence of brucellosis (undulant fever) in this country is not known, because it is not a notifiable disease, but Dalrymple Champneys[1] estimates that there are at least 500 cases annually Drinking raw milk is probably the commonest mode of infection, although farm labourers, veterinarians, and laboratory workers exposed to infection may and often do contract the disease The risk of brucellosis must be assumed whenever cow's milk has not been pasteurised or boiled In a series of 1134 cases reported by Dalrymple Champneys, 780 patients were known to have consumed unboiled or unpasteurised milk or cream, even tuberculin-tested milk cannot be assumed to be free from infection

Brucellosis must always be considered in any persistent pyrexia, or obscure febrile illness There is usually a prodromal period in which the patient complains of tiredness, frontal or occipital headache, and sweating, accompanied by a characteristic sour odour, although, on the other hand, the onset of the disease may be extremely sudden Anorexia, muscle pains, particularly in the lumbar region, arthralgia, rigors, an enlarged spleen, and constipation or digestive disturbances are common A lymphocytosis and polymorphonuclear leucopenia are often present The diagnosis is confirmed by the culture of *Brucella abortus* from the blood, or by an agglutination test, using a standard brucella antigen, to a titre of not less than 1 in 100 Cross agglutination may cause confusion in tularæmia and cholera, but this is of no significance in this country, though it is in the East and in America An intradermal test using "brucellin" or "brucellergen" is sometimes used as an aid to diagnosis There are often no clear cut symptoms, and brucellosis is sometimes diagnosed clinically as influenza, typhoid fever, tuberculosis or malaria, and in fact it may be confused with any pyrexial illness with few physical signs, the differentiation between brucellosis and typhoid fever may be particularly difficult Moreover the duration of the illness and the way it ends are variable Even in the absence of specific treatment the disease may last only a few days or weeks, or it may become chronic and last for years

A great many remedies have been tried in brucellosis vaccines, antisera hyperthermia blood from immunised subjects, 'brucellin" (made from the filtrate of a broth culture of brucella) and the sulphonamides have done little good But the newer antibiotics hold much more promise, and their value is now becoming established There seems to be little to choose between aureomycin, chloramphenicol, and terramycin[2–5] Streptomycin in doses likely to be effective is too toxic The relapse rate, using single antibiotics, is, however, high, in a series described by Killough et al[5] it was 69% But a big reduction in the relapse rate can be achieved by using antibiotics in combination Herrell and Barber[6] reported favourably on a combination of aureomycin and dihydrostreptomycin Magill and Killough[7] used a combination of terramycin and streptomycin (or dihydrostreptomycin) for a period of three weeks The initial response was good and the relapse rate was reduced to 14% The well known effects of cortisone on pyrexia and arthralgia suggest that it might usefully be combined with one of the antibiotics in acute brucellosis

There are hopes that contagious abortion in cattle, which is also caused by *Br abortus*, as well as brucellosis in man, may be stamped out by the vaccination of cattle with what is known as strain-19 vaccine This is having a great success in reducing the prevalence of contagious abortion, which is now down from something like 40% in herds in this country to about 15%[8] Eradication of the disease in cattle by slaughter can never be an economic means of control in Britain, where the infection is so common The present legal position is that no one may sell milk from a cow knowing that it is suffering from contagious abortion, but, as the presence of *Br abortus* would need to be demonstrated before the offence could be proved, the enforcement of the law is difficult At the moment there is only one sure method of prophylaxis against brucellosis—to boil or pasteurise all milk before consumption

THE CLIMBING OF EVEREST

THE good news from Colonel Hunt and his expedition on Mount Everest reached London on the eve of Coronation Day and this splendid addition to the excitement of the occasion was all the more stirring because earlier messages had suggested that the mountain's formidable barriers had again beaten back the climbers In the first strike for the summit, on May 25, Bourdillon and Evans used the closed circuit oxygen apparatus We do not know how far the difficulties that deterred them were the result of oxygen lack but certainly the closed circuit has not been so thoroughly tested under these extraordinary circumstances of weather and terrain as the more familiar open circuit apparatus And it was with open circuit apparatus that Hillary and Tensing left camp VIII, on the ridge below the South Summit, to grapple triumphantly with the last 1200 feet on May 29 Judging from the stories that have so far been told,[9] oxygen supply was the greatest worry for those who climbed from camp VII on the South Col, for the weather, so cruel to many of the earlier expeditions, seems to have been comparatively gentle this time The success of Colonel Hunt and his men owes much to the skill of those who planned the oxygen equipment and the other aids to survival and strength at great heights, and to the rugged Sherpas who carried the necessary supplies of oxygen up to the South Col—itself a dreadful mountaineering feat The members of the expedition are now descending the slopes they have conquered Colonel Hunt and Mr Hillary to be knighted by the Queen Sherpa Tensing to receive an honour not yet announced and the whole party to be acclaimed for their courage and endurance

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[2] Bryer M S Schoenbach, E B, Chandler C A Bliss E A Long, P H *J Amer med Ass* 1948, 138, 117

[3] Debono J E *Lancet* 1949 ii 326

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[8] Dalrymple Champneys, W *Vet Rec* 1953 65 89

[9] *Times* June [illegible] 1953

REPLACEMENT OF BOTH URETERS BY AN ILEAL GRAFT

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A woman, aged 29, had been treated several times for bilateral stenosis of the ureteral meatuses. This stenosis led to gross enlargement of both ureters and the pelvis of one kidney and consequent progressive destruction of the parenchyma of both kidneys. After the failure of various measures we performed a bilateral nephrostomy on Feb. 9, 1952, followed on Feb. 23 by resection of 50 cm. of ileum near its terminal portion. The remaining portions of the ileum having been anastomosed, the resected portion, with its mesentery, was drawn towards the bladder and arranged in a U-shaped loop. The base of this loop was anastomosed with the bladder, and two lateral limbs were substituted for the pelvic and iliac portions of both ureters. The remaining portions of the ureters were then anastomosed with the free lateral ends of the resected ileum (fig. 1).

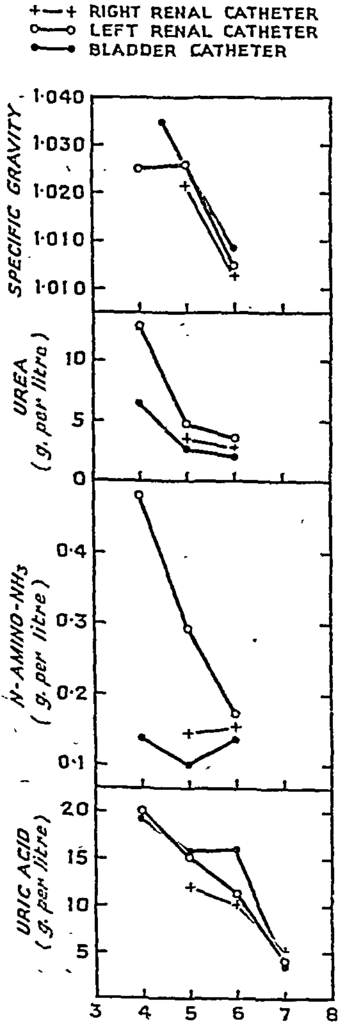

Fig. 2—Analysis of postoperative urine.

In the immediate postoperative period we collected the renal urine through nephrostomy catheters. After the third postoperative day, by temporarily obstructing these catheters we collected the vesical urine which had passed through the ileal loop.

The collected urine was examined for density, total nitrogen, urea, N-amino-NH_3, uric acid, and free and total creatinine. The electrolytes could not be determined daily, because of difficulties of collection. Fig. 2 shows the changes in specific gravity and in amount of urea, N-amino-NH_3, and uric acid. In our opinion this is the most important part of the postoperative problem.

It can be seen that, after the fifth postoperative day, the amounts of the main nitrogenous urinary compounds excreted began to approach stability, which was reached on the seventh or eighth postoperative day. The composition of the bladder urine, although disturbed at first, gradually became similar to that of the urine collected through the renal catheters. This indicates that the grafted section of ileum had become well adapted to its new function, with altered permeability. It became adapted to the flow of urine without producing any troubles except transient ones.

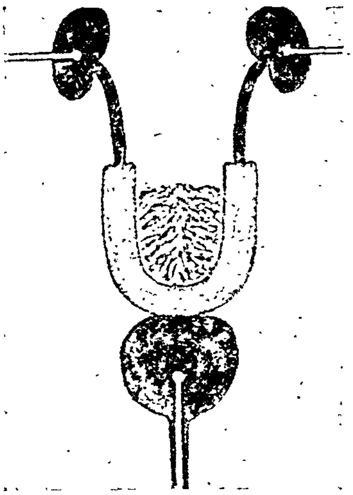

Fig. 1—Scheme of operation, showing ileal loop anastomosed to ureters and bladder.

Twelve months after the operation the patient has recovered normal micturition and a perfect state of health. She presents no biological abnormalities, and the renal function and pyelographic appearances have shown impressive improvement.

The complicated experimental conditions met with in such a case contribute to making the interpretation of our results difficult. Further research should be undertaken on this subject, directed at a more complete and precise study of the postoperative period of adaptation, especially as regards what is added to, and what is absorbed from, the renal urine by the intestinal graft.

DR. WILSON: REFERENCES

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HERPES-SIMPLEX HEPATITIS AND ENCEPHALITIS IN NEWBORN TWINS

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Evidence has been produced confirming that a pathologically distinct form of hepatitis, first described by Hass (1935), is the result of infection by the virus of herpes simplex (Quilligan and Wilson 1951, Zuelzer and Stulberg 1952).

Although virological studies were not made in the present cases, they correspond pathologically to those previously reported and are of interest in that they suggest the possibility of transplacental infection. We have been unable to find reports of any similar cases in the British literature.

CASE-RECORDS

A woman, aged 28, gave birth a month prematurely to binovular twin boys at the South London Hospital for Women and Children on Nov. 3, 1946. She had had a pregnancy, four years before, terminating spontaneously at six months with the delivery of stillborn twins, one of which was macerated. Her present pregnancy was complicated by hypertension (160/95–100 mm. Hg) during the last month;

Special Articles

JUNIOR HOSPITAL STAFFING

A MEDICAL VIEWPOINT

R M. Forrester
M A M B Camb, M R C P

When the National Health Service was established in 1948 it was clear that there would be many aspects needing review and revision It can hardly have been foreseen, however that after less than five years some sections of the hospital services would be within sight of breakdown because of shortage of junior medical staff This is nevertheless the problem which is troubling regional boards The first public indication was given in the House of Commons in 1951 [1] and the continued anxiety is reflected in letters reaching the medical press

An indication of the size of the problem came from the Manchester region in November 1951, when out of 570 posts (intermediate registrar senior house officer, and house officer) only 417 were filled—a deficiency of 27% [2] Of intermediate registrar posts 19 5% were unfilled, despite the fact that the regional board was trying to fill an establishment some 8% less than the minimum they had declared necessary a few months earlier There has since been very little change in the state of affairs

Regional boards find that the problem is worst in small peripheral hospitals but even in teaching centres some specialist hospitals are in difficulty In 1952 the Royal Manchester Eye Hospital had a quarter of its resident posts unfilled, and today there is only one resident out of the normal complement of five

It seems strange that this shortage should be present at a time when the medical schools of the United Kingdom are steadily increasing their output of doctors and when the total number of registered practitioners is rising rapidly (1932, 56,007, 1942, 69 428, 1947, 77,929, 1952, 83,914)

THE PAST

To understand the present position it is necessary to review certain aspects of the history of the hospital services since 1948

At the outset it was accepted that every general practitioner needed at his elbow a comprehensive specialist service to take the place of the uneven and inadequate service that had hitherto been provided in the lesser centres of population Much of the peripheral specialist work had been done by general practitioners themselves and many of the general-practitioner specialists were of the highest standing Rightly or wrongly, however, it was decided that the over-all quality of the service left much to be desired, and vast expansion of the specialist service was proposed Thus the divorce between hospital and general-practitioner services was arranged, and the great post-war hospital boom began There was talk of a "three-tier system" by which every hospital bed was to be watched over by consultant, registrar, and houseman The urge to increase medical staff in established units was stimulated It became a matter of competition between established consultants to build up the numbers in their teams

The flood of ex-Service doctors made it easy to find the man-power, and so the inflation of the service continued almost unchecked until the Ministry of Health published their memorandum on the registrar grades in November, 1950 This pointed out that there were at that time over 1400 doctors in each of the senior and intermediate registrar grades, and it was clear to everyone that the numbers bore no real relation to the eventual prospects of specialist posts The drastic Ministry proposals for reducing the numbers were acceptable neither to the profession [3] nor to Parliament [4], but it was clear that some attempt had to be made to achieve a balanced establishment It was agreed after discussion between the profession and the Ministry that for England and Wales the establishment of senior registrars should not exceed 960

This figure was based on a normal tenure of four years, and was reckoned to allow 75% of senior registrars the prospect of a specialist post Intermediate registrar establishments were left to the discretion of the employing authorities, whose ideas may be exemplified by those of the Manchester Regional Hospital Board In February, 1951, this board, which had on their staff 122 intermediate registrars, suggested that in fact 150–200 were needed in the non-teaching hospitals of the region to provide a moderately satisfactory service [5]

Here, then, in early 1951 was a hospital service gradually expanding with new specialist appointments still overloaded with registrars (there were three grades at that time) and moderately well staffed farther down the scale by hopeful house-officers who thought they might be on the road to a specialist career It must have been shortly after this that it began to occur to newly qualified and newly demobilised doctors that hospital work held a future for only a very limited number As early as July 1951 the first real signs of staff shortage were apparent, and *Lancet* editorials [6] drew attention to the serious lack of applicants for junior hospital posts Now in 1953 a steadily deteriorating position is said to be occupying the attention of the Minister of Health [7]

THE PRESENT

It seems quite clear that the flood of recruits to the hospital service in the post-war years is unlikely to be repeated They were swept in on a tide of optimism and expansion, and postgraduate deans were advised by the Ministry of Health to encourage large numbers of doctors to take higher degrees The success of this campaign may be judged from the figures of the Royal College of Physicians Over the period 1932–35 an average of 67 new members were admitted each year in 1948–51 the average was 269 per year

The new generation of doctors study the past and the future more carefully and this is the picture that they see Before the start of the health service the routine work of many hospitals was supervised by the senior resident, who had the title of resident medical (or surgical) officer Many such residents gained great experience and some of them higher degrees, but few had any illusions about their prospects of eventual specialist status They were, however anxious to have this experience because they knew that with such a background it would not be difficult to find a general practice—often in the vicinity of the hospital—where they would be welcomed Commonly too, they had a chance of returning to their own or another hospital as part-time specialists The numbers of men involved were small, the opportunities adequate, and a steady supply of labour was available to satisfy the modest demands of the hospital service of the time With the National Health Service there have been great changes Gone is the incentive to acquire experience and higher degrees before entering general practice No longer can the young man with his F R C S settle in practice and do some surgery The hospital beds now belong to the new consultant, and in many areas the general practitioner is prevented from having even the but albuminuria was noted for the first time only after labour had begun. The Wassermann reaction was negative and her blood-group was Rh-negative, but no antibodies were found in her serum.

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[1] *Hansard* July 9 1951 col 130
[2] *Lancet* 1952 i 706
[3] *Brit med J* suppl 1950 ii 225
[4] *Hansard* Nov 22 1950 col 472 *Ibid* Dec 15 col 1534
[5] Manchester Regional Hospital Board Minutes Feb 27 1951.
[6] *Lancet* 1951 ii 953 *Ibid*, 1952 i 705
[7] *Ibid* May 16 1953 p 998

Three days before delivery she developed severe generalised urticaria, with intense pruritus, which was considered to be a toxic rash. Labour started 2 days later and lasted for twenty-eight hours, the first infant being delivered by the vertex and the second by the breech. Twelve hours after delivery the urticaria was still severe and she developed pyrexia (103°F) accompanied by a rigor and delirium. Her temperature returned to normal within twenty-four hours, her skin improved, and she made a good recovery.

TWIN 1

Twin 1, a boy weighing 5 lb. 1 oz., was slightly cyanosed at birth, but rapidly improved and remained well until the 4th day of life, when mild jaundice appeared and he had two attacks of vomiting, followed by cyanosis, rolling of the eyes, and twitching of the face. His temperature rose to 100·4°F, this being the only occasion throughout his illness on which it was raised. The following day he had a further cyanotic attack and four attacks of twitching in spite of chloral-hydrate therapy. On the 7th day he no longer took his feeds and had four severe convulsions each lasting two or three minutes. He finally became deeply cyanosed and died at the age of 7 days.

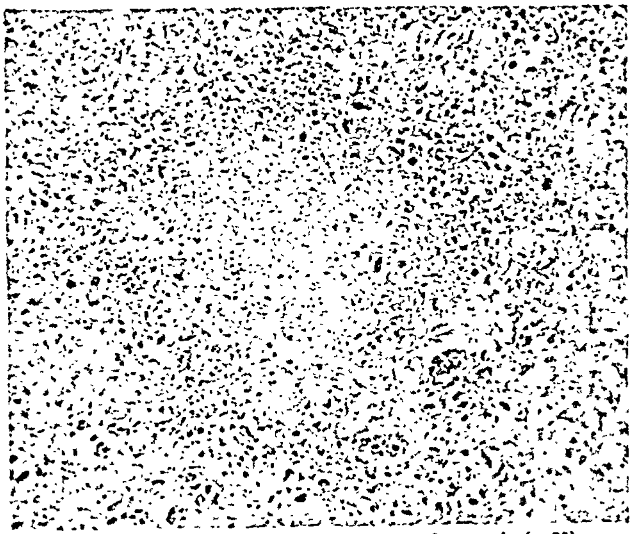
Fig. 1—Liver of twin 1, showing a focus of necrosis (×90).

Necropsy Findings

The *liver* was very firm and of about normal size. Numerous round white nodules were scattered evenly beneath the capsule but did not project above the surface, which remained smooth and glistening. Similar areas were present on the cut surface, varying in size from 0·5 to 2·0 mm. in diameter, most of them being about 1 mm. in diameter. They were diffusely distributed and bore no obvious relation to any particular region of the lobule. The *gall-bladder* contained normal green bile and the extrahepatic bile-ducts were patent. The *spleen* was slightly enlarged, but showed no abnormality. The *brain* was too diffluent to allow of detailed examination.

Microscopy

The *liver* showed extensive areas of necrosis of irregular size and shape (fig. 1). Although most of the lobules showed central necrosis only, in others the necrosis extended to the portal tracts or even involved several adjacent lobules. The necroses were all recent, judged by the persistence of the necrotic cells in situ and the absence of any great reaction to their presence. Bordering on the necrotic patches were occasional degenerate hepatic cells intermingled with viable cells. The degenerate cells were often irregular in outline and had more eosinophilic cytoplasm than normal. There was often a round, oval, or irregular and eosinophilic or faintly basophilic homogeneous structure almost completely filling the nucleus. Occasional cells showed condensations of chromatin on the nuclear membrane separated from a rather irregular eosinophilic inclusion body by a clear halo (fig. 2). All the other organs were normal.

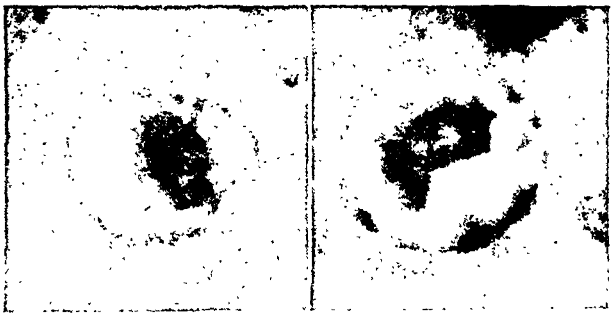
Fig. 2—Liver cells showing classical shrunken eosinophilic inclusions (×2100).

TWIN 2

Twin 2, also a boy, weighed 5 lb. 3 oz. and was well until the age of 10 days, when he was found to have lost 3 oz. during the previous twenty-four hours, his weight having fallen to 4 lb. 10 oz. No abnormalities were detected clinically, and there was no jaundice. Next day he became lethargic and reluctant to feed. He gained weight slowly until the 16th day of life, when he passed two motions containing a streak of bright blood. His colour became poor, and twelve hours later he had a convulsion accompanied by the passage of bright blood per rectum, and died at the age of 16 days.

Necropsy Findings

The *liver* was like that of twin 1. The *brain* was externally normal, but on section numerous white nodules, similar to those in the liver, were seen scattered throughout both cerebral hemispheres. They were present in both grey and white matter and involved the basal ganglia. Owing to their firmness they could be easily distinguished by touch from the surrounding brain tissue. There was no evidence of hydrocephalus or of meningitis. All the other organs appeared normal.

Microscopy

The *brain* showed areas of gliosis of different sizes. Such areas were widespread and lay in both grey and white matter, bearing no relation to the vessels. Many were tiny foci of small cells with deeply staining round nuclei almost completely filling the cells; others were more extensive and composed of numerous glial cells, resembling astroglia, together with smaller cells, some of which appeared to represent degenerate astrocytes (fig. 3). Gliosis was prominent beneath the ependyma of the lateral ventricles, and in some places the proliferated neuroglia had extended through the ependyma to produce small nodules on the lining of the ventricles. Less common were small patches of softening in

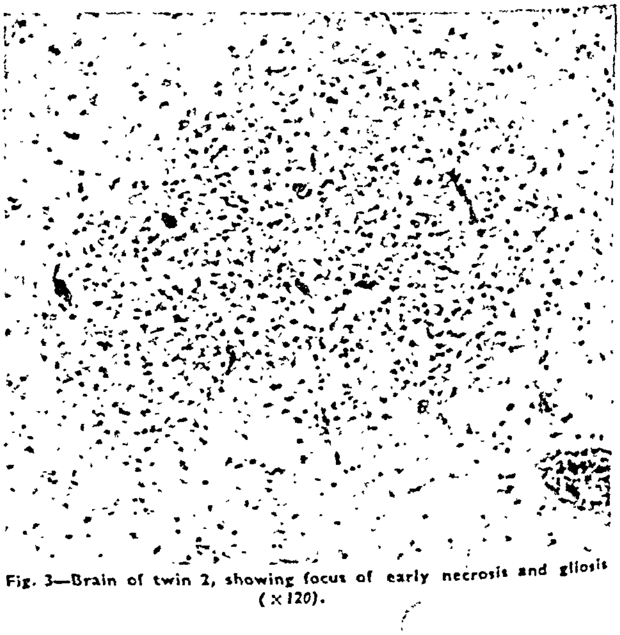
Fig. 3—Brain of twin 2, showing focus of early necrosis and gliosis (×120).

simplest investigation made on his patients Instead, for even a blood-count his patient must go through the formalities of an appointment with a consultant and so do his bit towards the overcrowding of an outpatient department already working below establishment for lack of a registrar This is a situation which Alice would have taken in her stride, but in the daylight outside the rabbit hole it is plainly ridiculous It certainly does not provide inducement to the young doctor to gain experience To this must be added the belief among registrars that to general practitioners the ex-registrar is necessarily a "failed specialist" who proposes to take to general practice as a poor second choice This is a regrettable attitude, but who can blame a principal if, under the present circumstances of general practice and its divorce from hospital work, he selects a man of 28 with a diploma in preference to a man of 38 with "F R C S—10 years' hospital experience"? So much, then, for the prospects in general practice

What about the future for the one in every four of intermediate registrars who may hope to become a senior registrar? His chance of becoming a specialist in some grade is now increased to 75%—but every step in this direction takes him farther away from the possibility of general practice as a reasonable alternative And what for the lucky few who do eventually reach specialist posts? At the end of 1951 there were 2445 whole time specialist medical and dental officers (including senior hospital medical officers and senior hospital dental officers)[7] A study of *The Lancet* for 1952 reveals that of the 887 specialist posts advertised that year 655 were full time It is idle to suppose that more than a small fraction of the doctors now in these posts will ever move on to maximum part-time posts The S H M O s among them are limited to the salary scale £1300–1750, and the full time specialists to £1700–2750 —without private practice, domiciliary visits, or reasonable income-tax allowances Fair salaries these may be for the work involved, but they are not the glittering prizes which induce a young man to commit himself to a specialist training—especially when compared with the money he is encouraged to earn as a partner in general practice According to *The Lancet* he can hope to achieve such partnership by the age of 36,[8] and with 2000 patients on his list his income from this source alone would be £2200[9] A man with a family may wisely decide that the D OBST and an ultimate £3000 offers better professional satisfaction than the M D, M R C P, and £1750 The general practitioners have arranged their affairs well and no one will begrudge them their award, but they have seriously undermined the hospital services

In addition to their financial handicaps specialists at peripheral hospitals are in an exceedingly difficult position because of the shortage of resident staff Were it not for the present unhappy situation of many senior registrars there might be considerable difficulty in filling some of the single-handed specialist posts

Never was there a bleaker prospect for the young man starting a hospital career Here lies the root of the hospital staffing problem

THE FUTURE

What are the possible remedies for this state of affairs? It is necessary to explode at once the myth that the year of compulsory preregistration residence will be of any real help in staffing hospitals A recent survey (July 1, 1951, to June 30, 1952) showed that 76 5% of all doctors entering the Armed Forces during that period had done at least a year in hospital posts and at least 27% had done considerably more than this

The Medical Act, 1950, will ensure that all doctors do a full year in hospital, but at the end of his year each liable individual will be called up unless there is some very special reason for his further deferment At the moment the need of a hospital for his services is not regarded as a valid reason In addition it must be recalled that preregistration appointments are in approved posts in the major specialties (medicine, surgery, obstetrics) It is difficult to see how the Medical Act makes any real contribution to the staffing of peripheral hospitals, and it will certainly not improve the figures for S H O s and registrars

The main solution must come from recognition that for the doctor a junior hospital post is a temporary affair For the hospital "the house surgeon" is a permanent need, but for the doctor the post is a stepping stone It must be made an effective step either to a career as a specialist or a career as a general practitioner

As far as specialisation is concerned, I have already pointed out that the balance of financial reward in general practice and specialist medicine needs redress Attention must be paid to the particular handicaps imposed on the full-time salaried specialist—whether of consultant or S H M O status—and the trend towards increasing the number of whole time appointments must be reconsidered Any attempt to introduce a new grade of specialist paid at a lower rate would certainly aggravate the position, for, although some posts might be filled now by ex senior-registrars, their existence would provide no incentive in the future

Apart from the eventual financial reward every effort must be made to ensure that the scales of promotion are not too heavily weighted against the man whose registrar experience has been gained at non teaching hospitals This problem will be solved, as far as senior registrars are concerned when the majority of senior registrar posts are held on a basis of rotation between teaching centre and periphery Such rotation hardly seems practicable for intermediate registrars who work on a 2 year tenure, and it must be acknowledged that the registrar from a teaching hospital will always be a strong candidate for a senior registrar post Here the interests of the registrars themselves as well as those of the peripheral hospitals might be best served if the teaching hospitals insisted that experience *as a registrar* in a non teaching hospital was a necessary qualification for appointment to a similar grade at the teaching centre There may well be other ways of tackling this side of the problem

As far as general practice is concerned, we are up against a much more formidable problem The opening of diagnostic facilities to general practitioners would be a first step which would make the background of hospital training a clear asset in practice Much more fundamental however, is the reintegration of the specialist and general practitioner services By this is not implied that regular contact between the G P and the specialist which is so hopefully discussed and so seldom achieved, but rather the replanning of the whole structure of hospital staffing at all levels to allow the general practitioner specialist to return to the scene Only by holding out the very real prospects of such posts will it be possible to fill those 75% of intermediate registrar posts which must in future be held by potential general practitioners

The British Medical Association are committed to this policy,[10] but improvement will not be brought about by grafting clinical assistants and part time G P consultants on to the present establishments There must be a complete reconsideration of the method of staffing at all levels The medical and political advice upon which the hospital service was initiated must now be reviewed, the lessons of the last five years learned, and the harsh facts faced for the first time since its inception which a few compound granular corpuscles were present, together with evidence of mild neuroglial proliferation at the periphery of the lesions. In neither the areas of gliosis nor in those of softening were any intranuclear inclusion bodies seen.

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[8] *Ibid* April 18 p 779

[9] *Brit med J* suppl 1952 i 28

[10] *Ibid*, p [illegible]

The *liver* and all the other organs showed histological features similar to those of twin 1.

DISCUSSION

Cowdry (1934) called certain intranuclear inclusion bodies "type-A inclusions" and thought them characteristic of infection by a virus. Cells containing such inclusions show accumulation of chromatin on the nuclear membrane, which is separated from a central intranuclear eosinophilic body by a clear zone. The cell ultimately disintegrates completely, and such cells are accompanied by a noticeable reaction in the surrounding tissues. Those associated with herpes simplex have been described by Scott et al. (1950), who state that when the inclusions first appear they are faintly basophilic and fill the entire nucleus; later, shrinkage takes place, and an eosinophilic body is produced, separated from the nuclear membrane by a clear halo.

Primary infection by the herpes-simplex virus commonly produces gingivo-stomatitis in children (Scott 1944), usually resolving after 1 to 2 weeks. Although rare in the neonatal period, primary infection is important in that it may produce lesions in organs other than the skin, and may cause death (*Lancet* 1952).

Although herpes simplex had for some years been suspected on morphological grounds as a cause of encephalitis, it was not until 1941 that Smith et al. (1941) isolated the virus from a child dying at the age of 5 weeks with extensive meningo-encephalitis in whose brain typical inclusion bodies were found in the nerve-cells. Since then the virus has been recovered from the cerebral lesions of two adults (Zarafonetis et al. 1944, Whitman et al. 1946) and from an infant aged 13 days born at full term of a woman who had genital herpes in the fifth month of pregnancy (Wildi 1951).

Wildi's case showed cerebral lesions of two types: in one there was non-specific inflammation and no inclusion bodies; and in the second type inclusion bodies were very numerous, especially in nerve-cells, and associated with much inflammation and necrosis. The specific ætiology of the lesions found in twin 2 is suggested by the associated presence of typical herpes hepatitis, although no inclusion bodies were found in the brain. Haymaker (1950) states that softening of the brain may be so severe that the pathologist omits histological examination; the possibility remains that encephalitis caused the diffluence of the brain of twin 1.

That herpes-simplex virus can produce lesions in organs other than the brain was first suggested by a case reported by Hass (1935). This was in a girl aged 14 days who had been born prematurely, and numerous necrotic areas were found throughout the liver, which on microscopy revealed many cells containing intranuclear inclusions resembling those found in herpes simplex. Similar microscopic foci of necrosis were also present in the adrenal glands.

Quilligan and Wilson (1951) described a similar case in a child aged 12 days, whose mother had herpes labialis 9 days before delivery. The baby showed herpetic lesions of the skin and, at necropsy, severe hepatitis with inclusions in the liver cells. The virus was isolated from the skin on the 2nd day of illness, and from the skin and liver at necropsy.

Zuelzer and Stulberg (1952) reported eight cases of generalised visceral lesions which were due to the herpes-simplex virus and in which hepatitis was a prominent feature. Their material was divided into two groups:

(1) Five babies who died 5 to 13 days after birth. Three of them were thought to have been infected during passage through the birth canal, thus acquiring herpetic conjunctivitis; in one case transplacental infection was suggested. The mother had clinical genital herpes simplex in one case, and the virus was isolated from her infant.

(2) Three older children in whom generalised spread followed herpetic gingivo-stomatitis.

As neither of the present cases showed any obvious portal of entry we believe that the infection was transplacental.

SUMMARY

Twin boys dying at 7 and 16 days showed the pathological features of herpetic hepatitis, associated in one case with encephalitis.

The ætiology of this condition is discussed.

We wish to thank Miss F. M. Humphries for technical assistance.

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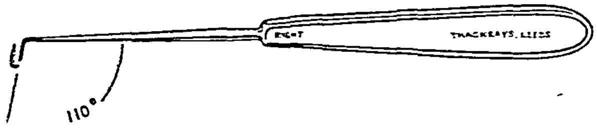
New Inventions

FEMORAL-HERNIA NEEDLE

THE common approaches for repairing femoral herniæ are the inguinal approach of Lotheissen and the older route below the inguinal ligament. After the hernial sac has been excised, an essential step in both methods is to pass two or three stitches through Astley Cooper's ligament. This is often done with a small-sized Symonds or J-shaped needle held at an angle of about 110° in a needle-holder. As such a needle is difficult to hold and to control, I use the needle shown in the illustration and find it simplifies the operation.



My own practice is to repair the non-strangulated femoral hernia by the lower route. It is a quick easy operation which does not weaken the inguinal canal by dividing the transversalis fascia. For strangulated hernia the inguinal route is preferred because it enables the strangulated bowel to be inspected and, if necessary, resected. In both operations two or three no. 35 unbleached linen-thread sutures are passed through Astley Cooper's ligament. Linen is chosen because it is strong, knots well, and being of vegetable origin is absorbable. In other parts of the body, where I have had opportunities of reopening the incision, thread takes about eighteen months to be absorbed. In contrast to 'Nylon' it encourages fibrosis. If sepsis is feared in a strangulated hernia, antibiotics, catgut, or nylon can be used, because infected thread is not absorbed and may cause a sinus to be formed.

In the lower operation Cooper's ligament is brought into view by retracting the inguinal ligament by passing a Kocher's blunt dissector or a narrow copper spatula through the femoral canal so that its end bears on the posterior surface of the pubic bone. If the lower half-inch of the copper spatula is bent to 60°, a better exposure is obtained. The femoral vein is protected with a Lane's retractor or with a finger. Since the sutures are inserted with the handle of the needle placed medially across the midline of the body, a separate needle is required for

Now at last there must be in this staff shortage, common ground between politician, bureaucrat, and doctor The time is surely ripe for realistic discussion and action

I am grateful to Dr John Walton, Dr E Grey Turner, Dr F J Harvey, and the registrar of the General Medical Council for various items of fact included in this article

SALARIES OF ASSISTANT MEDICAL OFFICERS

UNDER an Industrial Court award which operates as from June 1, the salary-scale of assistant medical officers or medical officers in departments is to be £950, rising by annual increments of £50 to £1300 This award supplants a 1950 award[1] by which the scale was £850 rising by annual increments of £50 to £1150 In seeking revision of the 1950 award the staff side of Whitley Council Medical Committee "C" claimed a scale of £1000 rising by annual increments of £50 to a maximum of £1400

The new scale is to be applied to the present holders of appointments Assimilation on the new scale will correspond with the medical officer's position on the old scale, but a medical officer now at the maximum (£1150) of the old scale is to be placed at the sixth point (£1250) of the new scale and thereafter will proceed to the new maximum

The salaries of other medical workers in the public-health service are governed by earlier decisions of the Industrial Court[1 2]

The Wider World

THE HEALTH OF A TROPICAL PEOPLE

A Survey in Ceylon

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III INCOME AND HEALTH

THE income of the individual or of the family is often used as an index of social environment It is an index which can be given a quantitative rating which is easily checked, and which is readily understood by all.

The income includes not only wages earned but also food and goods produced for family use, profits from investments, and an allowance for rent if the house is self-owned. When estimating the income all these sources should be checked and then counter-checked by reference to the employer and other interested parties For the household the total income may be reduced to so much a head, or it may be related to the number of food-consumption units in the household In Ceylon we have used the latter method because it enabled us to link the income classification with the dietary studies

An Inquiry Based on Income

In Ceylon, we usually divided our samples into three income groups:

(1) *Low income group* in which the families have an income of less than 20 rupees per adult food-consumption unit per month

(2) *Intermediate income group* in which the families have an income of between 20 and 50 rupees per adult food-consumption unit per month

(3) *Higher income group* in which the families have an income of more than 50 rupees per adult food-consumption unit per month.

TABLE I—AVERAGE INTAKE PER CONSUMPTION UNIT (INTERNATIONAL VALUES) PER DAY

—	Low incomes (441 families)		Intermediate incomes (681 families)		Higher incomes (185 families)	
	Mean consumption	S.E. of mean	Mean consumption	S.E. of mean	Mean consumption	S.E. of mean
Calories	2067	49·5	2593	48·5	3055	93·1
Protein (g.)	57·8	1·34	75·2	1·63	87·8	2·85
Fat (g.)	31·8	1·72	52·7	1·68	91·0	4·55
Carbohydrate (g.)	396	7·1	476	9·7	493	12·0
Calcium (mg.)	396	14·7	579	13·6	756	24·0
Phosphorus (mg.)	1475	51·4	1730	51·0	2080	51·7
Iron (mg.)	12·9	0·39	16·8	0·38	18·1	0·62
Preformed vitamin A (I.U.)	3180	103·2	4670	120·2	5700	331·0
Thiamine (mg.)	0·919	0·027	1·352	0·079	1·365	0·049
Riboflavine (mg.)	1·433	0·058	2·052	0·044	2·321	0·038
Nicotinic acid (mg.)	11·02	0·587	13·0	0·288	13·62	0·464
Ascorbic acid (mg.)	48·1	2·99	51·0	1·67	90·5	4·42

S.E. = standard error I.U. = international unit.

The low income group, which is the largest, contains mainly agricultural workers and the village peasant cultivators The intermediate-income group is predominant in the urban areas and on the estates and includes most of the estate labourers and clerical workers The higher-income group is found chiefly in the urban community, and includes the professional classes, the civil servants business men, and people from the supervisory grades of labour

CONSUMPTION OF FOOD

A sample survey of the whole island showed that the quantity and quality of the food eaten was largely determined by the economic status of the family (tables I and II) (Cullumbine 1951)

The calorific value of the total foodstuffs consumed, and the total amounts of the individual chemical constituents consumed, rose with the economic status of the consumers The variation in the consumption of individual foodstuffs with economic level is not so con-

TABLE II—AVERAGE DAILY INTAKES (OZ.) PER CONSUMPTION UNIT (INTERNATIONAL VALUE)

—	Foodstuffs	Low incomes (441 families)		Intermediate incomes (681 families)		Higher incomes (185 families)	
		Mean	S.E.	Mean	S.E.	Mean	S.E.
Cereals	Rice	9·95	0·31	11·22	0·26	10·80	0·73
	Wheat flour	2·96	0·044	4·27	0·092	3·69	0·124
	Other cereals	1·59	0·068	0·996	0·053	0·07	0·180
Vegetables	Roots	1·65	0·036	1·26	0·063	2·16	0·102
	Greens	1·37	0·064	2·08	0·122	1·32	0·963
	Pulses	0·582	0·051	1·33	0·079	0·517	0·082
	Veg. fruit	2·0	0·196	1·39	0·140	2·96	0·266
Fruit	Fresh	0·494	0·073	0·401	0·045	1·42	0·161
Dairy products	Fresh milk	0·470	0·120	1·25	0·141	3·19	0·345
	Powdered milk	0·042	0·006	0·111	0·024	0·24	0·053
	Butter	—	—	0·021	0·0043	0·31	0·028
	Ghee and curd	0·01	0·0006	0·004	0·0023	0·128	0·016
	Eggs	0·017	0·0053	0·047	0·0069	0·372	0·040
—	Meat	1·63	0·20	3·05	0·15	10·15	0·27
	Fish	14·1	0·30	16·44	0·32	22·81	0·89

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[1] See *Lancet* 1950 ii 918 *Ibid* 1951, p 58
[2] See *Ibid* 1951 i, 1176

each side: these needles are marked "right" and "left."

I normally pass three sutures through Cooper's ligament and next rethread the needle to the upper end of each thread. A finger can often be passed through the femoral canal which has been stretched by the hernia and the half-inch length of the anterior wall of the femoral canal appreciated. The lowest limit of the anterior wall of the femoral canal is in any case indicated anteriorly by the upper cornu of the falciform edge (Hey's ligament). The three sutures are passed in turn, from within the femoral canal, through the lowest part of the anterior wall of the canal. The sutures are then tied, fixing the anterior wall of the femoral canal to Cooper's ligament. This makes a good solid repair and does not distort the line of the inguinal ligament.

I wish to thank Miss Margaret C. McLarty for the clear illustration. The needles were made by Charles F. Thackray, of Leeds.

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Reviews of Books

Medical History of the Second World War

The Army Medical Services: Administration. Vol. I. F. A. E. CREW, M.D., F.R.S., professor of public health, University of Edinburgh. London: H.M. Stationery Office. Pp. 530. 50*s*.

THIS is a difficult book to review. The title is forbidding and the letterpress relieved only by a few pages of photographs of recruits in training. The subject is one which is unlikely to raise the pulse-rate of many of those who, willingly or otherwise, spent the war years under the motto *Per arduis fidelis.* It was so easy in our troubles to blame "them"—the gilded ones who came and left in large cars, who sent us hither and thither "forthwith," who settled our hash for good or ill. Twelve years or so later we can judge them with charity and, if we read this book carefully, with sympathy. It is not easy to manage a hospital: how much more difficult to manage a hundred hospitals, a hundred field ambulances, and a huge variety of other units, not in one country but scattered from the Falkland Islands to Manipur Road, and often in transit. These had to be staffed and administered by doctors from every walk of the profession, most of whom had been their own masters for years and were proud of it. The regular soldier upon whom fell the brunt of administration in the early days knew little more of the problems of war than the ex-civilian. The R.A.M.C. in peace was a hospital service; stretcher drill was an elegant manœuvre and the recruit knew the First Field Dressing only as a picture on the blackboard. Most of us who laughed or cursed in the autumn of 1939 had reason to be grateful to the regular soldiers who saved us from the major errors of procedure and behaviour. What we did not know then we can learn from this book.

The uncertainty in planning the medical services of the nation for war makes a sorry story. The pull-devil-pull-baker between the Armed Forces and the Ministry of Health took place across the Cabinet table. The first knew the number of doctors needed for the fighting Forces in being and projected, and perhaps they over-estimated their needs. The second had been warned of astronomical casualties from aerial attack at home and believed that they could not spare a man. Perhaps not so much harm would have been done if the fight had been settled twelve months earlier, irrespective of the issue. The finest testimony to the Army Medical Department is that, by the end of 1939, 61 fully equipped medical units had reached France while the health of the Army at home, left in the hands of the ill-trained and uninstructed, gave no reason for anxiety. All this is described critically and without acrimony, but it is past history. Yet there is much in this book which may be read with profit today. Our present problems are not identical but they are not so dissimilar that we cannot draw a parallel: too much to do, too many conflicting claims, not enough willing hands, and, above all, not nearly enough earnest minds willing to give and take responsibility. On a more technical level, the statistical appraisal of medical man-power might be applied to some staffing problems today, and some appreciation of the theory behind the military attempts at rehabilitation might lead to a more objective and less chancy approach to the problem than seems usual.

There is much more in this book which deserves attention. Is there any other country which would entrust an official military history to a distinguished geneticist who now holds a chair of public health? To quote the preface "the author alone is responsible for . . . the opinions expressed." They are shrewd and they aim straight, but they are fair and, as far as we may judge, they will be generally accepted. As an enlightened presentation of fact the book is a masterpiece.

Cardiography in General Practice

ABRAHAM I. SCHAFFER, M.D., assistant visiting physician, Metropolitan City Hospital, New York. Baltimore: Williams & Wilkins. London: Baillière, Tindall, & Cox. 1952. Pp. 135. 24*s*.

THE term "general practice" may not have the same connotation in the U.S.A. as it has here, but in this country the title of this small book must be called misleading. It is a technical account of cardiography, including electro-, vector-, and ballisto-cardiography, illustrated by diagrams to show the electrical changes, normal and abnormal, in the heart and their cardiographic representation, the appropriate placing of leads, and so forth. It is presumably intended for the student aspirant to whole-time cardiology; and even for him it is of academic rather than clinical value, though the cardiographic pictures of the various lesions and disorders of the heart are duly shown. The book shows clearly enough in how many conditions a cardiogram, expertly interpreted, can assist diagnosis; but most practitioners are probably ready to take this on trust, and only those among them determined to understand for themselves the mysteries of cardiographic script will be recompensed for the considerable intellectual effort of reading these pages.

Primary Love and Psycho-analytic Technique

MICHAEL BALINT, M.D., M.SC. London: Hogarth Press and the Institute of Psycho-Analysis. 1952. Pp. 288. 30*s*.

Dr. Balint is chiefly interested in the manifestations of human sexuality, especially as derived from the infant's early relationship with its mother, which he calls "primary love," and with the far-reaching effects which this experience has on the formation of object-relations, and, for the patient in psycho-analysis, on the course of the transference, especially in the closing stages. The papers start with one written in 1930, on psychosexual parallels to the fundamental law of biogenetics, in which the evolution of human sexuality and love is considered in relation to a phylogenetic background based on a wide knowledge of biology. The last paper appeared in 1952, and examines sympathetically some of the more recent findings of Mrs. Klein; so it may be said that the book gives a useful and valid conspectus of the developing viewpoints of psycho-analytic theory on its subject matter. It is simply and clearly written.

Office Management of Ocular Diseases

WILLIAM F. HUGHES, JUN., M.D., professor and head, department of ophthalmology, University of Illinois College of Medicine. Chicago: Year Book Publishers. London: Interscience Publishers. 1953. Pp. 452. 70*s*.

Professor Hughes has condensed current teaching on ophthalmic disease into a small and readable volume, though he does not always abide by the implications of his title, wandering off at times into the hospital treatment of glioma retinæ and retinal detachment. Some of the lid operations are also more than most of us would attempt in the surgery. Illustrations are, on the whole, good, but some photographs, such as fig. 89, are not sufficiently clear to demonstrate anything. Certain treatments, such as that of glioma retinæ, are not quite up to date, but, on the whole, the author has achieved what he set out to do: this is a concise and useful volume.

sistent In general, the intermediate-income families eat more cereals, green vegetables, and pulses, while the higher income families eat more root vegetables, fresh fruit, dairy products, meat, and fish

The proportion of the average total calories derived from protein, from carbohydrate, and from rice decreases while the proportion contributed by fat increases with rising economic status (table III)

The high contribution made by carbohydrates, and by rice in particular, shows the lack of variety in the diet of the average Ceylonese This is further emphasised by the meagre quantities of milk, butter, and other dairy products eaten by people at all economic levels

TABLE III—PERCENTAGE OF TOTAL CALORIES DERIVED FROM VARIOUS SOURCES

Income group	Protein	Fat	Carbo hydrate	Rice
Low	14 1	14 3	71 6	48 1
Intermediate	12 2	18 9	68 9	43 3
Higher	11 7	27 7	60 6	36 3

Only a few families were found to eat these foodstuffs (table IV)

The consumption of meat is also small, but fish is a common article of diet Most of the protein of the diet was of vegetable origin (table V) The percentage contribution to the total protein intake made by meat increases with rising income, but the average contribution to the total intake made by fish is more or less the same in all income groups

DEFICIENCIES AND PHYSIQUE

Many members of the families surveyed were examined for signs of deficient nutrition (table VI) Xerosis, ariboflavinosis, and anæmia are to be found more often among the low-income group Dental caries was found in all income groups, phrynoderma (follicular hyperkeratosis) is commoner in the intermediate income group

TABLE IV—PROPORTION OF FAMILIES CONSUMING VARIOUS FOODSTUFFS

Income group	Butter	Milk	Milk powder	Ghee	Eggs
Low	7/441	83/441	17/141	3/141	27/441
Intermediate	24/681	288/681	103/681	28/681	154/681
Higher	51/185	161/185	52/185	31/185	93/185

Physiques and body measurements differed widely in the three income-groups (table VII) Exercise performance ability is correlated with certain anthropometric characters (Cullumbine 1949), and table VIII correlates variations in strength, exhaustion, and speed with anthropometric characters

The differences in body configuration offer a reasonable explanation of the differences in dynamic fitness of the people at each economic level We find indeed the vicious circle—low income, poor nutrition, poor physique, poor functional or working capacity poor production, therefore low income

BIRTH WEIGHT

The low income/poor nutrition/poor physique correlation has other implications An analysis of 1311 consecutive full-term births in one ward of the De Zoysa Maternity Hospital, Colombo, suggested that the main factors influencing birth weight were the mother's weight, the number of gestations and whether the birth is a single or a multiple one (Cullumbine 1950) The heavier the mother the greater was the infant's birth weight, except that when the mothers weighed over 120 lb there was no further increase in the baby's weight with increasing maternal weight This relationship has been generally recognised by obstetricians, and it has also been found to be true in stock breeding (Walton and Hammond 1938) It is usually attributed to hereditary

TABLE V—PERCENTAGE OF TOTAL PROTEINS CONTRIBUTED BY VARIOUS FOODSTUFFS

Income group	Meat	Fish	Vegetables
Low	2 8	24 4	72 8
Intermediate	4 1	21 9	74 0
Higher	11 2	25 1	63 7

TABLE VI—SIGNS OF MALNUTRITION OBSERVED IN THE THREE INCOME GROUPS

Income group	Number of subjects examined	Number of subjects with signs of—					
		Under-nourishment	Xerosis	Phrynoderma	Riboflavine deficiency	Anæmia	Dental caries
Low	1936	575	1119	629	107	1141	697
Intermediate	2876	367	1099	1252	108	1066	908
Higher	583	79	243	173	3	102	182

TABLE VII—VARIATION OF THE MEANS OF ANTHROPOMETRIC CHARACTERS OF GROUPS OF SINHALESE SUBJECTS (AGED 21–30) WITH ENVIRONMENT AND ECONOMIC STATUS

Anthropometric character	Income group		
	Low	Intermediate	Higher
Weight	—	>a, P = <0 001	>a P = <0 001 >b P = 0 001
Height	—	—	>a P = 0 001 >b P = 0 001
Surface area	—	>a P = <0 001	>a, P = <0 001 >b, P = <0 001
Weight/height	—	>a P = <0 001	>a, P = <0 001 >b P = <0 001
Leg length	—	>a P = <0 001	>a, P = <0 001
Bi acromial	—	>a P = <0 001	>a P = <0 001
Bi iliac	—	>a P = <0 001	>a, P = <0 001
Bi zygomatic	>c, P = 0 001	>a P = <0 001 >c P = <0 001	— —
Chest circumference (Best)	—	—	>a P = 0 02
Chest circumference (inspiration)	—	>a P = 0 001	>a P = 0 001
Chest length	—	>a P = <0 001	>a, P = <0 001
Chest depth	—	—	—
Chest breadth	—	>a P = <0 001	>a P = <0 001 >b P = 0 001
Leg length/height	—	>c P = 0 05	—
Bi iliac/height	—	>a P = 0 05	—
Bi acromial/height	—	>a P = <0 01	—
Chest circumference height	—	—	—
Bi iliac/bi acromial	>b P = 0 01 >c P = 0 01	—	—
Chest depth/chest breadth	>b P = 0 01 >c P = 0 001	—	—
Chest length/sitting height	—	>a P = <0 001	—
Chest breadth/sitting height	—	>a P 0 001	< a P 0 021

P = Probability

ychological and prophylactic effect" of inducing dical experts on both sides to be careful in their sertions and claims, because these might always be viewed by an outstanding authority in their own ld.

For some years the State of Massachusetts has provided, civil proceedings, pre-trial examination of psychiatric ses by impartial medical specialists, and this arrangeent is said to be working well. The result of the ew and far wider experiment in New York may well fluence the development of practice in this country. ndeed, no legislative innovation would be required to troduce a parallel working system here, for under the ules of the Supreme Court (R.S.C. 0·37A, r.1) the court r a judge may already "in his discretion at any time n the application of any party appoint an independent xpert (to be called "the court expert") to enquire and eport upon any question of fact or of opinion not nvolving questions of law or construction." Unfortunately, applications under this rule have been but few nd far between, and it would perhaps be well if judges were given power to call in court experts from an ppropriately prepared list even where no such express equest is forthcoming from the parties.

TREATMENT OF BARBITURATE POISONING

SUICIDAL poisoning with barbiturate drugs is becoming increasingly common,[1] and the mortality may be high even in those who come under medical care. Nilsson in Sweden has shown the value of good medical treatment without convulsant drugs,[2] and Locket and Angus in this country have had similar results.[3] In their series of 84 patients who were not given convulsant drugs there were only 2 deaths. Analeptics are not a treatment for anoxia or asphyxia, and their value is obviously difficult to assess when survival may depend on the skill of the nurse and the doctor in managing an unconscious patient. Nevertheless it has become the practice to give analeptics for barbiturate poisoning because they reduce the mortality in poisoned animals; but then experimental animals do not enjoy the nursing attention that is the patient's right.

In comparing different analeptics the effect of chance on mortality-rates cannot be gauged when deaths are numbered in single figures. Mortality-rates depend on age, individual idiosyncrasy, and the condition of the liver and kidneys, as well as on more obvious factors such as the dose and type of the drug and the amount vomited. Hence little is to be gained from comparing the results of different workers, as Koppanyi and Fazekas [4] have done. They conclude in the end, largely from their own experience, that the best initial treatment is to give 5 ml. of a 10% solution of leptazol. If there is a response to this "orientation dose" they continue with the same dose given every 10 or 15 minutes. Otherwise they give picrotoxin 25 mg. followed by 15 mg. every 15 minutes, provided of course that convulsions are avoided. In general leptazol is more likely to be effective against the rapidly acting barbiturates, and picrotoxin against the slowly acting ones. Koppanyi and Fazekas do not recommend caffeine or nikethamide. Dick [5] discusses 160 reported cases and 11 of his own, all treated with amphetamine; and he favours this analeptic, if only because it is relatively safe. The Council on Pharmacy and Chemistry of the American Medical Association [6] point out that there are deficiencies in investigations of analeptics. Indeed, the evidence for giving picrotoxin at all must be judged inadequate by modern standards; and the cumulative effect of successive doses often means that too much is given, for it has a latent period of up to 30 minutes. On the other hand, leptazol acts quickly and for a short time, and it is often given in inadequate doses.

The use of ultraviolet absorption spectrophotometry has lately provided a satisfactory method of measuring the concentration of barbiturates in body-fluids. Apart from giving much-needed data on the distribution and excretion of barbiturates, this method may facilitate both treatment and diagnosis. By providing a measure of the severity of poisoning, it should make the comparison of the results of different treatments an easier matter.[7] Alwall et al.[8] in Lund have used the method to study means of increasing the elimination of barbiturates. The rapidly acting barbiturates are of course largely destroyed in the healthy liver, but the more slowly acting ones are mainly excreted in the urine. Alwall et al. were remarkably successful in speeding the elimination of phenobarbitone in poisoned rabbits by exchange ultrafiltration and by dialysis. Forced polyuria was less effective. They applied dialysis successfully in two patients, but the full details have not yet been given. Barbiturates are distributed throughout the body-water,[9] and it is unlikely that exchange transfusion [4] can aid elimination effectively; on the other hand where dialysis with an artificial kidney is practicable recovery may probably be hastened in patients poisoned with the longer-acting members of the group. But whether the mortality-rates can be improved with dialysis or with analeptics will remain in doubt until controlled clinical trials have been carried out.

RACIAL PREJUDICE

RACIAL prejudice is a powerful disruptive social force breeding violence and harming every community it touches; and its influence is becoming increasingly apparent in many parts of the world. There is every need therefore to understand its origins, to prevent its spread, and to control its manifestations. UNESCO, as the international organisation charged with the spread of peace and goodwill through education, is trying to play its part by calling together a number of sociologists, anthropologists, and geneticists to prepare joint statements on the subject of race, setting out the scientific aspects,[10] and by publishing popular booklets to carry the facts to lay discussion-groups, school-children, and others who may benefit from this information. The latest publication is *What is Race?* [11] which explains the elements of genetics, with a wealth of attractive diagrams, and scientifically refutes some popular ideas of inheritance and the belief in a master race. The scientists answer the three basic questions Is there a pure race? Is there a superior race? and Are there unchangeable race differences? with a definite No. The word "race" is used here in the genetic sense of a group of human beings with physically inherited characteristics differentiating them from other human beings. But in everyday usage race means a good deal more; it means, for instance, the classification of man by nationality, culture, religion, colour—or the shape of his nose; and the classification may have little to do with his ancestry. If scientists restrict the word to their own use and meaning, other people will have to find another word for what is after all quite a different meaning.

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[1] Moore, M., Alexander, L., Ipsen, J. jun. *New Engl. J. Med.* 1952, 246, 46.
[2] Nilsson, E. *Acta med. scand.* 1951, suppl. 253; see also *Lancet*, 1951, ii, 297.
[3] Locket, S., Angus, J. *Lancet*, 1952, i, 580.
[4] Koppanyi, T., Fazekas, J. F. *Amer. J. med. Sci.* 1950, 220, 559.
[5] Dick, H. L. H. *Ibid*, 1952, 224, 281.
[6] Eckenhoff, J. E., Schmidt, C. F., Dripps, R. D., Kety, S. S. *J. Amer. med. Ass.* 1949, 139, 780.
[7] Fisher, R. S. *New Engl. J. Med.* 1949, 240, 395.
[8] Alwall, N., Lindgren, P., Lunderquist, A. *Acta med. scand.* 1952, 143, 299.
[9] Symposium on Barbiturates. *Fed. Proc.* 1952, 11, 625.
[10] See *Lancet*, 1950, ii, 142.
[11] What is Race? Department of Mass Communication of UNESCO. 1952. Obtainable from H.M. Stationery Office. Pp. 85. 5s

UNESCO tells how an observer from Mars, the objective scientist, views the human species What we want to know is how men come to view one another as they do The fact, for example, that the relatively recent ancestors of present-day Scotsmen came from Ireland, Scandinavia, and France does not prevent Englishmen from recognising the Scots as a distinctive group (or from saying that "all Scotsmen are mean") Moreover, there are black Jews in Africa, yellow Jews in China, and every variety of white man among the Jews of Europe and America, so the "typical Jew" is different from country to country, and there can clearly be no "Jewish race" according to the canons of physical anthropology Nevertheless Jews are by and large a recognisable group of men marked by a common religion and common customs Ill-feeling towards such groups may be called racial prejudice, national prejudice, or cultural prejudice; but whatever its name it has very little to do with genetics or physical anthropology Thus we fear that the genetic approach to racial problems may do a disservice rather than a service to the cause UNESCO has at heart, because it hides the irrational basis of racial prejudice and pretends that it can be fought with scientific knowledge and reasoned argument The man who complains that all niggers smell is not interested in the scientific truth or otherwise of his statement, what he means is that he hates Negroes What has to be discovered is how he has come to feel such an emotion, and what are the circumstances which encourage its spread among his friends and neighbours

We are nearly all inclined to generalise about groups from single cases, and to view all foreigners with suspicion, even when they come from no further afield than Cornwall or Yorkshire We are prone to accept traditional judgments, like "the Irish are unreliable" or "the Italians excitable," because we believe we can recognise members of these groups at once by their speech and bearing, and often our experience bears out this belief In a few individuals this mild xenophobia becomes severe and pathological, and its origins require detailed case-histories to make them plain It is surprising how little psychiatric investigation there has been in the research on race prejudice To explain further how the virulent emotion of the few spreads at certain times and places to the whole community we must examine social conditions not only at the time of an outburst of violence but in the quiescent periods, and we must consider the reactions and motives of people who show no gross antiracial feeling as well as those of men who turn readily to lynching, the pogrom, and ritual murder Until this evidence has been collected we shall be unable to deal with racial prejudice other than empirically

HERPANGINA

FOR many years now a puzzling disease has reappeared in some areas of the United States each year during the summer or early autumn The illness, nearly always affecting children and generally those under 5 years of age, starts suddenly with fever, dysphagia, anorexia, sore throat, and pharyngitis, sometimes associated with vomiting and abdominal pain, usually it lasts 2–3 days Its most characteristic feature is the appearance in the mouth of a few greyish-white papulovesicular lesions, 1–2 mm in diameter and surrounded by an areola of erythema After 2–3 days these papules break down to give greyish-yellow ulcers which resolve after a few more days To this disease Zahowsky[1] gave the name herpangina, since it is somewhat similar to herpetic stomatitis Subsequent workers failed, however, to isolate the virus of herpes simplex The lesions in herpangina can be differentiated from those of herpetic stomatitis because they are limited to the anterior fauces, soft palate, uvula, and tonsils, while those of herpes are generally most pronounced on the buccal membrane and often associated with fœtor oris, gingival hæmorrhage and local lymphadenopathy Also herpangina occurs seasonally in small epidemics, whereas primary herpetic stomatitis is a sporadic disease rather more prominent in the winter[2]

Huebner and his colleagues[3] at Bethesda have shown that herpangina is probably the most common manifestation of infection with the A group of Coxsackie viruses In suckling mice, this group causes a diffuse myositis affecting predominantly skeletal muscles and not involving the brain, fat, or pancreas as the group-B viruses do Huebner and his associates surveyed a small community in the north west of Washington, D C, before, during, and after a small outbreak of herpangina for the presence of Coxsackie virus of the A group and for antibodies against six strains of Coxsackie virus, five of which had been isolated in cases of herpangina in this or neighbouring areas The virus was found only in those people who had herpangina or were contacts of cases and in whom antibodies to the infecting strain developed The level of antibodies to the other strains causing herpangina elsewhere remained constant in both the infected and the uninfected people The Bethesda workers also showed that the infected group had no previous antibody to the infecting strain, whereas in the non-infected group the percentage of people with neutralising antibody was very high In infected households contacts with antibody in their blood did not have the disease or harbour the virus Thus the localisation of the epidemic was apparently due to the majority of the population being immune because of previous infection, for, although coming into contact with the virus, these people were protected by their circulating antibody, which was shown to keep the same titre for at least a year So far Coxsackie virus has been isolated from either the throat-washings or the fæces of 90% of the 50 cases of herpangina investigated from 46% of contacts and from only 1% of the remainder of the population surveyed

Infection seemed to spread from case to case, the incubation period being 1–10 days Outbreaks were not explosive, as might be expected if the virus were spread by a vector such as food, drink, or infected flies. Coxsackie viruses have been isolated from flies, and Melnick and Penner[4] have shown that the virus may survive, although not multiplying, in this host for as long as 14 days So far it is not known where the virus hibernates during the winter and spring Nor is it known how long it can survive in carriers, the longest time after initial infection that it has been found is 78 days These viruses are fairly resistant, and possibly if conditions were suitable they might survive outside the body and be taken up by man or some other vector and so initiate another small outbreak if introduced into susceptible households, sporadic cases of herpangina almost certainly go unrecognised, and probably these keep the infection alive in a community

Coxsackie viruses have been associated with poliomyelitis and other diseases, but often such isolations may have been due to chance At present it seems that the commonest manifestation of infection with the group-A Coxsackie viruses is herpangina, and that perhaps the chief syndrome due to the B group is Bornholm disease either in its typical or in its more non specific form There is some evidence, however, that occasionally Bornholm disease may be caused by group A viruses also, although this disease might easily be wrongly diagnosed in cases of herpangina with abdominal pain and only a solitary lesion on the fauces influences (Bourne 1944) but it must also be remembered that the weight of the mother is in addition an index of her nutritional status. True it is usually accepted that the birth weight is only adversely affected when the mother's nutritional state is poor, but this may have been an influencing factor on the babies born in the lower-weight groups of this series. (The average weight of Sinhalese women, aged 26 to 30 years is 95·5 ± 1·23 lb., and 95 of these mothers were less than 90 lb. in weight.) Like the very undernourished mothers the very anæmic mothers (with hæmoglobin levels less than 5 g. per 100 ml.) had babies with significantly smaller birth weights. The reverse—i.e., increased birth weight after unlimited feeding during pregnancy—does not hold true, at least in rabbits (Wishart and Hammond 1933). The People's League of Health (1942) investigation, where a group of pregnant women were given supplements of iron, calcium, and vitamins A, B-complex, C, and D, also showed that these supplements did not significantly affect the birth weight.

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[1] Zahowsky, J *Arch Pediat* 1924 41, 181

[2] Parrott R H, Ross S, Burke, F G Rice E C *New Engl J Med* 1951, 245 275

[3] Beeman E A, Cole R M, Huebner, R J *Amer J Hyg* 1952 56, 215

[4] Melnick J L Penner, L R *J exp Med* 1952 96, 255

Birth weight bears a definite relation to the postnatal progress of the newborn baby. Thus, Illingworth and others (1949) have shown that in each age-group from 6·5 to 13 years children of higher birth weight are on the average significantly heavier and taller than those of lower birth weight. A similar relationship exists for the children of Ceylon, and in one group of 327 children, the weight at birth was positively correlated with the weight at 15 months (r = + 0·468), at 3 years (r = + 0·496), and at 6 years (r = + 0·423).

As birth weight is positively correlated with weight-growth during childhood, the latter will be indirectly influenced by the mother's weight and the number of her previous gestations. These again depend upon genetic and nutritional, and therefore socio-economic, factors. In other words heredity may determine the growth-potential of the individual, but the baby may yet be hampered at the outset in its chances of achieving this potential growth by malnourishment of the mother before its birth.

TABLE VIII—SIGNIFICANT VARIATIONS, WITH ECONOMIC STATUS, IN FITNESS INDICES AND RELATED ANTHROPOMETRIC CHARACTERS

Fitness index or related anthropometric character	Significant differences between income-groups
Strength, exhaustion-time, and speed	Higher > Intermediate > Low
Surface area	Higher > Intermediate > Low
Bi-iliac diameter	Higher and Intermediate > Low
Bi-zygomatic diameter.. ..	Higher > Intermediate and Low
Chest circumference/height ..	None
Leg length	Higher and Intermediate > Low
Bi-acromial diameter	Higher and Intermediate > Low
Weight	Higher > Intermediate > Low
Chest circumference	Higher and Intermediate > Low
Chest breadth	Higher > Intermediate > Low
Chest length	Higher and Intermediate > Low

Birth weight is also said to be related to the postnatal functional progress of the child (Bourne 1944). In 327 Ceylonese children the average birth weight was 6·51 ± 0·06 lb., the average age for first teething 9·5 ± 0·11 months, for first walking 12·7 ± 0·12 months, and for first talking 12·4 ± 0·14 months. By the method of least squares, it has been shown that the birth weight in this group of children was negatively correlated with walking-age (r = — 0·203, P = 0·05) but was not correlated with the teething (r = + 0·089) and talking ages (r = — 0·096). Walking-age was, however, positively correlated with talking-age (r = + 0·371, P = 0·001) and with teething-age (r = + 0·195, P = 0·05),

TABLE IX—MORBIDITY RATIOS FOR DIFFERENT CAUSES OF ILLNESS BY SEX AND FAMILY INCOMES, CEYLON, 1950

Cause of illness	Family income Rs. per month									All groups		
	100			100–300			300					
	M	F	All	M	F	All	M	F	All	M	F	All
Infective and parasitic diseases	105	99	102	98	94	96	92	92	92	102	98	100
Malaria	125	99	112	77	70	73	110	59	86	110	89	100
Common cold	—	—	—	—	—	—	—	—	—	—	—	100
Diseases of the nervous system	102	106	104	91	93	92	90	80	85	99	101	100
Diseases of the circulatory system	91	82	87	125	107	117	192	173	183	106	94	100
Diseases of the respiratory system	101	96	99	116	98	108	74	89	76	104	96	100
Bronchitis	107	95	101	115	96	106	55	40	54	107	93	100
Pneumonia	111	92	99	133	96	116	42	9	27	110	89	100
Diseases of the digestive system	110	94	102	104	87	96	93	89	91	108	92	100
Diarrhœa and enteritis	109	112	111	85	75	80	77	54	66	101	99	100
Dyspepsia	109	93	101	88	119	103	47	97	71	100	100	100
Diseases of the genito-urinary system	55	133	93	76	150	111	129	128	129	65	137	100
Normal and abnormal pregnancy	—	102	—	—	102	—	—	68	—	—	100	—
Diseases of the blood	82	157	118	46	95	69	14	46	29	68	134	100
Deficiency diseases	109	126	117	73	63	68	34	35	35	95	105	100
Diabetes	72	77	74	121	72	100	542	299	435	110	87	100
Chronic rheumatism	—	—	—	—	—	—	—	—	—	90	112	100
Diseases of the skin	126	82	104	123	71	98	71	33	53	122	76	100
Diseases of the eye	112	111	112	98	59	80	49	53	51	105	94	100
Accidents	154	55	106	120	54	89	110	44	79	142	54	100
All causes	103	104	104	93	95	94	78	84	81	99	101	100

prophylaxis for the gonococcal condition seem to me, to say the least somewhat uncertain, and, if prophylaxis is to be continued, it seems preferable to substitute penicillin for silver nitrate as you suggested.

Notification of the "sticky eye" is no doubt of little value, but notification of ophthalmia neonatorum, which includes possible cases of gonococcal ophthalmia, has evidently proved invaluable in (temporarily?) eliminating this condition. Unless we can be certain that blindness from this cause can no longer occur, notification would, like prophylactic measures, appear still to have a useful function.

London, W 1

H E HOBBS

LOCALISED MUSCULAR ATROPHY IN DIABETES

SIR,—I was interested in the article by Dr Hirson published on May 16. I was glad to read Dr Harris Jones's letter (May 30), and feel I must add my observations to his.

I entirely agree with Dr Harris Jones, for my feeling about Dr Hirson's paper was that he was, in fact describing fat atrophy rather than muscular atrophy. I have seen a number of cases where fat atrophy has occurred in areas where no insulin has ever been injected. I have never seen localised muscular atrophy associated with fat atrophy, as Dr Hirson described.

The photograph of his case 1 is very typical of fat atrophy in the arms of an old lady, and I am not convinced that it is true muscular atrophy as well. The most affected arm is the left, where the muscles are usually rather smaller than in the right. The localised patches of "atrophy" he shows in cases 5 and 6 look typically like fat atrophy, and I cannot see how there could be such a localised area of muscular atrophy in a long muscle.

I have discussed this article with my colleagues at King's College Hospital diabetic clinic, and they agree that, for the reasons given above and for those given by Dr Harris Jones, the evidence for a specific diabetic muscular atrophy is slight.

Diabetic Clinic
King's College Hospital,
London, S.E 5

JAMES A ROBERTSON

TRICHOMONAS VAGINITIS

SIR,—Concerning the correspondence on this subject, may I point out that trichomonas vaginitis in young girls is not rare in this country. In most of these cases the mother also has trichomonas vaginitis.

Tel Aviv Israel

S ROSENBAUM

THE INCONTINENT WOMAN PATIENT

SIR,—I was very interested in your annotation (May 23) on the incontinent woman patient and the use of sphagnum moss in dealing with this most distressing condition. As you say, any device which would reduce the burden of incurable incontinence is worthy of trial.

Another approach, which has been attempted from time to time, is the incorporation of a drainage system into the patient's bed. The disadvantage of such a system is that it inevitably requires a fair degree of immobility on the part of the patient. Enforced immobility is undesirable, but obviously many hopeless incontinents are also quite unable to move because of the nervous system disease or mental apathy, which is at the same time the source of their incontinence. Indeed it is almost a corollary that if mobility can be restored, incontinence will be cured.

On the basis of these facts some trials have been undertaken in Glasgow of a moulded bed with a drainage aperture and receptacle for urine and fæces. The principle of such a bed is that of the dorsal plaster shell, which not only maintains the perineum over the drainage aperture but reduces the liability to pressure-sores by distributing the patient's weight over a large area of soft tissue. Such a bed is made in sections, which can be approximated or moved apart to accommodate patients of varying heights. Adjustment of a standard mould to individual shapes is achieved by a specially prepared soft 'Dunlopillo' mattress. The bed is described elsewhere in detail.[1] Trials so far have shown that in selected cases patients can be kept dry and comfortable for longer than a year at a time. It is most satisfactory with females. In many cases they can be sat out of bed for some time each day.

At present an attempt is being made to modify this bed so that it may be used to nurse patients in an orthopnœic position while maintaining the principle of a moulded bed. If this can be achieved it should be possible to eliminate the menace of heavy patients with heart-failure and respiratory failure clambering on to bedpans.

London, W 12

JOHN C BROCKLEHURST

THE BRACHIAL-PALSY HAZARD

SIR,—I was very disappointed to read in THE LANCET of May 30 the editorial note which you saw fit to append to my letter.

The letter concerned a principle which seems to me important, and as its second sentence made clear, it used the matter of brachial-plexus injury only as an illustration. Thus your note setting out your beliefs concerning several technical procedures seems to me to obscure rather than illuminate the problem I tried to present.

A possible interpretation of your note would be that if I had been aware of the variety of prophylactic manœuvres to which you refer, I would have realised that the risk of plexus injury on the operating-table could clearly and certainly be eliminated and that I would not therefore have used this risk as an illustration. Ignorance of this variety of procedures is not the only possible explanation, however. Conviction comes to some of us more easily than others. When the complication is, in any event, unusual, it will need much more experience than has yet accumulated to allow me to follow you in describing these many prophylactic measures as successful. Meantime, whether the arm is betwixt or beyond the coronal plane I still feel justified in saying "Let us, *for argument's sake*, admit that there is a risk of brachial plexus injury following maintained abduction of the arm under anæsthesia."

It now seems to me that I owe your readers an apology. One purpose in writing my letter was to lend a grain of mutual support to those doctors who really have to deal with such conflicting risks in practice. Little did I think that I would release from your respected pen words which in a particular instance, will, I think, increase their embarrassment.

Department of Anæsthesia
Royal Victoria Infirmary,
Newcastle upon Tyne

E A PASK

⁂ An editor naturally finds it painful to see any subject discussed without mention of the many articles on it which he has recently published. Dr Pask must forgive our zeal for giving information. As for our convictions, we agree that the anæsthetist should do whatever he thinks best in the particular circumstances.—ED L

THE CORONATION

SIR,—May I congratulate you on the verse for the occasion of the Queen's Coronation in your issue of May 30? This surely must express the sentiments of thousands of her subjects. It is most felicitous. W R B has spoken well for us.

Frampton on-Severn
Gloucestershire

JOSEPH BOULTBEE

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[1] Brocklehurst, J C Incontinence in Old People Edinburgh, 1951

although the talking and the teething ages were not related significantly (r = + 0·105).

MORBIDITY

A low income is associated not only with a poor diet, poor growth, poor physique, and poor function but also with a higher incidence of disease. A morbidity survey in Ceylon (Cullumbine 1952), which collected data from 1 in every 80 families in the total population, showed that the general morbidity from all reported causes increased, for either sex, as the income fell (table IX).

As the family income fell, the incidence rose of the parasitic and infective diseases (including typhoid fever, tuberculosis of the respiratory system, malaria, "influenza," ankylostomiasis, and dysentery), diseases of the digestive system (including diarrhœa, enteritis, and ulceration of the bowel), normal and abnormal late pregnancy, childbirth, and puerperium, diseases of the blood, deficiency diseases, the rheumatic diseases (including rheumatic fever and chronic rheumatism), diseases of the skin, diseases of the eye (including conjunctivitis), infirmities such as deafness, dumbness, blindness, accidents, and senility. Most of these relationships between low-income and disease-incidence can be reasonably explained by the association of poverty with overcrowding in the homes, poor sanitation, deficient nutrition, dirt, increased hazards from heavy manual labour, and ignorance and low standards of nursing care and personal hygiene.

By contrast, as the family-income rose so also did the morbidity-rates for diseases of the circulatory system (including hypertension, pericarditis, endocarditis, myocarditis, and diseases of the coronary arteries), pleurisy, diseases of the buccal cavity, appendicitis, hernia, diseases of the genito-urinary system, abortions, and diabetes. Most of these causes are the so-called diseases of civilisation.

The intermediate-income group had the highest morbidity-rates for respiratory diseases (including bronchitis and pneumonia), indigestion or dyspepsia, and possibly hæmorrhoids and peptic ulcer.

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Personal Papers

POLIOMYELITIS

I was driving home after watching the hospital rugger-team play when my attack of poliomyelitis began. I felt cold and unwell, and shortly after arriving home I had a rigor. After twenty-four hours in bed I felt almost normal but lassitude and general malaise cut short two attempts to return to work. Five days after the onset I was apparently completely recovered and resumed all my usual activities. Two days later I attended a social function with my family. My youngest daughter was overcome by shyness and insisted on my carrying her for so long that my arms and shoulders ached intolerably. I have no doubt that this episode was of importance in determining the distribution of the paralysis which was soon to follow. The same evening I noticed a trivial pain in my neck. In retrospect I do not see how the ultimate diagnosis could have been made during the minor illness.

THE MAJOR ILLNESS

The next morning I awoke with a headache and general malaise. The headache was so severe by lunch time that I retired to bed. It was predominantly occipital and accompanied by sharp pains in the neck and back of the head. There was moderate fever, but no neck stiffness, at this stage. Still, I became apprehensive, and remembering Ritchie Russell's dictum—too late as it proved—clung to my bed. The headache was intense and aggravated by coughing and straining. Vomiting began the next day, and though I only vomited four times the experience was memorable: intense and exhausting retching lasted for about a quarter of an hour and was accompanied by the involuntary swallowing of large volumes of air, which led to a most unpleasant gastric distension. On the third morning of the major illness it was suggested that I should go into hospital, but at my request the decision was deferred for a few hours. Shortly after the consultation I rose to brush my hair and found that I could not use the comb owing to weakness of my left arm and shoulder. Within a few hours I was in my own hospital having a lumbar puncture performed by my *senior registrar*. This was an entirely painless procedure.

There was no spread of the paralysis until the next afternoon, when I suddenly felt that a curtain was being drawn across my pharynx. On trying to drink I found that swallowing was extremely difficult. My voice began to weaken. At this point I was transferred to another hospital where special nursing facilities were available. The headache remained intense, and the pains which had previously been limited to my neck spread slowly down my back.

Next morning, when I found that my dysphagia had apparently become complete, I became extremely agitated; fortunately it was soon demonstrated to me that I could swallow fluids with the aid of a straw, provided I drank very slowly. My voice grew progressively feebler. Finally on the fourth day of the paralytic phase my right shoulder-girdle and arm became affected, but I was so preoccupied with my bulbar palsy that this last blow seemed unimportant.

At the end of the paralytic phase I was left with a bilateral affection of the arms and shoulder-girdles, a severe but incomplete bulbar palsy, and relatively mild involvement of the intercostals and various trunk muscles. It was surprising to discover the extent to which paralysis was perceived as a numbness or heaviness rather than weakness—a point which Gooddy has made.

THE MENTAL STATE

The mental state during the first week or ten days of the major illness was of considerable subjective interest. I felt all the time that I possessed complete insight and awareness, though in retrospect this was clearly not the case. For instance, when I first noticed the weakness in my left upper limb I returned to bed and thought hard for some twenty minutes before I was able to decide what had happened. Again, I am told that when I heard I was to be transferred to another hospital I remarked in my disappointment, "If I had not told them about my bulbar palsy they would have allowed me to stay here." Yet I was able to navigate the ambulance from a stretcher for the whole of the 7-mile journey from my home to hospital, and on my transfer to the second hospital I regaled myself and my companions by naming the various streets as we crossed London.

I was much troubled by flight of ideas: a succession of confused and unrelated thoughts sped through my mind so rapidly that I was unable to seize and hold any one of them. This experience was particularly frustrating and annoying at night, preventing any sustained thought or contemplation during many sleepless hours. Nevertheless it had its compensations, for the serious nature of my illness caused me relatively little appre-

Obituary

GEORGE SCOTT WILLIAMSON

M C, M D Edin

At the age of 69 Dr Scott Williamson died on June 4 Joint founder, with Dr Innes Pearse, of the Pioneer Health Centre at Peckham, he gained most honour outside his own profession and his own country But by any reckoning the Peckham achievement was remarkable, and no experiment that has made so many people think—and will probably set them thinking again—can be considered more than superficially a failure His last years were spent in the shadow of disappointment, but in preferring the study of health to the study of disease he had trodden a new path that may some day become a highway

He was born at Ladybank, in Fife, the son of Captain David Williamson, and was educated at Barnard Castle and Edinburgh After qualifying with the Scottish Conjoint diploma in 1907, he took up pathology and held posts at Nordrach-on-Dee Sanatorium, at the West Riding Asylum, and with the Clinical Research Association, before becoming pathologist to the Bristol General Hospital and assistant to the professor of pathology at Bristol Having taken his M B at Edinburgh in 1914, he saw service in France from 1915 to 1918, commanding the 2/3 South Midland Field Ambulance, with the rank of lieut -colonel, and winning the Military Cross After demobilisation he graduated as M D Edin, gaining the gold medal, and was appointed director of pathological studies at the London School of Medicine for Women, and pathologist to the Royal Free Hospital and the Central London Ear, Nose, and Throat Hospital He had already shown an unusually wide range of interests, writing ably on bacteriological, biochemical, and histological subjects At the Royal Free his research concentrated increasingly on the structure and function of the thyroid gland, and after retiring from his post at that hospital in 1928 he chose the thyroid and thymus glands as the subject of his investigations undertaken as first holder of the Mackenzie-Mackinnon research scholarship of the Royal Colleges of Physicians and Surgeons In 1925 he had given Arris and Gale lectures to the College of Surgeons on the anatomy and physiology of the thyroid apparatus

But Scott Williamson's major contribution to medicine arose out of work done outside working hours With Dr Innes Pearse, who had collaborated in his thyroid investigations, he began to think in larger terms of human welfare, and (unlike so many thinkers) they lost little time in putting their ideas into practice Their first centre, a club for working-class families was opened in 1926 and with this experience behind them they produced in 1931 *The Case for Action* The support that enabled them to create a big new building and organisation at Peckham was won because they had something more than a building scheme to offer they had a new message which attracted people far and wide

The medical approach, said Scott Williamson is derived from pathology—the study of what is *wrong* with people (physically mentally or socially) The Peckham approach is derived from "ethology"—the study of what is *right* with them

> "Having determined what is right you *must then proceed* to cultivate and educate or grow the *right* by *ecological* methods Just as therapy is the technological aspect of the science of pathology, so is ecology the technological aspect of the science of ethology Hitherto what is right—health or wholeness—has been assumed to be able to look after itself In fact even the proposed new medical services assume that all those who can look after themselves by whatever means are ipso facto the healthy and vital—a most disastrous error We have not only adopted, but deliberately enforced a laissez faire attitude to personal health so that any individual concerned for his own health is dubbed a *neurotic* or psychotic'
>
> The systematic study of *pathos* of the people, or pathology has proved its worth but the best that can be made of a bad job with it is to stop the bad from getting worse In the Peckham Health Centre we have begun a systematic study of the *ethos* of the people, and have made a first tentative technological approach to their ecology Health, we have discovered, is like a seed it must be sown, grown, and cultivated in the seed bed, garden, or tilled field—the homestead—of the social soil "[1]

The work at Peckham, and its philosophical basis were described in *Biologists in Search of Material* (1938), and in *The Peckham Experiment* (1943), the Pioneer Health Centre (so different in conception from the kind of health centre envisaged for the National Health Service) was filmed by the Ministry of Information and became well known abroad, and as "the first serious attempt to found sociological work upon a biological basis" the whole project was continually under discussion The advantages of periodic medical examination, on which the founders insisted, are of course a perennial subject of controversy, and this was extended to the technique of the family consultation, which put the members in possession of whatever information the centre had obtained about them But sympathisers as well as critics could not help remaining doubtful about the scientific value of the biological data to whose accumulation and analysis Scott Williamson attached so much importance; and, looked at purely as a new form of community centre, Peckham failed to justify itself by acquiring a life and vigour of its own apart from the inspiration and vigour of its founders "The centre," wrote one who had worked in it, was "lacking in an essential social activity peculiar to humans, and in this sense it was biologically inadequate to its task "[2] Many, none the less, will share the same commentator's hope that the ideas that underlie its conception "will one day be put to a searching though sympathetic test"

S T writes

Scott Williamson's dream was of a day when it would be within the power of the family doctor to create individual health rather than treat disease But his enthusiasm raced far ahead of work a day medical science So he failed to convince the age in which he lived of the validity of his message

His conviction of the need for action to raise health standards among the industrial population found practical expression in April, 1926, when the original Pioneer Health Centre was opened in a small house in Peckham It was a family club, with a subscription of 6*d* a week for the whole family In return, there were club rooms for various activities welfare clinics, an afternoon day nursery, and a compulsory annual health examination for every member The centre was, in fact a community centre, with health examinations as a pill in the sugar, and "the doctors moving freely among the people, and making observations to supplement those gathered in the consulting room' "By adjusting bad habits observed at the centre, we were able to prevent the onset of disease ' It may well have been true, indeed, I believe it was true But the evidence presented was certainly not enough to convince the scientific sceptic

On their experience, Dr Scott Williamson and Dr Pearse were soon convinced that they were on the right lines They shut down the little centre, and made preparations for something much more ambitious With great difficulty, funds were raised, and in 1935 the new Pioneer Health Centre was opened It was a striking concrete and glass building created around a magnificent swimming pool A cafeteria and a dance room overlooked the pool A pool for toddlers could be filled to any depth required There was a gymnasium a day nursery, quiet rooms and clinic rooms, and a whole suite of medical consulting rooms and laboratories Today we could take many of these facilities for granted in a community centre, though they are still rare enough To have created them by voluntary effort in the ' bad old 1930s was a *miracle*

To meet costs family membership subscription was raised to 1*s* a week With 2000 families it was calculated that it would be self supporting Yet somehow it never quite came off Income never matched expenditure and help had to be sought first from one charitable body, then from another With the war and evacuation it had to close down and weeds grew in the gardens the windows cracked, the concrete began to look very shabby Afterwards, it never got fully into its stride

The coming of the National Health Service brought no hope to the organisers of the Pioneer Health Centre It was

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1 Williamson G S *Lancet* 1916 i 393
2 Chance M R A *Ibid* 1950, i 726

hension during these early days; it was later that I was assailed by fears, both reasonable and otherwise. This lack of concern extended to my family: I did not begin to worry about the chance of their contracting the infection until that possibility had become remote.

During this period of confusion I had fantastic day-dreams. My favourite was one in which I lay couched in my own medulla watching the outfall of nerve-cells from my nucleus ambiguus, an experience characterised by the complete absence of any affective element. For several days I was unable to appreciate the size and arrangement of my cubicle: at night, for instance, it expanded to an enormous room in a mythical "house on the South Downs," or contracted to the box-like compartment where the stable-lad sleeps at my daughters' riding-school. In the confusion resulting from this uncertainty as to my whereabouts I was prone to get out of bed at night. Even by day I was unable fully to appreciate the organisation of extrapersonal space. It was some three weeks before I was able to read with normal enjoyment, and about a month before my mental state was completely normal. Insomnia was a most unpleasant symptom. For seven to ten days I had very little sleep at all, in spite of the administration of various hypnotics. Indeed, normal sleep did not return for some six weeks.

FASCICULATION

Fasciculation appeared on the second day of the major illness, but it was not sufficiently obtrusive to warrant attention, in my case, until paralysis had actually appeared. The movements then became more widespread and of sufficient violence in one muscle at least to deserve the term myoclonus rather than fasciculation. Admittedly the fasciculation was predominantly situated in the areas which became paralysed, but it also affected parts where there was no demonstrable weakness. Moreover, the muscles in which fasciculation was most active were not those which were most severely paralysed. Fasciculation continued at a reduced rate for many weeks, and though now slight is still felt and seen six months after the onset of symptoms. I have used the term to denote spontaneous fasciculation and not the action fasciculation which has long been recognised as a phenomenon encountered in muscles partially denervated as the result of poliomyelitis.

RATE OF RECOVERY

I have been relieved to find that neuronal recovery clearly continues for much longer periods than one might imagine from a study of the literature. I suppose my bulbar palsy began to improve in ten days, but I did not derive any comfort from the degree of improvement until the fifth and sixth weeks, when there was a dramatic change for the better. The ninth and tenth weeks saw a similar rapid improvement. As late as the fifteenth week my voice made great progress quite suddenly in a matter of three days; this could only have been due to central factors. I was particularly exercised about my bulbar palsy, as I had had a patient under my care who, after bulbar poliomyelitis, had been left with a degree of dysphagia and aphonia which would have been crippling in a doctor. Consequently I did not accept the well-founded reassurance I was given as readily as I should have done. It is, of course, a commonplace that recovery of muscular power in the early months proceeds by fits and starts. The improvement in the limbs has generally followed a similar pattern, though some muscles have lagged far behind others. Generally, six months after onset, improvement is more slow and gradual, but there are still surges of returning power in the weakened muscles.

Muscular fatigability has been a prominent though variable phenomenon. On some days all exercises and activities are well carried out, on others performance is poor and fatigue develops early. These "bad" days sometimes occur spontaneously, but more often they follow an exceptionally vigorous or prolonged period of physiotherapy or some foolish physical activity on my part. The other day I was stupid enough to spend three hours gardening; it has taken several days for my muscles to return to their previous average level of performance. The fatigue is always generalised and may affect muscles which have apparently been untouched by the disease. This fatigability also affects the bulbar muscles on occasion, but it is more difficult to assess at this level.

During rehabilitation, cramps began to occur in a few muscle groups on exertion. They still persist but are lessening in severity. Apart from specific muscular fatigability, there is a troublesome and recurrent general tiredness which limits both physical and mental activity. Adequate periods of rest are required to prevent this symptom arising.

TREATMENT

Ritchie Russell has given an excellent account of the management of the patient with poliomyelitis in his recent book. He has anticipated most of the points I would have raised from the patient's point of view. Whilst supporting his teaching on the value of early active movements in rehabilitation, my own experience is that exercises should be continued to a point just short of fatigue and not beyond it; if I proceed further than this point it only means that my physical activity has to be correspondingly reduced the next day, so the net gain is nil.

The importance of the physiotherapist in treatment can hardly be over-emphasised. She requires not only a good knowledge of the anatomy of movement, and considerable intelligence, but also the ability to maintain the patient's enthusiasm by varying his exercise programmes and sparing him the boredom which follows too much repetition. If she is a good conversationalist with a wide range of interests so much the better.

There is need for an authoritative statement on safe means of sedation in bulbar poliomyelitis. I found the lack of sleep the worst feature of the acute stage. I was fortunate to have a "functional leucotomy," as my physician termed it; but for those who are less favoured prolonged sedation would clearly be a great relief. At the height of the major illness only large doses of 'Sodium amytal' were effective in my case. I did not require analgesics so long as I was nursed on a 'Sorbo' rubber or interior-spring mattress: the pains and stiffness in my neck and back rendered a hard mattress intolerable.

Ritchie Russell has emphasised the need for training nurses in the management of poliomyelitis. I was fortunate not only in my physicians but also in my nurses, who were well versed in the care of bulbar poliomyelitis. This was a considerable source of confidence to me, and one that should be available to all afflicted with the disease. It is difficult to imagine a more terrifying predicament than that of the patient with bulbar poliomyelitis who lies in the care of the ignorant, and it is to be hoped that integrated plans for medical and nursing care will soon be introduced throughout the country. The present dissolution of clinical responsibility is unsatisfactory: there seems to be no reason why the physician initially in charge of the patient should not look after him throughout the whole course of the illness, seeking such help from his colleagues as circumstances might demand. A physician with neurological training is best qualified for the task.

* * *

There are compensations for most misfortunes. My illness gave my friends and colleagues an opportunity to show me the way in which the sick should be treated. I was privileged to learn many lessons from many people. Doctoring will never be quite the same again.

not, and refused to become, a local-authority health clinic It was not a G.P health centre And it refused to regard itself as a community centre So at last it had to be disposed of

In December, 1950, it was bought by the London County Council, for the use of their educational, health, and welfare services As a condition of purchase, the L C C agreed not to use the title Peckham Health Centre or Pioneer Health Centre So today, in the Queen s Road Health Centre, Camberwell, school-children are once more using the lovely swimming-bath A day nursery is open An antenatal clinic is functioning And evening classes of all kinds are in progress In an outbuilding the L C C welfare department is running a workshop for blind people One day, it is hoped to add a G.P health centre Finally, a research programme will be begun

What went wrong ? Why did the original Pioneer Health Centre fail ? Perhaps it is that the Englishman likes to keep his community life separate from his health service Perhaps he resists unconsciously any potential medical dictator—no matter how benign—who requires him to surrender both his health and leisure And although the family is obviously enough the right unit in the home, it is not necessarily the right unit for club life The Athenæum and the Women's Institute, the dance club and the working men's club, each owe their success to the clear cuts that they make across family life

And yet, when all is said and done, the Pioneer Health Centre was a noble experiment People from all over the world came to draw inspiration from the idea it represented We can only build positive individual health on a basis of knowledge of the working of the normal human being in society Such knowledge must come from experience And such experience can only come from the study of prophylactic communities Fifty years from now, when the angularities of the prophet have been rubbed off by time, we may be ready to accept Scott Williamson s message

Dr Scott Williamson married first Nell, daughter of Captain Madden, and secondly Dr Innes Pearse

CLAUDE BLAXLAND LEVICK

O B E , M.B , Ch M Sydney, F R C P

Dr C Blaxland Levick, physician in charge of the cardiology department at St George s Hospital, London, died on May 31, at the age of 56

Dr Levick was educated at Sydney Grammar School and the University of Sydney where he held Aitken and Cooper scholarships and was awarded John West and Grahame medals He graduated M B in 1920 and CH.M. in 1922 ; and in 1923 he became a M R C.P As a postgraduate he worked in Manchester, where he was a senior house-physician at the Royal Infirmary

Coming to London, he held resident posts at St George's Hospital and at the Victoria Hospital for Children, Tite Street, before being appointed physician to outpatients at the Victoria Hospital for Children in 1925 and assistant physician to St George's Hospital in 1928 He was elected F R C P in 1934 During the late war he served in the Middle East. He was appointed O B.E in 1943 and was twice mentioned in despatches

Dr Levick's two main interests were cardiovascular disease and disease in children , and he was one of the earlier physicians to use the electrocardiograph clinically. He always remained, however, a general physician, seeing each problem against the background of the whole patient , and it was this, together with care for detail, that made him a valuable consultant

C P. P writes "I knew Blaxland Levick for the thirty years he was associated with St George's Hospital He was an excellent teacher with a precise mind, so that his students were trained to think and express themselves clearly. When he became resident assistant physician he showed that he was a first-class administrator, and this was repeatedly evident from his advice over hospital matters and in committee, and during the war with the success that came to him in his Middle East appointment

'Blaxland was a shy man, but he was the most generous and helpful of colleagues and a good friend to his juniors. In his early days at St George's he was an enthusiastic skater, and he was a keen lawn-tennis and squash player He was fond of good music and had a large collection of classical records

"He will be sadly missed by his colleagues and friends, with his sense of humour and devotion to work"

In 1934 Dr Levick married Miss Stella Kent who survives him

HUGH MORLEY OLIFF LESTER

O B E , Ph D , B Sc. Lond., M R C S

THE death of Dr H M O Lester, director of medical services in Malaya was announced at the end of last month

Dr Lester graduated B SC with first-class honours in 1922, and three years later he qualified as M R C S from St. Thomas's Hospital For a time he was a demonstrator of physiology at St Thomas's , but in 1926 he gained the diploma in tropical medicine and hygiene, and the rest of his professional life was spent overseas He graduated PH D in 1935

P A. B writes "When Dr Lester first arrived in Nigeria after his appointment to the Service, some happy chance sent him to work in the north with senior men who were studying tsetse flies and sleeping-sickness He then carried out researches comparing different strains of trypanosomes in respect of their virulence and so forth As he became more senior and his administrative gifts developed, he was put in charge of the very large Sleeping Sickness Service of Nigeria. He developed the method of mass treatment of infected people in their villages, and reduced what had been a formidable and uncontrolled epidemic to a disease of quite minor importance In the period after the war he directed the research and reclamation against the same disease in British territories in East Africa His writings on the subject were always from a broad view and with a clear and definite expression of opinion

"Towards the end of his career Lester was first of all director of medical services in Palestine at the time when the mandate terminated, and finally he held the same position in Malaya It would be difficult to say which of these two posts was the more important or the more difficult Lester had an industrious and serious nature and this tended to isolate him His treatment of others and of himself was always honest and sometimes severe He is a very great loss to the public service and to tropical preventive medicine '

REGINALD JOHN STILWELL

M R C S , J.P

R J Stilwell died at his home in Hillingdon on June 5 in his 81st year Born in 1872 he was educated at Harrow and at the Westminster Hospital and qualified in 1899 He came of a long line of Stilwells interested in the care of mild psychiatric conditions As far back as 1799 patients were first received at Moorcroft, then an extensive farm in open country For 154 years a Stilwell has been associated with Moorcroft House, which became widely known for the care and treatment of psychiatric conditions of all kinds

After working at Bethlem Royal Hospital he settled, in 1903, at Moorcroft House and remained there for fifty years Handsome in appearance and always immaculately groomed, "Reggie" possessed a charming personality which endeared him to all who were associated with him Generations of patients and their relatives will remember him with affection. Those who have worked with him in any capacity will feel his loss as if he was a brother In 1907 he married his cousin Gertrude Stilwell, whose father, Dr Henry Stilwell, was physician in charge of Moorcroft House from 1860 to 1906 All who were privileged to know Dr and Mrs Reggie will recall their charming house and their enduring devotion. Mrs Stilwell died in 1947 and there were no children

Stilwell was a man of many interests He had travelled widely, and in his youth had acquired an unusual knowledge of the old masters of the Italian school of painting He was a good tennis-player and a devotee of cricket, seldom missing an important match at Lord's, and being for many years a member of the M.C C He took an active interest in farming, and the attractive herd to be seen on the home farm of Moorcroft House was evidence of his knowledge and skill He was a Justice of the Peace for Middlesex and most regular and punctual in his attendance at the Uxbridge Magistrates' Court

Medical Congresses

FERTILITY AND STERILITY

THE First World Congress on Fertility and Sterility, sponsored by the International Fertility Association and by the American Society for the Study of Sterility, was held in New York City from May 25 to 31, and combined the first congress of the former association with the ninth of the latter. The scientific programme was covered in five days and involved twenty-four sections; more than one hundred and fifty papers were read. Over 1100 registrants, representing fifty-three countries, were in attendance.

Ovulation in Hirsute Amenorrhœic Women

R. G. **Greenblatt** (Augusta, Georgia) discussed a group of 27 women who had prolonged administration of cortisone. The drug may modify the rate of bodily hair growth. Of patients with menstrual disorders, some may respond by cyclic ovulatory menses and ultimate conception, and others simply by an increased number of menstrual periods, many of which may be anovulatory; others again may show no improvement. In the hirsute female cortisone may act not merely by depressing 17-ketosteroid excretion through its inhibition of corticotrophin (A.C.T.H.) production, but by a balancing action on growth hormone and adrenal steroids which leads to a more orderly release of pituitary gonadotropins.

Respiratory Physiology and Ovulation

W. T. **Pommerenke**, R. L. **Goodland**, and J. G. **Reynolds** (Rochester, N.Y.) investigated the effects in men of injections of progesterone and œstradiol benzoate, alone and in various combinations, on basal metabolic rate, alveolar carbon dioxide tension, basal body-temperature, and serum-sodium and serum-chloride concentrations. Progesterone caused a significant increase in basal body-temperature and a decrease in alveolar pCO_2. It seemingly produced a rise in the basal metabolic rate, and an increase in serum concentrations of both sodium and chloride. A significant increase in serum-sodium and a decrease in serum-chloride was noted following œstrogen administration. The thermogenic effect of progesterone was diminished when œstradiol benzoate was simultaneously administered. The suppression of alveolar pCO_2 by progesterone was prolonged when œstrogen was also injected. Under these conditions both serum-sodium and serum-chloride levels appeared to be lowered. Studies of electrolytes and respiratory gases may be employed as substitutes or supplements to morphological criteria of œstrogen and/or progesterone activity.

Genital Tuberculosis in Sterile Women

I. **Halbrecht** (Hadera, Israel) stated that he found tubercle bacilli by means of cultures of the menstrual and intermenstrual cervical and vaginal discharges in 60 women with primary sterility, in whom tubercle bacilli were being discharged continuously or intermittently from the genital organs. In 32 of these 60 women the diagnosis of genital tuberculosis was first established by endometrial biopsies and later confirmed by the cultures of the uterine discharges. In 22 cases genital tuberculosis was detected only by cultures of the menstrual discharges, whereas the endometrial biopsies were negative. The relatively great number of cases in which tubercle bacilli were found growing in cultures of the menstrual discharges and in the cultures of the intermenstrual, cervical, and vaginal secretions, while endometrial biopsies gave negative results, enhances the value of these cultures as a factor in diagnosing latent genital tuberculosis in its earliest stages, when the disease is still limited to the fallopian tubes.

Pre-adolescent Hypogonadism

C. W. **Charny**, A. S. **Conston**, and D. S. **Meranze** (Philadelphia, Pa.) described 3 cases which were suspected to be of mild hypogonadism when first examined. Follow-up study by means of testicular biopsies revealed the progressive pathological changes leading to the adult infertile state. A constant feature is the lack of uniformit of the histological picture: relatively healthy seminiferous tubules may be seen next to tubules which hav been irreversibly damaged.

Time of Ovulation

C. G. **Hartman** (Raritan, N.J.) said that inspection c the ovary at laparotomy will often provide useful information about the time of ovulation; but in his opinion i is impossible to estimate with any precision when a give follicle will rupture. Observation of hundreds of monke ovaries, when the exact day of ovulation was know made him doubt the accuracy of estimating the ag even of "newly ruptured" follicles.

Ovulation Timing

H. **Knaus** (Vienna) described his early work o uterine muscle contractility, when he found that huma uterine muscle is controlled by the hormone of the corpu luteum in the same way as it is controlled in the rabbit Ovulation in women normally takes place on the 15t day before the onset of menstruation. In a woman wit a cycle varying from 26 to 30 days, ovulation will occu between the 12th and 16th day of the cycle, but whe the cycle is one of 21–24 days it will occur between th 7th and 10th days. The "safe period" as a method o birth-control has confirmed the practical validity of thi view of the determination of the time of ovulation.

Outcome of Pregnancy

G. I. M. **Swyer** (London) presented data on the outcom of 220 pregnancies in 207 patients, attending the fertilit clinic at University College Hospital, London. There wer 19·1% of abortions and 3 ectopic gestations. Labour wa normal in 123 patients. There were 15·4% of forcep deliveries, 5·7% of cæsarean sections, and 4·6% of breec presentations. The total fœtal-mortality and congenital malformation rates were 0·57%. Toxæmia occurred i 11·4% of pregnancies.

Peritoneal Factor in Sterility

E. G. **Murray** (Buenos Aires, Argentina) stated that alterations of the pelvic peritoneum near the tubal ovarian junction are an important cause of sterility Their frequency is 11·6% (234 cases in 2017 patients). The peritoneal disturbances were grouped as morphological and functional. The morphological changes consist of ovarian blockage (intrinsic or extrinsic), tubal blockage, blockage of the tubal-ovarian junction (simple or in pockets), and combined blockage. In functional blockage ovular migration is disturbed even in the absence of morphological changes. Diagnosis may be difficult, and often has to be based on auxiliary diagnostic aids, such as radiology. The treatment has two important stages: firstly, prophylaxis; and secondly, treatment of the pelvic blockage—the purpose being to prevent or cure the peritoneal cicatrisation and the resulting retractions. In prophylaxis the best results have been obtained with local intra-uterine or peritoneal penicillin. In rats abnormal cicatrisation has been reduced by administration of cortisone and corticotrophin. In women their use is still in an experimental stage.

Non-surgical Treatment of Tuberculosis

T. **Barns** and **Linton Snaith** (Newcastle upon Tyne) gave a preliminary report on the response to isoniazid of 43 cases of pelvic tuberculosis.[1] These 43 cases with endometrial tuberculosis, of which 3 had also infection of the cervix, were treated with isoniazid, after preliminary confirmation of the diagnosis by biopsy, animal inoculation, and culture: in all cases where typing was possible

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[1] Barns, T., Smith, H.G.M., Snaith, L.M. *Lancet*, April 25, 1953, p. 817.

His experience of clinical psychiatry was extensive and his opinion always worth having Colleagues have often expressed their indebtedness to a quiet hint, modestly expressed, regarding the treatment of a difficult case His management of the truly objectionable patient sometimes met with in psychiatric practice was instinctively successful and the admiration and envy of the beginner

In Reggie Stilwell psychiatry has lost a senior practitioner of great distinction and charm It is sad indeed to think that he is the last doctor in a family which has done so much for the enlightened care of psychiatric illness

G W B J

Diary of the Week

JUNE 14 TO 20

Monday, 15th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 12
4 P M Prof T L Hardy Colon Neuroses
UNIVERSITY OF EDINBURGH
10 A.M (University New Buildings, Teviot Place, Edinburgh) Sir Geoffrey Jefferson, F R.S Variations in Behaviour of Pituitary Adenomas (First of three lectures)

Tuesday, 16th

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St Mary's Hospital Medical School, W 2
5 P M Prof Gerhard Domagk Development of Chemotherapy of Tuberculosis (Almroth Wright lecture)
INSTITUTE OF DERMATOLOGY, St. John s Hospital, Lisle Street, W C 2
5 30 P M Dr Phyllis Wade Treatment of Cancer of Skin
UNIVERSITY OF EDINBURGH
10 A.M (University New Buildings) Sir Geoffrey Jefferson Affections of Trigeminal Nerve (Second of three lectures)

Wednesday, 17th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M Dr M G P Stoker Q Fever
4 P.M Dr B Ackner Depression (Last of three lectures)
INSTITUTE OF DERMATOLOGY
4 30 P M Dr H Haber Histopathology of Tuberculosis and Syphilis of Skin
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P M (Chelsea Hospital for Women, Dovehouse Street, S W 3) Mr J W A Hunter Pregnancy Following Fothergill's Operation

Thursday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr J W D Bull, Neuroradiology
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P.M (Queen Charlotte s Hospital, Goldhawk Road, W 6) Mr V O'Sullivan Acute Inversion of the Uterus
LONDON JEWISH HOSPITAL MEDICAL SOCIETY
8.30 P M (11 Chandos Street, W 1) Mr C S Bangay, Dr F Gray, Dr Max Sorsby National Health Service
NORTH WESTERN TUBERCULOSIS SOCIETY
3 P M (Hefferston Grange Hospital Weaverham near Northwich, Cheshire) Summer meeting
UNIVERSITY OF EDINBURGH
10 A M (University New Buildings) Sir Geoffrey Jefferson Applied Physiology of Cerebellum (Last of three lectures)
HONYMAN GILLESPIE LECTURE
5 P.M (University New Buildings Teviot Place, Edinburgh) Dr Robert Brown Contracted Pelvis

Friday, 19th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Prof J D Boyd Pigment Cells in Body
4 P M Dr R I S Bayliss A C T H and Cortisone
INSTITUTE OF DERMATOLOGY
5 30 P M Dr P F Borrie Vascular Diseases

Saturday, 20th

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
12 noon (Hammersmith Hospital Ducane Road W 12) Mr J Peel Diabetes in Pregnancy
BIOCHEMICAL SOCIETY
11 A M (Department of Biochemistry South Parks Road, Oxford) Scientific papers

Appointments

THOMAS DAVID M B B.SC Wales D P M asst psychiatrist (S H.M O) Belmont Hospital Sutton and clinical asst St George s Hospital London

Factory Doctors

FORSYTH MARY M B Edin appointed factory doctor Normanby Yorkshire
HUGHES T H M R C S appointed factory doctor Wembley Middlesex
LOWRY W G M B Belf appointed factory doctor W Hartlepool Durham

Notes and News

DEVELOPMENT OF ENDOCRINOLOGY

Now in its seventh year, the section of endocrinology of the Royal Society of Medicine held its first dinner on June 4, to celebrate the Coronation

Lord Horder, the chief guest, said that it seemed odd that a long struggle had been needed to get endocrinology put on the map as a section of the society It had been feared that the proposed new section would split the subject of Medicine into watertight compartments, and also that the other sections would be denuded of much of their subject matter At this distance of time, however, the objections sounded quite medieval "Some of you," Lord Horder continued, "have visions of a body, organisation, institute—call it what you will—which might place endocrinology on a still higher footing in the hierarchy of Medicine than it now occupies as a section of the Royal Society of Medicine The subject has made such strides, it has demonstrated so fully the depth and breadth of its penetration into the pathogenesis of disease, that it surely cries out for a special hospital with its attached research department As an interested outsider I would strongly support such a scheme" The progress of endocrinology had made us all breathless—or would do so if we did not exercise control The patient (impatient because human) needed protection from his credulity , the chemist must not be allowed to dictate to the clinician about the use of the substances he produced , and we must check the tendency to divorce endocrinology from general medicine He agreed with Dr S Leonard Simpson, president of the section, that while every general physician must have a good working knowledge of endocrinology this did not exclude the need for collaboration and consultation with the endocrinologist—though the latter, in his turn, must avoid taking over departments of Medicine as his special field because hormone therapy played an important part in them There was no ceiling to the reach and grasp of this branch of Medicine it began at the start of life, and it pursued life through growth, puberty, adolescence, maturity, to old age "Use your influence," Lord Horder concluded, "to get the basic and established facts of your specialty interwoven with the student's curriculum Then teach them to the practitioner"

Mr L R Broster, first president of the section, said that its strength resided in its application of applied sciences It worked in closest harmony with the Society of Endocrinology, and the collaboration between clinician and scientist was enabling them to understand each other s problems The future rested on the foundation of some institution where it would be possible to coördinate all these aspects Meanwhile, at a time when Medicine was disintegrated by splintering, the section of endocrinology was doing much to bring its parts together , for it had proved a meeting ground for surgeons, physicians, psychologists, biochemists, medicolegal experts, and many more

Dr Leonard Simpson, who presided proposed The Guests , and Dr F M R Walshe, F R S , president of the Royal Society of Medicine, reflecting the faint uneasiness of those who dine under the diagnostic eye of psychiatrists or endocrinologists, replied "on behalf of my fellow syndromes"

MEDICINE UNDER THREE QUEENS

On June 5 Sir Zachary Cope opened a new exhibition at the Wellcome Historical Medical Museum, 28, Portman Square, London, W 1

Dr E Ashworth Underwood, director of the museum, explained that the exhibition was designed as a tribute to the Queen on her Coronation, and its theme was a comparison of the state of medicine in the reigns of Elizabeth I, Anne, and Victoria The real beginnings of British medicine were undoubtedly in the reign of Elizabeth I, but compared with the Continent, England in those days was backward in the art and practice of medicine The Elizabethan age was characterised by buccaneers and a spirit of adventure, finding their expression in medicine in the heroic surgery of William Clowes (1544–1604) But by the time of Queen Anne, English medicine was represented by great physicians such as Richard Mead, John Radcliffe, and Hans Sloane During the long Victorian era, there were numerous discoveries, but only a few of the discoverers could be mentioned in the exhibition

Sir Zachary Cope began by paying a tribute to the Wellcome Trustees for their foresight and wisdom in providing and maintaining a historical museum and library of such excel the organism was of human type. Only 2 patients, with massive caseation, did not respond; 40 cases showed no infection after treatment, and 1 became pregnant. These workers are sceptical about the permanence of apparent cure, since a caseating focus elsewhere, especially in the fallopian tube, may be resistant to the antibiotic and may reinfect the endometrium.

Uterotubal Insufflation

I. C. Rubin (New York City) declared that the value of uterotubal insufflation in tubal occlusion encountered in hydrosalpinx, clubbed fimbrial ends, or atresia of the tubal lumen is purely diagnostic. Its therapeutic value is restricted to certain degrees of tubal obstruction produced by mild to moderate mucosal agglutination, perifimbrial adhesions, and tubal kinks which are amenable to improvement by repeated insufflation. In the last analysis tubal obstruction refers to barriers which block the normal passage of the ovum through the tubal lumen into the uterus. The degree of luminal constriction can be estimated by the pressures obtained during kymographic uterotubal insufflation, which are correlated with the diameter of the ovum. If these pressure-levels can be reduced to 100 mm. Hg or below, intra-uterine pregnancy can be expected. When the pressure-levels remain higher than 150 mm. Hg, tubal pregnancy is more likely. Pressure-levels persistently above 200 mm. Hg are incompatible with conception, because the lumen of the corresponding fallopian tubes requiring these high pressures is too narrow for the free transport of the ovum. Tubal obstruction refers to the blocked passage of the ovum and not to the failure of CO_2 gas or radio-opaque liquids to escape under pressure from the fallopian tubes into the peritoneal cavity. Kymographic uterotubal insufflation is very suitable for the determination of the calibre of the lumen, which is correlated with intratubal pressures. A significant difference was noted in the percentage of pregnancies following uterotubal insufflation demonstrating tubal strictures and the percentage following the test demonstrating normal tubal patency. There were, for example, 118 (31%) out of 379 patients with tubal strictures who became pregnant, as against 316 (26%) out of 1210 with normal tubal patency who became pregnant. The therapeutic value of uterotubal insufflation in cases of tubal stricture appears to be appreciable. Chance and coincidence may play their part in this treatment as in all other forms of therapy; but, after subjecting the data to the strictest criteria, it seems justifiable to conclude that uterotubal insufflation exerts a therapeutic effect in sterile women whose fallopian tubes obstruct the ovum; the obstruction is improved by repeated insufflations, and conception ensues the same month or shortly thereafter.

Ovulation Around the Menopause

A. Sharman (Glasgow) stated that the modern literature on pregnancy records no parturition after the age of 52 years. An investigation was made into ovulation, using the histological method, in 249 women 40 or more years of age. The oldest age at which ovulation was detected was 52 years: this occurred in 5 cases. In no case was secretory endometrium obtained more than ten days before a menstrual period. Ovulation dissociated from menstruation was detected in 2 women, aged 47 and 49 years. In the age-group 40–45 years, 19 out of 76 biopsies performed within ten days of a supervening menstruation revealed anovular cycles. In a group of women aged over 45 years, of 15 premenstrual biopsies 6 revealed anovular cycles. In 12 out of 49 biopsies after irradiation no endometrium could be obtained; and none of the other 37 specimens showed a secretory pattern.

Tubo-ovarian Physiology

A. Westman (Stockholm, Sweden) studied the tubo-ovarian physiology in rabbits through an abdominal window and in *Macacus rhesus* monkeys by aid of a laparoscope. During ovulation strong contractions were observed in the tubal wall, producing suction into the tube. The fimbrial apparatus swayed to and fro over the surface of the ovary, which slowly rotated round its longitudinal axis, presenting its medial or its lateral surface to the ostium of the tube. By this device the ovum is directly sucked from ruptured follicles into the fallopian tube. Some observations on radiographs gave indirect evidence of the same mechanism in human beings.

Ovulation after Ectopic Pregnancy

A. M. Siegler (New York City) studied 27 patients after operation for tubal pregnancy. A normal, ovular menstrual cycle is immediately re-established after operation.

The conference concluded with a banquet, at which it was announced that the next world congress of the International Fertility Association will be held in Italy in 1956.

Public Health

Recruits to the Local Health Services

In his report for 1952, Dr. I. A. G. MacQueen, medical officer of health for Aberdeen, says that there are grave and increasing shortages of nurses, dentists, and doctors in the local authority services. He attributes the situation mainly to the financial disparities between these members of the service and their opposite numbers in other branches of the National Health Service. He points out that the nurse who undertakes additional full-time study to secure the health visitor's certificate is rewarded by a salary which is less than she would have received had she remained a ward sister without the certificate; and there are comparable differences in the case of medical officers. Dr. MacQueen concludes: " It is obvious that, unless both the quality and the quantity of recruits to the local health authority service improve, the preventive health services will inevitably decline, as they are already doing in some places . . ."

Medical Statistics for 1948 and 1949

The medical text of the Registrar-General's Statistical Review of England and Wales for 1948 and 1949 is published this week.[1] It is primarily a commentary on the mortality and notification statistics for these years; and many of the figures it deals with have been published previously in part I of the statistical reviews for 1948 and 1949. Separate volumes giving some results of morbidity inquiries will be published as supplements to the review for 1949.

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[1] The Registrar-General's Statistical Review of England and Wales for the Two Years 1948–1949. Text, Medical. H.M. Stationery Office. Pp. 370. 10*s.*

Infectious Diseases in England and Wales

Disease	Week ended May				
	2	9	16	23	30*
Diphtheria	13	22	17	19	21
Dysentery	466	729	736	754	505
Encephalitis:					
Infective	6	—	2	3	2
Postinfectious	1	—	2	4	1
Food-poisoning	86	137	234	155	147
Measles, excluding rubella	10,768	9810	10,034	10,279	9012
Meningococcal infection	32	37	43	31	41
Ophthalmia neonatorum	29	46	47	46	41
Paratyphoid fever	6	14	11	4	8
Pneumonia, primary or influenzal	551	479	515	505	446
Poliomyelitis:					
Paralytic	19	28	25	22	30
Non-paralytic	10	10	11	7	22
Puerperal pyrexia	226	216	254	267	283
Scarlet fever	1140	1388	1286	1307	1084
Smallpox	—	2	1	1	—
Typhoid fever	—	1	2	3	2
Whooping-cough	3376	3462	3312	3104	2476

* Not including late returns.

lence both were at the service of the medical historian, and deserved to be better known because of the unfailing courtesy and erudition of those in charge of them

Before the days of Elizabeth I men had ideas about medicine but there were no facts Progress dated from the time when practitioners of the art decided to collect facts The whole of modern medicine was based on the facts of anatomy and physiology, both of which subjects, so far as England was concerned, saw their beginnings in the days of Elizabeth When she was 10 years old, Andreas Vesalius in Padua wrote his famous work on anatomy, and in 1578, when she had been on the throne for twenty years, William Harvey was born Most great thoughts had come to men in their twenties and there could be little doubt that it was during the reign of Elizabeth that Harvey first theorised on the circulation of the blood And so one could say that it was in her reign that anatomy was fertilised by physiology and modern medicine was conceived

After the important episode of its conception, the embryo entered upon rather a long period of gestation The quickening was in the reign of Queen Anne, for it was then that the first serious medical teaching was undertaken William Cheselden, produced his syllabus of anatomical lectures within a year of completing his own studies in 1710, and with Francis Hauksbee, a physiologist, as his partner he provided the first attempt at systematic medical education in this country Then came William Hunter, who founded his school of anatomy and was joined by his brother, John By the end of the 18th century there were many efficient private schools of anatomy and medicine The same century, following a lead given in the reign of Queen Anne, saw the foundation of many of our great hospitals, which provided the clinical material for the teachers Inevitably medical schools became attached to hospitals

The period of gestation of modern medicine was almost terminated by a pseudo labour in 1815, when the Apothecaries Act was passed and the first attempt made to secure a proper standard of professional skill The Act was, however, not sufficiently comprehensive, and there was no agreed minimal standard of competence for all medical practitioners until the passing of the Medical Act in 1858 and the formation of the General Medical Council That year, Sir Zachary regarded as signalising the true birth of modern medicine It was a memorable year in medicine, for Virchow was publishing his famous work on cellular pathology, Pasteur was working on fermentation, and Florence Nightingale was crystallising her ideas on nursing About this time, too, anæsthetics were being tried and the first practical applications were being made in surgery of Pasteur's important discoveries "Yes," he said, "it was a long period of gestation—from the birth of Harvey to the passing of the Medical Act was 280 years Interesting, isn't it, because it was almost for medicine in years what it is for a human being in days"

From the time of the passing of the Medical Act until now, the baby had grown, through childhood and adolescence, into manhood For the first fifty years the child was most of the time with his mother, anatomy, it was only during the present century, when he had come under the influence of his father, physiology, that real growth and development had taken place Sir Zachary concluded "Now is a time of great promise—big developments are pending I know it from reading the journals, although I do not always understand what it is all about"

After Sir Gordon Gordon-Taylor, seconded by Sir Allen Daley, had proposed a vote of thanks to Sir Zachary, the party viewed the exhibition, for help in the preparation of which Dr Underwood had expressed his thanks to Miss M E Rowbottom and to the technical staff It contains a variety of instruments of ages past, including a beautiful set of surgical knives and a miniature axe, the purpose of which is obscure they date from 1570 and were formerly the property of General William Earle Bulwer of Heydon Hall, father of Lord Lytton Among other instruments are bullet extractors of the late 16th century, spearhead removers, Savigny's syringe for blood transfusion using Blundell's technique (1818), a portable leech jar, Messrs Kidstone's 1850 novelty of the mechanical leech, an intriguing miniature stethoscope to fit snugly into the hat, and the prototype of Mackenzie's polygraph Queen Anne it seems, when touching for the King's Evil, objected (and rightly) to touching the scrofulous ulcers, so she carried a lodestone for the purpose she later presented it to John Rooper, her deputy cofferer, in whose family it remained until presented to the Wellcome Museum Also associated with the King's Evil are two examples of Queen Elizabeth's "gold angels" There is on view, too, a handsome alembic of green glass, and also one of John Marshall's compound microscopes complete with a fine adjustment screw, which were being made in 1688 There are many striking photographs of Victorian doctors, and a series of contemporary prints are set up to illustrate the many social evils which encouraged the dissemination of disease in the 1840s and 1850s The exhibition also includes numerous prints and engravings, some of which are scarce and illustrate the beginnings of English engraving Of particular interest is the handsomely rubricated and illuminated manuscript on vellum of Pierre Boaistuau's *Histoire Prodigieuses* which, following a visit to England in 1559, he dedicated to Queen Elizabeth It seems likely that the dedication was rejected, for the book was published in Paris in 1560 That the evils which the Act of 1858 eventually eradicated troubled the legitimate members of the medical profession three centuries earlier is evidenced by a copy of John Halle's (1529 ?–66) *An historicall expostulation against the beastlie abusers, both of chyrurgerie and physyke in our time*, published in London in 1565

The exhibition remains open for several weeks (Mondays to Saturdays 10 A M to 5 P M)

A FILM ON DEXTRAN

A NEW thirty minute sound and colour film, *Dextran*, deals with the theory of shock, the history of plasma substitutes, the manufacture of narrow fraction dextran, and its use in surgery It was made by Dr Brian Stanford in collaboration with Prof A M Boyd at the Victoria Hospital, Manchester, for Benger Laboratories Ltd The colour photography is superb In the operation sequence at the end of the film, the stages of a difficult operation are correlated with the patient's response on a Nosworthy chart while the blood-pressure is maintained by regulating the rate of a dextran drip But the animated diagrams, used to explain the behaviour and fate in the body of different sizes of substitute colloids could have been clearer, and, with the exception of the operation sequence, the clinical aspects of shock are omitted The emphasis of the film is on the commercial preparation of a particular plasma substitute, and a large section is devoted to factory and laboratory scenes during the production and investigation of narrow fraction dextran, with only a brief reference to its use in a case of shock The film will be useful for medical societies, but it is unlikely to be used much for teaching purposes in its entirety, though parts of it, if available separately, would be valuable to pharmacists, medical students, surgeons, and anæsthetists

NEW ZEALAND HOSPITALS INQUIRY

A CONSULTATIVE committee has been set up to advise the government on the best way of administering the New Zealand hospital system, and the other services provided by hospital boards The following have been appointed members Mr H E Barrowclough (Auckland), Dr D S Wylie (Tauranga), Dr P P Lynch (Wellington), Mr H W Shove (Auckland), Mr C A Campion (Ashburton), and Mr H S Williams (Christchurch)

This committee has been set up at a time when local rating is about to disappear from hospital finance, with assumption by the government of full responsibility The system of thirty seven local hospital boards will thus become an anachronism Discussions have already taken place between the minister, the Hospital Boards' Association, and others about regionalisation and the issue of block grants to larger regional boards The constitution of boards will have to be reviewed, at present all members are elected by popular vote The position of the health department will also be studied, it now shares with the local boards the responsibility for hospital planning and provision

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University of London

On Nov 27, the honorary degree of D SC will be conferred on Dr H E Sigerist

Faculty of Radiologists

The following have passed the examination for fellowship of the faculty

Radiodiagnosis—D Lloyd Dick, D E Fletcher, P F New, J N Pattinson, E G Redman T R Riley, D Stenhouse, J Sutcliffe, D Sutton C K Warrick

Radiotherapy—J Boland, Mary Douglas, W B Lawson, J A Orr

In England Now

A Running Commentary by Peripatetic Correspondents

ALTHOUGH they are both more than twice my age, I established a firm friendship with Mr. and Mrs. Broadbridge soon after they moved here several years ago. Mr. Broadbridge found that he and I hold similar religious views, and he was delighted to lend me various aged books, his dearest treasures, written, as he said, by very clever men, who made short work of religions and superstitions. During our acquaintance this delightful old couple have several times peered into death's door, but have decided not to go in. Last winter they were obliged to take to the same bed at the same time, where they lay, blue and panting. I stood by and administered various medicaments, which I am sure were without effect, but for which they gasped out their unlimited thanks through cyanosed lips. Thanks, presumably, to a merciful providence that looks after these charming old heathens, they have always slowly recovered.

Mr. Broadbridge's zest for life is enormous. He is a great gardener, the best player in his bowls club, and an expert at draughts. But his chief joy is the horses, and however blue and dyspnœic he may be, he never ceases to study form. He came to see me last Friday; we exchanged a few conventional expressions of regret that the Coronation was a religious ceremony, and we were briefly indignant at the use of the title Doctor by Anglican bishops. Mr. Broadbridge then said that in the morning he would know the winner of the next day's big race, and that he would let me have it, but I must keep it under my hat. I thanked him, promised I would, and forgot all about it. Not so Mr. Broadbridge, who dragged his dyspnœic old frame to my house on Saturday morning and personally handed me a letter which was addressed to me and marked "Private and confidential." The letter read:

June 6, 1953.

Dear Doctor,
As promised I have sent the winner of the Derby.
Pinza it is.
There is no bunk about this.
Get on. Price will be short—about 9-2. But little fish are sweet.

Yours with compliments,
P. E. BROADBRIDGE.

I dare not tell Mr. Broadbridge that his efforts on my behalf were in vain. Until I had his letter I did not know what the big race was, and I have no idea of how to put money on a horse.

* * *

A strong case could be made out for strangling us amateur actors, if not at birth, at any rate as soon as we show histrionic stigmata. The plea that we get a lot of fun out of it and harm nobody is at once specious and unsound; it argues an unpardonable indifference to the sufferings of our audiences who are expected to pay good money for the dubious privilege of sitting for hours on chairs uncomfortably hard, in a hall uncomfortably hot (or cold) and deficient in emergency exists, with nothing better to do than to watch us act.

Closeted thus, and (as we insist) in darkness, they can neither read nor knit; they must merely endure. If they refuse to support us, we dub them stuffy and unsporting. If they come, we demand their attention during the performance and their adulation afterwards, sometimes even to the extent of providing bouquets or chocolates for all the ladies of the company and perhaps a box of cigars for the producer. Respites are few, for no sooner do we complete a mercifully brief run than we go into rehearsal for the next production.

At a recent performance inflicted on a sanatorium last week not only were the convalescents herded into the hall by the staff, probably armed with knouts, but the show was relayed to the wards where, it may be suspected, the more serious cases were chained to their beds with headphones clamped to their ears.

If we amateur players are to escape the violent deaths we so richly deserve, surely some compromise is possible? Might we not, for example, be allowed to act only in camera? If nobody saw us at it there might be less cause for shame. Incidentally, the same might apply to some professionals.

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It isn't really too bad being a pathologist. And when I say pathologist, I mean what they do in Edinburgh—a thoroughbred morbid anatomist and histologist.

The pathologist's apprenticeship is long and hard. You are blooded in the deadhouse, whence you graduate to biopsies, and if you manage to avoid pricking your finger, you become, when bald or greying, an authority. As such, your function is to pronounce upon the difficult section. The difficult section may originate anywhere in the region; born in obscurity, it travels by devious routes, pausing here and there at conferences and laboratory meetings, and finally comes to rest on your bench when you are out for lunch. It always consists of innumerable small round cells of a nondescript type, and though recognisable tissues, varying from case to case, may be present, the Thing Itself is as clueless and inscrutable as the Sphinx. Pictures of it are common in the journals, where it is variously described as sarcoma, carcinoma, blastoma, reticulosis, hyperplasia, a peculiar inflammatory reaction, or an atypical this or that. If you send it to a panel of experts, they will suggest all these possibilities, though perhaps in a different order. The correct diagnosis is of course *incognoma* or *incognitis* (whichever you prefer). In my report I explain this in simple language, and—as requested—enclose a modest bill, but I can't remember ever being paid for my candour.

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Well, the Coronation is over and as far as we can tell the hundred thousand who slept on the pavements and the thousands who got chilled in the stands seem to have thriven on it. I don't know how it all worked. Colds, we are taught, come through contact of a susceptible person with a subject who is already infected, or, as the lay person prefers it, through sitting on cold stones, leaving off winter pants, standing in the draught, getting wet feet, and the like. But witness my spinster patient who always gargles with salt and water before venturing into the germ-infested atmosphere of my waiting-room. Sustained only by swigs of brandy and the excitement of the occasion she sat for twelve hours in a draughty stand wringing the water from her clothing and enjoying it all to the full. And then there was my P.A. case with her thyrotoxic daughter. They stood for fourteen hours in Oxford Street enjoying a good view of the whole proceedings. Three others of my patients staked their claim on a patch of pavement fully twenty-four hours before the procession was due and saw everything in cold and discomfort, and loved it all. None of these have been laid low by a chill, and yet how often in the past have I treated them for colds caught through leaving off winter woollies just a few hours too soon.

It all goes to show; but what it shows I don't know, except perhaps the power of mind over matter and the fact that it takes a Coronation and a wet one at that to demonstrate this to perfection.

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Every medical school has its human landmarks, comfortingly immutable in a changing world. Thus when Queen's men meet their first question is likely to be: "How is Sister Dynes?"; for Sister Dynes (her Christian name is Catherine, though this is unknown even to some of her friends) has been night superintendent at the Royal Victoria Hospital, Belfast, since December, 1909. In these forty-four years she has never been absent through illness; and during her early days, when the hospital was in financial difficulties, she might have no night off for weeks on end while an assistant was on holiday. To her work she has brought not only skill but an uncanny knack of arriving, without being summoned, at the place where she is needed; and many hundreds of ill patients have been the better for her humane attention. The not so ill—those who sought to use the hospital for bed and breakfast—could be spotted by their whispered: "Is Sister Dynes on tonight?" It is only some of these who will not share the general pleasure at the appointment of Sister Dynes as M.B.E. in the Coronation Honours list.

Royal College of Physicians of Ireland

The following have been admitted to fellowship of the college

George Gregg R H O'Hanlon R W M Strain P J Sweeney, W D Hughes, Muhammad Aslam Pirzada (in absentia)

The following have been admitted to *membership*

J P A Ryan J D Sullivan

Society of Apothecaries of London

The following candidates have been granted the diploma of the society (L M S S A Lond), enabling them (upon complying with the requirements of the Medical Acts) to practise medicine, surgery, and midwifery

A Booth, G I Taylor, H A Whitehouse, G J John, J G Cooper, V R Jones R G Jones G R. Vesey, C M Stevenson, J D Spouge, J W S Webb, D J Waller G L Haworth, L Chapman, C L Smith, W G Rhys Jones, D Porter E W Fowler, T C Ryan, E R Lester, E McK Sycamore, R A Cooper, W G Nethery, B Lewis, and J A Scanlon

Members of the livery are summoned to attend at Guildhall at 11 45 A M on Wednesday, June 24, for the election of sheriffs and other City officers annually chosen on Midsummer Day

West London Medico-Chirurgical Society

The society's annual banquet is to be held on Thursday, June 25, at 7 30 P M, at the Apothecaries' Hall, Blackfriars Lane, E C 4

National Smoke Abatement Society

A proposal to form a south east divisional council will be considered at a meeting to be held at Caxton Hall, London, S W 1, at 2 30 P M on Friday, June 26 Dr A J Shinnie, medical officer of health for Westminster, and Sir Ernest Smith, D SC, will open a discussion on pollution problems in this division

Princess Tsahai Hospital

A general meeting of subscribers to this hospital's Fund is to be held on Tuesday, July 7, at 3 P M, at Tuke Hall, Bedford College, Regents Park, London This meeting, at which a film of the opening of the hospital will be shown, is to be followed by a garden party The hon secretary is Miss Sylvia Pankhurst, 3, Charteris Road, Woodford Green, Essex

South African College of Physicians and Surgeons

A College of Physicians and Surgeons may be established in South Africa before the end of the year The new college would enable South African doctors to take higher qualifications without leaving established practices to go overseas In an editorial the *South African Medical Journal* says that the founding of the college would be one of the major achievements of the South African Medical Association and one which would have far reaching effects on the quality of medical practice in the Union

Westminster Hospital

The annual dinner of old students was held in a happy pre Coronation atmosphere on May 29 The toast of The Hospital and Medical School was proposed by the chairman, Dr I W Magill, in a single sentence Mr H E Harding, the dean, admitted that such brevity caught him a little unprepared, but went on with customary ease and wit to welcome The Guests each as an old friend In reply, Sir Robert Young spoke of the phenomenal advances in medicine he had witnessed In his early days there were no X rays and the clinical laboratory was only just being established There was thus far less help and more uncertainty, but much more thrill in being right In anæsthesia the contrast between the days of Clover's inhaler and the present time was very great and he had much admired the contributions of Dr Magill to this change But, although science must play its part, he hoped the *art of medicine* would not be neglected, and most of all that the real flower of the profession—the general practitioner with his knowledge and interest in personality—would be restored to his rightful position in the family of his patients Dr Robert Machray, in proposing The Chairman, voiced the regret of all on Dr Magill's impending retirement after 29 years on the honorary staff Responding Dr Magill said that intubation had become commonplace and was taken for granted by the young anæsthetist and surgeon who now had relaxants, a bloodless field, and perhaps refrigeration in the offing He would warn both however against placing too much reliance on resuscitation or using sledge hammer methods in anæsthesia as a cover for lack of gentleness in surgery

Osler Club of London

At a meeting to be held at 1, Wimpole Street, W 1, on Friday, June 19, at 7 45 P M, Mr A Dickson Wright will speak on Some Royal Case Histories

Electronics Exhibition

The 8th annual exhibition of the north western branch of the Institution of Electronics is to be held at the College of Technology, Manchester, from July 15 to 21 The exhibition, which will be opened by Sir Geoffrey Jefferson, F R S, will include displays of the medical applications of electronics

Royal Society of Tropical Medicine and Hygiene

At the annual general meeting of this society, to be held at 26, Portland Place, London, W 1, on Thursday, June 18, Sir Neil Hamilton Fairley, F R S, the retiring president, will induct Dr F Norman White as president for 1953–54

Welsh National School of Medicine

Dr A S Duncan has been appointed the first whole time professor of obstetrics and gynæcology in the school He will succeed Prof G I Strachan, who retires on Oct 1

Dr Duncan, who is at present senior lecturer in obstetrics and gynæcology at the University of Edinburgh, graduated M B Edin in 1936 He took the F R C S E three years later and the M R C O G in 1941 During the late war he served as a medical officer in the Royal Naval Volunteer Reserve and he was awarded the D S C in 1943 In 1946 he was appointed lecturer in obstetrics and gynæcology at the University of Aberdeen, a post he held till he took up his present appointment in 1950 He was one of the authors of a *Combined Textbook of Obstetrics and Gynæcology* (1950), and he has also contributed chapters to the *Encyclopædia of Medical Practice* (1951), and to *British Gynæcological Practice* (1952)

World Health Organisation

At the meeting of the executive board in Geneva on May 28, Dr Melville Mackenzie, a principal medical officer of the Ministry of Health was elected chairman of the board The board decided that the topic for the technical discussions to be held at the Seventh World Health Assembly next year will be Public Health Problems in Rural Areas—a subject proposed by the Yugoslav delegation at the sixth assembly, which has just ended in Geneva The director general of W H O was asked to study with the International Labour Organisation what measures can be taken for strengthening activities in the field of occupational health The board also approved publication of expert committee reports on plague, mental health, and nutrition, and it reviewed the procedure for the selection of non proprietary names for drugs

Faculty of Anæsthetists

On June 3 Lord Nuffield received the diploma of honorary fellowship of the Faculty of Anæsthetists of the Royal College of Surgeons of England At a luncheon in the college after the ceremony, Dr Bernard Johnson, dean of the faculty, proposing the health of the new fellow, praised Lord Nuffield's foresight and originality in proposing and endowing the chair of anæsthetics at Oxford University, and, he added, the new Nuffield College of Surgical Sciences, presently to appear next to the Royal College of Surgeons, would include provision for research in anæsthesia These generous gifts would benefit the practice of anæsthetics throughout the world Lord Nuffield spoke warmly of Prof R R Macintosh's work in the Oxford chair of anæsthetics He thought that the anæsthetist's job should certainly include the responsibility of deciding whether the patient was fit for a particular form of anæsthesia, in the past the surgeon had often had to accept this and other duties that could usefully have been undertaken by the anæsthetist

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Number 4 of the *Proceedings of the Society for the Study of Fertility* which has now been issued covers the conference held last year in London The proceedings are published for the society by W Heffer & Sons Ltd Cambridge at 10s

The 10th edition of the *Register of Speech Therapists* is obtainable without charge by doctors from the Board of Registration of Medical Auxiliaries Tavistock House (North), Tavistock Square London W C 1

Births, Marriages, and Deaths

BIRTHS

DALEY —On May 2, in London to Alison (née Miller) and Raymond Daley, M D —a daughter

MOLLOY —On May 30 at University College Hospital to Audrey Molloy (née Mounce), wife of Robert Molloy M B —a daughter (Penelope Anne)

MARRIAGES

THOMAS—OWEN —On June 4 at Llanbeblig Church Caernarvon Robert Garym Thomas M A B M Oxfd, to Nansi Wyn Owen

Letters to the Editor

THE NURSE'S RESPONSIBILITY

SIR,—Your leading article last week will give rise to criticism. It suggests that the doctor wishes to shift much of his responsibility on to the nurse's shoulders. The Royal College of Nursing is a highly organised body for which I have great respect, but it does not seem anxious to move with the times and recommend ways and means for the young nurse to gain an extra skill which, as you state, she enjoys. I use the word "nurse" in its legal sense of a State-registered nurse. I shall try to put the case of the house-officer, who has no organised body behind him, and I shall make some suggestions to remedy what may become a deadlock.

Many house-physicians are responsible to physicians for some forty "acute" beds. They probably assist in three outpatient sessions weekly and do a share of casualty. They are called at night for emergencies. They have a half-day off a week, every third weekend, and a fortnight's holiday for every 6 months of service. Theirs is a busy life with no thought of a 48-hour week or 96-hour fortnight.

The problem of the house-officer's and nurse's responsibility is exemplified by a patient admitted with suspected diabetes. At outpatients it is decided that a glucose-tolerance test is needed. All will agree that the early morning is the best time. Is the house-officer to be called five or six times for this, or should a nurse be trained to do this as a part of her nursing duties? I maintain that she can be taught and also that she is doing more useful work than any other nursing activity for him or her. I will forge the routine temperature, pulse, and respiration record if need be. If the diagnosis is confirmed, she will later teach the patient to test his urine for sugar and acetone, to understand his diet, and to give himself insulin. I can quote a case of a patient who died because he infected himself when he gave himself insulin, and I have no doubt whatever he would have done the same if a doctor had taught him. Single cases like this make bad laws. The disaster you record was not due to the nurse's getting "a reading of less than 80 mm. Hg," but to group-A blood being supplied instead of group-O.

What therefore is the remedy? Whoever performs these special tasks should be trained. That principle is already established for midwives. Nurses, after becoming S.R.N.S, should have a 6–12 months' course in a medical, surgical, or other ward and be taught the special procedures. Postgraduate education would also be given, best done by ward-rounds; and at the end she should be given a diploma comparable to the S.C.M.

In the early 'thirties THE LANCET organised a Commission on Nursing which did great good. The time is now ripe for another commission to decide who, in the best interests of patients and realising the limitations of medical and nursing personnel, should carry out certain procedures.

Rugby. R. E. SMITH.

THE ILLEGIBLE CANDIDATE

SIR,—May a layman express regret at the defence of illegible writing that has appeared in your columns? Doctors are often accused of bad writing, but I never thought to find them complacent about it. Sir John Conybeare's defence of it (May 16) rests on the assumption that a man's handwriting is finally stabilised in his twenties; but he offers no proof, and in fact the evidence is to the contrary. I know of many who have reformed or changed their hand, at all ages up to 60; I have never heard of anyone who tried to do so and failed. I changed my hand when I was 22, in preparation for an examination where bad writing was penalised. It took only a few hours stretched over three days, and left me with a handwriting which was easier not only to read, but also to write, since it was less jerky.

Bad writing is more like bad manners than bad features: it is unpleasant to the beholder, like an ugly face, but, unlike it, is easily corrigible. There is little excuse for anyone to emerge from a liberal education with so antisocial a habit, and therefore much to be said for penalising illegibility in examinations, provided always that students are forewarned and helped to improve their writing. This is not difficult, as there are plenty of good examples and manuals available, and anyone can teach himself. *Nullius in verba:* but could not Guy's try an experiment?

Stansted, Essex. E. W. Playfair

EFFECT OF GLUTAMIC ACID ON THE COMA OF HEPATIC FAILURE

SIR,—We have read with interest Dr. Walshe's preliminary communication (May 30). We have treated one similar case with a single dose of 20 g. of glutamic acid introduced through a stomach-tube, passed while the patient was in coma. Since we obtained a gratifying response we feel it worth recording this case briefly.

A man, aged 29, suffered from infective hepatitis in April, 1950. The attack did not appear to be severe and he was not immediately admitted to hospital, but shortly afterwards he developed ascites which necessitated paracentesis on two occasions. He was treated with a high-protein diet and recovered sufficiently to return to work after a few months.

He was admitted to hospital a year later with a recurrence of ascites but again responded to treatment. He remained at work for a further year until October, 1952, when he had a sudden hæmatemesis. This was followed by a period of alternating violence and semi-coma lasting 36 hours. Nevertheless he left hospital in a few weeks and continued at work until May 9, when he had a further hæmatemesis of about $1^1/_2$ pints.

He was readmitted to hospital in a rational state, but 16 hours after the hæmatemesis he became extremely violent for a period of 3 hours and then lapsed into deep coma. Treatment with glucose, B vitamins, and plasma was given for 4 days without apparent benefit. Liver-function tests were not significantly altered compared with results obtained on previous admissions; these showed only moderate impairment of liver function, as in Dr. Walshe's second case. However, chromatographic examination of the amino-acids present in the cerebrospinal fluid on the 4th day of coma showed a striking increase of glutamine. It was therefore decided to give 20 g. of glutamic acid suspended in 20 oz. of water introduced through a stomach-tube. All other treatment was stopped. Within 8 hours the patient became less comatose, and 24 hours after the glutamic acid had been given he was sitting up in bed eating breakfast.

During the last decade, and especially during the war years in Egypt, we have treated several cases of hepatic coma with intravenous glucose, B vitamins, and plasma. Although on occasions we have obtained some response to this form of treatment we have not hitherto observed such a striking recovery as that which followed the administration of glutamic acid. We agree with Dr. Walshe that this form of treatment deserves further trial.

W. M. PRIEST
T. P. WHITEHEAD
Warwick. S. R. F. WHITTAKER.

SIR,—We have read with great interest the preliminary communication by Dr. Walshe, as during the past three years we have been treating cases of delirium tremens by oral administration of glutamic acid. We hope to publish our results later; but in view of the interest aroused by his article it was thought that our findings should be disclosed now.

CHEMICALS AND FOOD

A RECONSIDERATION *

E C Dodds

MVO, MD, DSc Lond, FRCP, FRIC, FRS

COURTAULD PROFESSOR OF BIOCHEMISTRY IN THE UNIVERSITY OF LONDON, AT MIDDLESEX HOSPITAL MEDICAL SCHOOL

It is generally admitted that certain subjects, when introduced into a conversation, have the curious power of robbing the talker of his powers of logic They appeal so strongly to the emotions that they are seldom considered coolly and critically

High on the list of these dismissers of reason and logic is the question of food One only has to think of the brown versus white bread controversy to realise that this is so Even the dignified calm of the Upper House has been rent by sharp cries of the noble contestants in this famous controversy Similarly, adulteration and chemical treatment of food has an irresistible fascination for the press Journalists seem to take a delight in painting pictures of people sitting round a family table eating what looks like a fine and wholesome meal yet is really a poison

Last year in this very room Sir Edward Mellanby thrilled and horrified an audience with his cinematograph pictures of dogs suffering from running fits due to eating treated flour Observations such as his must of necessity focus the attention of the public, and also of the medical profession and scientists in general, on this question of the chemical treatment of food But we should, I believe, be wrong to judge such treatment by the few alarming exceptions which it is possible to quote It is not true, as the general public is sometimes led to suppose, that food manufacturers can do what they like with the people's food, but, even if there were no supervisory authority to control them, it seems unlikely that these manufacturers, who, after all, must be astute business men, would deem it sound policy to produce products that would eventually poison their customers I think it must be admitted that there is a first check in this respect by the manufacturers themselves—though unfortunately it must also be admitted that this has not stopped them making mistakes in the past from lack of knowledge

Preservation of Food

Chemicals may find their way into food either accidentally or deliberately, but in this lecture I am considering only those which are added deliberately for some specific purpose Again, I shall have nothing to say about the addition of substances for the purpose of misrepresenting the food—though on occasion such fraudulent practices have of course had serious results

From the earliest times man has been interested in doing things to his food, either by treatment such as cooking or by the addition of substances for various purposes The main purposes of the additions are (1) to alter or improve the taste of the food, and (2) to preserve it We are not not concerned here with substances like spices, which were originally employed to cover the fact that the food was often slightly putrid Far more important is the preservation of food, which in the past has been the main object of adding chemicals

That food needs preserving is obvious when one thinks of the seasonal nature of its production, also it has to be stored for periods of want and famine, and for purposes of travel The classical methods of preserving it were drying, salting, smoking, and refrigerating To these were later added the methods which we now know as hermetically sealing—the art of sterilisation—which was used for vegetables in glass jars as far back as the 17th century but became of great importance when the canning industry was firmly established towards the end of the last century All early attempts at food preservation were handicapped, however, by lack of knowledge of the cause of putrefaction It was firmly believed that putrefaction was due to a spontaneous process occurring in the tissues of the food when kept in presence of air, and it was felt that if all air could be excluded putrefaction would be arrested Later the cause of putrefaction was put down to the oxygen in the air, and storage in an atmosphere of nitrogen was recommended to prevent it Not until the middle of last century was the true nature of the putrefactive process understood, through Pasteur's demonstration that it was airborne microbes, not the air itself, that caused putrefaction

Just as Lister in surgery used carbolic acid sprays to eliminate microbial action as a cause of infection, so did the food manufacturers try to use powerful antiseptics in the preparation of their products Thus in the 1870s we find such powerful substances as formalin being extensively employed, particularly as a preservative for milk The surgeon quickly learned that it was better to exclude the micro organisms, by the process of asepsis, than to kill them by the violent and harsh process of antisepsis The food manufacturer learned this very much later, and we see the persistence of powerful antiseptics in food long after antiseptic surgery had disappeared

Many people unthinkingly ask why it is necessary to add chemicals to food at all The answer is obvious —namely, that if one has a highly urbanised population such as we have in this country one must be able to preserve their food Unless a person lives on a farm by the sea, his milk, butter, eggs, and fish must be brought from a considerable distance, and this in itself demands some form of preservation So long as our population is of the size it is, and is grouped in large cities and towns, some form of chemical treatment of food is an absolute necessity Again, the preservation of food enables the products of other lands to be enjoyed

If we accept the thesis that food preservation is essential, we can turn to the two vital questions of the methods to be used and the way in which these methods should be controlled by the Government Let us consider first the question of control

Control and Supervision

From the time of the Norman Conquest our legal records show a continuous series of prosecutions for contaminating food or for purveying food unsuitable for human consumption In the absence of detailed laws and regulations, however, prosecution depended largely on the opinion of the prosecutors The control of many of the food industries was in the hands of guilds—the vintners, the bakers, the salters, and so forth—and supervision was vested in these City companies The methods they employed make interesting and amusing, if unscientific, reading It must be remembered that chemical analysis was rarely applied to food before the last century The only form of analysis of a Governmental nature that was performed was undertaken for the Board of Excise at Somerset House, which needed an estimate of the alcohol content of beverages imported into the country

As chemical theory and practice developed, it was natural that the Government should turn to the newly developed science of analytical chemistry, and in 1842 the first Government laboratory was set up in Somerset House for the Board of Excise In 1875 the laboratory facilities were considerably extended, and Dr James Bell, who was appointed in 1875 as head of the labora-

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* Sanderson Wells Lecture delivered at the Middlesex Hospital on May 20, 1953

In all, some twenty cases of delirium tremens have been treated by this method, giving 12–16 g. of glutamic acid daily by mouth or, in restless patients, by tube feeding. The first few cases were also given vitamin B_1 100 mg. intramuscularly daily, but later cases were given glutamic acid alone, and showed equally favourable results. Within a few hours the restless delirious patient becomes quiet and easily managed, and within a week he has usually become rational, so that treatment can be discontinued.

The possibility has occurred to us that the mental symptoms of delirium tremens might be due to a disturbance of brain metabolism secondary to hepatic failure. Two of the patients had been jaundiced, and recent investigations by chromatography have shown biochemical similarities with cases of hepatic failure. Mental confusion, restlessness, and delirium are moreover common in hepatic failure; but so far as is known no instance has been reported where visual hallucinations were present, though these are a fairly constant feature of delirium tremens.

Warwick.

R. F. CHATFIELD
C. TETLOW.

RESEARCH ON POLIOMYELITIS

SIR,—In your annotation of May 30 you ascribe to me the observation that there is a high prevalence of paralytic attacks of poliomyelitis in school-teachers. This is not in accordance with my experience. I did, however, draw attention to the fact that a disproportionate number of patients in the recent outbreak of poliomyelitis in Southend-on-Sea came from the families of, or were intimately associated with, school-teachers.

Municipal Health Centre,
Southend-on-Sea.

J. STEVENSON LOGAN
Medical Officer of Health.

THE PROBLEM OF PEPTIC ULCERATION

SIR,—The repeated writings on peptic ulceration by a surgeon of such eminence and standing as Sir Heneage Ogilvie must inevitably induce many of our younger colleagues to regard the operation of partial gastrectomy as one which not only gives absolute cure, but is also unaccompanied by any long-term postoperative ill effects. The student of medicine with lesser experience may even wonder why the physician attempts to cure the condition by a long period of inpatient hospital treatment when but a fortnight's stay, accompanied by a gastrectomy, will cure the condition once and for all. He may wonder too, why it is suggested that those of a younger age-group, in which duodenal ulceration predominates, should be advised to restrict their normal way of life, when the operation would seem to be as beneficial to them as to older sufferers from this condition.

As a result of long apprenticeship to surgery, in which I have had the privilege of being house-surgeon and registrar to a number of distinguished surgeons, and because of my own personal experience, I am convinced that postoperative ill effects occur in a very substantial number of patients, especially when the operation has been performed for duodenal ulcer. They have certainly occurred amongst the patients of all surgeons for whom I have worked and also in my own series. Judging from the reports in the literature these disabilities are a widespread experience of many surgeons. Cattell told me in a private communication that only 85% of his patients are symptom-free following a gastrectomy, and that in 5% ulceration recurs.

If gastrectomy is the perfect operation for peptic ulceration of all types, research into other ways and means of curing the condition is a waste of time. I believe, however, that this mutilating operation, which removes an essential part of the digestive tract, does not give anything like perfect results, and that further research for the cure of a condition which seems ever increasing in its numbers is essential.

I have previously described an operation applicable to cases of duodenal ulceration in which the stomach is preserved.[1] My experience of this operation, in approximately 100 cases, suggests that, so far, it is greatly preferable to a gastrectomy in such a condition, and the results will be reported shortly.

Although the patients of one surgeon may very seldom have disturbances following gastrectomy, there is no doubt that, whatever technique is used, these are, throughout the country, comparatively common, and we would be unwise to underrate their number.

London, W.1.

STANLEY AYLETT.

TUBERCULOSIS IN GLASGOW

SIR,—In the absence abroad of my friend, Dr. Brailsford, may I be permitted to reply to Dr. James's astonishing letter in your issue of May 30. It is true that Dr. James's address seems to suggest that he is "trailing his coat," but nevertheless there is a possibility that some of his arguments will be taken at their surface value.

Dr. James complacently states that there is no evidence that good housing and a good standard of living will eradicate tuberculosis; in fact there has been such evidence for two or three generations right throughout the world. It is well known that in this country tuberculosis is and always has been very much less common amongst the well-to-do than amongst the poor, and the general difference between these two groups has been, not their access to doctors, but the good housing and the good standard of living which the well-to-do have enjoyed. The two world wars brought to Europe a sudden deterioration in living conditions, and in each case the falling incidence and death-rate from tuberculosis both were interrupted in a disquieting fashion to fall again when more normal conditions of nourishment and living returned. In Scandinavia, which probably enjoys the highest standard of living in Europe, the death-rate and incidence of tuberculosis have steadily declined long before the discovery of modern antibiotics, and although much of this may be ascribed to vaccination it may safely be claimed that most of it is due to a high standard of living and housing. Is Dr. James aware of the epidemiological history of, for example, the Netherlands and Germany during the late war? The Dutch passed through greater malnutrition than almost any other nation in Europe, and by 1945 the incidence of tuberculosis had risen to 208% of the normal. In Germany, Poland, Hungary, and Austria a similar position arose.

It is surely ironical to suggest that the solution of the tuberculosis problem depends on a "final assault" on an "extremely resilient organism," especially during a period when every civilised nation is vigorously engaged in injecting live tubercle bacilli into the largest possible number of their *non-tuberculous* subjects! More than 40 million persons have been vaccinated during the past few years, and each year there are in the world more persons infected with tuberculosis and fewer with tuberculous disease.

The tubercle bacillus is ubiquitous, and it is ridiculous to suggest that the disease can be conquered by physical eradication of the organism itself. History does not give any instances of the eradication of any such epidemic disease in this way. Diphtheria has been conquered in this country, not by treatment of the disease itself, not by any mass attack on the *corynebacterium*, but by immunisation of the host; and for the past half-century tuberculosis has been attacked in the same way. It will not have escaped general notice that tuberculosis is less common in the civilised countries with a high standard of living and most deadly in countries where the standard of living and housing is low. Dr. James would do well to read the transactions of last year's Commonwealth Health and Tuberculosis Conference in London, in which tory, became responsible for analysing not only alcoholic beverages but also food and drugs In the same year the first important Act controlling chemicals in food and the composition of drugs was passed and in 1893 an Act dealing with fertilisers and feeding-stuffs brought a further inrush of work The Government Laboratory, as we now know it, was brought into being by the appointment of Sir Edward Thorpe in 1894 as the first Government Chemist This post has been continued to the present day, and its scope and importance have increased from year to year To get an idea of the amount of work now required, compared with what was required in 1894, one has only to think of the advances since that time in biochemistry, chemistry, and nutritional science in general In 1894 we had no knowledge of even the existence of the vitamins apart from certain hints with regard to the antiscorbutic factor of lemon juice and the possible bearing of rice polishings on beriberi

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[1] *Brit. med. J.* 1951, i. 154.

THE LANCET'S CAMPAIGN

The attention of Parliament and the public was focused on food adulteration towards the middle of the last century by a very curious series of writings and happenings conducted by THE LANCET The first editor Thomas Wakley, is well known to all readers of the period as one of the outstanding figures in medical and other reforms of the day This fiery courageous man jumped into the most dangerous of situations without any thought for himself or for the financial implications in which he might involve his journal During the years approaching the middle of the century he became more and more worried about the adulteration of food and decided to found in 1850 a body which he called THE LANCET Analytical Sanitary Commission This flourished from 1851 to 1854 inclusive—i e , for about four years The principal analyst attached to the commission was Dr Arthur Hill Hassall, who was born in 1817 and died in 1894 He had been trained as a doctor under the old system of apprenticeship in Dublin, and came to this country to set up in general practice He was admitted to membership of the Royal College of Physicians, but during his early training he came under the influence of Sir William Hooker, director of Kew Gardens, and became not only an excellent botanist but a trained microscopist As an expert on the application of the microscope to botanical specimens, such as seeds, he had peculiar knowledge of the job that Wakley had in mind With Hassall at the head of the team, Wakley examined some 2500 samples of food during the five to six years from 1850 onwards A high proportion of these were found to be adulterated, and in order to bring the matter to the attention of the authorities Wakley published the names of firms, suppliers tradesmen—in fact the name of everyone connected with the exploitation of the particular food These were all published openly in THE LANCET One can well understand the anxiety of Wakley's friends and relations during this period, for some of the companies and individuals mentioned might well have brought legal proceedings against him, and a successful action of this kind would probably have ruined him and his enterprise

As a contemporary put it a gun suddenly fired into a rookery could not cause a greater commotion than did the names of dishonest tradesmen ' Nearly 3000 names were published yet only one legal action was started, and this was dropped The type of adulteration varied from relatively harmless frauds such as the dilution of coffee with chicory to some very dangerous adulterations employing sugar of lead, mercury, sulphuric acid, and even nitric acid in vinegar It is estimated that as a result of these publications adulteration of food dropped from 65% to under 25%

In 1855 Hassall published a book called *Food and its Adulteration*, and this included the report of THE LANCET Analytical Sanitary Commission This was the spearhead of the attack, and the same year saw the appointment of a Parliamentary committee, under the chairmanship of Mr Scholefield to investigate the whole question of the chemical treatment and adulteration of food In its report published in 1856 this committee pointed out that not only were the public defrauded but their health was endangered, while the export of adulterated food would damage our prestige overseas

LEGISLATION

As a result of these activities the first Adulteration of Food and Drugs Act was passed in 1860 Though it only scratched the surface of this very difficult problem, credit must be given to those who devised it for foreseeing the need for the appointment of public analysts to the various cities and corporations Unfortunately the Act did not make it compulsory to appoint them and there was therefore no adequate machinery for enforcing the law The first public analyst was Dr Letheby, for the City of London, but it is reported that in the first three months of his office he examined only four samples of food—all of which were adulterated

When this 1860 Act was found to be largely in abeyance, a new one was passed in 1872 This imposed severe restrictions on manufacturers and purveyors of food, and it caused a strong reaction in the food manufacturers, who, it is said, influenced Parliament to produce a third Act in 1875 which was more favourable to them This 1875 Act, despite its shortcomings remained in force for sixty years and was not revised until the 1930s Its two principal points were first that nothing injurious should be added to food and secondly that the food when supplied to the public must be of the nature, substance, and quality demanded by the purchaser When one considers how difficult it is today to decide whether a chemical is poisonous or not, one can well understand the difficulties that faced those trying to administer the Act of 1875 Again it is a tribute to the 1875 Act to note that there has been a steady fall in prosecutions and convictions for food adulteration since it was enforced

The success of the 1875 Act was due almost entirely to the early public analysts They developed methods of analysis which were able to withstand criticism in the courts, and these methods have been copied throughout the world Their position was further established by the arsenic in beer tragedy in Manchester at the turn of the century, when some 6000 people were poisoned and 70 died, and by the mayoral banquet at Winchester in 1902 when contaminated oysters caused many illnesses and 4 deaths The analytical work for many of these outbreaks if one can call them that, was undertaken by central authorities such as the Government Laboratory but it was soon found that these were too numerous to be attacked centrally and that more local organisation was needed 1906 saw the food departments of the Local Government Board constituted—mainly to deal with tinned meat from Chicago, which was found to vary widely in quality The Public Health (Regulations as to Food) Act of 1907 gave importing authorities the right to examine foreign meat and unsound food

During this period no special attention had been paid to milk, and it is interesting to note that after the Wakley affair there was an increase in the addition of powerful antiseptics such as formalin and borax, to many foods and particularly to dairy products By 1912 the authorities were beginning to be worried about milk and a Milk and Dairies (Consolidation) Act was passed in 1915, though it could not be brought into action until 1918 Amended in 1922, this Act defined the different grades of raw milk and prohibited the addition of any chemical whatsoever Pasteurisation was the only form of treatment permitted, and the authorities wisely con he would find some figures relating to the Commonwealth which would surprise him. Special attention might be paid to the incidence and death-rates in India and Pakistan. Dr. James, however, is most provocative when he suggests that at long last and for the first time tuberculosis is being tackled by modern drugs such as streptomycin, but the facts do not support him. The death-rate from tuberculosis in 1950 was approximately one-tenth of the figure 100 years previously, and during this century the drug treatment of the disease contributed practically nothing to its eradication. The fall during this 100 years was fairly steady and followed closely the steady improvement in the standard of living.

Dr. James again suggests that because the price of food has steadily increased during the past four years this is an argument to show that the standard of living has not affected the tuberculosis incidence or death-rate during this period. May I suggest that improved housing and improved standards of living do not miraculously and in a period of a weekend or even a full year result in the complete transformation of a badly nourished man. Improved housing and improved nutrition take years to operate, and it is an unchallengeable fact that the people in this country are enjoying a vastly higher standard of living than they did at any previous time of their existence. Even during the past four years the *real* standard of living has slightly improved.

The claim that the modern drugs will cure tuberculosis is a little premature, is it not? We are perfectly aware that patients treated by streptomycin and so forth have their deaths postponed, but there is no convincing evidence that they have been completely cured and no evidence whatsoever that all the mycobacteria in their bodies are completely killed.

While full acknowledgment must be made to the use of modern antibiotics as one of a half-dozen potent weapons in the fight against this disease, it still remains that their use is only one weapon, and it is fortunate indeed that this weapon was not discovered 50 years ago before the well-tried methods of prevention by attention to the well-being of the host had been shown to be so successful.

Public Health Department,
Smethwick, Staffs.

HUGH PAUL.

POSSIBLE HAZARD WITH SUXAMETHONIUM AND SUXETHONIUM

SIR,—Because of the increasing use of the short-acting muscle relaxants suxamethonium and suxethonium, we believe it desirable to draw the attention of anæsthetists to a possible complication when a procaine infusion is administered to a patient receiving either of these compounds.

Dr. Victor Goldman[1] reported some fourteen months ago that he had observed prolonged apnœa in a patient receiving procaine who had been given 60 mg. of suxamethonium cation followed six minutes later by a further dose of 30 mg. The first dose produced relaxation lasting four to five minutes, while the second caused most profound paralysis of thirty minutes' duration which necessitated artificial respiration with oxygen.

Since it is now known that pseudocholinesterase is responsible for the hydrolysis of both procaine and suxamethonium compounds, it is not inconceivable that the frequent use of procaine during thoracic and cardiac surgery in conjunction with the short-acting relaxants may give rise to further similar cases. Foldes et al.[2] have recently confirmed the observation of Goldman both experimentally and clinically. The intravenous injection of procaine during suxamethonium administration increased the inhibitory effect of the latter on neuromuscular transmission, resulting in increased respiratory depression in patients and a decreased response of the sciatic-gastrocnemius preparation to electrical stimuli in animals. Foldes et al. also demonstrated in vitro substrate competition for pseudocholinesterase between procaine and suxamethonium.

It seems important that anæsthetists should be aware of the possible additive effects of these agents.

Medical Information Division,
May & Baker Ltd.,
Dagenham, Essex.

C. R. DAY.

MISDIAGNOSIS

SIR,—In your excellent annotation of May 23 you quote Professor Bürger, who poses five direct questions to the clinician who has been mistaken: (1) was a thorough physical examination of the patient undertaken? (2) were diagnostic investigations carried out—and which? (3) was the history properly assessed? (4) were the signs correctly evaluated? (5) were there superadded symptoms obscuring the diagnosis?

This reminded me at once of the last paragraph of Sir William Osler's book *Diagnosis of Abdominal Tumors*, published in 1902:

> "Amid many pleasant memories of Berlin. just twenty years ago this session, none recur more persistently than those associated with that true Asclepiad, Ludwig Traube, who, adding probity to learning, sagacity, and humanity, reached the full stature of the Hippocratean physician. When acknowledging some error he would say—often in a soft, meditative manner, as if gently reproaching himself—Have we carefully observed all the facts of the case? Yes. Did the art permit of a judgment on the facts under consideration? Yes. Did we reason correctly upon the data before us? No. Wir haben nicht richtig gedacht. And with these significant words—may they long echo in your ears!—let us close the exercises of the session."

Tonbridge, Kent.

P. T. COOPER.

JUNIOR MEDICAL STAFFING

SIR,—I think that the article by Mr. Hurst and his colleagues in your issue of May 23 calls for further comment.

The authors appear to base their claim that there are too few doctors on the fact that there are fewer entrants to the medical schools each year than there are preregistration posts; but they seem to forget the fallacious appearance of shortage of doctors at junior hospital staff level owing to many of these doctors being temporarily in the Forces. In any case they should surely base their estimate on the number of permanent established medical posts available (hospital, general practice, local authority, Forces, industry, Colonial Service, &c.) unless they envisage a new grade of permanent junior house-officer. If they will study the figures of the total number on the Medical Register and the numbers of posts available in the various major sources of permanent employment as above listed, they will scarcely fail to be struck by the fact that these established posts account for little more than, if as many as, half of the 83,914 doctors already registered. (It is worth recalling that the numbers on the Register in 1933, 1940, and 1946 respectively were 56,741, 64,679, and 76,292: and there have not been so many retire or emigrate.) Sober calculation shows that there is already an overabundance of doctors, though admittedly there are anomalies in distribution. Are the authors not aware of the plight of the senior registrars and of many others in, or not even in, unestablished medical posts? It is high time that medical man-power figures are looked at as a comprehensive whole right from student to professorial, general practitioner, and consultant level.

Some of their suggestions for remedying this alleged shortage of doctors are open to question. The employment of non-medical technical assistants to carry out

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1. Personal communication.
2. Foldes, F. F., McNall, P. G., Davis, D. L., Ellis, C. H., Wnuck, A. L. *Science*, 1953, 117, 383.

centrated on the production of better conditions in the preparation and distribution of milk

FOOD STANDARDS

A study of food standards was begun in 1886 and a Select Committee of the House of Commons suggested the formation of a Court of Reference to deal with standards But no real progress was made until after the 1914–18 war

Between 1919 and 1934 a large number of committees were appointed to consider the control of the quality of food and of various substances added to it—e g , colouring matters and flour improvers Out of the report of an interdepartmental committee in 1934 came the new Food and Drugs Act of 1938 This Act was never fully used owing to the imminence of the war, and when the Ministry of Food was formed the Ministry became the operative authority

At the present time yet another Act is being worked upon, and in the near future we may expect an Act which will embody the experience and wisdom gained from 1850 onwards The Ministry of Food has returned to the old problem of devising standards for food, and today there exists a Food Standards Committee which is in process of laying down the requirements

Chemicals in Food

As things stand at present, with few exceptions the manufacturer can add to food, or treat food by chemical process, without obtaining the permission of any Government department But though no Government department is officially charged with advising manufacturers of the toxicity of chemicals added to food, the Ministry of Food is frequently consulted and has given very valuable advice on the use of chemicals in food

MINERAL OILS

The addition of mineral oils to food became a common practice in the early part of the war Fat was scarce and the addition of pure liquid paraffin to certain food products increased their keeping qualities and palatability Researches officially instituted showed, however, that the addition of liquid paraffin was actually dangerous in that it reduced the absorption of certain vitamins, while the paraffin itself might be absorbed and deposited in certain parts of the body In 1949 its use was prohibited

ETHYLENE GLYCOL AND DIETHYLENE GLYCOL

The use of these substances as solvents for sulphanilamide led to the death of 107 persons in the United States, and it is amazing that this could happen in a country so far advanced in the control of substances offered for sale Another American tragedy was caused by the use of ortho-cresyl-phosphate as a substitute for ginger It produced serious permanent damage in the central nervous system

FLOUR IMPROVERS

After Sir Edward Mellanby's classical experiments on the production of running fits in dogs by feeding them with flour treated by nitrogen trichloride, it was only natural that alarm was caused in both official and lay circles The first question that the layman asks is "why have flour improvers at all ?" and he reinforces this by the statement that improvers are not used in certain countries such as France The answer is very simple In this country during the last fifty years the small baker has gradually been replaced by the big scale bakers known as "plant bakeries" This has resulted in shortening the time of production of the loaf and has simplified delivery On the other hand, the operation of a plant bakery demands a rigidity of process which is unnecessary for the small baker

It must be remembered that the composition of flour varies very considerably from time to time The British miller has to depend on imported wheat and wheat from different districts, and his flour will vary in its behaviour in the bakehouse The small baker can modify his baking process, time of fermentation, and so on to allow for these differences in the types of flour, but the plant baker cannot do this In order to overcome this difficulty the chemical treatment of flour, with so called improvers, was devised. Acting on the gluten of the flour these chemical agents change its physical properties and make its behaviour, as regards baking, more or less constant Most improvers are oxidising agents, and substances such as bromates and persulphates have been employed About thirty years ago the treatment of flour with gaseous nitrogen trichloride was introduced it had the same effect as prolonged storage and was called the "agene" process Nutritional experts have always been a little unhappy about the use of highly reactive chemicals, and in 1923 Mr Neville Chamberlain, then Minister of Health appointed a departmental committee to study the treatment of flour with chemical substances The report of this body, issued in 1927, makes fascinating reading, for the committee seems almost to have foreseen the work of Sir Edward Mellanby Paragraph 54 reads

> "Our observations upon chlorine apply also to nitrogen trichloride It is true that the quantity of the latter substance used per sack of flour is very much less than the quantity of chlorine introduced in the chlorine process, but nitrogen trichloride is very highly reactive, and evidence has been given that its action on the protein of flour is probably similar to what we have already described in the case of chlorine We are, therefore, compelled to extend our disapproval of chlorine to nitrogen trichloride also"

This paragraph has a distinctly prophetic tone, although at that time there was no evidence that improved flour had any biological properties other than those of normal flour The subject is now receiving the most careful attention by all concerned

COLOURING OF FOOD

The use of dyes is a very old practice in fact the oldest records of food include descriptions of how to make it more attractive in this way The early pigments were natural ones and therefore free from risk burnt sugar was used to give food a rich brown colour, while cochineal and similar pigments were used for sweets With the development of the synthetic dye industry the use of dyes in food was greatly increased At first no thought of harm occurred to the official mind, which was concerned mainly with the possibility of colouring to make foods appear better than they really were

Towards the end of the last century the attention of health administrators was drawn to the so-called aniline workers' cancer This was a malignant papillomatosis, occurring in the bladder of a significant proportion of persons engaged in the production of aniline dyes A great deal of hard work has been done on this problem and we now know most of the compounds responsible, which incidentally do not include aniline itself Some of the compounds used in the colouring of food were known to belong to this series of cancer-producing substances, and the question of control immediately arose One method is to follow the American practice and issue a *permitted* list of compounds This consists of some 20 pigments which have been subjected to extensive pharmacological and biological study, and the American industry is said to be able to manage with these The alternative is to compile a *prohibited* list, and it is this technique which has been adopted by our own authorities It is giving away no secrets to say that the official mind is much concerned about the present position, for the English method virtually gives carte-blanche to the manufacturer to colour his wares with any pigment provided it is not on the proscribed list preliminary investigations on patients is wasteful and psychologically harmful; in short it is push-button medicine at its worst, as any experienced clinician knows. Are lay administrators really the right people to advise on these matters? And do members of our profession really think that more and more regulations should be made forcing longer hospital service on all young graduates, forcing whole-time status on consultants, and barring doctors from more non-clinical, presumably medical administrative, posts?

C. D. NEEDHAM
Aberdeen. Consultant Physician.

SIR,—Dr. Greenwood Wilson suggests, in his letter last week, that the junior resident staff in the National Health Service are nowadays too concerned with working hours and conditions. He then gives us an account of his days as a houseman at Westminster Hospital when apparently he never knew that time existed. Presumably this description is meant for comparison with present-day disgruntled house-officers. Such an attitude of mind is all too common among senior medical men, but it disregards several important factors.

Firstly, since the days when Dr. Wilson was a houseman the practice of medicine has undergone considerable changes. The modern resident doctor is responsible for the proper management of complicated techniques unheard of thirty years ago. Instead of remaining impotent by the bedside counting the pulse and percussing the chest, he is able to carry out active measures which require thorough knowledge of many branches of medicine.

An obvious example is intravenous-drip therapy. This requires among other things a knowledge of the technique of blood-grouping and cross-matching, together with a basic understanding of the electrolyte balance of the body under both normal and abnormal conditions. At the same time the conscientious houseman will keep a close watch to see that the patient is being neither over- nor under- "dripped." Finally the actual setting up of the drip requires a certain degree of manual skill, particularly in severely dehydrated infants.

Another example is tuberculous meningitis. In the days of Dr. Wilson a patient with this disease slowly slid into the necropsy room, whereas now the management of such a case requires months of special daily treatment, the bulk of which falls on the houseman.

Surely these procedures carry more responsibility than those practised in the time of Dr. Wilson.

Secondly, since the end of the war the majority of housemen have encountered some form of National Service. Either they are ex-Servicemen who have taken up medicine since leaving the Forces, or they have to contend with two years of National Service after finishing their house-appointments. As a result nowadays the average doctor has to wait longer for a settled existence than his more senior colleagues. Does Dr. Wilson really imagine that an ex-Serviceman with, for example, two children is happy to find himself on the threshold of his chosen career, being rewarded with £1 a week and all found, including laundry, plus the odd theatre ticket from the matron's office?

If Dr. Wilson chose to become resident in any National Health Service hospital for only a week, I am sure he would discover that the great majority of housemen are just as conscientious as in his day. This does not prevent them from being sufficiently intelligent to ask for better working conditions.

Waltham St. Lawrence,
Berkshire. M. ANTHONY PEYMAN.

SIR,—I cannot, as a houseman, let Dr. Greenwood Wilson's letter go unchallenged.

I take it that it is some considerable time since he was a houseman. During the intervening years the value of the pound has altered somewhat, not to mention the rate of income-tax. From what one gleans from the consultants today, the pound-a-week houseman did occasionally lean on his parents, and in the years before the late war parents could afford to subsidise their housemen sons. Nowadays, as Dr. Wilson probably has noticed, there is less money about, and most parents expect their children to keep themselves on completion of their medical-school education.

One hears so many hard-luck stories today, on the lines of "the senior registrar with a triple fellowship who had to take up chicken-farming," that not many newly qualified men will gamble on the poor odds of reaching consultant status. Hence, they do a minimum time in hospital and endeavour to get into general practice and, they hope, Security.

At one time one had only to remain on the house staff for long enough to be fairly certain of a staff appointment. This is no longer so—hence the shortage.

May I assure Dr. Wilson that some of us at least are managing to be "happy round the clock," even if we don't get any theatre tickets from matron's office?

General Hospital,
Nottingham. R. W. POOLE.

KWASHIORKOR

SIR,—I am beginning to feel that we are making rather heavy weather over this word, and perhaps the time has come to simplify the whole issue. When I attended a conference in The Gambia last November one of the members described finding a child with this disorder in an up-country village in West Africa. He asked an old granny what it was called, and she knew the name. He then asked her what the name meant, and she said "the deprived child." This seems to me to be a far better explanation than to drag in red devils and other mythology. In any case it so exactly describes the child concerned that the story has the ring of truth.

Institute of Child Health,
The Hospital for Sick Children,
Great Ormond Street,
London, W.C.1. ALAN MONCRIEFF.

CONTRACEPTIVE TECHNIQUE

SIR,—The prejudice demonstrated by Dr. Marie Stopes (May 30) towards a much-needed progressive step in contraceptive technique must surely surprise many of your readers when she makes it clear that her disapproval is not founded on any clinical familiarity with the method she too readily condemns. In the curiosity she displays in its evaluation, however, there may be a brighter gleam of hope for the patient.

Copies of published reports following studies in evaluation of the effectiveness, tolerability, and acceptability of the 'Preceptin vaginal gel' method are available to Dr. Stopes—or to any interested medical practitioner—on request to the professional service department of this company. Supplies of the gel are also available to any clinic at moderate cost.

REGINALD GEORGE
High Wycombe, Managing Director,
Bucks. Ortho Pharmaceutical Ltd.

OPHTHALMIA NEONATORUM

SIR,—There would, I think, be fairly general agreement with Dr. Williamson's contention, in his letter last week, that the number of cases of ophthalmia neonatorum notified must represent but a small proportion of minor conjunctival infections in the newborn; but it is surely because they are limited to the conjunctiva that they respond to purely symptomatic treatment. Such treatment may include penicillin or, as Dr. Williamson suggests, other antibacterial agents.

Your recommendation of penicillin, however, was for the *prophylaxis* of gonococcal ophthalmia which, with its almost inevitable corneal involvement and very serious prognosis in spite of treatment, must be regarded in a very different light from the "sticky eye" which is now the only form of neonatal ophthalmia commonly seen in this country. The consequences of abandoning

Again the layman asks "why colour food?" Excluding fraud, with which we are not concerned here, there can still be no doubt that the use of pigments in certain food preparation is essential Sweets, jams, and confectionery would look very drab if they were not coloured, and the public would certainly take a considerable time to get used to uncoloured products But the protection given to the public must obviously be as complete as possible

Better Protection of the Public?

Presuming, as I think we must, that under modern conditions the chemical treatment of food, or chemical additions to food, are necessary, we can examine the question of whether the existing *regulations* are satisfactory and what can be done to improve them As I have already said, the whole subject of the Food and Drugs Act and of the regulations regarding preservatives is at present being reconsidered, and therefore one can speak only in the broadest possible terms Clearly, however, a new Act would embody the experience gained by the Ministry of Food during the war, and one can predict that many of the war-time orders of the Ministry will be included in the new Act or regulations made under it What is perhaps more appropriate for us to consider is whether sufficient information about the power of chemical substances to injure health is available, and (if not) how and by whom can it be acquired?

A great deal is known about the toxicity of a number of substances used in the food industry The minimum lethal dose, for rats and mice, of most of these substances is well known, but this of course does not give the food technician the answer that he wants He wants to know what would be the effect of consuming a minute quantity daily of a given substance during the course of a life time It is obvious that no-one possesses this information

Prof A C Frazer has given a great deal of study to this question and has suggested a series of tests Very briefly, he suggests testing the compounds at various levels for acute toxicity and lays down a very rigid lethal dose above which the compound should in no circumstances be employed by the food manufacturer To try to assess the compound over a longer period he has devised a test in which three generations of laboratory animals are exposed to the drug or chemical When the rates of growth, reproduction, and so on, of these animals remain unchanged, it is concluded that the substance is possibly harmless This appears to be a very reasonable assumption, and it is difficult to see how better information could be obtained within a reasonable time

The next and vital question is "who is going to do this work?" The amount to be done is enormous Should it be done by a central laboratory? This would be rather cumbersome, and the charge, surely, should not fall on public funds Perhaps a series of laboratories which produce chemicals for food could undertake the work, and many of us would think the *onus of proving* that a substance is harmless should properly rest on the shoulders of those who propose to use it Some chemical manufacturers have established very elaborate laboratories where extensive experiments of the type described are conducted and they are able to recommend their products with every confidence that they have eliminated the risk of chronic toxicity '

An entirely new aspect of the problem has arisen through the use of insecticidal sprays on crops, for, unless great care is taken the food may be contaminated with traces of the insecticide used This important subject is being considered by a committee under the chairmanship of Prof S Zuckerman Again, the use of insecticides is an absolute necessity today because very large quantities of potential food are destroyed by insect pests

Conclusion

Discussions in many places show that there is a group of people—often highly scientific people with well balanced outlooks—who feel that the addition of chemicals *to food is fundamentally unsound* and that our aim should be to abolish any form of chemical treatment or addition to food The argument is an unsophisticated one, based on the grounds that "Nature has provided the food, and who are we to interfere?" But why should we apply this type of argument to only one aspect of our existence? If we are to adopt a "hands off Nature" attitude towards food, then logically we should adopt it towards all other aspects of living We certainly should not live in towns, and possibly we should not wear clothes It seems to me that if we accept the so-called advances offered by the technologists in heating, transport, housing, and so forth, it is reasonable to accept similar advances in the *technology of food*—always with the proviso that the procedures are controlled as fully as possible The solution to the problem of deaths on the road is not to ban all motor traffic but to control it in such a way that the deaths are reduced and eventually, one hopes, abolished Surely the same applies to food

Using preservatives and other means it is now possible to distribute food at a cost within the grasp of all, and to maintain a uniformity which would be quite impossible without the labours of the food technologist Surely we are not going to throw away all these advantages because *of one or two* unfortunate episodes in which a doubtful or bad process has slipped through the existing system of control? The moral is to *perfect* the system of investigation and control so that we can gain the full advantage of the work of the food technologist but at the same time make sure that we are not doing ourselves any harm

MANAGEMENT OF ANÆSTHESIA OF THE SEVERELY BURNED PATIENT

JOHN R ROOK
M B Edin, D A

CONSULTANT ANÆSTHETIST, BIRMINGHAM ACCIDENT HOSPITAL

DURING the five years from February, 1948, to February, 1953, at the Birmingham Accident Hospital increasing numbers of extensive burns have been treated each year, and, since *skin-grafting* is a life saving measure in these cases, the anæsthetists have accepted worse anæsthetic risks than previously

PREOPERATIVE MANAGEMENT

Severely burned patients are a group on their own and behave differently from any other type of injured patient The *motor-accident* case is admitted to hospital in a condition of surgical shock due to multiple injuries but, once resuscitation has taken place, the injuries can be surgically treated, whereupon the patient's general *condition improves rapidly* Not so the extensively burned patient because after resuscitation he has to wait for two or three weeks till the dead skin and other tissues have separated and the burn is ready for skin grafting During those two or three weeks of waiting the patient's general condition is likely to deteriorate Consequently at the preoperative examination the anæsthetist often finds a patient with a *high temperature* and a rapid pulse, as if he had a severe respiratory *infection* Ideally *one does not* like to anæsthetise any patient with a high temperature and who looks ill but if operation is postponed in the hope of improvement the patient continues to get weaker and the ideal moment for grafting is missed sometimes with disastrous results The correct management *of such a case* is to

MITRAL STENOSIS

MEDICAL knowledge has been built up largely by nicopathological correlations based on necropsy udies. But this method, however well it served our cestors, had many disadvantages. It only revealed the ate of affairs at the time of death, and the accompanying hysiological conditions had to be reconstructed by mple clinical observation supplemented by shrewd uess-work. The advent of cardiac surgery in mitral enosis has persuaded many physicians to adopt the bolder ethod of cardiac catheterisation in order to assess the hysiological effects of valve disease likely to be amenable o surgical treatment.

In Stockholm 49 cases of mitral stenosis have been arefully investigated in this way.[1] The patients were ubdivided according to degrees of breathlessness on ffort into four functional grades. By passing a catheter own the branches of the pulmonary artery to a point t which it occludes one of the subdivisions, a pressure record can be obtained which is probably the pressure in he pulmonary capillaries and which also reflects to ome extent the pressure changes in the pulmonary veins. This information, together with pressure records taken from the pulmonary artery and right ventricle, and also the cardiac output, gives a remarkably complete picture of the dynamics of the circulation. In groups 1 and 2, with little limitation of physical activity, cardiac output was normal and there was only slight abnormality n pulmonary arterial and pulmonary capillary pressures. In groups 3 and 4, with incapacitating dyspnœa, cardiac output was reduced and pulmonary arterial pressure was raised; while in group 4 pulmonary capillary pressure averaged 29 mm. Hg (close to the osmotic pressure of the plasma-proteins). In these two groups exercise increased the pulmonary capillary pressure to a level above the protein osmotic pressure at which œdema of the lungs could readily occur. In each functional group auricular fibrillation was associated with a lower average cardiac output than in the patients with sinus rhythm. A "diffuse" cardiac impulse was taken to indicate right ventricular hypertrophy, and in patients with this clinical manifestation the mean pulmonary arterial pressure was nearly always above 30 mm. Hg (normal 13 mm.). Other clinical signs said to indicate pulmonary hypertension (accentuated pulmonary second sound, pulmonary systolic murmur[2]) were found to be unreliable. The electrocardiogram was unreliable as evidence of *absent* right ventricular enlargement. Bifid P waves suggested hypertrophy of the left auricle, since they were associated with a high presystolic pressure wave in the pulmonary capillary pressure tracing. A loud apical systolic murmur was evidence of mitral incompetence, as indicated by a high systolic wave in the record of pulmonary capillary pressure, though sometimes pulmonary capillary tracings showed a high systolic wave in the absence of such a murmur.

Gorlin and Gorlin[3] have suggested a hydraulic formula for calculating the area of the mitral valve orifice; but the Swedish workers point out certain fallacies in this, particularly when the mitral valve is incompetent. In this connection it is interesting that Brock[4] holds that in mitral stenosis the mitral valve is nearly always oval-shaped and measures about 1 by 0·5 cm. This nearly standard size is encountered whether the symptoms are mild or severe; he holds that the fusion of the valves always takes place at the critical areas of insertion of the chordæ tendineæ, which are at the junction of the middle and outer thirds of the valve edges. If this is true, then we cannot picture the course of mitral stenosis as related to progressive narrowing of the valve; the varying clinical course in different types would depend on various physiological adaptations, perhaps determined by different effects of the rheumatic process on other valves and on different parts of the myocardium.

Another interesting point brought out by the Swedish investigators is the relatively slight increase in blood-content of the lungs even in the presence of high pulmonary vascular pressures. This agrees with the findings of Kopelman and his associates in this country[5] [6] and is possibly related to reactive narrowing of the pulmonary vessels.[7]

While the Swedish work lays an excellent practical foundation for further studies of mitral stenosis, it leaves many questions unanswered. Why do some patients develop such an extremely high pulmonary arterial pressure, which may reach or even exceed that in the systemic arteries? Why do those patients who develop massive left auricles or tricuspid insufficiency have such a relatively benign course?[8] If the stenosed valve orifice is of Brock's standard size, why are there such varied courses of different clinical severity? Closer study of the various subvarieties of mitral valve disease will be necessary, and each individual patient will be found to vary in some respect from his neighbour.

A NEW ANTIPRURITIC

THE best treatment of an itching dermatosis is to remove the cause; and to do so an accurate diagnosis and the choice of an appropriate remedy are essential. Unfortunately, there is as yet no specific treatment for a large number of pruritic conditions, which must be dealt with empirically and largely symptomatically. Of the older local antipruritics, many are messy or relatively ineffective, or they smell disagreeably. Local-anæsthetic ointments of the benzocaine class often sensitise the skin, and the contact dermatitis so provoked may become very severe before the doctor or the patient realises that it is being caused by the supposed remedy for the itching. Such a patient may be sensitised to related chemicals such as the sulphonamides, *p*-aminosalicylic acid, and hair dyes.

In the absence of a really effective antipruritic which can be given by mouth, we need good local applications of low sensitising power. N-ethyl-*o*-crotonotoluide, which is on the market in a vanishing-cream base, seems to be highly effective and relatively harmless. This compound was developed after the discovery that certain substituted crotonamides increased the "knock-down and kill" power of insecticides. It was found to have a potent action in vitro on rabbit itch-mites,[9] and extensive trials in human scabies gave excellent results.[10–12] During these trials, the application was shown to have a considerable antipruritic action, and this observation led to its use in non-parasitic itchy dermatoses.

Hitch,[13] who used 'Eurax,' a preparation of N-ethyl-*o*-crotonotoluide, on 200 patients suffering from a variety of skin disorders, said that over 75% found greater relief from this preparation than from any of the others previously used. The improvement in the itching was described as excellent or good in 65%. He had 4 patients who were sensitised by the application, but only one of them was affected by the active principle itself. Similarly, Peck and Michelfelder,[14] reported 1 case of sensitisation to N-ethyl-*o*-crotonotoluide in a series of 400 patients. A further case has been seen by Bereston,[15] in which

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1. Wade, G., Werkö, L., Eliasch, H., Gidlund, A., Lagerlöf, H. *Quart. J. Med.* 1952, 21, 361.
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3. Gorlin, R., Gorlin, S. G. *Amer. Heart J.* 1951, 41, 1.
4. Brock, R. C. *Brit. Heart J.* 1952, 14, 489.
5. Kopelman, H., Lee, G. de J. *Clin. Sci.* 1951, 10, 383.
6. Ball, J. D, Kopelman, H., Witham, A. C. *Brit. Heart J.* 1952, 14, 363.
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11. Couperus, M. *J. invest. Derm.* 1949, 13, 35.
12. Appel, B. *New Engl. J. Med.* 1950, 243, 74.
13. Hitch, J. M. *Brit. J. Derm.* 1952, 64, 408.
14. Peck, S. M., Michelfelder, T. J. *N.Y. St. J. Med.* 1950, 50, 1934.
15. Bereston, E. S. *Arch. Derm. Syph., Chicago*, 1952, 65, 100.

UNESCO tells how an observer from Mars, the objective scientist, views the human species What we want to know is how men come to view one another as they do. The fact, for example, that the relatively recent ancestors of present-day Scotsmen came from Ireland, Scandinavia, and France does not prevent Englishmen from recognising the Scots as a distinctive group (or from saying that "all Scotsmen are mean") Moreover, there are black Jews in Africa, yellow Jews in China, and every variety of white man among the Jews of Europe and America, so the "typical Jew" is different from country to country, and there can clearly be no "Jewish race" according to the canons of physical anthropology Nevertheless Jews are by and large a recognisable group of men marked by a common religion and common customs Ill-feeling towards such groups may be called racial prejudice, national prejudice, or cultural prejudice; but whatever its name it has very little to do with genetics or physical anthropology Thus we fear that the genetic approach to racial problems may do a disservice rather than a service to the cause UNESCO has at heart, because it hides the irrational basis of racial prejudice and pretends that it can be fought with scientific knowledge and reasoned argument The man who complains that all niggers smell is not interested in the scientific truth or otherwise of his statement, what he means is that he hates Negroes What has to be discovered is how he has come to feel such an emotion, and what are the circumstances which encourage its spread among his friends and neighbours

We are nearly all inclined to generalise about groups from single cases, and to view all foreigners with suspicion, even when they come from no further afield than Cornwall or Yorkshire We are prone to accept traditional judgments, like "the Irish are unreliable" or "the Italians excitable," because we believe we can recognise members of these groups at once by their speech and bearing, and often our experience bears out this belief In a few individuals this mild xenophobia becomes severe and pathological, and its origins require detailed case-histories to make them plain It is surprising how little psychiatric investigation there has been in the research on race prejudice To explain further how the virulent emotion of the few spreads at certain times and places to the whole community we must examine social conditions not only at the time of an outburst of violence but in the quiescent periods, and we must consider the reactions and motives of people who show no gross antiracial feeling as well as those of men who turn readily to lynching, the pogrom, and ritual murder Until this evidence has been collected we shall be unable to deal with racial prejudice other than empirically

HERPANGINA

FOR many years now a puzzling disease has reappeared in some areas of the United States each year during the summer or early autumn The illness, nearly always affecting children and generally those under 5 years of age, starts suddenly with fever, dysphagia, anorexia, sore throat, and pharyngitis, sometimes associated with vomiting and abdominal pain, usually it lasts 2–3 days Its most characteristic feature is the appearance in the mouth of a few greyish-white papulovesicular lesions, 1–2 mm in diameter and surrounded by an areola of erythema After 2–3 days these papules break down to give greyish-yellow ulcers which resolve after a few more days To this disease Zakowsky[1] gave the name herpangina, since it is somewhat similar to herpetic stomatitis Subsequent workers failed, however, to isolate the virus of herpes simplex The lesions in herpangina can be differentiated from those of herpetic stomatitis because they are limited to the anterior fauces, soft palate, uvula, and tonsils, while those of herpes are generally most pronounced on the buccal membrane and is often associated with fœtor oris, gingival hæmorrhage, and local lymphadenopathy Also herpangina occurs seasonally in small epidemics, whereas primary herpetic stomatitis is a sporadic disease rather more prominent in the winter[2]

Huebner and his colleagues[3] at Bethesda have now shown that herpangina is probably the most common manifestation of infection with the A group of the Coxsackie viruses In suckling mice, this group causes a diffuse myositis affecting predominantly skeletal muscles and not involving the brain, fat, or pancreas as the group-B viruses do Huebner and his associates surveyed a small community in the north west of Washington, D C, before, during, and after a small outbreak of herpangina for the presence of Coxsackie virus of the A group and for antibodies against six strains of Coxsackie virus, five of which had been isolated in cases of herpangina in this or neighbouring areas. The virus was found only in those people who had herpangina or were contacts of cases and in whom antibodies to the infecting strain developed The level of antibodies to the other strains causing herpangina elsewhere remained constant in both the infected and the uninfected people The Bethesda workers also showed that the infected group had no previous antibody to the infecting strain, whereas in the non-infected group the percentage of people with neutralising antibody was very high In infected households contacts with antibody in their blood did not have the disease or harbour the virus Thus the localisation of the epidemic was apparently due to the majority of the population being immune because of previous infection, for, although coming into contact with the virus, these people were protected by their circulating antibody, which was shown to keep the same titre for at least a year So far Coxsackie virus has been isolated from either the throat-washings or the fæces of 90% of the 50 cases of herpangina investigated, from 46% of contacts and from only 1% of the remainder of the population surveyed

Infection seemed to spread from case to case, the incubation period being 1–10 days Outbreaks were not explosive, as might be expected if the virus were spread by a vector such as food, drink, or infected flies Coxsackie viruses have been isolated from flies, and Melnick and Penner[4] have shown that the virus may survive, although not multiplying, in this host for as long as 14 days So far it is not known where the virus hibernates during the winter and spring Nor is it known how long it can survive in carriers, the longest time after initial infection that it has been found is 76 days These viruses are fairly resistant, and possibly if conditions were suitable they might survive outside the body and be taken up by man or some other vector and so initiate another small outbreak if introduced into susceptible households, sporadic cases of herpangina almost certainly go unrecognised, and probably they keep the infection alive in a community

Coxsackie viruses have been associated with poliomyelitis and other diseases, but often such isolations may have been due to chance At present it seems that the commonest manifestation of infection with the group-A Coxsackie viruses is herpangina, and that perhaps the chief syndrome due to the B group is Bornholm disease either in its typical or in its more non specific form There is some evidence, however, that occasionally Bornholm disease may be caused by group-A viruses also, although this disease might easily be wrongly diagnosed in cases of herpangina with abdominal pain and only a solitary lesion on the fauces

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[1] Zakowsky, J *Arch Pediat* 1924 41, 181

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[3] Beeman E A Cole R M, Huebner R J *Amer J Hyg* 1952 56 215

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estimate the hæmoglobin level, to adjust to 100% or slightly more by blood-transfusion if necessary, and to anæsthetise the patient so that he may have his life-saving operation without delay.

Fig. 1 is the temperature, pulse, and respiration chart of a girl, aged 12 years, who sustained a 25% burn, 11% of which was full-thickness skin loss. In our experience such a child has a 90% chance of survival (Bull and Squire 1949), but without surgery she might well be in hospital for more than a year and perhaps succumb to added infection. The points of interest on this chart, which are typical of most severe burns, are as follows:

(1) The temperature did not settle to normal till a week after the second operation (about Dec. 30), when all the burned areas had been grafted and the grafts were nearly healed.

(2) The pulse-rate was still raised, even when the child was healed and discharged home; it will gradually return to its normal level.

(3) The respiration-rate never reached a level typical of a *severe respiratory infection.*

Most of the severe burns are dressed the day before operation, which provides an opportunity to examine the unbandaged chest. This child had her first operation on Dec. 6, having been dressed and checked as ready for operation on Dec. 5. Occasionally a patient develops a chest infection coinciding with the time of operation. If the infection is only developing on the day of operation, it has been found to be in the patient's interest to proceed without any postponement. Later, if the chest infection becomes fully developed, the burned areas are already covered with skin grafts. This is particularly important in the bigger burns of over 20% full-thickness skin loss, if the patients are to have a reasonable chance of survival.

TABLE I—THREE CASES IN WHICH ENDO
LED TO LARYNGITIS AND ŒDEMA OF
TRACHEOTOMY

Case no.	Age (yr.)	% burn	Area	Pr oper hæ gl		
1	4	13	Fronts of thighs, chest, and axilla	100·0%		
2	6	19	Trunk, thighs, and buttocks	97·5%	Yes	Yes
3	3	9	Whole arm up to shoulder	83·5%	Yes	Possibly but not essential

However, if the infection has already reached its height, there is no alternative but to postpone operation.

INDUCTION OF ANÆSTHESIA

Infants and children were all carefully premedicated so that they should have no unpleasant memories of their visit to the operating-theatre. Since they would all require several operations, efficient premedication was of the utmost importance. No child was ever subjected to the minor operation of a "cut-down" under local analgesia for setting up a transfusion in the ward before coming to the theatre. The mild vasodilatation produced by the anæsthetic almost invariably reveals previously hidden veins, and "cut-downs" can be avoided.

Anæsthesia was induced with nitrous oxide and oxygen, followed by trichloroethylene or with ether. A few patients in whom the premedication had not been perfect were given rectal thiopentone.

The passing of endotracheal tubes calls for particular care, because three children developed laryngitis and œdema of the glottis postoperatively of sufficient severity to require tracheotomy.

The details of the children are given in table I, which shows that none were burned over the glottis, and that only case 2 really required the passing of an endotracheal tube, because both buttocks were burned and she was required to lie prone. All three children received a mouth pack to make the tube airtight; possibly the presence of the pack may have influenced the severity of the postoperative laryngitis. Therefore, where possible, tubes are avoided, and the patients, especially children, are turned on the side only and not fully prone.

Adults.—Five years ago adults were induced with thiopentone and maintained on nitrous oxide and oxygen combined with trichloroethylene or ether or intermittent injections of thiopentone. In those days it was noticed that in major cases the blood-pressure would often sink to about 80/50 mm. Hg, even if the patient was being fairly adequately transfused. With the advent of new techniques combining pethidine, a muscle relaxant, thiopentone, and nitrous oxide and oxygen it is now possible to complete bigger operations

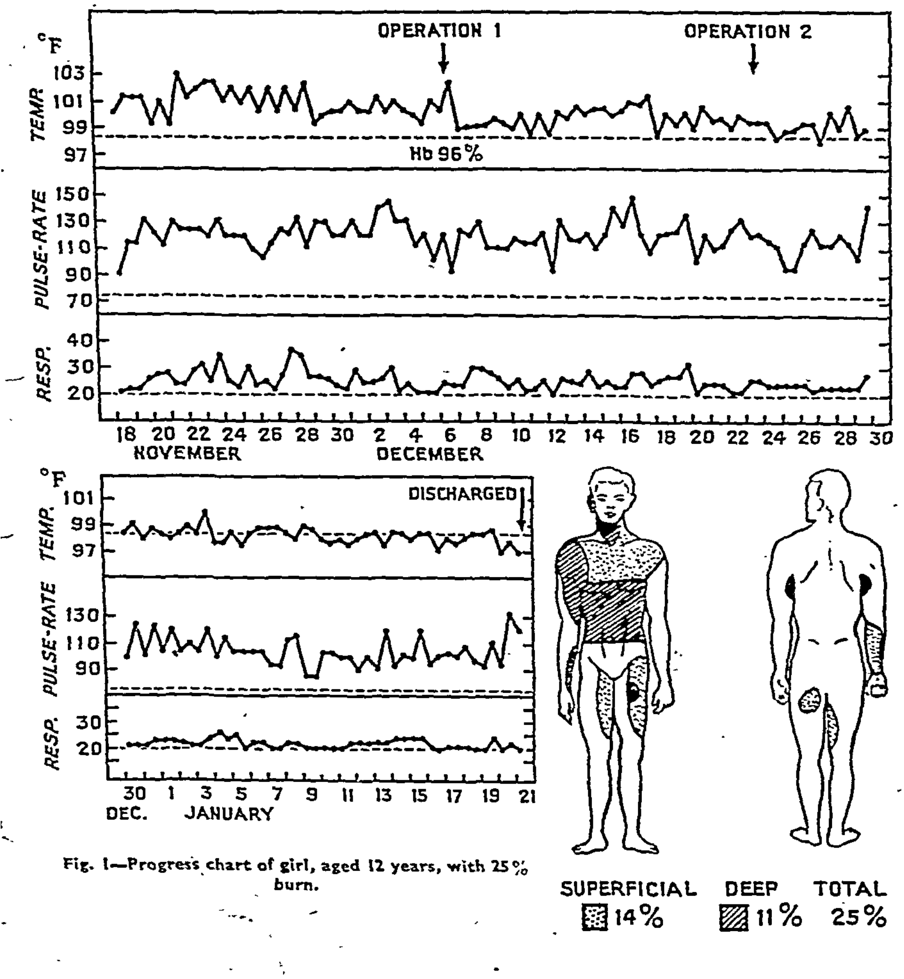

Fig. 1—Progress chart of girl, aged 12 years, with 25% burn.

But, though the ulceration is thus widespread throughout the colon, it in no way resembles that of ulcerative colitis, nor is the distribution alike Further, the condition more commonly attacks the ileum, and the burden of the argument has been that the ileal lesions associated with ulcerative colitis are only incidental It therefore seems unlikely that the two conditions are of the same parentage, their only similarity is that in Crohn's disease the colon may become ulcerated and the diarrhœa can be so severe that it simulates ulcerative colitis

Summary and Conclusions

The colon can be affected by three distinct conditions ulcerative colitis, ileocolitis, and proctosigmoiditis, all of which are customarily diagnosed as "ulcerative colitis"

It is suggested that ulcerative colitis is not a specific disease but a pathological state, behaving not unlike chronic ulcers of the leg The causes are to be looked for in the numerous primary conditions that initiate in the colon the degenerative process which is ulcerative colitis If the original trauma is severe, the case will pass directly into one of ulcerative colitis with continuous, though possibly abated, diarrhœa without remissions If healing with degenerate epithelium takes place, a latent interval, or "remission" will occur between the initial injury to the colon and the onset of ulcerative colitis, this form will be marked at first by remissions but later is likely to become chronic, with persistent diarrhœa In many instances the colon heals perfectly after damage by infection, stress, chemical agents, or whatever the cause may be, the patient is then spared from ulcerative colitis

The ileum is only involved in ulcerative colitis as a secondary phenomenon, either when the ileocæcal valve has become incompetent or, after operations that include an ileostomy, because of technical defects at the ileal stoma

Though Crohn's disease of the colon is more widespread than the gross changes suggest, it does not have any clear relationship to ulcerative colitis

I wish to thank Dr R St Johnston and Prof A P Thomson for permission to publish cases 1 and 2 respectively

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PREVENTION OF POSTOPERATIVE CHEST COMPLICATIONS

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The prevention of postoperative chest complications is still a very real problem, despite advances in their treatment It is agreed by most workers that the primary cause of such complications is impairment of respiratory movement following surgery, particularly, of course, abdominal surgery Churchill and McNeil (1927) demonstrated that one day after laparotomy the patient's vital capacity was half its preoperative value If it is assumed that the chief factor in this reduction is voluntary restriction of respiratory excursion, due to muscle spasm and pain arising from the site of incision, then one can confidently argue that if this postoperative pain is relieved or greatly diminished, a greater depth of respiration will be possible and thus increased aeration of the lung bases

Such an assumption is supported by the following report on 76 patients, all of whom had undergone upper abdominal operations, and in whom analgesia of the wound site was produced by intercostal block, using benzocaine (2%) and urethane (6%) to give prolonged analgesia This combination of drugs has been known to prolong analgesia for ninety days or even longer

Mode of Action

The rationale for this method is the chemical action which precipitates crystals of a drug in the tissues The crystals being relatively insoluble, they remain in situ, prolonging the action of the drug until absorption is complete In this instance urethane precipitates benzocaine crystals around the nerve, producing a long-acting analgesia Benzocaine, being almost insoluble, is made up in olive oil as a base The 6% urethane is in aqueous solution

Technique

At the end of operation, before the patient leaves the theatre, an intercostal block is carried out in the mid-axillary line, using 1 ml of benzocaine, followed by 1 ml of urethane, leaving the needle in position but changing the syringe For upper midline or paramedian incisions, a bilateral block of nerves T6–T10 is used, and for Kocher incisions, a block of T6–T12 on the right and T7–T9 on the left Accurate placing of the needle is imperative, for failure to block one nerve endangers the success of the whole procedure

A weak solution of benzocaine (2%) was used in order that the block should be purely sensory Walshe (1924) showed that weak solutions do not penetrate the neurilemmal sheath of the motor nerve, and therefore produce no motor paralysis The importance of this is obvious

The Patients

All these patients had been operated upon under general anæsthesia There were 60 cases of partial gastrectomy, 11 of perforated peptic ulcer, 3 of cholecystectomy, and 2 of gastro-enterostomy There was 1 death There were 5 failures or partial failures of the analgesia, due to incorrect placing of the block Apart from the death, there were no complications due to the analgesia—i e, sepsis, toxic absorption of the drug, or local necrosis

The effectiveness of the analgesia may be judged from the reduced number of doses of morphine required in the postoperative period (see table) Sedatives themselves often contribute to the production of chest complications An effort was made to select the cases for this procedure, for example, only those who had a definite pathological condition in addition to the disease for which the operation was performed, or who were considered likely to develop postoperative chest complications, were chosen This concurrent disease varied from simple obesity to chronic bronchitis and emphysema The ages ranged from 29 to 74 Those cases which are described in the table as having no preoperative concurrent disease were considered to be in poor physical condition, and therefore bad, or at the best only moderate, surgical risks There was no clinical evidence of pneumothorax in any of the cases

All the patients recovered from the analgesia The patient who died (case 64) remained quite well for twenty-four hours and free from pain She then developed signs of peritoneal irritation, and died seventy-two hours later Necropsy revealed a "blown" duodenal stump *It is interesting* to note that in this case the signs of peritoneal irritation did not arise until twenty-four to thirty-six hours after operation This may have been due to desensitisation of the parietal peritoneum by the block

In this connection it should be pointed out that attempts to eliminate the pain of peritonitis due to perforated peptic ulcer, using 2% benzocaine solution, Again the patient becoming shocked. Today the fraudque of nitrous oxide and oxygen analgesia comstilli with initial overventilation, as introduced by Brennan (1952), seems a good technique for the severely burned adult for the following reasons:

(1) The patient can be kept lightly anæsthetised and in possession of his protective vasomotor reflexes.

(2) He can tolerate an endotracheal tube and be turned prone without coughing.

(3) He wakes up almost immediately on completion of the operation.

(4) This greatly lessens the risk of any untoward occurrence in a helpless patient who is spreadeagled after the application of crêpe bandages and plaster-of-paris.

(5) Patients with burned faces and scalps can be intubated after the injection of pethidine, muscle relaxant, and thiopentone, without wearing a mask on the burned face.

MANAGEMENT DURING OPERATION

Blood-transfusion

During the grafting operation blood-transfusion is essential, and it is our practice for the anæsthetist to take charge of the drip. The aim is to have the blood drip running at the start of the operation and to replace any blood lost with an equal volume, or slightly more, from the transfusion. The scraping and excision of the sloughs from the burned areas often promotes a temporary rapid blood-loss; to cope with this it is generally necessary to increase the drip-rate by attaching a bellows to the air intake of the giving set and blowing air into the transfusion bottle.

A bellows used in this manner must be thoroughly clean; otherwise the blood itself will be contaminated. Since it is difficult to make sure that the inside of the bellows is sterile it is essential to fit a sterile air-filter between the bellows and the blood bottle (Bull and Hurst 1953).

The reason for scrupulous blood replacement as and when blood is lost is that, if the blood volume is allowed to decrease, the patient may become shocked and the systolic blood-pressure fall to 60 or 70 mm. Hg. While the surgeon is operating it is practically impossible to reverse this condition, even though blood be transfused rapidly, and there is no alternative but to stop the operation.

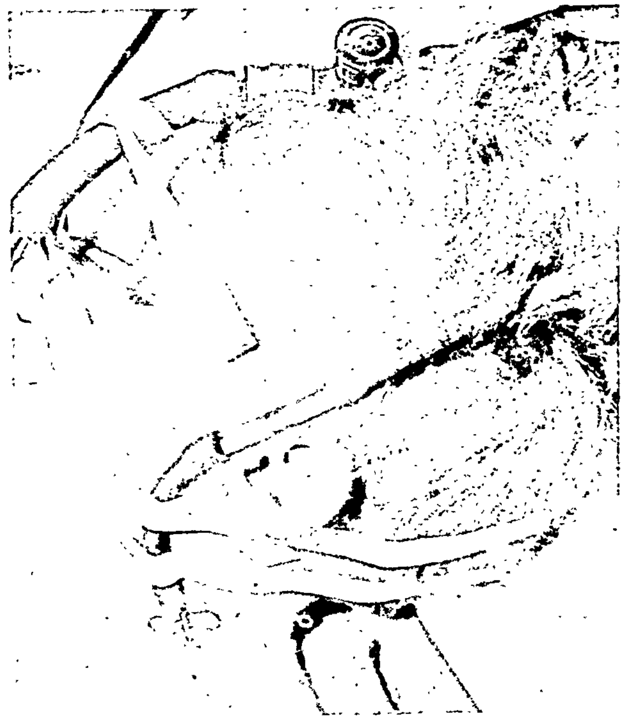

Fig. 2—External jugular vein being used for blood-transfusion.

Since the adoption of the practice of blood replacement in volumes equal to blood-loss it has become possible to cover larger percentages of burn at one operation; hence fewer operations are required to achieve full skin cover. This is very important; fig. 1 shows that it is only when the burn is completely grafted that the general condition of the patient begins to return to normal.

A convenient vein for transfusion is not always available. At the shock stage some veins have been used up by "cut-downs" on admission, and some patients are burned over their cubital fossæ, ankles, &c. However, a good standby on these occasions is often the external jugular vein (fig. 2). Whenever there is a dearth of convenient veins, or it is essential that a needle should not damage an awkwardly placed vein—e.g., the external jugular—the Guest (1941) cannula (fig. 3) is most useful. If only a quarter of an inch of vein is palpable, this cannula can be introduced with care and advanced an inch or more up the vein with safety.

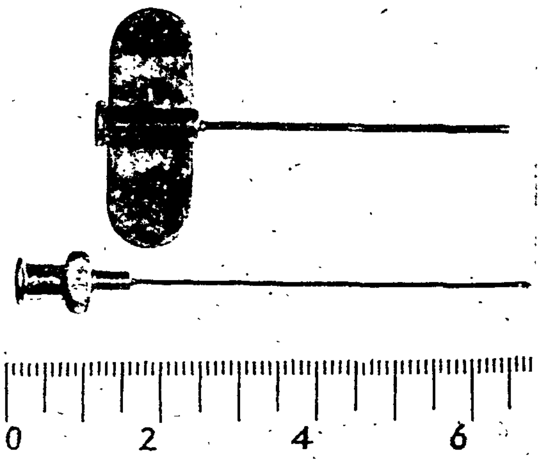

Fig. 3—Guest's cannula. Scale is in centimetres.

The use of hypotensive drugs was considered but not adopted. The policy has been not to interfere further with the already upset physiology and, if at operation blood is unavoidably lost in large quantities, to replace it with stored blood.

Collapse

In the last year three children collapsed during operation despite adequate blood-transfusion. All three showed a similar prodromal sign: cyanosis round the burns and widely dilated pupils, followed quickly by irregular respiration and then cessation and finally cardiac arrest. Details of these cases are shown in table II.

In all these cases the anæsthetic was discontinued at the first sign of any untoward occurrence and the lungs were inflated with oxygen. None of the patients were deeply anæsthetised, and all had spontaneous thoracic respiration before the sudden collapse. In cases 4 and 5 the lungs inflated easily at first but only with difficulty later when resuscitation was abandoned. Cardiac massage was done late on case 5 but promptly on case 6, who recovered. Cardiac massage seems to be the only satisfactory remedy, and it has to be early and by whatever method the surgeon is conversant with (Dark et al. 1952).

The general collapse associated with massive collapse of the lungs in cases 4 and 5 in table II may be partly explained as follows. All three children had fairly severe burns and scalds, and at the time of operation their injuries were several weeks old, during which time the were unsuccessful But the danger of masking of pain due to peritonitis may exist, and it is therefore advisable to watch for other clinical signs of peritoneal irritation

RESULTS OF PROLONGED ANALGESIA OF OPERATION SITE

Case	Sex and age	Operation	Preoperative condition	No of doses of morphine	Result
1	M 41	Partial gastrectomy	Cough	1	Good
2	M 37	" "	Bronchitis	1	Good
3	F 53	Cholecystectomy	Obesity	3	Failed
4	F 47	Partial gastrectomy		0	Good
5	M 60	" "	Hypertension	1	Good
6	M 52	" "		3	Partial failure
7	M 50	" "	Bronchitis and emphysema	4	Failed
8	M 40	"		0	Good
9	M 38	Repair of perforated D U	Cough	1	Good
10	M 51	Partial gastrectomy	Alcoholism	3	Partial failure
11	M 51	" "	Cough	1	Good
12	M 53	" "	Hypertension	1	Good
13	F 46	Cholecystectomy	Obesity	3	Failed
14	M 29	Partial gastrectomy	Bronchitis	0	Good
15	M 68	" "	Chronic bronchitis	1	Good
16	M 71	" "	Hypertension	1	Good
17	M 39	"	Bronchitis	0	Good
18	M 35	Repair of perforated D U		1	Good
19	F 48	Partial gastrectomy	Obesity	0	Good
20	M 74	"	Bronchitis	0	Good
21	M 37	"		0	Good
22	M 29	Repair of perforated D U		0	Good
23	F 35	Gastro enterostomy	Cough	0	Good
24	M 47	Partial gastrectomy		1	Good
25	M 42	" "	Cough	0	Good
26	M 36	"		0	Good
27	M 34	" "		0	Good
28	M 48	" "	Bronchitis	0	Good
29	M 53	" "		0	Good
30	M 48	" "		0	Good
31	F 52	"		0	Good
32	M 58	Gastro enterostomy	Bronchitis and hypertension	1	Good
33	M 51	Partial gastrectomy	Emphysema	0	Good
34	M 49	" "	Bronchitis	0	Good
35	M 32	Repair of perforated D U		1	Good
36	M 51	Partial gastrectomy	Bronchitis	0	Good
37	F 42	" "	Obesity	1	Good
38	F 49	" "	Hypertension	1	Good
39	M 43	" "	Bronchitis	0	Good
40	M 37	Repair of perforated D U		0	Good
41	M 36	Repair of perforated D U	Cough	1	Good
42	M 36	Partial gastrectomy		0	Good
43	M 31	" "	Cough	0	Good
44	M 37	" "	Bronchitis	0	Good
45	M 47	" "	Alcoholism	1	Good
46	M 47	" "	Bronchitis	0	Good
47	M 31	Repair of perforated D U	Cough	0	Good
48	M 36	Repair of perforated D U	Bronchitis	1	Good
49	M 39	Partial gastrectomy	Bronchitis	1	Good
50	M 51	" "	Hypertension	0	Good
51	M 55	"	Emphysema	1	Good
52	F 72	Cholecystectomy	Obesity	0	Good
53	F 56	Partial gastrectomy	Bronchitis	1	Good
54	M 48	" "	Bronchitis	0	Good
55	M 42	" "	Hypertension	0	Good
56	M 43	" "	Bronchitis and emphysema	1	Good
57	M 61	" "	Obesity	0	Good
58	M 59	" "	Hypertension	0	Good
59	F 48	"	Bronchitis	1	Good
60	M 43	Repair of perforated D U	Cough	0	Good
61	M 57	Partial gastrectomy	Bronchitis	0	Good
62	M 61	"		1	Good
63	M 49	" "		0	Good
64	F 52	" "		1	Died
65	M 31	Repair of perforated D U	Cough	1	Good
66	M 53	Partial gastrectomy	Emphysema	0	Good
67	M 41	"	Bronchitis	0	Good
68	F 48	"	Emphysema	0	Good
69	M 38	"	Bronchitis	1	Good
70	M 55	"	Hypertension	0	Good
71	M 39	Repair of perforated D U	Bronchitis	1	Good
72	M 51	Partial gastrectomy	Obesity	0	Good
73	M 41	" "	Bronchitis	1	Good
74	M 46	" "	Emphysema	1	Good
75	M 48	" "	Bronchitis	0	Good
76	M 70	" "	Bronchitis and emphysema	1	Good

Results

Of those cases which were classified as failure or partial failure, 4 developed postoperative chest complications This represents 5·3% of the total, which compares favourably with recent figures of 6%, 8·9% (Langton Hewer 1943), and 10% (Lee 1947) All the other patients had complete analgesia of the site of operation and made normal recoveries

Other Uses of Benzocaine and Urethane

Ritchie Russell and Spalding (1950) have described the use of benzocaine and urethane in the treatment of painful amputation stumps It is now being used in various orthopædic conditions—e g, causalgias and fractured ribs—and for neuromata It has a particular use in the old patient with fractured ribs who often gets pneumonia and collapse, and it has been used as a prophylactic in such circumstances A patient who had continuous pain for several years from a developmental anomaly in the 5th left lumbar transverse process, making a false joint with the ilium, has been completely relieved for over ninety days

Summary and Conclusion

In a series of 76 cases of upper abdominal operations treated with long acting analgesics (benzocaine 2%, urethane 6%) the postoperative incidence of chest complications was 5·3% Its value in the prevention of these conditions is demonstrated Other uses for this long acting analgesic are also described Its effect may last for ninety days or more An additional advantage is that it is much less expensive than other long acting analgesics

I should like to thank the surgeons whose patients I treated in this investigation, and also the hospital dispensers for their help in preparing the solutions

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LIQUID AIR FOR CASUALTIES IN MINES

THE EAST MIDLAND LIFE SUSTAINAER

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J TREFOR WATKINS
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IN coal-mining it is essential to have adequate means of rescuing and protecting people who have been or may be overcome by exposure to irrespirable atmospheres The equipment for this purpose should be easy to apply and easy to carry, for those who have to use it will already be weighed down by apparatus for their own protection

The apparatus in general use consists of cylinders of carbogen (93% oxygen, 7% carbon dioxide) fitted with suitable breathing masks But even the smaller pattern of this type weighs 32 lb and the carbogen supply lasts only twenty minutes There are therefore very substantial advantages, we believe, in our 'East Midland Life Sustainaer,' which weighs only 16 lb fully charged and affords protection for two hours without recharging

The purpose of this apparatus is to provide respiratory protection for asphyxiated men while they are still in an atmosphere polluted by toxic gases It is of simple design and comprises the following parts (see figure) *

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* An application for a patent has been made by the National Coal Board

TABLE II—CHILDREN WHO COLLAPSED DURING OPERATION

Case no.	Age (yr.)	Injury	Premedication	Anæsthetic	Remarks
4	2	10% scald: chest, abdomen, right shoulder, and thigh	'Omnopon' gr. $^{1}/_{12}$, hyoscine gr. $^{1}/_{400}$	Nitrous oxide and oxygen, trichloroethylene	40 minutes after start of operation: less bleeding from donor area; cyanosis round burn; respiration irregular and ceasing after 30 sec.; cardiac arrest after further $1^{1}/_{2}$ minutes *Outcome.*—Death *Necropsy findings.*—Bilateral total collapse of lungs which in life had been healthy
5	$3^{1}/_{2}$	30% burn: chest, both legs, both arms, neck	'Nembutal' gr. 1, omnopon gr. $^{1}/_{12}$, hyoscine gr. $^{1}/_{400}$	Nitrous oxide and oxygen, ether, trichloroethylene, orotracheal tube size 2	45 minutes after start of operation: cyanosis at top of legs, followed by cessation of respiration and cardiac arrest 1 minute later *Outcome.*—Death (cardiac massage failed) *Necropsy findings.*—Bilateral total collapse of lungs which in life had been healthy
6	6	24% scald: trunk, thighs, axillæ, and back	Nembutal gr. 1, omnopon gr. $^{1}/_{6}$, hyoscine gr. $^{1}/_{400}$	Nitrous oxide and oxygen, ether	55 minutes after start of operation: cyanosis of chest round burn; respirations became irregular and ceased, together with cardiac arrest 8 minutes later *Outcome.*—Survived after cardiac massage for 15 minutes and is a normal child

general condition of each had deteriorated owing to the burn. Secondly, each was burned over the chest or trunk. In the preoperative period all had their chests bandaged, and probably the burns plus the dressings tended to limit full respiratory excursions. Part of the routine preoperative preparation is breathing exercises and blowing through bubble bottles; but, in spite of this, mucus may have collected in the lower bronchioles, and the child would then have come to the theatre with lungs susceptible to atelectasis. However, this is thought to be only a part of the problem, the remainder being still unsolved.

Bandages

At the end of the operation all the skin grafts have to be fixed in position with bandages. Many patients have burns of the trunk; hence both the chest and the abdomen are eventually swathed in crêpe bandage. In view of the danger of chest complications, either the chest or the abdomen is left loosely bandaged, and care is taken to ensure that the tightest part of the dressing exerts only firm pressure. On the discontinuation of the anæsthetic, with its high oxygen content, the patient occasionally becomes cyanosed, and if there is any reason to believe that this is due to inefficient aeration of the chest the bandages are removed and reapplied. Consequently it is our practice to retain any patient in whom both the chest and abdomen are bandaged for at least ten minutes after the anæsthetic has been discontinued. Any adjustments to bandages can be made at once instead of cutting the bandages as an emergency procedure in the ward.

TABLE III—EXAMPLES OF HEAT LOSS DURING OPERATION

Case no.	Age (yr.)	% burn	Duration of operation	Rectal temperatures (°F)		Decrease
				Start	Finish	
7	47	35	2 hr. 10 min.	101·8	95·4	6·4
8	3	35	2 hr.	100·7	93·0	7·7
9	$2^{1}/_{2}$	40	1 hr. 40 min.	103·4	95·3	8·1
10	7	37	1 hr. 15 min.	98·8	90·0	8·8

POSTOPERATIVE MANAGEMENT

Oxygen Tents

A feature of the skin-grafting operation for severe burns is that the patient lies on the operating-table almost completely uncovered for the duration of the operation. Since a patient becomes poikilothermic when anæsthetised, the body-temperature drops during the operation, and in several cases it has dropped to 90°F. Examples are shown in table III. This drop may be partly due to the amount and temperature of the transfused blood, which on occasion may be equal in amount to the whole blood volume and is always well below normal body-temperature. As consciousness is being regained and the patient is leaving the theatre, sometimes violent shivering develops as the body endeavours to recover its lost heat. If the operation has been extensive, the general condition of these patients may deteriorate considerably, and they become cyanosed in proportion to the violence of the shivering.

At the end of the operation these patients were dry and warm, their faces were pink, and they were showing no signs of clinical shock, because they had been adequately transfused. The rational treatment of the developing shivering and cyanosis is to aid the recovery of warmth by applying blankets, and to make up deficiencies in oxygen by placing the patient in an oxygen tent during the immediate postoperative hours—i.e., to treat the case as one of exposure to cold. This combination of warmth and oxygen on return to the ward prevents the shivering almost entirely, and no cyanosis develops. Patients treated in this way have a quiet and uneventful immediate postoperative period.

Nasal Feeding with Ryle's Tube

Sometimes a child may be too ill to take its food normally and require to be fed with concentrated fluid nourishment through a Ryle's tube.

Before the feeds are ever commenced one must be sure that the tube is in fact in the stomach and not in the trachea. There is only one infallible test, apart from radiography for proving that a Ryle's tube is in the stomach. If 5–10 c.cm. air is injected into the Ryle's tube while the ear or a stethoscope is placed over the left hypochondrium, there is an unmistakable loud rumbling noise.

Plasma Jaundice

Plasma jaundice occurs occasionally while the patient is undergoing a series of operations to cover the burn with skin grafts and to deal with contracture deformities. It used to be thought that thiopentone was metabolised in the tissues and not the liver; therefore it was not contra-indicated in jaundice. The following case suggests that this is not true:

A few years ago a man, aged 46, had had a 35% burn successfully treated, becoming healed in seven weeks. At this stage he developed plasma jaundice, and at the same time his left shoulder movements were very limited owing to the burn. A week later the shoulder was given a short manipulation under thiopentone 0·3 g. Ten hours later the patient recovered consciousness for a short while, and then succumbed to fulminating hepatitis thirty-six hours after the manipulation.

—COMPLICATIONS WITH TIME OF ONSET

	Week of treatment							Total	No stopping treatment
	1	2	3	4	5	6	6+		
	5				1			6	1
	1							1	1
a	18	3	3	1			3	28	16
	2				1			3	1
	5	3	1	2	1	2	1	15	7
	3		1					4	1
	2	3	1					6	2
	1							1	1
	3	1	1			1	1	7	7
		2	1	1	1	1		6	3
				1				1	1
	1	1	1					3	3
			1					1	0
	1					1		2	2

l no of patients 164
no with complications 67 (40 8 %)
no stopping treatment 33 (20 %)

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is an analgesic than salicylate, amido-
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The occurrence of a sore mouth or ulceration of the buccal mucous membrane was in no case associated with a leucopenia This agrees with Kuzell's findings (1952) No case of agranulocytosis has occurred, and earlier reports (Etess and Jacobson 1953, Kuzell 1952, Stifel and Burnheimer 1953) suggest that it is a sudden event due to idiosyncrasy, and it is doubtful whether serial white cell counts will be of value in anticipating this complication Enlarged submandibular and cervical lymph glands were not necessarily associated with a sore mouth

4 patients complained of increasing dyspnœa, which stopped after withdrawal of phenylbutazone This has been attributed to the retention of water in the lungs or to pleural effusion In our series we had no positive evidence of this, but since then another patient has *shown small bilateral pleural effusions when taking* phenylbutazone, and, as suggested by Cudkowicz and Jacobs (1953), the presence of heart-disease may contra indicate the use of this drug

Hæmorrhagic complications have been reported by Rhys Davies et al (1952) Our patient with melæna was shown to have a gastric ulcer One other case had epistaxes Stephens et al (1952) noted a fall in platelets, although this was not associated with hæmorrhagic phenomena, and a prolonged clotting-time was demonstrated in 1 patient by Cudkowicz and Jacobs (1953)

Headache and dizziness were not severe, and did not necessitate the cessation of treatment

The dosage we employed in the series was usually 200 mg three times a day, but in some patients a smaller dose was effective, and it remains to be seen whether reduction in the dose will diminish the number of toxic effects

CONCLUSIONS AND SUMMARY

Phenylbutazone is an effective drug in the treatment of many cases of rheumatoid arthritis In a controlled trial, no change has been noted in the E S R , hæmoglobin, or white cell count If a beneficial effect is to be obtained at all, it is usually evident within two weeks

Toxic effects are common (40%), they usually occur early, and may cause treatment to be stopped (20% in our series) These are occasionally serious, and, in our opinion, peptic ulceration and renal or cardiac disease are contra-indications to the use of phenylbutazone

Because of its potential danger, phenylbutazone should only be given to patients under close medical supervision, and it is hoped that a less toxic substitute may be elaborated

We wish to thank Dr W S Tegner, physician to the department, for his advice and criticism in the preparation of this paper

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The following case shows how an urgent operation complicated by infective hepatitis was done successfully :

Not long ago an epileptic boy, aged 12 years, had a fit and fell face down in the fire. His nose, one ear, mouth, and one eye were completely destroyed, and the eyelids of his second eye were affected by contractures and would not close. To prevent injury to his remaining eye it was necessary to repair the eyelids. Two weeks earlier he and his whole family had developed infective hepatitis. It was impossible to do the operation under local analgesia because of the septic burns round his mouth, nose, and head. The operation was successfully done under general anæsthesia using a modified Brennan's technique and no thiopentone.

After premedication with omnopon gr. $^{1}/_{6}$ and hyoscine gr. $^{1}/_{200}$ the patient was given intravenous pethidine 50 mg., and 2 ml. of 2% xylocaine was injected into the trachea and sprayed over the nares. While the patient was still conscious, a size-5 cuffed endotracheal tube was passed by blind intubation, because the scarred mouth would not admit a laryngoscope. After the injection of gallamine 60 mg. the patient was anæsthetised, and the anæsthesia was maintained by hyperventilation with nitrous oxide and oxygen throughout the operation, which lasted 70 minutes. A further 40 mg. of gallamine was required in divided doses.

MANAGEMENT OF THE AGED

Bull and Squire (1949) compiled tables from previous results which showed, for example, that a patient aged 80 with a 17% burn has a less than 5% chance of survival. This leads one to wonder if operation is worth while and whether the patient will tolerate a general anæsthetic. The answer to this problem appears to be that, provided the patient has not got congestive heart-failure concomitant with the burn, he is unlikely to die in the operating-theatre.

In the last five years forty-nine patients aged more than 70 who have survived about three weeks to be ready for grafting have been successfully anæsthetised without any death associated with the anæsthetic. One woman, at the end of operation and when the last bandage had been applied, collapsed suddenly and died from a large pulmonary embolus, but the remaining aged all returned to the ward having been given a further chance of life.

The induction of anæsthesia was similar to that described for younger adults, except that pethidine was never given in excess of 10 mg., nor was thiopentone given in excess of 0·15 g. Muscle relaxant and hyperventilation with nitrous oxide and oxygen were the main agents in keeping the patient very lightly anæsthetised. A cuffed endotracheal tube was always passed to maintain a scrupulously clear air-way and to enable endobronchial suction to be applied if required.

SUMMARY

The courageous acceptance of poor anæsthetic risks is necessary if extensively burned patients are to be saved.

Adequate blood-transfusion must accompany the operation and is best supervised by the anæsthetist.

Three unexplained collapses in children are described.

A burn is a big open wound, and its exposure *during* operation under general anæsthesia is associated with great heat loss.

An oxygen tent is an essential part of the postoperative facilities.

A technique for the management of a patient with plasma jaundice or infective hepatitis, who requires *urgent operation*, is suggested.

The aged patient who has survived a few weeks to be ready for skin grafting is a surprisingly safe anæsthetic risk.

My thanks are due to Mr. D. MacG. Jackson, surgeon in charge of the burns unit of the Birmingham Accident Hospital; my anæsthetist colleagues, Dr. L. J. Wolfson and Dr. D. J. Carter, for their most helpful criticism; and Mr. N. R. Gill and Mr. C. E. Richardson, of the photographic department of this hospital, for the photographs.

References at foot of next column

THE TREATMENT OF BULBAR POLIOMYELITIS IN CHILDREN

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IN poliomyelitis the issue of life and death does not usually depend on treatment. In bulbar poliomyelitis treatment is of paramount importance; and, although unfortunately recovery cannot be guaranteed, death will certainly ensue unless efficient and prompt treatment is given. Since the apparatus required is not usually to hand in a ward, and since bulbar poliomyelitis is relatively rare, perhaps when the emergency arises much time is lost in rushing about and searching for the various articles which are normally kept scattered about the hospital in different departments. Experience has shown that it is a great help to have the essential apparatus kept ready and for everyone to know what each has to do. It is hoped that this paper may help those who, not having had to deal with such a case before, are suddenly faced with the problem.

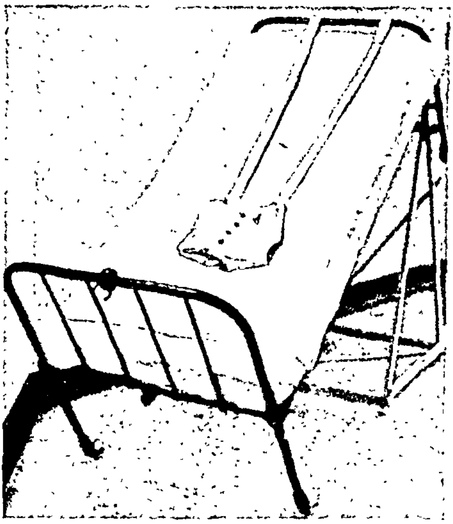

Fig. 1—Canvas jacket and webbing straps for suspending patient.

In our wards at Pembury and Tunbridge Wells we keep all the necessary small articles ready in a "Bulbar Palsy Box," which must not be used for any other purpose. The large heavy apparatus is sent for as soon as we know a child with poliomyelitis is to be, or has been, admitted.

APPARATUS REQUIRED

The apparatus required consists of the following items:

(1) Nuffield-Both respirator.
(2) Electric sucker.
(3) Jacques catheters of various sizes with additional side holes cut into the distal 1 in.
(4) Lengths of pressure tubing.
(5) Glass connection to join Jacques catheter to pressure tubing.
(6) Glass Y-piece to insert into pressure tubing.
(7) Canvas jacket with webbing straps (fig. 1).
(8) Tipping-frame 3 ft. 6 in. high (fig. 2).

It is important to make sure that the electrical apparatus has the correct "plug tops" and a sufficient length of cable to allow it to reach where it is proposed to work it. At least two "plug points" should be available.

It is not within the scope of this article to discuss the pros and cons of tracheotomy, which figures *so largely in*

DR. ROOK: REFERENCES

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TABLE I—SUBJECTIVE ASSESSMENT

—	Worse	No change	Slightly better	Much better	Total no of patients
Control group	4	12	7	4	27
Phenylbutazone group	4 (3 toxic)	2	8	14	28

Between control and drug groups $\chi^2 = 23.57$, $p < .01$

alterations in the diameter and range of movement of the joints

Our grades were

(1) Much better, meaning a definite improvement in the patient's symptoms and signs
(2) Slightly better
(3) No change
(4) Worse

The hæmoglobin, total white cell count and differential count, erythrocyte sedimentation rate (E S R) (Westergren), and weight were recorded before and after the trial

A larger group of 164 patients with rheumatoid arthritis was treated with phenylbutazone (200 mg three times a day or less) for periods of from one to six months Subjective improvement was assessed as in the controlled investigation Only when the subjective response was "much better" was the dose decreased below 200 mg three times a day

RESULTS

Controlled Investigation

5 patients failed to take the tablets for one month 3 in the drug group experienced toxic effects so severe that they were forced to discontinue phenylbutazone before final assessment, and are reported as "worse" Another patient failed to report because of domestic trouble, and 1 had bronchopneumonia

The subjective and objective assessments are shown in tables I and II The results of the special tests are shown in table III

Prolonged Treatment

The subjective assessment in the large group is shown in table IV 4 patients who were receiving corticotrophin or cortisone at the same time as phenylbutazone are not included, although 2 of them noted additional benefit from phenylbutazone

Toxic effects noted in this large group and their time of onset after treatment, are shown in table V Some patients experienced more than one toxic effect and are included in more than one column of the table

TABLE II—OBJECTIVE ASSESSMENT

—	Worse	No change	Slightly better	Much better	Total no of patients
Control group	3	19	3	2	27
Phenylbutazone group	5 (3 toxic)	11	3	9	28

Between control and drug groups $\chi^2 = 28.09$, $p < .01$

Anuria, which occurred in one patient and was associated with a sore mouth and swelling of the face, lasted thirty six hours and recovered spontaneously when phenylbutazone was withdrawn The urine showed no abnormality four days later A similar case was reported by Kling (1952)

Another patient was admitted to hospital with a history of three days melena After preliminary transfusion, partial gastrectomy was performed The stomach showed a chronic gastric ulcer half an inch in diameter on the lesser curve but no evidence of recent ulceration The patient gave no history of indigestion before taking phenylbutazone

More recently a man aged 72, died following five weeks' treatment with phenylbutazone (200 mg three times a day) Necropsy showed myocarditis, hepatitis, and tubulo interstitial nephritis (This case is being reported in detail separately)

DISCUSSION

The assessment of improvement in rheumatoid arthritis, particularly with a new drug, is notoriously difficult This is emphasised by the fact that, in the controlled series, all the patients were deprived of their usual analgesic drugs, and yet out of 27 subjects in the control group, 11 claimed to be improved

Other workers have advocated the use of the joint tenderness test in the assessment of objective improvement We have found it difficult to standardise the pressure exerted on the joint, and have found the patients' response inconstant and therefore unreliable We have, therefore, continued to use measurement of joint movements and size, and performance tests in assessing objective improvement

TABLE III—CHANGE IN WEIGHT, HÆMOGLOBIN, WHITE CELL COUNT AND ERYTHROCYTE SEDIMENTATION RATE IN PATIENTS TAKING PHENYLBUTAZONE

Weight

—	Mean weight before trial (lb)	Mean change in weight after 2 weeks (oz)	Level of significance	Mean change in weight after 4 weeks (oz)	Level of significance
Control group	133·7 (±25)	−10 (±27·7)	p < 0·01	−6 (±61·2)	p < 0·01
Drug group	144·4 (±20)	+53 (±52·8)		+42 (±47·2)	

Hæmoglobin

—	Mean value before trial (%)	Mean change after 4 weeks (%)	Level of significance	
Control group	80·7 (±10·4)	+2·5	0·2 > p > 0·1	p ≏ 0·02
Drug group	82·3 (±17·9)	−3·2	0·1 > p > 0·05	

White-cell Count

—	Mean value before trial (per c mm)	Mean change after 4 weeks (per c mm)	Level of significance
Control group	7970 (±842)	−376	Not significant
Drug group	8050 (±1024)	−379	

Erythrocyte sedimentation Rate

—	Mean value before trial (mm per hr)	Mean change after 4 weeks (mm per hr)	Level of significance	
Control group	14 (±20·1)	−14·5	p > 0·01	p > ·01
Drug group	41·1 (±19·5)	+3·1	0·5 > p > 0·4	

Standard deviations in brackets

The number of patients showing subjective and objective improvement is significantly greater in the phenylbutazone group than in the control group ($p < 0.01$)

The patients in the control series were comparing their tablets with other analgesic drugs (usually compound codeine tablets *B P*) and a large number found phenylbutazone in this dosage better than codeine tablets

TABLE IV—FOLLOW UP OF PATIENTS TAKING PHENYLBUTAZONE OVER PERIODS UP TO SIX MONTHS

Length of follow up	Total no of patients	Much better	Slightly better	No change	Worse or stopped for toxic effects
1 month	164	72 (44%)	43 (26%)	27 (16%)	22 (13%)
2 months	134	65 (45%)	26 (20%)	24 (18%)	19 (14%)
3 months	115	50 (44%)	20 (17%)	21 (18%)	24 (21%)
4 months	86	37 (43%)	14 (16%)	15 (17%)	20 (23%)
5 months	47	25 (53%)	3 (6%)	10 (21%)	9 (20%)
6 months	18	9 (50%)	—	4 ([illegible])	5 (28%)

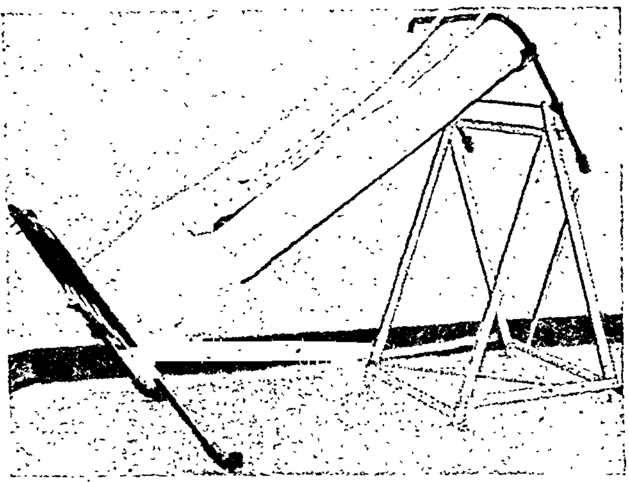

Fig. 2—Wooden frame for tipping bed.

American reports. Suffice it to say that it appears to be unnecessary. The use of positive-pressure artificial respiration has also been recommended recently, but it must be remembered that the apparatus is expensive and very few hospitals have it, whereas the Nuffield-Both respirator is to be found in practically every hospital in this country. Everything required for the treatment suggested here is normally found in hospitals or can be made in them at small cost.

TREATMENT REQUIRED

The paralyses which require treatment in bulbar palsy are those affecting deglutition and respiration. Paralysis of deglutition prevents the intake of food and drink, but because of its limited duration this is of minor importance compared with the inability to swallow saliva and nasopharyngeal and pulmonary secretions, which are consequently inhaled and drown the child. The result of respiratory paralysis is obvious. The treatment to overcome these paralyses can be listed as follows:

(1) Tipping.
(2) Suction.
(3) Artificial respiration.
(4) Feeding.

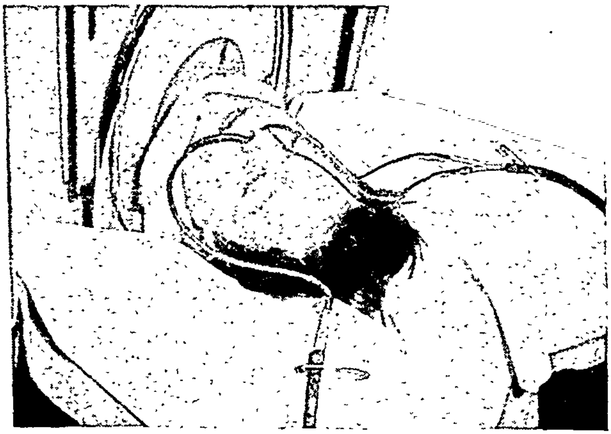

Fig. 3—Large Jacques catheter, used for suction, in left nostril, and oxygen catheter in right nostril.

Tipping

With the patient lying on his back, the trachea runs posteriorly at an angle of about 20°; hence to reverse this the angle of tip must be greater than 20°. If the trachea were simply a tube, any angle above 20° would allow fluid to run out of it; but in practice air is drawn into the trachea more forcibly than it is expelled, and in the Both respirator the difference is considerable. Therefore to prevent fluids from being inhaled the angle of tip needs to be about 40°; this means that the foot of the bed has to be about 3 ft. 6 in. higher than the head. To effect this we use a simple wooden frame (figs. 1 and 2). In an emergency, hospital furniture can be used instead.

Suspending the patient.—When a child is tipped to an angle of 40°, secure suspension provides something of a problem. Originally we used lengths of 6-in. bandage, with cotton-wool over the points of pressure, but the sense of insecurity to both patient and staff was considerable. We now use the canvas jacket with webbing straps (made in the hospital workrooms), and this has proved satisfactory and can be used both on a bed and in the respirator.

The child is always laid on its back, and though, from the point of view of angle of tip, a much lesser degree would be required if it lay on its face, we have found in practice that the weight of the body pressing on the chest and abdomen makes respiration almost impossible, and we have had to abandon the position whenever we have tried it.

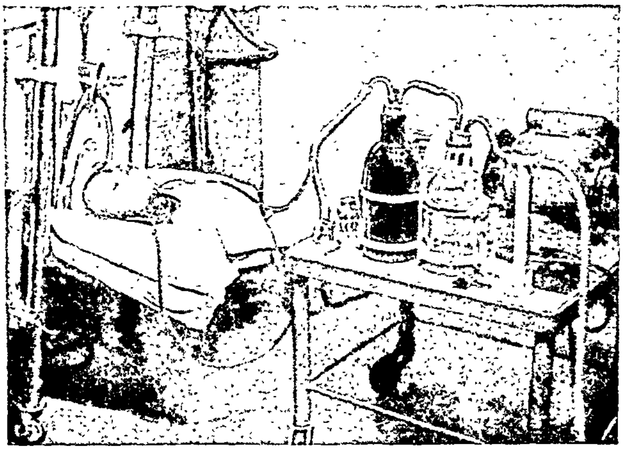

Fig. 4—Patient connected up, through catheters and rubber tubing, with powerful suction plant.

Suction

It is impossible to overemphasise the importance of efficient suction. Much of the secretion is saliva, which is easily removed; but there is also a good deal of thick tenacious mucus, which only a powerful electric sucker will remove. Our practice is to pass the largest possible Jacques catheter (fig. 3) down the nostril for 2 or 3 in. Some force may be required. The catheter is connected by pressure tubing to the sucker (fig. 4), but at some point the tube is broken for the insertion of a Y-piece (fig. 5). Thus suction can be turned on and off at will by closing the open limb of the Y-piece with the thumb. Rapid intermittent suction for periods for $^1/_2$–1 minute, at intervals of about 10 minutes, will remove all secretions very well.

Artificial Respiration

A large proportion of patients with bulbar poliomyelitis develop respiratory paralysis and have to be transferred to a respirator. A constant watch must be kept on them because the paralysis may develop with dramatic suddenness. As soon as this happens the child is put in the

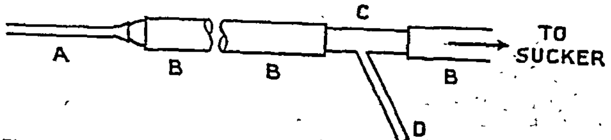

Fig. 5—Method of control of suction: A, Jacques catheter; B, pressure tubing; C, glass Y-piece. By closing Y-piece with thumb at point D, pressure of suction can be controlled.

TABLE V—COMPLICATIONS WITH TIME OF ONSET

—	Week of treatment							Total	No stopping treatment
	1	2	3	4	5	6	6 +		
Diarrhœa	5				1			6	1
Constipation	1							1	1
Indigestion, nausea	18	3	3	1			3	28	16
Dyspnœa	2				1			3	1
Skin rashes	5	3	1	2	1	2	1	15	7
Headache	3		1					4	1
Œdema	2	3	1					6	2
Anuria	1							1	1
Sore mouth	3	1	1			1	1	7	7
Lymphadenopathy		2	1	1	1	1		6	3
Melæna				1				1	1
Vertigo	1	1	1					3	3
Epistaxis			1					1	0
Malaise	1					1		2	2

Total no of patients 164
Total no with complications 67 (40 8%)
Total no stopping treatment 33 (20%)

Steinbrocker et al (1952) have found phenylbutazone more effective as an analgesic than salicylate, amidopyrine, or gentisate Currie (1952) reported subjective and performance improvement in 92% of cases with rheumatoid arthritis treated with phenylbutazone intramuscularly, while Rhys Davies et al (1952) performed a controlled experiment with 32 patients, using phenylbutazone intramuscularly, and reported a considerable difference between the groups treated with saline and with phenylbutazone Using smaller numbers of patients, with no control groups, Dudley Hart and Johnson (1952) reported improvement in 81% of patients

In our large series we found that 70% showed subjective improvement in a follow-up period of one month, a figure lower than that reported by these observers, and agreeing more with Stephens et al (1952) and Steinbrocker et al (1952) This figure became less with a longer follow-up period, until only about half the patients were still benefited at the end of six months

Objective improvement has been reported by other authors, we found it in 11 out of 27 patients (40%) This is less than the number reported by Rhys Davies et al (1952) The difference may be accounted for partly by the length of the trial period Some patients experienced transient benefit which wore off before the end of the trial

Kuzell et al (1952) have suggested that patients suffering from psoriasis associated with arthritis may derive benefit from phenylbutazone We have treated 7 such patients In only 1 was there a slight improvement in the skin condition, although the joints were improved in 3

There was no significant change in the hæmoglobin, white-cell count, or E S R in those treated with phenylbutazone in the controlled series The fall of the mean E S R in the control group remains unexplained, and did not parallel any change in the clinical condition of these patients

Minimum perceptible erythema times were estimated by Partington (1952) on this controlled series and showed no alteration

A fall in the hæmoglobin level was reported by Stephens et al (1952), while Currie (1952) reported a fall in the E S.R of patients taking phenylbutazone We could not confirm these findings

The phenylbutazone group show an average gain in weight at two and four weeks, which is statistically significant ($p<0\ 01$) An increase in weight has been shown to be due to a retention of water and sodium (Green and Williams 1953, Wilkinson and Brown 1953)

Toxic Effects

The toxic effects in this series have been similar to those already reported, and occurred in 67 (40%) out of 164 cases In half the cases the toxic effects wore off, although the drug was continued

Swelling of the face occurred apart from œdema of the ankles, and was often associated with a rash, which was usually maculopapular, or a generalised erythema with intense pruritus

The occurrence of a sore mouth or ulceration of the buccal mucous membrane was in no case associated with a leucopenia This agrees with Kuzell's findings (1952) No case of agranulocytosis has occurred, and earlier reports (Etess and Jacobson 1953, Kuzell 1952, Stifel and Burnheimer 1953) suggest that it is a sudden event due to idiosyncrasy, and it is doubtful whether serial white cell counts will be of value in anticipating this complication Enlarged submandibular and cervical lymph-glands were not necessarily associated with a sore mouth

4 patients complained of increasing dyspnœa, which stopped after withdrawal of phenylbutazone This has been attributed to the retention of water in the lungs or to pleural effusion In our series we had no positive evidence of this, but since then another patient has shown small bilateral pleural effusions when taking phenylbutazone, and as suggested by Cudkowicz and Jacobs (1953), the presence of heart-disease may contra-indicate the use of this drug

Hæmorrhagic complications have been reported by Rhys Davies et al (1952) Our patient with melæna was shown to have a gastric ulcer One other case had epistaxes Stephens et al (1952) noted a fall in platelets, although this was not associated with hæmorrhagic phenomena, and a prolonged clotting-time was demonstrated in 1 patient by Cudkowicz and Jacobs (1953)

Headache and dizziness were not severe, and did not necessitate the cessation of treatment

The dosage we employed in the series was usually 200 mg three times a day, but in some patients a smaller dose was effective, and it remains to be seen whether reduction in the dose will diminish the number of toxic effects

CONCLUSIONS AND SUMMARY

Phenylbutazone is an effective drug in the treatment of many cases of rheumatoid arthritis In a controlled trial, no change has been noted in the E S.R, hæmoglobin, or white cell count If a beneficial effect is to be obtained at all, it is usually evident within two weeks

Toxic effects are common (40%), they usually occur early, and may cause treatment to be stopped (20% in our series) These are occasionally serious, and, in our opinion, peptic ulceration and renal or cardiac disease are contra-indications to the use of phenylbutazone

Because of its potential danger, phenylbutazone should only be given to patients under close medical supervision, and it is hoped that a less toxic substitute may be elaborated

We wish to thank Dr W S Tegner, physician to the department, for his advice and criticism in the preparation of this paper

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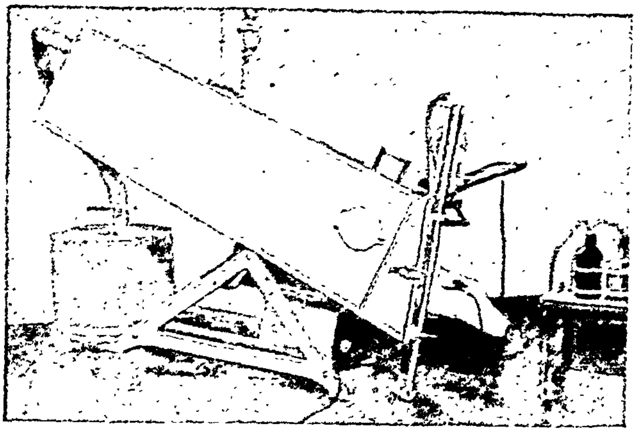

Fig. 6—Respirator tipped to required degree. Note blocks under one foot of stand.

respirator, which must now be tipped to the required degree (fig. 6). It is important that the canvas jacket should also be used in the respirator; otherwise the child's weight will be carried by the shoulders pressing against the lid of the box, and this causes great pain.

Feeding

For the first 24–48 hours we have found it best to make no attempt at feeding, but simply to make good the loss of fluid with a rectal drip of 5% dextrose in N/5 saline solution. After this period the child can usually swallow small amounts by mouth, or tube feeding can be used.

COMMENTS

This treatment has now been used on seven children aged 4–13 years. Six of them recovered. The duration of treatment averaged about seven days. In the children who survived, residual paralysis was less than might have been expected. All the children had rhinolalia, which recovered within a year. Five children had diaphragmatic paralysis: one died, and in the others function returned. Two children had a sternomastoid paralysis which recovered within two years, and 2 had moderate paralysis of one upper limb, with almost complete recovery of function. One child had gross paralysis of both upper limbs, and another had gross paralysis of all four limbs. These last two children made only a slight recovery of function.

I wish to thank Dr. L. Sagorin and Dr. S. Jarvis for their help in treating these cases; and my E.N.T. colleagues Mr. J. V. Clark and Mr. N. Asherson for refusing to do tracheotomies.

WHAT IS ULCERATIVE COLITIS?

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The cause of ulcerative colitis has eluded us, and it is my belief that there are two reasons for this. First, the diagnosis of ulcerative colitis has been applied to patients with chronic or recurrent diarrhœa, which, apart from Crohn's disease (which will be considered later) can be caused by three different diseases, of which only one should be termed ulcerative colitis. Secondly, this true "idiopathic" ulcerative colitis is probably not a specific disease entity so much as a pathological state arising from damage to the colon by a number of different agents.

Causes of Chronic Ulceration of Colon

The three conditions which give rise to chronic ulceration of the colon and thus chronic diarrhœa are indicated in fig. 1.

(1) *True "idiopathic" ulcerative colitis* affects the sigmoid and descending colon maximally—though this is not to say that it starts there—extends downwards into the rectum and proximally to a variable distance; it stops abruptly at the ileocæcal valve, except when the disease has been present long enough to damage the structure of that valve and render it incompetent (see below). This is, therefore, a primary colitis—primary in the sense that the colon is the organ primarily involved.

(2) "*Right-sided*" *colitis* is almost certainly a secondary colitis, in which the ascending and adjacent transverse colon are involved initially, while the bowel beyond remains radiologically normal (fig. 2) but *not* always sigmoidoscopically so. In the later stages the whole colon is involved. The colonic changes are secondary to an ileitis which may be difficult to detect by barium studies but is sometimes indicated by a defect of fat-absorption (Brooke and Cooke 1951). A comparison of the radiographs (fig. 3) and anatomical specimen (fig. 4) shows this difficulty in case 1:

Case 1.—A man, aged 40, had had diarrhœa for as long as he could remember, with four or five soft bulky motions daily, increasing in recent years to double that number, while the stool became more watery, presumably as the secondary colitis advanced. He eventually developed a carcinoma in the transverse colon.

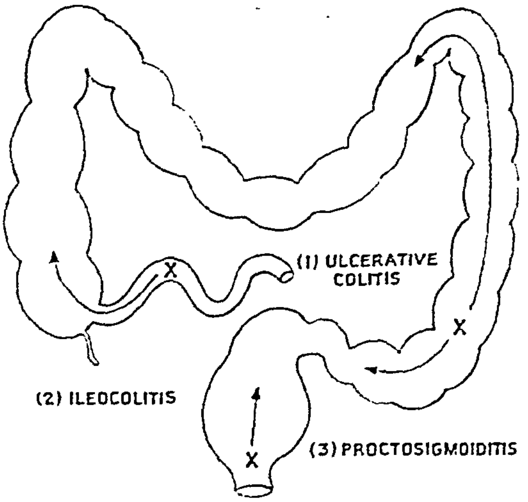

Fig. 1—The three conditions which cause chronic ulceration of colon and chronic diarrhœa.

The small bowel in enterocolitis or ileocolitis, as this condition should be called, is involved over a considerable distance—in case 1 from the lower part of the jejunum onwards, with small shallow ulcers and intervening mucosal œdema. The recognition of ileocolitis is rendered more difficult by the fact that on external examination of the ileum—e.g., at laparotomy—no abnormality may be detected, and in this respect, as in the appearance of the ulceration, ileocolitis is unlike Crohn's disease.

Case 2.—A woman, aged 24, who had had diarrhœa and right-sided abdominal pain for 3 months, was submitted to laparotomy because vomiting, abdominal distension, and an increase of pain suggested a perforation supervening on ulcerative colitis. At the time of her admission she was passing five motions by day and five at night. Though her rectum appeared normal at sigmoidoscopy, the cæcum and colon were seen to be thickened and red at laparotomy: no perforation was found, and the ileum appeared normal. However, at necropsy 10 days later the jejunal mucosa was swollen and hyperæmic and the ileum had shallow ulcers of irregular distribution throughout its length, with partial healing in some places.

In this case severe and acute enterocolitis was accompanied by fatty degeneration of the liver: *this change seems to be a constant finding in ileocolitis or enterocolitis* and was present also in case 1.

That the ileocæcal valve is intact in ileocolitis is an indication that the ileitis is not due to a "flowback"

FATAL AGRANULOCYTOSIS AND GASTRIC ULCERATION DUE TO PHENYLBUTAZONE

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THE value of phenylbutazone (1 2 diphenyl-3 5-dioxo-4-*n*-butylpyrazolidine, 'Butazolidin') in giving symptomatic relief in rheumatoid and other forms of arthritis has been established since its introduction by Currie in 1952 Its comparatively simple structure, related to that of amidopyrine, has stimulated large scale production , and the drug is now widely used, sometimes perhaps without full awareness of the risks In the past month 2 cases of agranulocytosis attributable to phenylbutazone have occurred in this area, one terminating in death This case is described here

CASE-HISTORY

The patient, a woman aged 53, had suffered from rheumatoid arthritis for seventeen years , although her deformities were crippling, she had not had any treatment other than physiotherapy and mild analgesics of salicylate type She was not known to have any disorder of the cardiovascular or alimentary system, and had never had an allergic reaction

At the request of the patient and her relatives, her family doctor agreed to try a course of phenylbutazone On March 13 this year treatment was begun with 600 mg daily by mouth. After five days of therapy œdema of the legs and arms developed , treatment was suspended, and the œdema subsided rapidly during the next forty eight hours Seven days later therapy was recommenced, but the dosage was reduced to 400 mg daily After three days the patient complained of epigastric pain and diarrhœa, and she vomited some bloodstained fluid Next day she had a sore throat and dysphagia

A day later (April 2) the patient was admitted to hospital She was found to have ulceration of the pharynx and a temperature of 104 8°F Examination of the blood showed absolute agranulocytosis, the white cells being made up of 1440 lymphocytes and 60 monocytes per c mm In addition there was severe anæmia, with hæmoglobin 8 g per 100 ml (51%) and red cells 3,300,000 per c mm No other significant symptoms or physical signs developed, and the patient died in coma three days after admission

Necropsy Findings

The necropsy was done forty eight hours after death, during which time the body was refrigerated

Pharynx and œsophagus—The pharynx was extensively ulcerated, and the œsophagus showed œdematous thickening of the wall with destruction of the surface epithelium throughout the whole length Microscopic examination of the œsophagus showed complete replacement of the squamous epithelium by eosinophilic amorphous material, while the subepithelial layer of connective tissue contained young fibroblasts which extended into the muscle coats, separating the individual muscle fibres There was pronounced round cell infiltration of all coats, but neutrophil polymorphs were not present

Stomach—In the stomach there were about a hundred superficial ulcers ranging 1–5 mm in diameter These lay in parallel rows in the long axis of the stomach, and most of them situated on the ridges of the gastric rugæ Unlike acute gastric erosions the ulcers were craterous, heaped up inflamed mucosa surrounding a small central area of necrosis Microscopically the base of each ulcer was formed of amorphous eosinophilic material overlying an area of submucosa heavily infiltrated with young proliferating fibroblasts Around the periphery a dense ring of lymphoid tissue beneath the mucosa explained the macroscopic appearance of the elevated and swollen mucous membrane surrounding the ulcer pits Neutrophil granulocytes were not found in the sections No other lesions were found in the alimentary canal

Spleen—The spleen was enlarged (200 g) and pale, but otherwise normal macroscopically Microscopically the splenic pulp was largely replaced by loose fibrous tissue containing very few cells and while there were a few lymphoid aggregations, true malpighian corpuscles were not evident The vessels were normal This medullary endothelial proliferation was probably part of the chronic rheumatoid arthritis syndrome, and not a result of phenylbutazone therapy

Lungs—Both lower lobes were grossly œdematous and congested The alveoli were œdematous and many were packed with red blood cells There was no inflammatory reaction

Knee joint and femur—The articular surface of the right knee joint showed gross destruction of the type seen in active rheumatoid arthritis The marrow of the femur contained confluent erythroblastic foci in the head and upper third of the shaft

DISCUSSION

The commonest complications of treatment with phenylbutazone have been generalised œdema, digestive disturbances, skin eruptions, granulopenia, and hæmorrhage from the gastro intestinal tract Rarely jaundice has been reported, and a fall in the platelet-count has been noticed in a few cases

Œdema

Currie's (1952) original series of 81 cases, in which 1 g of phenylbutazone was given daily for ten days, included none in which œdema developed, but of 100 cases treated by Davies et al (1952) with 1 g daily 8 developed œdema of the legs , while Kuzell et al (1952) found œdema in 17 out of 140 cases treated Both groups of workers report that the œdema subsided rapidly within two days after either reducing the dosage or restricting sodium intake Green and Williams (1953), in a study of healthy volunteers, constantly found that between the second and eighth hour after injection of 1 g of phenylbutazone there was a reduction in urinary output associated with a fall in urinary sodium It seems therefore that sodium retention results directly from phenylbutazone medication, and that œdema indicates overdosage rather than idiosyncrasy Green and Williams also observed that the phenylbutazone level in the blood, though high soon after injection, fell rapidly in the next forty eight hours, and was undetectable after ninety-six hours Hinz et al (1953), however, found in a case of agranulocytosis which had resulted from treatment with 400 mg of phenylbutazone by mouth daily for forty six days that traces of the drug persisted in the plasma fifteen days after administration was discontinued

Gastro intestinal Tract

Bleeding from the gastro intestinal tract has been reported (Dudley Hart and Johnson 1952, *British Medical Journal* 1952, Ross and Baldwin 1953, Benstead 1953) In this total of 7 cases, 2 of which were fatal, each of the patients received the drug by mouth Of the cases reported by Dudley Hart and Johnson (1952) 1 developed bleeding from an acute duodenal ulcer two days after starting a third course of 800 mg of phenylbutazone daily , and in the other 2 cases melæna appeared after four weeks' and after two days' treatment Ross and Baldwin (1953) report melæna after three weeks' treatment with 400 mg daily, and hæmatemesis after administration of 1 g daily for seven days

Of the 2 cases in which the patient died, 1 was in a woman of 65 who had received 600 mg orally each day for fifteen days (Benstead 1953) She developed hæmaturia and died next day The stomach was normal but at the lower end of the œsophagus there was an ulcer 1/ in in diameter, and in the duodenum a subacute ulcer 1/4 in in diameter which had perforated and caused general peritonitis In the other case a woman of 75 had received 1200 mg of phenylbutazone daily for eight days, when massive hæmatemesis supervened (*British Medical Journal* 1952) At necropsy the stomach contained multiple superficial ulcers 1–2 cm in diameter, mostly in the fundus

In none of these accounts is it suggested that the gastro intestinal lesions were other than acute, and in none is any previous dyspepsia mentioned

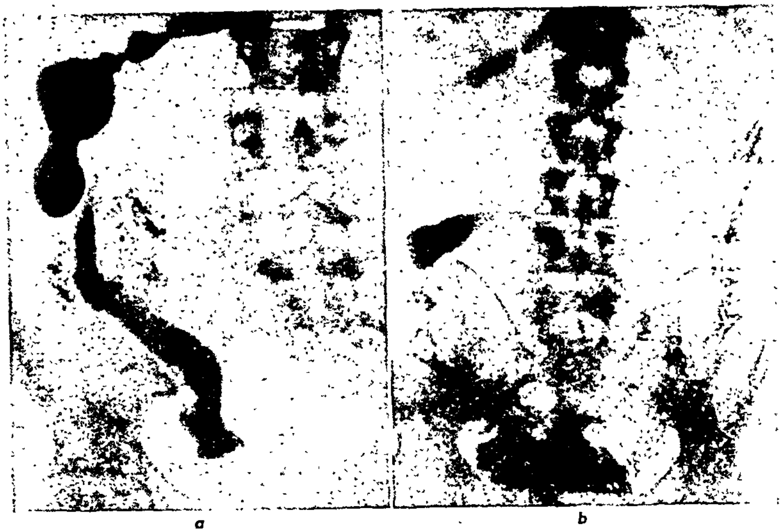

Fig. 2—Radiographs from a man, aged 33, with diarrhœa (6 motions daily) and defective fat-absorption : a, after barium meal to show ileal involvement ; b, after barium enema to show colonic involvement.

of infected material, in contrast to the ileitis associated with ulcerative colitis. Though clinical recognition of the one disease from the other is difficult, one point in the history is of value. Whereas ulcerative colitis tends to fluctuate between remission and recrudescence in its earlier stages, only to become continuous later when the bowel is so utterly destroyed that no attempts at healing can take place, in ileocolitis these fluctuations are less well defined and, indeed, no remission may occur at all. In its commonest form ileocolitis starts with four to eight soft motions daily, not always containing pus, and this continues ; in ulcerative colitis the onset of an attack of diarrhœa is usually sudden, with ten, fifteen, or even twenty fluid fæcal motions daily, containing pus and blood, and during the intervals of remission the motions may be normal in character and frequency.

(3) *Proctosigmoiditis* is better recognised but seldom referred to. Hess Thaysen (1934) gives an excellent account of it and states that Strauss gave the first description in 1910. As Thaysen points out, it is thought by some to be a subgroup of the more usual form of ulcerative colitis, a view not well substantiated by the facts. A mild chronic intractable inflammation is to be seen in the lowermost reaches of the rectum ; its upper limit is often sharply defined, the area involved being no more than the last 2 or 3 inches of the rectum, and less often its distribution in the rectal ampulla is patchy. In the earlier stages no frank ulceration is to be seen, though the mucosa is inflamed and bleeds if touched, this general appearance suggesting the name, sometimes applied, of granular proctitis. It presents in various ways as " bleeding piles," as diarrhœa, and even through anæmia, which is the only general disturbance associated with the disease. Though diarrhœa can be the patient's complaint it is spurious, for proctosigmoiditis is associated with constipation ; it is the blood and pus collecting in the rectum and passed in several fluid motions, notably earlier in the day, which give rise to the complaint. The condition is singularly indolent ; it may remain localised for years or gradually pass upwards into the sigmoid ; it is at this stage of proctosigmoiditis that ulcerative colitis is simulated, particularly since anal fissures and fistulæ complicate both conditions. One example indicates the degree of constipation in these patients :

Case 3.—A woman, aged 34, who had had proctosigmoiditis for 7 years was submitted to surgery because of chronic severe secondary anæmia (Hb 41%, red cells 2,900,000 per c.mm.), tenesmus, and an anal fistula which would not heal after excision. Since colostomy might have precipitated trouble higher in the colon, ileostomy was performed, but not before it was noted that barium was still present in the colon 3 weeks after a barium enema. 3 months after ileostomy, when the large bowel was excised because of the persistent tenesmus and discharge of pus, scybala were still present.

Nature of Ulcerative Colitis

It seems therefore that the first group described is the only type which can be reasonably termed ulcerative colitis, for here alone is a generalised primary ulceration of the colon. Is it a specific disease entity ? Recourse must now be had to the histological appearances. For those who look for a sign, for some specific cell change, there will only be disappointment. Surgical removal of the colon has enabled us to see that the over-all picture is one of destruction of epithelium and underlying mucosa followed by attempts at healing from epithelial islands remaining from the bottom of the crypts (fig. 5*a*). The situation is in every way analogous to a burn of the skin, except that in the colon secondary infection *always* supervenes, rendering healing more difficult. A burn heals from the epithelial cells at the bottom of hair follicles and sweat ducts which dig deep into the dermis ; if destruction goes beyond this level, healing will not take place. Thus in the colon some agent destroys mucosa to a variable depth ; even if epithelium is renewed it is often debased in form, no longer columnar, a weak " rice-paper " scar prone to break down at the slightest provocation (fig. 5*b*). Furthermore, the

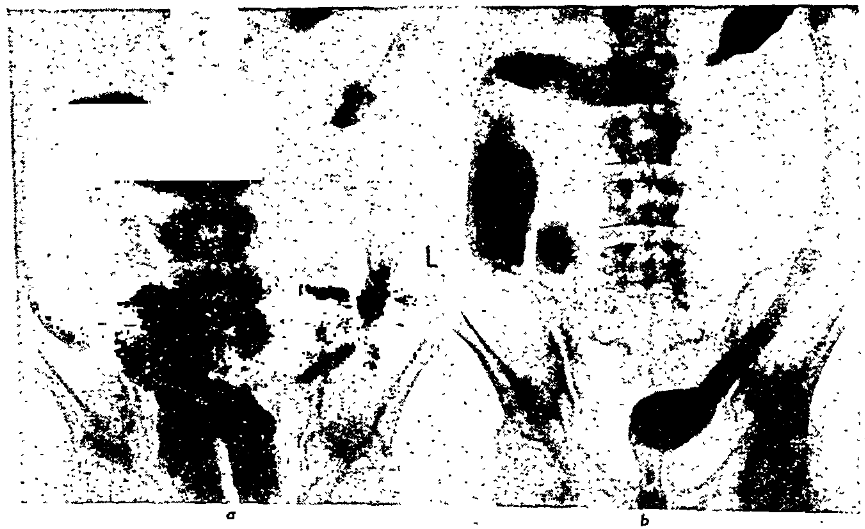

Fig. 3—True "*idiopathic*" ulcerative colitis in case I, showing ileal changes, colitis, and carcinoma in transverse colon : a, after barium meal ; b, after barium enema.

Kuzell et al (1952) report in 4 of their cases severe digestive disturbances during treatment, associated with reactivation of pre existing duodenal ulcers, 1 of these patients had been receiving the drug intramuscularly. Cudkowicz and Jacobs (1953) mention 2 cases in which peptic ulceration was reactivated—in 1 case after fourteen years' quiescence. These 6 cases do not seem to justify including reactivation of peptic ulceration among the toxic effects of phenylbutazone, and the risk of acute ulceration is probably the same with or without previous dyspepsia.

Skin Reactions

These have been fairly common varying from slight petechial rashes to severe maculopapular eruptions. Most cases have, however, been mild and have cleared up with administration of anti-histamine drugs. Rashes are said to be rare at the start of treatment but to develop usually after ten to fourteen days or at the start of a second course.

Granulopenia

Granulopenia has been reported in at least 11 cases (*British Medical Journal* 1952, Crowther and Elgood 1952, Loxton et al 1952, Hinz et al 1953, Jarvis 1952, *Lancet* 1953, Tait 1952).

In the case described by Crowther and Elgood (1952) the patient had been receiving 1200 mg daily by mouth for ten days when she developed a facial rash and slight œdema of the ankles. The dose was reduced to 600 mg daily, but a week later she became jaundiced and pyrexial, and the drug was discontinued. After a further week, during which she continued to be pyrexial, she was found to have an absolute agranulocytosis. In a case reported by Jarvis (1952) severe neutropenia developed after fifteen days' treatment with 1200 mg daily by mouth. Hinz et al (1953) report neutropenia arising after forty-six days' treatment with 400 mg daily by mouth. In a case of agranulocytic bronchopneumonia which terminated fatally (*British Medical Journal* 1952) the patient had received 800 mg daily for a total of four weeks the drug having been given in two fortnightly courses separated by an interval of two weeks.

Discombe (1952) has suggested that agranulocytosis after treatment with other drugs known to be occasionally toxic, such as amidopyrine, may be an allergic manifestation and therefore develop only after initial sensitisation. Israels and Wilkinson (1937) noted that in certain patients who had recovered from amidopyrine agranulocytosis a subsequent dose of the drug caused leucopenia.

Purpura

Purpura has been reported by Stephens et al (1952) and Davies et al (1952). In none of these cases was the condition attributable to a fall in the platelet-count. Stephens noticed thrombocytopenia in 31 of a series of 188 cases, usually this complication appeared only after three to four weeks of treatment, and in none was there purpura.

Jaundice

Jaundice has been reported by Solomon (1953) in 2 cases, but he presents little evidence that phenylbutazone was responsible.

SUMMARY

Complete agranulocytosis developed in a 53-year-old woman during treatment with phenylbutazone. Post mortem the stomach contained many superficial erosions.

I wish to thank Dr W J Hay, consultant physician, for permission to report the case and for help in the inquiry, and Dr A. G Rickards for his advice and criticism.

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Phenylbutazone

At its annual general meeting on June 10, with the president, Dr **Donald Wilson**, in the chair, the section of physical medicine discussed Phenylbutazone ('Butazolidin') as a Therapeutic Agent in Arthritis.

Dr **John Shulman** said that phenylbutazone had been used by a number of clinicians for about a year, and some assessment of its value in rheumatic disease should now be made. His first experience of the drug had been in the form of 'Irgapyrin,' which was a mixture of phenylbutazone and amidopyrine, he felt certain that neither drug modified the toxic effects of the other, as had been suggested. Turning to the pharmacological effects of phenylbutazone, he said that there was no doubt that the drug raised the pain threshold; and it was also claimed that it had an anti-inflammatory action and a possibly associated effect on capillary permeability. In gout the blood uric-acid level was reduced. The most important side-actions were fluid and sodium retention and a toxic action on the bone-marrow. Although reduction of urine volume and sodium output were also found with corticosterone, phenylbutazone had no effect either on 17-ketosteroid or potassium output, or on the eosinophil-count, and the urinary effects could perhaps be attributed to increased reabsorption in the tubules. With regard to the toxic effects on the marrow, Dr. Shulman suggested that these could be minimised by confining phenylbutazone treatment in rheumatoid arthritis to active cases, as in gold therapy. He thought it likely that as much of the functional marrow was supplied by blood-vessels of epiphyseal and thus para-articular origin, there was in the active stage of rheumatoid arthritis a barrier to the blood-supply of the marrow which protected it against the harmful effects of toxins and drugs such as gold and phenylbutazone. Among diseases other than rheumatoid arthritis gout and ankylosing spondylitis had shown the best response. From his experiences in the treatment of 500 cases, mostly rheumatoid arthritis he thought phenylbutazone was valuable as maintenance therapy after cortisone or gold. but that it should never be used in the quiescent stage of disease. The maximum maintenance dose should not exceed 400 mg per day—if possible, 200 mg per day. Repeated regular blood-counts were essential to detect incipient agranulocytosis. The future of phenylbutazone therapy probably lay in the management of cases unsuitable for gold or cortisone.

Dr **Rhys Davies** had had eighteen months' experience of phenylbutazone. Initially, 12 patients with rheumatoid arthritis were treated in a pilot experiment, and most of them benefited. showing few toxic effects. Then 16 further cases carefully controlled, had confirmed initial conclusions and were reported elsewhere. He described a third group of 145 patients with rheumatoid arthritis all of whom were under observation before beginning treatment. Phenylbutazone was given by mouth starting with not more than 1 g daily, and reducing to a maintenance dose of not more than 800 mg on alternate days. Other drugs especially barbiturates,

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DR. DILLING REFERENCES—*continued*

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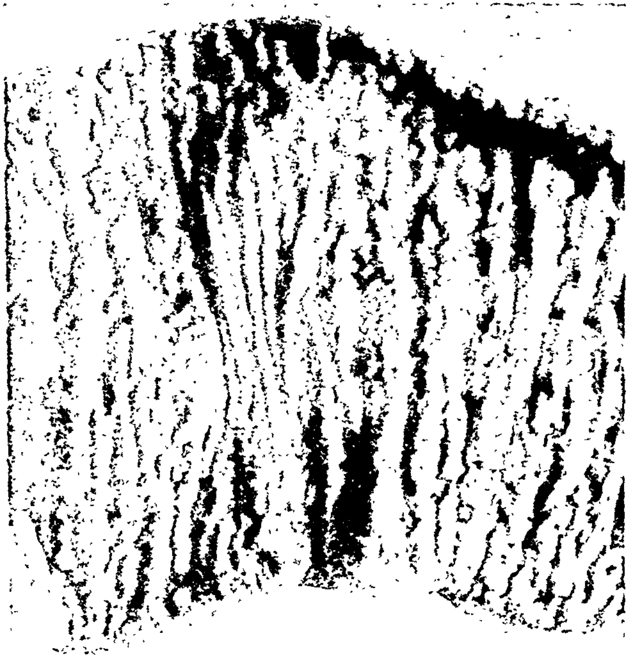


Fig. 4—Mid-ileum from case I. These changes were present from jejunum onwards.

orifices of crypts become blocked, with the result that small intramural abscesses remain buried in the mucosa to start the ulceration anew (fig. 5c).

These facts point in one direction. Ulcerative colitis is essentially recurrent or persistent; *one limited attack of diarrhœa does not constitute the disease: surely*, then, it must be the outcome of an initial blow to the colon of such severity as to leave the mucosa either in a permanently unhealed state or so weakened as to be prone to break down recurrently at the slightest strain, as in chronic ulcers of the leg. Put another way, ulcerative colitis is not a specific disease which hangs about the system to flare up from time to time.

The clinical facts support this. The history, in a definite proportion of cases, starts with a recognised attack of bacillary dysentery, and rarely amœbiasis is to blame; by the time ulcerative colitis has supervened all evidence of bacillary or amœbic infection has passed away. The fact that a clinically normal interval may occur between the definitive infection and the onset of ulcerative colitis does not invalidate the argument, for the bowel can heal, but sometimes imperfectly with the result that its breakdown later under the stress, perhaps, of another disease or a mild non-specific colon infection, is inevitable. The interval may be long.

Case 4.—In 1929 a man, then aged 23, had an attack of dysentery (thought to be bacillary) while resident in Aboukir. In 1948 he developed ulcerative colitis with persistent diarrhœa until he was operated on in 1952. In the interval he had had two mild attacks of diarrhœa lasting no more than 3 days.

Whether an attack of bacillary dysentery is to be followed by ulcerative colitis or not is a matter of the degree of destruction in the first instance. There are, of course, many cases with no past evidence of dysentery; but, since most of them had their first attack of diarrhœa outside hospital, an unnoticed food-poisoning, of the type which recurs so commonly in modern communities, may have started the chain of events. Even the failure to find incriminating organisms in the rather rare acute fulminating attack does not exclude this explanation, for the colon must be subject to chemical and biochemical traumata whose nature we do not at present understand, as recent experiences with chloramphenicol and aureomycin have shown (Reiner et al. 1952); the sensitisation phenomena suggested by Andresen (1940, 1951) may on occasion provide the initial blow. I have never seen ulcerative colitis follow typhoid fever or other members of the enteric group; the rarity of this combination can be explained by the distribution of the original ulceration, which leaves ample mucosa intact for purposes of healing.

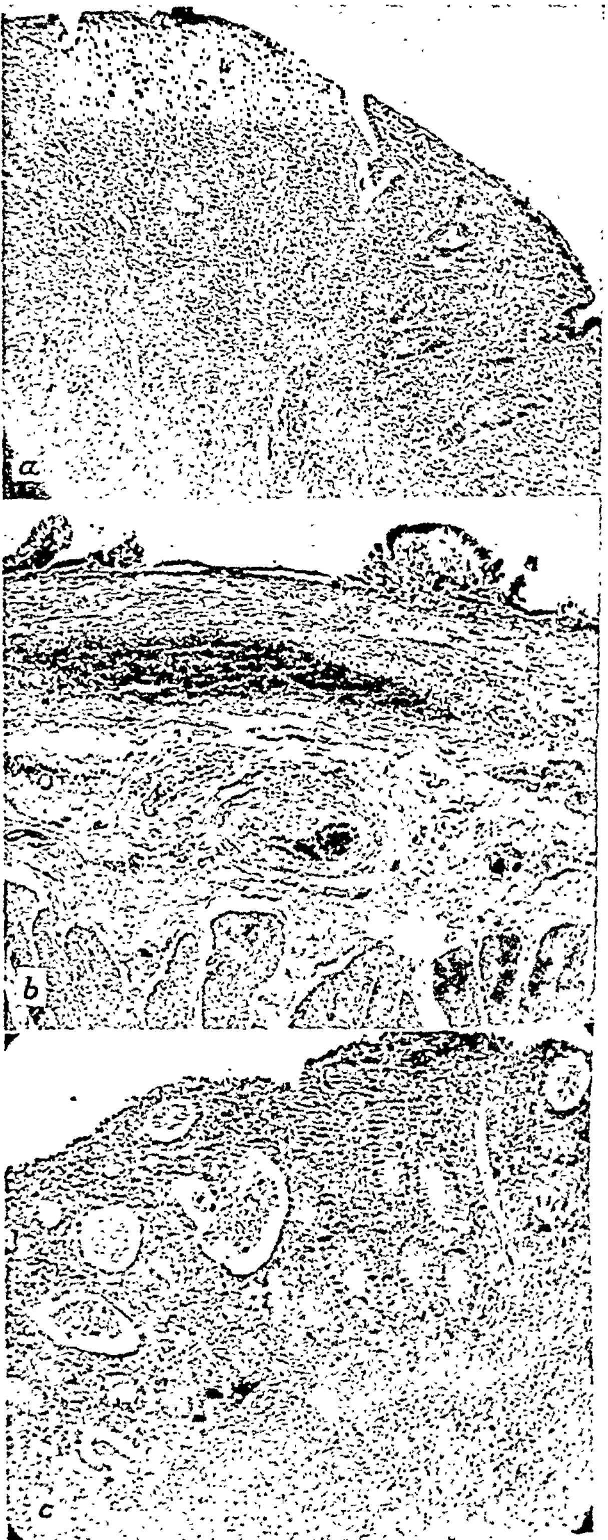


Fig. 5—True "idiopathic" ulcerative colitis: *a*, low and almost *cubical epithelium growing out from crypts and covering inflamed mucosa*; *b*, mucosa lost down to muscularis mucosæ, which is covered with flattened debased epithelium (a small pseudopolyp is *visible*); *c*, unobstructed crypts alongside crypts distended with pus.

which may mask toxic effects, were avoided. When the cases were assessed on a grading basis, there was no evidence of an effect on the rheumatoid process. A third of the patients showed some improvement in function, but the main effects were analgesia (only 10% showed no relief) and euphoria. Dr Davies thought that this euphoria was a very great help in the management and rehabilitation of patients with rheumatoid arthritis. Patients with ankylosing spondylitis, gout, and sometimes osteo-arthritis of the hip often improved when other analgesics had failed. Salt restriction was an important precaution in patients on phenylbutazone, and regular blood counts, especially during the first six weeks of treatment, were essential. Side effects could be allergic (rashes, angioneurotic œdema, asthma) or toxic. 10% of the patients had gastro-intestinal symptoms of more or less severity. Granulocytopenia had occurred in only 1 of his cases. Dr Davies had seen 2 deaths in patients taking phenylbutazone, and he thought that possibly a generalised drug sensitivity was responsible. He urged that phenylbutazone should not be used unless other analgesics had failed. It was to be regarded as a useful ancillary to rest, physical measures, and chrysotherapy.

Dr **Wilson** emphasised the great care needed in using phenylbutazone. He described a patient with renal dystrophy who had died in uræmia three months after starting and a month after finishing a course of the drug. He also believed that the severity of intercurrent infections was increased by phenylbutazone treatment.

During the discussion, Dr G O **Storey** described an elderly man, with typical rheumatoid arthritis treated with phenylbutazone, who died suddenly after admission to hospital with signs of toxicity. There was microscopical evidence at necropsy of a general hypersensitivity response. He emphasised the importance of careful post-mortem examination of patients dying suddenly while under treatment. Dr **Michael Mason** showed two slides illustrating a series of comparisons made between phenylbutazone and corticotrophin therapy in rheumatoid arthritis. Subjective and functional improvement produced by the two drugs appeared similar in his series; the erythrocyte-sedimentation rate, which fell during corticotrophin treatment, was unaffected by phenylbutazone. Dr J B **Jessiman** had observed toxic effects in 20 out of 22 patients with rheumatoid arthritis treated with phenylbutazone. All these cases had had previous treatment with gold or copper, to which they were sensitive. Dr N S **Craig** pointed out that aplastic anæmia may supervene very suddenly, and that regular white counts were no insurance against this. He thought that phenylbutazone was a highly dangerous drug. Dr C J S **O'Malley**, speaking of his experience in a rehabilitation centre, said that phenylbutazone enabled patients to undergo the rehabilitation course who, without the drug, would have been unable to attempt it. Dr **Cedric Hirson** said that Dr Craig's view of phenylbutazone, had it been applied to the sulphonamides when they were first introduced, as some people had advocated, would have led to their abandonment. Other speakers commented on the lack of unanimity in the dosage schemes used.

In reply to some of the points raised, Dr **Rhys Davies** said that in his experience sudden death attributable to the drug was due to acute pulmonary œdema, probably a manifestation of generalised drug hypersensitivity. With regard to blood-uric-acid levels in acute gout he had observed levels to fall from 7–10 mg. to less than 4 mg. within three days of starting phenylbutazone. He pointed out that the drug was detectable in the blood for forty-eight hours after a single dose, and that therefore maintenance doses every two days should be adequate. Dr **Shulman**, while recognising the occurrence of unheralded aplastic anæmia and agranulocytosis, thought that in most cases it could be anticipated by routine white-cell and platelet counts.

AMERICAN RHEUMATISM ASSOCIATION

In his presidential address at the annual meeting held in New York on May 28-29, Dr C **McEwen** (New York) said that in its twenty-two years the association had seen great advances in the scientific quality of the papers presented, and now counted 800 members. Yet this advance was slow when compared with advances in other fields of medicine. There was still only one member of the association for every 12,000 victims of the rheumatic diseases, and only four or five of the major universities in the United States had an established arthritis department supporting full-time faculty members interested primarily in the problems of these diseases. It was time to seek from the Federal government, via the Public Health Service, support for further such departments. Only in this way could the study of the rheumatic diseases attract more workers and advance more rapidly.

Rheumatic Diseases

S **Cobb**, F **Anderson**, and W **Bauer** (Boston) reported a life-table study of 583 patients admitted to hospital at some time with rheumatoid arthritis, and followed for an average of 9.6 years. There had been 137 deaths, which on analysis showed that while the development of this disease did not influence the longevity of patients over 50, under that age expectation of life was considerably reduced: such patients succumbed to valvular heart disease, to infections of all sorts, or to pulmonary embolism, with a much greater frequency than others of the same age group.

WORK IN PROGRESS

E **Gardner** (Detroit) reviewed the blood and nerve supply of articular structures.

The synovial membrane was, he said, a highly vascular structure, which showed, besides an abundant capillary network, a type of thick-walled arteriole associated with arteriovenous anastomoses, and probably concerned with the regulation of local blood flow and temperature. He analysed the various types of nerve ending found in the joint, and showed that stimulation of some of these could produce visceral reflexes (i.e. hypotension) as well as local reflexes. J H **Kellgren** (Manchester), reporting studies of incorporation of labelled glycine into the tissues of rats, noted that adult collagen, once formed, showed little if any metabolic activity. However there were more soluble forms of collagen which did show a change. Formed collagen could not be regarded as necessarily inert. There was evidence that in rheumatoid tissues the normal collagen was replaced by an amorphous fibrinoid material—possibly a glyco-protein. These changes had been followed by electron microscopy, by X-ray diffraction, and by chemical analysis. K **Meyer** (New York) reported work on hyaluronidase preparations. Those of animal origin differed from those of bacterial origin. Of particular interest was the fact that bacterial enzymes not only split the hyaluronic acid chain molecule, but also modified the end grouping of the hexuronic acid component. This might have antigenic significance. **James Rhinehart** (San Francisco) had treated tissues with hyaluronidase, and had stained them before and after with a colloidal iron stain specific for sulphated polysaccharides. He showed that the mucoid polysaccharide-containing, interfibrillary substance of connective tissue seemed to be the site of the earliest lesion of rheumatic fever. This material swelled and became infiltrated with fibrin and possibly other components of the blood.

L **Sokoloff** (New York) had studied very early nodules of rheumatoid arthritis and had found that such lesions were highly vascular. This contrasted with the necrotic, avascular, and fibrous mature nodule. Necrosis, when it occurred, did so in relation to the blood vessels in such a way as to suggest that some

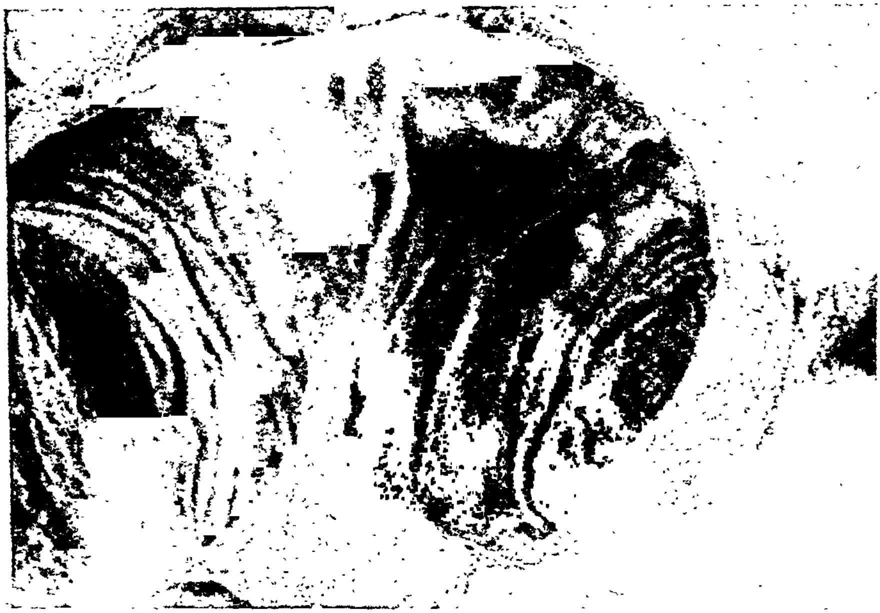
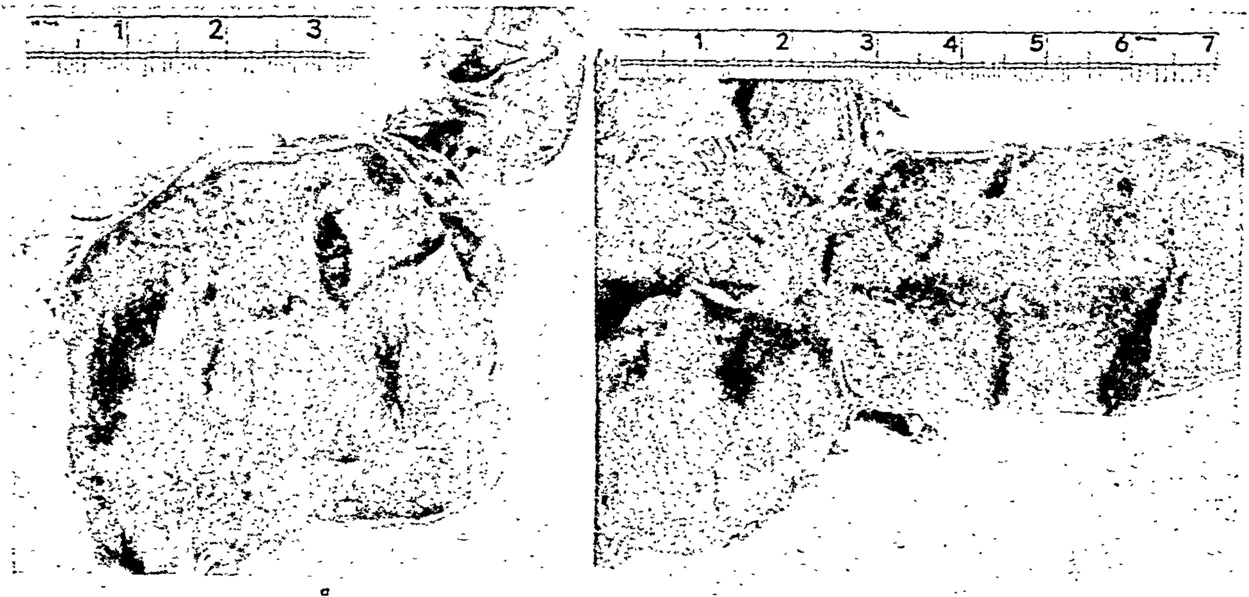


Fig. 6—Normal ileocæcal valve, showing crescentic fold.

There remain two questions regarding the significance of the pseudopolyps and the site of greatest destruction. The pseudopolyps have no significance in relation to the origin of ulcerative colitis; they are evidence only of bowel damage, being more often islands of mucosa remaining in a sea of destruction, less often granulomata covered with debased epithelium. It seems likely that there is a physiological reason why the left colon bears the brunt of the inflammation; the fact that the damage is greatest here cannot be taken as evidence that the disease starts at this site, but only that the weakened mucosa is broken down more readily and more completely here.

The Ileum in Ulcerative Colitis

As indicated above, it remains to explain why the ileum is sometimes involved in ulcerative colitis. Crohn (1949) rightly described it as due to a backwash of infected material from the colon, though he placed "right-sided colitis" with its associated ileitis in the same group and thereby inflated the incidence to 24%. In a personal series of 55 patients operated on I have seen ileitis only 3 times: during the same period 9 additional cases of ileocolitis were observed. This complication of ulcerative colitis is entirely due to the destruction of the ileocæcal valve. If the large bowel, removed at operation, is first distended to its natural size with fixative before being cut open for examination, the many mucosal folds, caused by contraction following fixation in the more usual way, are smoothed out and the bowel lumen can be studied in its natural form. (I am indebted to Dr. Cuthbert Dukes for drawing my attention to this method.) In normal bowel it will be seen that the cæcum is separated from the ascending colon by a crescentic fold, which is quite constant and passes about three-quarters of the way round the bowel lumen (fig. 6). On the cæcal side of this fold lies the ileocæcal valve, a horizontal slit, its upper lip formed by the fold which overhangs the lower lip in such a way that the orifice is directed towards the cæcum and away from the fæcal column contained in the colon. As the lips have a depth of ¼–½ in., the mechanism is similar to that of the mitral valve. It is quite competent, as handling of the cæcum and colon at laparotomy will reveal, when neither air nor fluid can be expressed into the ileum. The fact that barium can flow into the ileum from a barium enema in normal people does not argue that the valve is physiologically incompetent, for these are abnormal circumstances. The weight of barium, together with the head of pressure behind it, causes the cæcum to sag; this pulls down the medial wall together with the lower lip of the valve; the orifice opens and barium spills through into the ileum.



a

b

Fig. 7—Incompetent ileocæcal valve in ulcerative colitis: a, with ileum intact; b, with ileum slit open to show changes due to "backwash." Scale in inches.

blood-borne necrotising agent seeped out of the vessels into the tissues around, finally affecting the wall of the vessels itself, which then became obstructed by thrombosis J P KULKA (Boston) confirmed this work and had shown, by serial section, that many of the vessels involved in such early lesions were venules In lesions only one or two days old there was an œdema of the ground substance of the tissues near such a vessel, and then infiltration of it with a fibrin-like material apparently exuding from the vessel W D ROBINSON (Ann Arbor) described 4 cases of rheumatoid arthritis which developed diffuse or localised arteritis The lesions of the vessel walls differed from those of polyarteritis nodosa, and resembled rheumatoid granulomata elsewhere Clinically these patients had shown peripheral neuritis and/or lesions due to coronary or cerebral occlusion M A OGRYZLO (Toronto) drew attention to those cases of classical rheumatoid arthritis with nodules, which developed a fulminating involvement of other viscera manifested by fever, weight loss, nodule formation, cardiac and pulmonary disorder renal changes, and severe myositis In some the lupus erythematosus cell phenomenon was present, but, as several speakers pointed out, this could no longer be considered diagnostic of this disease

T B BAYLES (Boston) reported some of the many ways in which scleroderma may affect viscera as well as the skin Of his 15 patients, 14 had cardiac involvement Bronchiectasis, breast changes, ulceration and stricture of the intestinal tract, and myositis were not uncommon

The differential sheep cell agglutination titre was discussed by A S JACOBSON (New York) Using Heller's modification, he had found it to be positive in 74% of cases of active peripheral rheumatoid arthritis A positive test was found most often in cases with nodules and was more frequent in the male sex There were 2 6% of false positives, and most of these were in cases of other "collagen" disease In the subsequent discussion other workers reported attempts at characterising the factor responsible It seemed probable that it was a macromolecule, of molecular weight 15,000, stable between pH 3 and pH 11 and in the presence of 30% alcohol It reacted unlike a protein, although it seemed to be associated with the γ globulin fraction of the plasma-proteins

SURGICAL MEASURES

R L PRESTON (New York) described his method of reconstruction of the knee-joint in rheumatoid arthritis In the more severe cases he used both anterior and posterior arthrotomy, followed by synovectomy and removal of intra-articular deformities and adhesions The tibial tubercle was moved distally to restore function to the stretched quadriceps Corticotrophin (A C T H), 100 mg daily, was given for one week before and two weeks after operation to reduce pain and scarring Exercises maintained muscle strength and joint range Before operation all 18 of his patients were disabled by flexion deformity In 16 the operation was satisfactory, and 11 who had been followed more than six months had maintained good function

M C COBEY (Washington, D C) had experimented with combining plastics with other materials for splints Finally he had evolved a mixture of plaster of-paris and 'Melmac' resin, combined in such a way that plaster bandages would be impregnated with both simultaneously, so that wetting was followed by setting of both the plaster and resin The resulting splint was more resilient, lighter, and cheaper than plaster alone As it was four times as strong as plaster, less material was required Two 4-inch plaster bandages would make a satisfactory leg cast which with a little reinforcement could be used for weight bearing Such casts were porous but unaffected by moisture or urine, and were often in satisfactory use continuously for a year

MEDICAL TREATMENT

From the Mayo Clinic L E WARD (Rochester) reported a study of cortisone and hydrocortisone, and their esters in rheumatoid arthritis Although weight for weight the various steroids differed in their antirheumatic potency, the more powerful the preparation the more likely it was to produce undesirable toxic effects

J H KELLGREN (Manchester) and A BRADFORD HILL (London) described the early results of a small but strictly controlled Medical Research Council therapeutic trial of cortisone and aspirin, as suppressive agents in rheumatoid arthritis Selecting only early cases, before permanent deformity had occurred, and judging the results by the ability of their patients to return to work or normal daily activity, they found no differences between the two treatments It was as yet too early to assess results in the prevention of permanent deformities

Members of a committee of the American Rheumatism Association, who also were concerned with assessment of the benefits of cortisone in rheumatoid arthritis, reported a preliminary inquiry into the ways in which the clinicians were already using cortisone for this disease This was not a controlled study, so the results could not be used for the comparison of cortisone against other treatments Nevertheless it showed that there were in practice a surprising number of limitations to the use of this preparation They hoped to use the information thus collected in setting up a large scale controlled study covering both early and late cases

Three papers reported on the use of cortisone in rheumatic carditis MAY G WILSON (New York) treated carditis in 33 patients, using an average of 150 mg of corticotrophin or 300 mg of cortisone daily for about seven days She thought that carditis could be terminated in this way, and her patients became ambulatory in two to three weeks In her long experience of rheumatic fever covering many thousand patients over twenty years, she had not seen so effective a remedy as cortisone On the other hand ANN G KUTTNER and JANET S BALDWIN (New York) had treated 7 patients, fourteen days or less from the onset of their first rheumatic attack, with cortisone or hydrocortisone for from twenty one to sixty three days, and had found that 5 of these patients (after follow-up periods up to two years) had established valvular damage, in 1 other the rheumatic progress was still active LAWRENCE GREENMAN (Pittsburg) had treated 49 children in their first attack of rheumatic carditis with cortisone in a dosage of 300 mg per day for six weeks, decreasing to zero during the next two weeks He found, on follow up, that 9 out of 10 patients whose duration of disease was less than fourteen days before treatment, recovered with normal hearts The results were less good in those cases whose carditis had been active for longer than fourteen days B F MASSELL (Boston) agreed that massive suppressive dosage continued for several months was effective in preventing permanent cardiac damage EDWARD E FISCHELL (New York), discussing these results, noted the great variability of the clinical course of rheumatic fever Although the results were encouraging they were from uncontrolled studies and this fact should be remembered in assessing their significance and the discrepancies between them

W C KUZELL (San Francisco) had treated 800 patients suffering from a variety of rheumatic diseases with phenylbutazone ('Butazolidin') and had found it an effective and useful, though temporary, suppressive agent Patients with gout and ankylosing spondylitis showed the best responses Toxic effects had been fairly common, occurring in 381 out of the 800 patients and in sufficient severity to cause discontinuation of therapy

When ulceration has persisted in the cæcum for some time, the crescentic fold is destroyed, the lips of the valve are then lost, and the cæcal wall is directly continuous with that of the colon. At this stage the ileocæcal junction appears as a circular porthole constantly open. The ileum beyond then develops a granular mucosa and a thickened wall (fig. 7). That this ileitis is of no more than secondary significance is shown by the fact that ileostomy can be performed in such cases above the site of gross change without subsequent inflammation developing above the stoma, provided, of course, the stoma is efficient. Ileostomy dysfunction (Warren and McKitterick 1951), from stenosis of the stoma and partial obstruction, will induce an inflammation in the ileum which has nothing to do with the original disease, as will the simple trauma of an indwelling tube. A significant point in the ætiology of ulcerative colitis is the fact that the bowel does not become affected with the original disease above an ileal stoma; if ileitis does develop, it is due to one of the factors just mentioned or because the case is an unrecognised ileocolitis.

Crohn's Disease and Ulcerative Colitis

A study of ulcerative colitis cannot be complete without considering Crohn's disease. It is true that when Crohn's disease attacks the colon primarily it can be widespread and far more so than is generally recognised from the study of the gross lesion, which is usually circumscribed. If a colon, attacked by this disease, is prepared in the manner described by Dr. Dukes, lesions can sometimes be observed beyond the area of gross damage. In the specimen shown in fig. 8 the ascending colon was grossly disorganised; yet the *external* appearances of the bowel beyond the hepatic flexure were perfectly normal, with no thickening. However, scattered rather sparsely throughout down to the sigmoid, shallow "aphthoid" ulcers about $^{1}/_{8}$–$^{1}/_{4}$ in. in diameter were visible, while here and there scars, resembling those seen in an atheromatous aorta, indicated an area which had healed. It would be impossible to detect these changes on external observation of the bowel at laparotomy, and their unsuspected presence may explain the high recurrence-rate following resection in this disease.

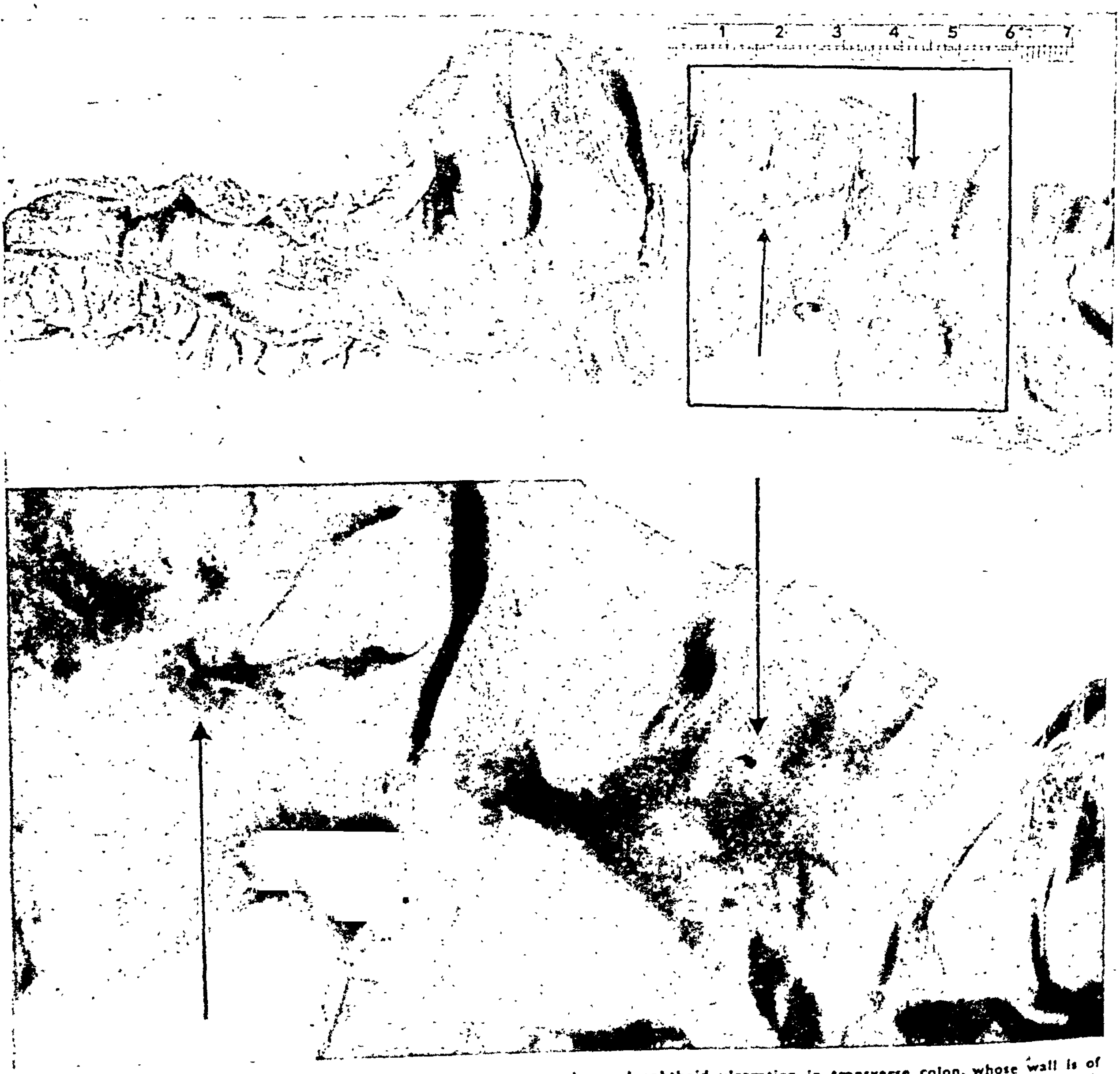


Fig. 8—Crohn's disease of cæcum and ascending colon: above, scarring and aphthoid ulceration in transverse colon, whose wall is of normal thickness; below, enlargement of inset. Arrows point to scarring on the left and an "aphthoid" ulcer on the right. Scale in inches.

in about 15% **Elmer E Yeoman** (Tucson) had treated 40 patients suffering from rheumatoid spondylitis with this drug for periods up to two years In his series the drug had been discontinued in only 1 because of toxic effects 11 patients had gone back to work and 3 became fit enough for surgery He emphasised that the maintenance dose should not be above 200 mg per day **Ephraim P Engleman** (San Francisco), on the other hand, found the toxic effects of this drug to be both serious and frequent Jaundice occurred in 4 patients, of whom 1 died 4 patients showed heart-failure 1 of these died, and at necropsy there was a diffuse arteritis involving most of the viscera, including the heart 2 patients developed optic neuritis, 1 becoming permanently blind 2 had granulocytopenia, with 1 death Other toxic reactions included peptic ulceration, psychosis, and purpura His patients had received the drug for from two to twenty-eight days at a dose level of between 300 and 800 mg daily

DeWitt Stettin (New York) reviewed recent work employing tracer substances bearing on the metabolic defect in gout In normal men there was a miscible pool of uric acid of about 1 1 g which was replaced each day to the extent of 75% by newly formed uric acid About 80% of the uric acid disposed of each day appeared in the urine as uric acid The remainder was broken down into urea and ammonia In the gouty subject the miscible pool of uric acid might increase to 30 g This was greater than the amount that could exist as a saturated solution in the total body-water, and it appeared certain that uric acid tophi could contribute to the pool by continuous resolution and precipitation Uricosuric drugs such as 'Benemid' could shrink this miscible uric acid pool in gout In some, but not all, gouty patients there was an increased rate of synthesis of uric acid from dietary glycine

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Reviews of Books

Ciba Foundation Colloquia on Endocrinology

Vol 5 *Bioassay of anterior pituitary and adrenocortical hormones* Editor G E W Wolstenholme, O B E, M A, M B, assisted by Margaret P Cameron, M A, A B L S London J & A Churchill 1953 Pp 228 25s

The bulk of this book consists of the texts of individual papers presented at the colloquium Most of these papers describe one or more methods of assay of each of the anterior pituitary hormones or of the adrenal corticoids Although most of the papers are complete, self-contained, and descriptive accounts, the book as a whole suffers from the lack of a critical appraisal of the merits of the different methods, and the reader may find it difficult to make his own assessment Moreover, as the chairman pointed out in his summing-up, the different purposes for which bioassay is required—namely, the control of manufacture, fundamental research, and the clinical diagnosis of hormonal dysfunction—make different demands on the design of the assays, thus, clinical diagnosis demands an assay method of high sensitivity, but not necessarily of great precision, while control of manufacture requires precision but not necessarily sensitivity There is no clear indication of the part that the assays described can play in these very different fields The fault does not lie with the authors nor with the editors it results from the written reproduction of the spoken word, which cannot recapture the inflexion of voice, the subtle emphasis, or the flat uninterestedness that provided a constant critical commentary at the meeting itself And if this is true of the papers themselves, it applies even more to the verbatim reports of the discussion which, on the whole, make colourless reading

Nevertheless in this single volume are to be found up-to date accounts of bioassays of all the anterior pituitary hormones and of the adrenal corticoids, and the collection of these methods from the literature would otherwise be a formidable task The book is likely therefore, to be of considerable value to endocrinologists in both the clinical and the research fields It is arranged in six parts, covering general principles, thyrotrophic hormone, gonadotrophins and prolactin, growth hormone corticotrophin, and the adrenocortical hormones respectively It is well turned out, with admirably clear tables and figures, and the latter, including some line drawings of a bioassayist at work, should have a wide appeal

The Œsophagus and its Diseases

Eddy D Palmer, M D, F A C P, lieut colonel, Medical Corps, U S Army, chief, gastro intestinal section, Walter Reed Army Hospital London Cassell 1953 Pp 553 93s

The foreword of this book states that "the œsophagus is coming into its own from a sort of 'No Man's Land'" and the author supports this contention by discussing the many and diverse disorders to which the œsophagus is heir He correlates and analyses various views advanced in recent years, but is perhaps too reticent about his own opinions

The opening chapters survey œsophageal anatomy and physiology, and illustrate the difficulties of studying any abnormality of deglutition Congenital abnormalities are well handled, but the section on diaphragmatic hernias, particularly the hiatus type, is not satisfactory, and the work of Allison and Johnstone is not mentioned in this connection The ætiological factors in achalasia and cardio spasm are fully discussed, but the reader will find it hard to decide which form of treatment, if any, is recommended A number of operations for cardiospasm are described which must inevitably lead to the undesirable reflux of gastric contents into the œsophagus (Accepted teaching in this country favours the Heller type of operation) Some of the most interesting and informative chapters are concerned with more unusual disorders, such as benign tumours, scleroderma, and varices

No attempt is made to go into operative and technical details, which would have made the book too long It is well produced and adequately illustrated, and will be valuable for reference

Histochemistry

Theoretical and Applied A G Everson Pearse, M A, M D, D C P, lecturer in histochemistry, Postgraduate Medical School of London London J & A Churchill 1953 Pp 530 60s

The author follows Prof J R Baker in acclaiming Francois Vincent Raspail (1794–1878) as the founder of histochemistry The science received a temporary set back after the introduction into histology of aniline dyes by Beneke in 1862, but it revived with the publication in 1936 of Lison's *Histochimie Animale* Since then its growth has been rapid—so rapid, in fact, that it has been hard for the histologist and histopathologist to keep level with developments There are many, therefore, who will be grateful to Dr Pearse for amassing so much information and treating it so ably and critically The work includes a useful chapter which deals briefly with the various physical methods which can help the modern microscopist There are many helpful illustrations, while technical methods are conveniently contained in a series of appendices which correspond to the various chapters This book will be of value to all concerned in the preparation and interpretation of tissues for microscopy

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Medicine (Vol 1 *The Patient and His Disease* 2nd ed Edinburgh E & S Livingstone 1953 Pp 410 25s) — Never have so many textbooks of medicine appeared in such a short time as in this post war period We welcome this second edition with its implication that the first edition is sold out Among the few that are good, Dr A L Clark Kennedy's ranks high mainly because it is not a catalogue of *facts, nor yet an omnibus of authors* nor even a practical guide but a straightforward account of how the problems of health and disease appear to a thoughtful and gifted physician Knowledge and experience seasoned with sincerity, humility and humanity are the ingredients A book to be read with profit by all from the senior physician to the junior clerk

Special Articles

SUSPECTED VIRUS INFECTIONS OF RESPIRATORY TRACT AND CENTRAL NERVOUS SYSTEM

DIAGNOSIS BY SEROLOGICAL METHODS

REPORT BY THE VIRUS REFERENCE LABORATORY,* PUBLIC HEALTH LABORATORY SERVICE, COLINDALE, LONDON

THE Virus Reference Laboratory, Colindale, began to make certain serological tests for the diagnosis of suspected virus infections of the respiratory tract and central nervous system in 1947–48. New tests were added as conditions permitted; and by 1949 cases of suspected virus infection of the respiratory tract were being investigated for antibodies to influenza viruses A and B, the psittacosis-lymphogranuloma-venereum (L.G.V.) group of viruses, *Rickettsia burneti*, and *Streptococcus M.G.*, and cases of suspected virus infection of the central nervous system for antibodies to the viruses of lymphocytic choriomeningitis (L.C.M.) and of mumps and to leptospires. In the ensuing two years a considerable number of serological tests were made on, and some viruses were isolated from, material from patients, mainly in hospitals, from all parts of England and Wales and to a small extent from Scotland; most of the specimens have, however, come from London and the Home Counties. A number of the positive results have already been recorded in papers by different physicians on series of patients (Crofton et al. 1951, Jennings 1952) or interesting individual cases such as Q fever, psittacosis, mumps-meningoencephalitis without parotitis, and lymphocytic choriomeningitis; and brief remarks on part of the respiratory-tract and neurological series have been reported from the laboratory (Marmion 1951, MacCallum 1950).

Although the Virus Reference Laboratory has coöperated with many hospitals and physicians and provided pamphlets on instructions for the collection of specimens and for the interpretation of results of the various tests, many doctors are probably still unfamiliar with the types of test that can be usefully made and are now available for the diagnosis of certain virus diseases. Since the complement-fixation tests for influenza A and B viruses, the psittacosis-L.G.V. group of viruses, and *R. burneti*, and the agglutination tests for *Strep. M.G.* are being made at public-health laboratories at Cambridge, Cardiff, Hull, Manchester, Newcastle, Northampton, Nottingham, and Winchester, and agglutination tests for leptospires at Birmingham, Bradford, Cambridge, Cardiff, Exeter, and Portsmouth, in addition to the Central Health Laboratory at Colindale, and by Dr. J. C. Broom, of the Wellcome Laboratories of Tropical Medicine, London, it seems an opportune time to report briefly the results of tests made in 1949–51, so as to show the relative incidence of causal organisms in suspected virus infections in Great Britain and to indicate whether certain tests are likely to be of help or not in diagnosis. Similar reports are available from various centres in the United States of America (Milzer 1950, Sigel 1950, Smadel 1950).

Information about what specimens are required for the investigation of suspected virus diseases, and the manner of their collection and transport to the laboratory, is given in recent textbooks—e.g., Bedson et al. (1950) and MacCallum (1951)—and papers and is not dealt with here. Serological diagnosis is, of necessity, the routine method of diagnosis in virus diseases. The isolation of viruses necessitates the use of fertile hens' eggs or animals such as mice, guineapigs, rabbits, hamsters, ferrets, and monkeys, making it a more expensive and formidable task than the isolation of bacteria. In addition, most of the laboratory animals carry latent viruses; therefore any virus isolated must be tested against the patient's acute and convalescent serum to confirm its origin. In addition, not only may there be human carriers of viruses, but also there can be dual infections—e.g., influenza and Q fever, poliomyelitis and Coxsackie viruses, and poliomyelitis and hepatitis. The examination of a pair of sera collected in the acute stage (ideally before the fifth day of the disease) and the convalescent stage (about the twenty-first day), with the demonstration of a rising titre of antibodies in the second specimen, is essential for an accurate diagnosis. The examination of the serum in the acute stage is necessary since the titre of antibodies may rise to a peak very early in the illness; and the demonstration of an increased titre in the serum in the convalescent stage is essential since antibodies may persist from nine months to two years in different infections.

RESPIRATORY TRACT

We originally intended to concentrate our attention on cases of suspected virus influenza and of primary atypical pneumonia (virus pneumonia). Table I shows that many specimens were also received from patients with a clinical diagnosis of lobar pneumonia or of bronchopneumonia. Influenza B was epidemic from January to the end of April, 1950, and influenza A was epidemic from December, 1950, to the end of April, 1951. The results from sera from patients in outbreaks of influenza in institutions or schools were not included in the table. The term "psittacosis" covers viruses of the psittacosis-ornithosis group. Of the 35 patients considered positive among the 1660 analysed, only 1 had any known contact with a parrot and only 1 with budgerigars; in neither was there a history of concomitant illness. The cases were, on the whole, considered to be examples of ornithosis resulting from contact with pigeons or other domestic birds carrying viruses of this group. The Q-fever figures are slightly greater than might be expected, because the disease was discovered in Kent and Devon at the beginning of the period under discussion, and an intensive search was made.

Of the total number of patients from whom samples were examined in the period from July, 1949, to June, 1951, about a third were rejected from the analysis because the clinical details were either inadequate or described conditions unlikely to be due to a virus infection, or because the sera were taken too early for antibody to be present and no further specimen was sent. Of the remainder (1660), which have been analysed, 44% had only a single sample of serum taken during convalescence and 23% had two or more specimens of serum taken during convalescence. In only 33% of patients were two or more specimens of serum collected of which one was obtained earlier than the tenth day of the illness and a subsequent one from fifteen to thirty days after the onset. It is realised that in some patients the onset may be mild and they do not present themselves until a stage when antibodies are already present; but the idea of infection by a virus or by a rickettsia often appeared to have been an afterthought.

Table I presents the results in the 33% of patients from whom adequately timed sera were collected. (The results in the 23% of patients who had two or more specimens of serum taken during convalescence were of the same order.) It can be seen that about 30% of the patients had antibodies to one or other of the antigens. Of the patients diagnosed as having virus or atypical pneumonia, about 34% reacted to one of the five reagents. The remainder may have been caused by some other unidentified sensitivity developed after only twenty-four hours' treatment The ointment was not tolerated by acute or oozing lesions, possibly because of the nature of the vehicle

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* Those participating in this work during all or part of the period were Dr. F. O. MacCallum (director), Dr. B. P. Marmion, Dr. A. D. Macrae, Dr. B. Andrews, Dr. A. P. Goffe, J. A. L. McDonald, A.I.M.L.T., and P. Phipps, A.I.M.L.T. The tests for leptospirosis were made by Dr. J. C. Broom, of the Wellcome Laboratories of Tropical Medicine, and for mumps by Dr. C. L. Greenbury, of Stoke Mandeville Hospital.

Topical applications are unexpectedly difficult to assess, for no two skin conditions are identical and all are subject to changes independent of treatment Moreover, symptoms cannot be measured objectively, and they can be influenced by the enthusiasm of the doctor armed with any new preparation Treating a symmetrical eruption on one side only might seem to be the answer, but it has been found in various skin diseases that the untreated side may respond as well as the treated The effect of the vehicle must be considered for example, Reiss and Kern,[16] when testing an anti-histamine ointment, found that over 28% of their patients were relieved of itching by the base alone In these investigations the main control has been the patients' experience with previous preparations, which may have had quite dissimilar bases The reports are therefore open to criticism, but they can at least be taken as an indication that the substance is useful and safe It seems unwise to use it combined in an ointment with an anti-histamine (as is the case in 'Teevex'), for antihistamines can also cause sensitisation dermatitis after repeated local applications On the other hand, it would be helpful to have the pure substance available for incorporation in different media

CHOROIDEREMIA

PROGRESSIVE degenerative lesions of the retina that have been grouped as "abiotrophies" include the different kinds of retinitis pigmentosa, gyrate atrophy of the retina, choroideremia, and several types of macular dystrophy In choroideremia the earliest symptom is night-blindness, then peripheral vision is gradually lost and finally central vision, so that the patient is blind In advanced cases ophthalmoscopic examination shows that the choroidal vessels have disappeared and there is extensive retinal atrophy, affecting the central area least At necropsy the choroidal vessels are either sclerosed or absent, and the outer layer of the retina is extremely degenerate Earlier workers thought that this condition might be a variant of retinitis pigmentosa, with which it shares several features—the strong genetic determination, the progressive nature of the lesion, and in some instances pigmentation of the retina Furthermore some of the female relations of patients with choroideremia were thought to have retinitis pigmentosa

A few years ago American workers[17] described a family of some 600 of whom 33 had choroideremia Sorsby and his colleagues[18] have now given an account of three further affected families These studies show clearly that the condition is distinct from retinitis pigmentosa, which did not occur in these families They also show that the condition is progressive, and in different members of the family at different ages all stages can be seen from symptomless pepper-and-salt changes in the periphery of the retina to the unmasking, sclerosis, and finally disappearance of the retinal vessels Professor Sorsby found advanced choroideremia in a boy aged only $4^{1}/_{2}$, and one man was blind at 25, but blindness is rare before the age of 40, central vision being well retained while peripheral vision is gradually lost

Only males have symptoms of choroideremia, but many of the females in these families had retinal changes typical of the earliest stages of the disease in males There is thus no doubt that the condition is due to a sex-linked gene which is intermediate between a dominant and a recessive, it produces a severe lesion in the male, but in the heterozygous "carrier" state m female it produces only a mild and apparentl progressive disturbance Sorsby and his colleagues that the exceptions to this mode of inheritance de in earlier reports are due to errors in diagnosis, and the carrier state in the female relations of men choroideremia was mistaken for retinitis pigmento

With any genetically determined disorder the ab to recognise the carrier state is most helpful in adv parents on the chance that their children will be affec The sisters of men with choroideremia have an e chance of being normal or of being carriers It important to them to know which they are, since the sons of carriers on the average will go blind Th with normal retinæ can be reassured that there i risk that their sons and grandsons will be affected.

NEW YEAR HONOURS

IN the select company of the members of the Order Merit the place left vacant by the death of Sir Char Sherrington is filled by the appointment of a surge Prof Wilder Penfield, F R S, of the Montreal Neur logical Institute A leader in neurosurgery, he has de classical work on cerebral localisation and the relat problems of epilepsy, and the profession in this country as in Canada, will welcome his new distinction Of th doctors to be created knights bachelor, three a Australians—Mr N M Gregg, the Sydney ophthalm surgeon who first drew attention to the relation congenital cataract to maternal rubella, Dr E Britte Jones, of Adelaide, who has been vice-president of th Royal Australasian College of Physicians and presider of the Medical Board of South Australia, and Dr Pet MacCallum, professor of pathology at Melbourne fo 26 years and chairman of the Australian Nation Research Council and of the Australian National Re Cross Nearer home it is a pleasure to see a knighthoo conferred on Mr Zachary Cope, of St Mary's Hospital who has so well earned this honour as a teacher, as former vice-president of the Royal College of Surgeons as chairman of the Cope Committees—and simply a Zachary Cope Another welcome name is that of Prof Arthur Ellis, once of Toronto but afterwards of th London Hospital and the regius chair at Oxford, whos uncommon sense—whether directed to the kidney or th curriculum—has done so much, in quiet ways, fo medicine and its students We are happy to note that Dr Pridie's notable and far-flung work as chief medic officer of the Colonial Office since 1948 has been reco nised by promotion in the Order of St Michael an St George, and that the distinguished medical head of the Navy and Army, Admiral MacKenzie and Gener Harris receive knighthoods in the Order of the Brit Empire Many other familiar and respected names wi be found in the list we publish on p 87, and to thes we would add that of Mr A Landsborough Thomson D SC, now knighted, whose long service as second secretary of the Medical Research Council makes almost able to claim him as a member of our profession

VACANCIES

READERS who reached the concluding pages of ou last issue will have noticed the analysis of vacan appointments which was printed so conspicuously then As we explained in an annotation, this analysis is to serve as a key, and will be published weekly But now that we have prominently drawn attention to its existence, we are transferring it to our advertisement columns, where it will be found this week on p 30

Dr G F ABERCROMBIE has been elected chairma of the foundation council of the College of Gen Practitioners

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[16] Reiss F Kern B B *J Allergy*, 1950 21 160
[17] McCulloch C McCulloch R J P *Trans Amer Acad Ophthal Oto laryng* 1948 52 160
[18] Sorsby A Franceschetti A Joseph R Davey J B *Brit J Ophthal* 1952, 36 517

THE LANCET

LONDON: SATURDAY, JUNE 20, 1953

Bread

When submarine warfare caused a critical food shortage in 1917 the amount of food available to our human population was increased by milling wheat to a higher percentage—first to 80% and then to 90%. The Food (War) Committee of the Royal Society investigated the "higher extraction" bread, and noted its nutritive superiority: even at a time when the importance of vitamins was but dimly appreciated, the scientific advisers of the Government told the public that "the part of the grain which was formerly rejected contains valuable flesh-forming material and salts." Within a fortnight of the Armistice, however, the Government announced a reduction in the extraction-rate of flour, which would release approximately 18,000 tons of "wheat offal" weekly for farmers, pig-keepers, and others to feed their animal stock. We deplored in 1918 this post-war reversion to whiter bread,[1] and we deplore it again today. Admittedly the changes now proposed will be popular with the uninformed public, and they include compensating safeguards for health. But it is hard to believe that in framing them it is health that has been the first consideration.

During the second world war the history of bread repeated itself with variations. A new and fundamental departure was made when in 1940 the Government announced[2] that, because the 73%-extraction flour at that time in use was lacking in vitamin content, it had been decided to fortify it with vitamin B_1. In making the announcement Mr. (now Sir Robert) Boothby said that this new policy of "fortifying" bread, which had been adopted after receiving a report from the Scientific Food Committee, would be "hailed by scientists everywhere as a great advance"; but in fact it was widely regarded as retrograde. Such fortification with vitamin B_1 became unnecessary when the acute shortage of shipping space obliged the Government to abandon white flour in favour of National flour of not less than 85% extraction and including the maximum amount of wheat-germ. At the end of 1944, when the war in Europe was drawing to a close, it was found possible to reduce the extraction-rate to 80%; but this reduction could be justified by research which had shown that at this extraction flour could be milled which would contain most of the aneurine (thiamine), nicotinic acid, and iron. In January, 1945, the Ministry of Food convened a conference to advise on post-war bread policy and in particular on any regulations that might have to be made when wartime control ended. The members[3] included Lord Horder and the late Sir Jack Drummond, F.R.S., for the Ministry of Food, Sir Wilson Jameson for the Ministry of Health, Sir Edward Mellanby, F.R.S., for the Medical Research Council, and Prof. E. C. Dodds, F.R.S., for the National Association of British and Irish Millers; and though their conclusions suggest compromise for the sake of unanimity they include some important statements. Members of the official side of the conference had made it clear, said the report, that "all flour sold in this country for human consumption should, if practicable, be subject to regulation, so as to maintain a desirable nutrient standard." They had reached this conclusion as a result of "the very definite view expressed by the official medical and scientific members of the conference that a return to white flour, such as was commonly in use before the war, would be thoroughly bad for the nation's health." These members of the conference had said emphatically that "if the extraction rate of flour falls below a certain level and nothing is done to replace the lost nutrients, human beings dependent on bread for a supply of these nutrients are likely to suffer in health." "Limiting consideration to what is desirable and ignoring whether it is practicable or enforceable," the conference was not prepared to differ from the view that "natural food is to be preferred to food reinforced with so-called synthetic vitamins." The official scientific and medical members considered "that the retention of the natural constituents of the wheat grain is so incomparably preferable to reinforcement that they are not prepared to contemplate the adoption of" reinforcement. The conference was unanimous in recommending that it would be practicable for regulations to provide that flour (per 100 g.) should contain not less than the following amounts of three "token" nutrients: thiamine, 0·24 mg.; nicotinic acid, 1·60 mg.; iron, 1·65 mg.

In contrast to the uninstructed haste of 1918, the arrangements now being made for returning to white bread are cautious and complex. At the coming harvest, we are told,[4] the controls on cereals will be removed, the existing subsidy on flour will cease, and there will be an end to the restrictions on the type of flour which may be produced; but a National flour of 80% extraction is still to be available, and bread made from this will presumably be cheaper because it will be subsidised and subject to price control. Moreover, as a concession to nutritionists, the white flour of lower extraction is to have some of its deficiencies made good.

> "This whiter flour will . . . be fortified by the addition of nutrients equivalent to those lost in the further refining which it undergoes (so far as these can at present be identified) as well as the calcium which is already added to the National flour; and this will ensure that freedom to produce whatever flour the public prefers will not result in any avoidable lowering of nutritional standards."

But is there in fact any intention to add more than the three "token" nutrients—thiamine, nicotinic ous devices to keep particular muscle groups exercised, or to the warm plunge-bath, where physiotherapists exhort and persuade the gaily clad bathers to achieve the next stage of activity, or to the gymnasium, where the instructor notes with pride the gain in power of limbs impaired by poliomyelitis or other disorder From 4 30 to 9 30 P M the patients are off duty They can have tea in the handsome lounge, rest and read in the quiet room, chat or play games in the common-room, walk in the grounds, go out and visit friends, or join in the programme arranged by their own entertainments committee On three evenings a week the education and recreation department provides programmes of documentary and instructional films, or arranges discussions, games, or plays by local amateur dramatic societies or by the patients themselves All the patients have physical disabilities Treatment for industrial patients with neuroses is, of course, available at Roffey Park, near Horsham The average stay at Farnham Park is four weeks—the longest ten weeks The food is very good, and so is the morale of the patients, perhaps the two are linked

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[1] *Lancet*, 1918, ii, 755, 788.

[2] *Ibid*, 1940, ii, 117.

[3] Ministry of Food. Cmd. 6701. London: H.M. Stationery Office. 1945; see *Lancet*, 1945, ii, 789.

[4] Decontrol of Cereals and Feedingstuffs. Cmd. 8745. London: H.M. Stationery Office. 1953.

The Slough Industrial Health Service is thus a comprehensive scheme for the welfare of workers in industry, and has already shown its member firms a good return in the saving of working-time The workers themselves at first regarded it with the customary scepticism of the British working man, who is always wary of institutions outspokenly designed to do him good Gradually, however, they have come to recognise the value of the service, and now make full use of it

SCURVY

The Edinburgh Meeting

As already recorded in these pages, the Royal College of Physicians of Edinburgh and the Nutrition Society combined during the weekend of May 22 to celebrate in Edinburgh the bicentenary of the publication of Lind's *Treatise of the Scurvy*[1]

The proceedings opened with a "special graduation ceremonial" at which the Vice Chancellor (Sir Edward Appleton, F R S) conferred the honorary degree of doctor of laws upon Surgeon Vice-Admiral Sir **SHELDON DUDLEY**, F R S In a fighting speech Sir Sheldon said that the medical officer in the Royal Navy must educate his executive superior in practical hygiene, and that the importance of this subject was so great that there should be a health officer on the Board of Admiralty There was, he declared, no such entity as subclinical scurvy, and he believed that less than 15 mg daily of ascorbic acid was a maintenance dose although during the war dietitians had tried to persuade him that the figure was 300 mg At the conclusion of the ceremony a bronze plaque commemorating Lind was unveiled, the gift of the Sunkist Growers of Citrus Fruit in California and Arizona Later in the day another formal speech was made—this time by Prof V P **SYDENSTRICKER** (Augusta, Georgia), who gave the Sydney Watson Smith lecture in the Royal College of Physicians on the Impact of Vitamin Research on the Practice of Medicine

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The scientific meetings of the Nutrition Society were opened by Sir **EDWARD MELLANBY**, F.R S, who stated that Lind was the first to introduce the experimental method into medicine He cruised in safer waters when he came to contemporary history and reminded us of the service Sir Sheldon Dudley had performed in establishing the Royal Naval Personnel Research Committee, and of the careful researches on nutrition of Dame Harriette Chick over many years, he and she were the only two surviving members of the original Accessory Food Factors Committee set up jointly in 1917 by the Medical Research Committee and the Lister Institute Dame **HARRIETTE CHICK** then reviewed the early investigations of scurvy and incidentally differed from Sir Sheldon in affirming the existence of the prescorbutic state Later in the symposium a paper on authors on scurvy before Lind was read on behalf of Mr A J **LORENZ**

Perhaps the most important contribution of the session was given by Mr C G **KING**, PH D (Nutrition Foundation, New York City), who by labelling compounds with ^{14}C has indicated how L-ascorbic acid is formed in the body of the rat from D-glucose, D-glucuronic acid being an intermediate He has also made the interesting observation that with deficiency of ascorbic acid there is an increased formation of cholesterol from acetate, but, although he is a champion of high human allowances of ascorbic acid, he was careful not to claim that ingestion of the vitamin would decrease atherosclerosis

This relation to cholesterol metabolism is possibly related to one of the most interesting aspects of ascorbic acid, its connection with the adrenal cortex Ascorbic acid may form as much as 4% of the dry weight of the adrenal cortex, and the vitamin was of course initially isolated from adrenals by Szent-Györgyi in 1927 Sayers[2] and his colleagues have shown that adrenal ascorbate is reduced by corticotrophin (A C T H) or by various stresses It is possible that an oxidation product of ascorbic acid is required for the synthesis of adrenal cortical hormone from cholesterol and it may be that corticotrophin promotes the oxidation of ascorbic acid Cornforth and Long[3] have suggested that cortisone promotes the peripheral oxidation of ascorbic acid

Prof R M **KARK** (Chicago) reviewed the relation of ascorbic acid to scurvy, corticotrophin, and surgery he claimed that there was no evidence that cold or adrenal cortical activity increases the human requirement of ascorbic acid, and he did not believe that ascorbic acid or a derivative of it is used in synthesising adrenal hormones

The Lind tradition of experimental work on man was upheld by papers from Dr J H **CRANDON** (Boston) and Prof H A **KREBS**, F R S Dr Crandon described the now classical experiment[4] in which he subsisted for six months on a diet containing no vitamin C subsequently he has investigated the relation of ascorbic acid to surgery Professor Krebs described the similar experiment later conducted in Sheffield on conscientious objectors[5] In the latter experiment a supplement of 10 mg of ascorbic acid daily was found to cure clinical scurvy in all six volunteers and protected three volunteers from scurvy for 424 days, this figure of 10 mg was somewhat arbitrarily trebled to arrive at a figure which would satisfy "ill-defined additional needs and to allow a margin of safety" Even this figure of 30 mg is of course very much lower than that required for saturation in a delightful paper Prof **GOUNELLE**, of Paris, informed the meeting that he had found that tuberculous prisoners-of-war did not become saturated until they were given 300 mg daily The question whether saturation is desirable or necessary was taken up by Dr King in the discussion at the end of the sessions when he defended the daily allowance of 75 mg of ascorbic acid recommended by the National Research Council Mr L J **HARRIS**, SC D, had suggested that the question of requirement was one that needed discussion and, after pronouncing himself in favour of saturation, he called on Dr King Dr **KING** said that 75 mg gave only half-saturation, the guineapig allowed to choose its diet kept itself saturated, and animals that synthesised their own ascorbic acid were saturated, it could be shown that guineapigs survived diphtheria toxin better on high levels (5–10 mg daily) than on lower levels (2–5 mg), even though these lower levels completely protected acid, and iron? Is riboflavine, for example, to be added? The Conference on the Post-War Loaf[3] appointed a subcommittee under Lord Horder's chairmanship which set the minimum for riboflavine at 0·14 mg. per 100 g. of flour—an amount unlikely to be included in flour of less than 80% extraction. Riboflavine is a nutrient "lost in the further refining" and "can . . . be identified"; it is clear therefore that it comes within the definition of required fortification. Pyridoxine and pantothenic acid could be supposed to come within it also; for both these substances are known to play a part in normal nutrition. Are pyridoxine and pantothenic acid, we may ask, to be restored in the quantities removed by the milling of white flour? If not, what nutrients "equivalent" to them are to be introduced, so that there shall be no "avoidable" lowering of standards? The truth is that, though the Government have explicitly stated that the white flour will be fortified with the identifiable nutrients lost in the further refining, there are grave doubts whether this will in practice be done. In the debate in the House of Lords last week Lord Carrington, for the Government, said that "the makers of whiter flour will be required to restore to that flour the same amounts of the main nutrients as are present in 80% extraction flour. The nutrients which will be put back are iron, vitamin B_1 and nicotinic acid." This statement conflicts with that in the white-paper on Decontrol of Cereals,[4] and it appears that the Government now intends to restore the same amounts of the *main* nutrients that are lost (iron, thiamine, and nicotinic acid), rather than all the identifiable nutrients that are lost. If so, the white bread will be *demonstrably* of lower nutritional value than the 80%-extraction National bread—quite apart from any deficiencies which may or may not exist in substances which the young science of nutrition does not yet recognise as significant. In times of poverty and scarcity, such as may lie ahead of us, good bread is the chief nutritional safeguard of Western peoples. Yet mainly, it seems, for the sake of economic or commercial convenience the public are once again to be encouraged to cultivate a taste for an inferior product.

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[1] *Lancet* May 16 1953, p 988

[2] Sayers G *Physiol Rev* 1950, 30, 241

[3] Cornforth J W, Long D A *Lancet*, Jan 24 1953 p 160

[4] Crandon J H, Lund C C Dill, D B *New Engl J Med* 1940, 223 353

[5] *Lancet* 1948, i, 853

In his Sanderson-Wells lecture which we publish this week, Professor Dodds launches a brilliant counter-attack against those of us who demand "natural" food. Certainly few would nowadays care to maintain that the seeds of wheat, maize, and rice were primarily and perfectly devised for the nutrition of mankind and must therefore be eaten exactly as provided by Nature. Most of us, when driven by his arguments, will go so far as to agree with Professor Dodds that in the modern world wheat and the like should not be regarded as sacrosanct entities but rather as food materials to be adapted to our purposes as may seem best for the satisfaction or preservation of our urban communities. Even so, having lived satisfactorily on natural foods for hundreds of thousands of years, we may fairly plead for the least possible interference with their character. Professor Dodds can easily persuade us that refrigeration, or heating, or sterilisation are essential; but it is a sound instinct that makes us unwilling to accept the chemical treatment of food as comparable with these traditional physical methods. Moreover, food chemistry is a new technique, and even the kind of elaborate animal experiments that Professor Dodds envisages would be a sketchy basis for chemical alteration of any of the basic nutrients of a nation. All sensible people will accept what is necessary; but the duty of proving that some chemical must be added to a traditional food rests squarely on the people who add it and the Government who authorise its addition. As regards the agene treatment of flour, this duty remains undischarged[5]; and the speech of the Government spokesman in the Lords reflects once again an attitude which Sir Edward Mellanby described two years ago[5A] as "disturbing, not only in itself, but because it indicates a reluctance to consider seriously the wider problem of chemical manipulation of food and its relation to health and disease."

Hazards of Phenylbutazone Treatment

Since the encouraging first reports by Currie[6,7] of the clinical use of 1 : 2-diphenyl-3 : 5-dioxo-4-*n*-butylpyrazolidine (phenylbutazone, 'Butazolidin') in the treatment of rheumatoid arthritis it has been widely used, both here and in America, against this and other rheumatic conditions, including ankylosing spondylitis, osteo-arthritis, and gout. Subsequent investigations[8,9] have confirmed the value of the drug in relieving symptoms, but have revealed a high incidence of toxic side-effects. Recent reports emphasise the more serious of these, and it is now clear that phenylbutazone can be dangerous. The physician, as so often happens, has to weigh advantage against risk.

The superiority claimed for phenylbutazone in the treatment of rheumatism lies in its analgesic property. In a discussion last week at the Royal Society of Medicine (reported on an earlier page) many physicians agreed on this point; and Dr. Freeland and his colleagues, whose article appears on p. 1227, offer further evidence of the subjective improvement induced by phenylbutazone in active rheumatoid arthritis. Objectively they find equally favourable results—although it should be noted that relief of pain may contribute to abatement of signs. It is clear that no permanent improvement is to be expected from phenylbutazone in rheumatoid arthritis. At the Royal Society of Medicine Dr. Rhys Davies showed that the grading of severity is not significantly affected by treatment. He is impressed, however, by the feeling of well-being induced in such cases by the relief of pain and by the accompanying functional improvement. Phenylbutazone may give this relief when other drugs have failed—a feature of undoubted importance to the patient. It is not seriously contended that phenylbutazone exerts any specific antirheumatic effect; no constant fall in sedimentation-rate accompanies its administration, and serial biopsy of rheumatoid nodules shows no change in the microscopic appearances.[10]

Dr. Freeland and his colleagues encountered no major toxic complications, perhaps owing to their prudence in stopping the drug in half the cases against scurvy After Professor **Kark** had made the observation that Gurkhas with low dietary levels of ascorbic acid had better physical achievements than a Harvard crew, Dr **King** emphasised that the National Research Council allowance should not be regarded as a "requirement", Prof E J. **Bigwood** (Brussels), however, equated "requirements" with "allowances" Mr A L **Bacharach** thought that the National Research Council figure ought to be high, because if it applied to foods as purchased there could be losses in cooking, and if it applied to the average person there would be a frequency distribution about the mean and therefore about half the population would need more than the mean Dr **Harris** closed the discussion with the remark that we must agree to differ on the question of requirements

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[5] *Lancet*, March 21, 1953, p. 581; April 4, p. 686.
[5A] Mellanby, E. *Brit. med. J.* 1951, ii, 863.
[6] Currie, J. P. Proceedings of the 2nd European Congress of Rheumatology, 1951; p. 417.
[7] Currie, J. P. *Lancet*, 1952, ii, 15.
[8] Kuzell, W. C., Schaffarzick, R. W., Brown, B., Mankle, E. A. *J. Amer. med. Ass.* 1952, 149, 729.
[9] Davies, H. R., Barter, R. W., Gee, A., Hilson, C. *Brit. med. J.* 1952, ii, 1392.
[10] Engleman, E. P. *Ann. rheumat. Dis.* 1952, 11, 297.

It may be noted, however, that the National Research Council figures are specifically stated to refer to the "content of foods as eaten and [they] do not allow for losses in storage, cooking, and serving", further they are "levels enough higher to cover substantially all individual variations in the requirements of normal people"

* * *

Lack of time for full discussion immediately after papers was the obvious defect of the symposium which had been otherwise excellently arranged by Mr C P **Stewart**, PH D, and Dr A P **Meiklejohn** This lack was most obvious in the case of a paper from Dr S B **Wolbach** (Boston, Mass) on the histology of scurvy, extracts of which were read in his absence

Wolbach's views are controversial, but could not be controverted The controversy concerns the nature of the defect in connective tissue in scurvy In the scorbutic animal fibroblasts produce a metachromatic-staining material containing polysaccharides, and collagen is not formed, it is not certain whether the defect is in extracellular gelation or in the production of a precursor or factor by connective tissue cells There seems little doubt that collagen can be maintained but not adequately formed in the scorbutic animal, and King[6] has shown that ascorbic acid is not part of the chondroitin sulphate or collagen molecule Wolbach believes the defect is not in the production of the precursor of collagen, but in the extracellular conversion of the precursor into collagen, he thinks[7] that the pink-staining amorphous extracellular material in scorbutic tissues is the precursor of collagen Follis,[8] however, showed that this material was not produced in the bone of scorbutic animals unless those bones are subjected to stress, he regards Wolbach's gelation theory as unproved Both schools regard the changes in bone, teeth, and gums in scurvy as secondary to the failure to form connective tissue This has been summarised by Meiklejohn, Passmore, and Stewart

> "Wolbach showed a loss of collagen from connective tissues and a disappearance of intercellular cement As a result the cells forming the walls of the capillary blood vessels fail to stick together and this gives rise to the characteristic hæmorrhages There is also defective formation of dentine in the teeth and of the special tissue (osteoid) responsible for the growth and repair of bones Thus the three outstanding anatomical lesions of scurvy—the hæmorrhages, the loosening of teeth, and the bony deformities—can be traced to a single cause the failure in the supply of collagen for maintenance of connective tissue and intercellular cement"[1]

Here we can see that the controversy is even broader than the precise defect in production of collagen for, first, it is generally believed that in scurvy there is no *loss* of collagen but a failure to form it (once formed it can be maintained), secondly, capillary *permeability* is probably a function of the intercellular cement and is independent of ascorbic acid, whereas capillary *strength* is often but not always decreased in scurvy since there is weakening of the collagen surrounding the capillary wall and no weakening of the wall itself the endothelial intercellular cement being normal in scurvy[9], thirdly, the defective formation of dentine has no causative relation with the loosening and shedding of the teeth in scurvy which Lind so graphically described

The biochemical lesion underlying these histological changes is not known Possibly ascorbic acid or its oxidation products are concerned in setting up -S S bonds that link the protein chains in collagen A most important metabolic defect in scurvy concerns the oxidation of tyrosine Sealock[10] showed in 1940 that the metabolism of this amino-acid was defective in scurvy, next year Levine[11] and his colleagues reported that premature infants fed on cow's milk, a diet high in protein and low in ascorbic acid, excreted large amounts of derivatives of tyrosine in the urine unless ascorbic acid was given

Dr W J **Darby** (Tennessee) discussed the relation of ascorbic acid to tyrosine and hæmopoietic vitamins He supported the view that both ascorbic acid and folic or folinic acid are concerned in the oxidation of *p* hydroxyphenylpyruvic acid to 2, 5 dihydroxyphenylpyruvic acid which is then decarboxylated to give homogentisic acid he also supported the need of ascorbic acid for the conversion of folic to folinic acid

In the last year or two the stages in the oxidation of tyrosine through the compounds just mentioned have been elucidated and, although it is not certain that folic acid plays any part in them, ascorbic acid or its oxidation products are known to be concerned in the oxidation of *p* hydroxyphenylpyruvic acid and possibly in the later oxidation of homogentisic acid These biochemical aspects should have been discussed and it was a pity that there was no time for discussing each paper after it was presented, the short and somewhat desultory discussion at the end of the sessions achieved little

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CHILD HEALTH IN SCOTLAND

In 1949 a committee of the Scottish Health Services Council was set up, under the chairmanship of Mr Alexander Cunningham to review provision for child health in the country The committee has now reported,[12] and it suggests that the position should again be surveyed at the end of the first decade of the National Health Service

The committee urges the need for bringing together prevention and cure in all aspects of child care Other recommendations include the following

Antenatal period—In domiciliary practice there should be close coöperation between doctor and midwife and health

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8 Follis R H jun Pathology of Nutritional Disease Oxford, 1948
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12 Child Health Report of the Committee on Child Health of the Scottish Health Services Council H M Stationery Office Pp 21 9d

showing side-effects. Among the serious complications are sodium and water retention, leading to œdema; bleeding from the intestinal tract; and granulopenia. How far these are due to direct toxic action on tissues, and how far to acquired sensitivity is not known. Withdrawal of the drug may reverse the progress of complications; but at least 4 deaths from agranulocytosis attributable to phenylbutazone have been reported,[11] and the case described this week by Dr. DILLING adds another to this total. If granulopenia is a manifestation of drug allergy—and with amidopyrine (to which phenylbutazone is chemically related) this is probably so [12]—prolonged or repeated treatment may be expected to favour its occurrence. How this aspect of sensitisation is related to dosage is not known.

In these circumstances phenylbutazone should not be used merely as an alternative analgesic in rheumatism. Careful selection of patients and close attention to signs of toxicity are now rightly demanded [13]; and it is questionable whether these conditions can be fulfilled without hospital supervision.

Chemotherapy of Cancer

ADVANCES in chemotherapy of cancer have been slight in the past ten years,[14] save in the number of compounds tested, which now exceed 10,000. The sole gains relate to what is termed "management" in some forms of the disease, and to a little prolongation of something more than the mere spark of life in others. GELLHORN [15] has lately reviewed the most recent applications of chemical and hormone therapy based on extensive trials in man. The ideal would be chemicals with selective toxicity for tumour cells, leaving those of the host undamaged. This ideal is not yet in sight; for each of the effective chemical compounds is destructive to both. In judging the value of palliative drugs GELLHORN rightly insists on objective indices, such as fluctuation in size of lymph-nodes, fall in temperature, and restoration towards normal character and number of blood-cells. None of these criteria are applicable, however, to the largest group of tumours—those derived from epithelium.

Opinion about the value of œstrogens in breast cancer remains unchanged. As WALPOLE and PATERSON [16] suggest, their use should be limited to postmenopausal patients. Modifications in treatment of prostatic and mammary cancer have lately been summarised.[17] Adrenalectomy, combined with ovariectomy in the female, and cortisone substitution are being tried by HUGGINS.[18] This may be valuable when a tumour is adrenal-dependent, but dependence cannot be predicted before operation. In the late stages of lymphosarcoma and Hodgkin's disease cortisone and corticotrophin (A.C.T.H.) may bring the temperature back to normal and increase appetite; and bone-marrow function sometimes improves. The high hopes that these compounds would prolong life have not been realised: in acute leukæmia in children the prolongation of life is very small. Urethane is of use in chronic leukæmias when radiotherapy is contra-indicated or not available. Remissions lasting several months occur in about 30% of cases of acute leukæmia of childhood treated with modifications of folic acid (the anti-folic-acid chemicals aminopterin and A-methopterin); the median duration of life in those with remissions is twelve months, and further courses of treatment are progressively less effective. In the adult the disease is not modified at all. This disappointing outcome is in accordance with a previous forecast.[19] These drugs may be exceedingly toxic to normal blood-cells and to epithelium—more so, perhaps, than to the leukæmic cells, at least some of which eventually become drug-resistant. Refractoriness to these compounds and to cortisone and corticotrophin is, however, unrelated, so alternation in their use is worth a trial.

In Hodgkin's disease, in chronic leukæmias,[20] and to a less extent in disseminated lymphosarcoma, the nitrogen-mustard group of compounds is considered useful. When HN_2 is combined with radiotherapy the amount of irradiation required is materially reduced; patients remain symptom-free for the greater part of the treatment; and the burden of the illness is also significantly lessened owing to shorter periods in hospital and fewer applications of radiotherapy. The only other tumours which have responded to nitrogen mustards with sufficient regularity are bronchogenic carcinomas. Brief remissions of signs and symptoms, lasting two weeks to two months, have been induced. Similar or even longer remissions have been seen with X-ray therapy combined with administration of synthetic vitamin-K substitute ('Synkavit') in various tumours.[21]

There is something to be said for GELLHORN's suggestion that anti-tumour drugs should be screened clinically if and when criteria become available for measuring effects on tumours, especially those of epithelial origin. But not everyone will agree with some of his reasons. Experience has shown that there may be as much biological difference in behaviour between one human tumour and another at the same site as there is between similar animal and human tumours. Some respond to treatment while others, apparently identical, do not. Growth-rates of tumours, said to be so different in animals and man, must be related to the life-span of each species: the physiological events of three-score years and ten are crowded into the two and a half to three years of a mouse's life. Nor is it true that all animal tumours grow rapidly. Human tumours were always test objects for Coley's fluid and similar crude bacterial products [22] until SHEAR [23] with others identified the active necrotising agent in these products as a polysaccharide. Its action was analysed in animals, and has been ascribed to a capacity for inducing local hæmorrhage and thus inanition of the tumour. Against human tumours its performance has proved no better than in animals.[24] Keenly conducted screening techniques will take all these points into consideration.

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[11] *Brit. med. J.* 1952, ii, 1427; *Lancet*, Jan. 24, 1953, p. 192; Steinberg, C. L., Bohrod, M. G., Roodenburg, A. I. *J. Amer. med. Ass.* 1953, 152, 33; Etess, A. D., Jacobson, A. S. *Ibid*, 1953, 151, 639.

[12] Dameshek, W., Colmes, A. *J. clin. Invest.* 1936, 15, 85.

[13] Leonard, J. C. *Brit. med. J.* June 13, 1953, p. 1311.

[14] See *Lancet*, 1944, i, 21, 569; *Ibid*, 1944, ii, 20.

[15] Gellhorn, A. *Cancer Res.* 1953, 13, 205.

[16] Walpole, A. L., Paterson, E. *Lancet*, 1949, ii, 783.

[17] *Brit. med. J.* April 25, 1953, p. 924.

[18] Huggins, C. J. *J. Urol.* 1952, 68, 875.

[19] Dodds, E. C. *Lancet*, 1948, ii, 837.

[20] Gardikas, C., Wilkinson, J. F. *Ibid*, 1952, ii, 161.

[21] Mitchell, J. S. *Brit. J. Cancer*, 1949, 2, 251.

[22] Nauts, H. C., Fowler, G. A. A., Bogatko, F. H. *Acta med. scand.* 1953, suppl. 276.

[23] Shear, M. J. *J. nat. Cancer Inst.* 1943, 4, 461.

[24] Shear, M. J. *Ibid*, 1944, 5, 195.

visitor, where the last is not also the midwife, and the midwife should attend antenatal consultations. In some rural areas there may be room for more development of consultation clinics at which the general practitioner, the midwife, and the obstetric consultant should be present.

Neonatal period.—Special records should be kept of the condition of newborn infants, whether born in hospital or at home. The midwife engaged in domiciliary work should be able to detect conditions in the infant requiring medical attention. All maternity hospitals and maternity units of general hospitals should have special accommodation for sick, injured, and premature infants, and for isolation. Infants in maternity units should be under the care of a pædiatrician assisted by a house officer and, in a large unit, a registrar.

Child aged one month to one year.—Medical students should receive more instruction in infant hygiene and clinical pædiatrics, and general practitioners should attend refresher courses.

Pre-school child.—More advantage should be taken of the child welfare services by children of this age.

Child of school age.—A separate chief executive school medical officer should be nominated in the more populous counties. There should be an annual classroom inspection of all children who do not receive routine medical inspection during the year. The extent to which greater responsibility can be given to school nurses should be considered, and adequate clerical assistance should be provided for both medical and nursing staff.

Hospital and specialist services.—More bed accommodation should be provided, and the number of consultant pædiatricians should be increased. There should be interchange between clinical pædiatricians and medical officers engaged in child welfare work.

Integration.—In populous areas the child welfare clinic is essential. The coöperation of the consultant pædiatrician should be enlisted in the work of the welfare centres. The health visitor should play an important part in securing proper liaison between all parts of the National Health Service in relation to children. Where possible, institutes of child health should be established in which undergraduate and postgraduate training in pædiatrics could be undertaken.

MECHANICAL RESPIRATORS

The Ministry of Health, in a circular to hospital authorities (R.H.B. [53] 56), remarks that a working party has for some time been investigating problems connected with respirators. As a result a draft performance specification has been drawn up with which future respirators should comply.

Two entirely new respirators have been produced commercially, and have been approved by the working party. The cost of each will be about £800–1000; only a few will be available until 1954. Investigations are continuing into the development of a cuirass-type respirator, and of a simpler and cheaper cabinet respirator.

The working party has modified the Both respirator to make it more efficient. For this modification kits of manufactured parts are to be made available, and the work can be done by hospital engineers with simple tools. The cost of the kit is expected to be about £100. The changes, which agree closely with those devised in the Birmingham region,[1] are as follows:

Pump unit.—(1) a stronger motor platform; (2) a five step pulley pair; (3) improved bellows guides; (4) improved bellows, with extension pieces; (5) improved positive-pressure valve; and (6) improved hand-pumping gear.

Cabinet.—(a) Four arm ports each side of the body, one included in a bedpan port; (b) large window fitted into the top of the cabinet near the head end, the existing circular window being moved down towards the foot end; (c) alarm system, battery operated; (d) improved negative pressure valve fitted with friction stop and engraved calibration; (e) dial type aneroid pressure indicator; (f) improved body tilting gear; (g) raising the bed height and making the body unit mobile by fitting castors and brakes; (h) providing screws for tilting or raising the head end of the mattress; (i) providing a foot board; and (j) improved stretcher bearing roller.

It is likely that a split front and split collar will be recommended later when the parts become available. Meanwhile hospital authorities are asked to notify the Ministry without delay of the number of kits required.

The circular remarks that as an emergency measure the Both respirator may be further modified to make postural drainage possible. The patient is placed supine in a respirator of which the sloping front has been cut away vertically and replaced in this position with rubber seal and clips and head support.

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[1] Smith, P. E. *Lancet*, April 4, 1953, p. 674.

The Wider World

THE HEALTH OF A TROPICAL PEOPLE

A Survey in Ceylon

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IV. EASTERN AND WESTERN MEDICINE

The people of Ceylon have the choice of receiving their medical treatment from practitioners trained in either the Western or the Eastern systems of medicine.

The practitioners of the Eastern systems (in the following called Ayurvedic practitioners for convenience) include those trained in the Ayurvedic system, the methods of Siddha, and the Unani system. The practitioners of the Western system include, in Ceylon, graduates in medicine of recognised universities or medical colleges (in the following called Western practitioners), apothecaries in the Government service who have received a two year training in elementary medicine and, to relieve the shortage of fully trained Western practitioners, are attached mainly to out station, rural hospitals and dispensaries, and dispensers who have received some training in pharmacy and are to be found in charge of estate dispensaries.

Preferences of the People

The sample survey conducted in Ceylon in 1950 gave a general idea of the types of medical attention received by Ceylonese patients. It was based on door-to-door interviewing of 17,946 households, with 94,128 persons, from all districts, communities, and ethnic groups (Cullumbine 1952a), and one of the questions related to the nature of the medical care which was being given to the ill or disabled persons.

Western practitioners and Ayurvedic practitioners each treated a little over a quarter of the illnesses reported by the sample population. About 1 in every 20 sick people were receiving treatment from both types of practitioners and about 1 in 7 were not receiving any kind of specialised treatment (Cullumbine 1952b).

In general, Western practitioners treated a greater proportion of cases in the more serious diseases such as typhoid fever, tuberculosis of the respiratory system, malaria, dysentery, diseases of the circulatory system, bronchitis, pneumonia, and diseases of the genito-urinary system. By contrast, more cases due to the common cold, diarrhœa, dyspepsia, hæmorrhoids, deficiency diseases, rheumatic diseases, diseases of the skin, and conjunctivitis were treated by Ayurvedic practitioners. Western practitioners were, however, in charge of more of the normal and abnormal gestations, and this may be due to this provision of an antenatal and maternity service by the Government Medical Service. Illnesses of doubtful ætiology (e.g., the various mental disorders, paralyses, epilepsy, convulsions in children under 5 years) or illnesses which are refractory to treatment (e.g., the rheumatic diseases) received more attention from the Ayurvedic than from the Western practitioner. These were also the illnesses—along with tuberculosis, diseases of the genitals, and senility, all of

Annotations

EXPERIMENTAL INJURIES OF THE SPINAL CORD

It is generally recognised that in spinal injuries with involvement of the cord, damage to the cord occurs at the time of the injury, and that only in rare instances is it the result of continuing compression. For this reason, and because of the disappointing results of laminectomy in these cases, operative exposure of the cord is rarely carried out in the early stages of closed injuries; and in the later stages there is seldom much to be achieved by operation, except in the occasional patient where early improvement has given place to progressive impairment of cord function. Freeman and Wright[1] have investigated the question of spinal-cord damage experimentally, and they have produced evidence that, under the artificial conditions of their animal experiments, immediate operation on the cord may result in definite preservation of spinal-cord function. There is considerable difficulty in applying a standardised form of injury to the cord which can be reproduced in a series of experiments, and Freeman and Wright finally decided that direct, rather than indirect, trauma would be the most suitable. Their preliminary experiments were performed on rats. The spinal cord was exposed in the mid-dorsal region and a lucite rod, concave at one end, was placed vertically on the cord. A glass tube was placed over this lucite impounder, and trauma was applied by a mercury-filled glass rod which was dropped through this glass tube on to the impounder; this method made it simple to vary the force applied in different experiments. Three series of rats were studied: in one group a laminectomy alone was performed; in the second trauma was applied following laminectomy; and in the third group, immediately after the trauma, the pia mater was incised and an incision was made in the midline of the posterior aspect of the cord and extended for the length of the laminectomy through approximately half the thickness of the cord. With a force of 25 g. cm., paraplegia could be produced in the rats; and when they were studied for up to three weeks after trauma, recovery was commoner in the animals in which the pia had been opened and a blunt myelotomy performed.

These results suggested that operation might be helpful in diminishing the effects of the cord injury, so further studies were made on dogs. The experimental procedure used in two groups of dogs was the same as in the rat experiments, except that a force of about 400 g. cm. was used, and in the operation group, following posterior myelotomy, a gentle stream of warm saline was directed into the incision in the cord and necrotic tissue was washed out. Of the 9 animals in which immediate operation was performed following the experimental injury, 3 recovered sufficiently to walk reasonably well within a few days to five weeks, and another regained some power in the hind legs; but there was no recovery of function in the animals in which the cord was injured and no further operation was performed. In a further series of dogs a rather different procedure was used: a single laminal arch was fractured with an osteotome and then swung to one side; the impounder was then inserted and the spinal cord was injured as in the previous experiment. In the control group the lamina was replaced and the wound closed; and in the second group a formal laminectomy was carried out and the spinal cord was treated operatively as in the earlier experiments. In the control group only 4 out of 12 animals regained any function, and, of these, 2 were severely incapacitated: while in the operated group 8 out of 10 showed some degree of functional recovery. These results suggest that operation immediately after injury is of benefit in preserving some degree of spinal-cord function in a proportion of the animals, and Freeman and Wright propose to carry out further experiments to find out how long after injury operation can be delayed. The direct trauma used in these animal experiments is not really comparable with the indirect trauma which commonly causes spinal injuries in man; but if further work confirms these findings, early operation, by incision of the pia and posterior myelotomy, must be considered as a possible treatment of spinal injuries in man.

AN ANTIVIRAL SUBSTANCE

Hitherto the small viruses have been rather inaccessible to chemotherapeutic agents, so it is interesting to read a report by Shope[1] on an antiviral substance derived from *Penicillium funiculosum* (Thom). The active material, which he has called helenine, showed slight but definite antiviral action when tested against two neurotropic viruses—the Columbia SK encephalomyelitis virus of mice and the Semliki Forest virus. In early experiments slight activity against swine-influenza virus was noted, but this result could not be reproduced later. Helenine was most readily obtained by mechanical bruising in a Waring blendor of the pellicle formed in *P. funiculosum* cultures, followed by solution in culture fluid and precipitation by acetone. Its effect was most obvious when it was given in one or two injections from a few hours before until twenty-four hours after infection with 10 to 1000 minimal lethal doses of virus. Under favourable conditions helenine protected up to about half the treated mice or caused a significant delay in death. Its mode of action is not clear, but it seems either to slow the rate of virus multiplication or to prevent invasion of the mouse brain; for in the early stages of infection there was less virus in the brains of the treated animals than in the controls. Little is known of its chemistry, but extracts are viscous and contain a high proportion of polysaccharide.[2]

Shope tells us that the penicillium was recovered from the isinglass cover of a photograph of his wife, Helen—hence the name helenine. This method of naming chemotherapeutic substances is unusual and might cause difficulties if a mould happened to lodge on a *View of Battersea Power Station from Chelsea Bridge*, for example. But this is a matter which can safely be left to the nomenclature committees of the next Microbiological Congress, with perhaps a little assistance from the Royal Academy.

COLOURED NAILS

It is refreshing to read a description of a clinical investigation made without elaborate equipment. For centuries white spots on the nails have been found puzzling. They have their own folklore and an extensive medical "literature." Only now has an observer had the patience to study their natural history. Mitchell[3] charted the position of white spots on his nails daily for a year. He discovered that such spots not only may appear for the first time in the distal part of the nail, but may enlarge or disappear before the growth of the nail carries them to the free edge.

These white spots have commonly been ascribed to air-spaces in the nail, caused by small areas of imperfect cornification due to local or general disturbances affecting the nail matrix. The appearance of white spots in the distal portion of the nail suggests that the distal nail-bed may participate in the formation of the nail-plate. Many deny this, yet histological evidence supports the possibility. Nail and hair cortex are formed without the against scurvy After Professor **KARK** had made the observation that Gurkhas with low dietary levels of ascorbic acid had better physical achievements than a Harvard crew, Dr **KING** emphasised that the National Research Council allowance should not be regarded as a "requirement", Prof E J. **BIGWOOD** (Brussels), however, equated "requirements" with "allowances" Mr A L **BACHARACH** thought that the National Research Council figure ought to be high, because if it applied to foods as purchased there could be losses in cooking, and if it applied to the average person there would be a frequency distribution about the mean and therefore about half the population would need more than the mean Dr **HARRIS** closed the discussion with the remark that we must agree to differ on the question of requirements

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[1] Freeman, L. W., Wright, T. W. *Ann. Surg.* 1953, 137, 433.

[1] Shope, R. E. *J. exp. Med.* 1953, 97, 601, 627.

[2] Shope, R. E. *Ibid*, p. 639.

[3] Mitchell, J. C. *Brit. J. Derm.* 1953, 65, 121.

It may be noted, however, that the National Research Council figures are specifically stated to refer to the "content of foods as eaten and [they] do not allow for losses in storage, cooking, and serving", further they are "levels enough higher to cover substantially all individual variations in the requirements of normal people"

* * *

Lack of time for full discussion immediately after papers was the obvious defect of the symposium which had been otherwise excellently arranged by Mr C P **STEWART**, PH D, and Dr A P **MEIKLEJOHN** This lack was most obvious in the case of a paper from Dr S B **WOLBACH** (Boston, Mass) on the histology of scurvy, extracts of which were read in his absence

Wolbach's views are controversial, but could not be controverted The controversy concerns the nature of the defect in connective tissue in scurvy In the scorbutic animal fibroblasts produce a metachromatic-staining material containing polysaccharides, and collagen is not formed, it is not certain whether the defect is in extracellular gelation or in the production of a precursor or factor by connective tissue cells There seems little doubt that collagen can be maintained but not adequately formed in the scorbutic animal, and King [6] has shown that ascorbic acid is not part of the chondroitin sulphate or collagen molecule Wolbach believes the defect is not in the production of the precursor of collagen, but in the extracellular conversion of the precursor into collagen, he thinks [7] that the pink-staining amorphous extracellular material in scorbutic tissues is the precursor of collagen Follis,[8] however, showed that this material was not produced in the bone of scorbutic animals unless those bones are subjected to stress, he regards Wolbach's gelation theory as unproved Both schools regard the changes in bone, teeth, and gums in scurvy as secondary to the failure to form connective tissue This has been summarised by Meiklejohn, Passmore, and Stewart

> "Wolbach showed a loss of collagen from connective tissues and a disappearance of intercellular cement As a result the cells forming the walls of the capillary blood vessels fail to stick together and thus gives rise to the characteristic hæmorrhages There is also defective formation of dentine in the teeth and of the special tissue (osteoid) responsible for the growth and repair of bones Thus the three outstanding anatomical lesions of scurvy—the hæmorrhages, the loosening of teeth, and the bony deformities—can be traced to a single cause the failure in the supply of collagen for maintenance of connective tissue and intercellular cement"[1]

Here we can see that the controversy is even broader than the precise defect in production of collagen, for, first, it is generally believed that in scurvy there is no *loss* of collagen but a failure to form it (once formed it can be maintained), secondly, capillary *permeability* is probably a function of the intercellular cement and is independent of ascorbic acid, whereas capillary *strength* is often but not always decreased in scurvy since there is weakening of the collagen surrounding the capillary wall and no weakening of the wall itself the endothelial intercellular cement being normal in scurvy [9], thirdly the defective formation of dentine has no causative relation with the loosening and shedding of the teeth in scurvy which Lind so graphically described

The biochemical lesion underlying these histological changes is not known Possibly ascorbic acid or its oxidation products are concerned in setting up -S S bonds that link the protein chains in collagen A most important metabolic defect in scurvy concerns the oxidation of tyrosine Sealock [10] showed in 1940 that the metabolism of this amino acid was defective in scurvy, next year Levine [11] and his colleagues reported that premature infants fed on cow's milk, a diet high in protein and low in ascorbic acid, excreted large amounts of derivatives of tyrosine in the urine unless ascorbic acid was given

Dr W J **DARBY** (Tennessee) discussed the relation of ascorbic acid to tyrosine and hæmopoietic vitamins He supported the view that both ascorbic acid and folic or folinic acid are concerned in the oxidation of *p* hydroxyphenylpyruvic acid to 2, 5 dihydroxyphenylpyruvic acid which is then decarboxylated to give homogentisic acid he also supported the need of ascorbic acid for the conversion of folic to folinic acid

In the last year or two the stages in the oxidation of tyrosine through the compounds just mentioned have been elucidated and, although it is not certain that folic acid plays any part in them, ascorbic acid or its oxidation products are known to be concerned in the oxidation of *p* hydroxyphenylpyruvic acid and possibly in the later oxidation of homogentisic acid These biochemical aspects should have been discussed and it was a pity that there was no time for discussing each paper after it was presented, the short and somewhat desultory discussion at the end of the sessions achieved little

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But the meeting closed in the evening with an excellent dinner that included scurvy-grass, adrenal cortices, and paprika, a dietitian expressed herself satisfied that the vitamin-C content of the meal reached at least the 75 mg recommended by the National Research Council Here there was some confusion of sex, for the figure of 75 mg relates to men, but this confusion was perhaps started by Sir Edward Appleton who at the opening ceremony spoke of "the dietitian himself", and a few minutes later one wondered whether the dietitians who had pressed 300 mg daily on Sir Sheldon Dudley were male and if so were in fact dietitians But the presence of one of the four honorary members of the Nutrition Society at the dinner (Dame Harriette Chick) reminded us that excellent experimental work on vitamin C had during the past years been contributed by men and women working partly on guineapigs and partly on man This now knowledge is today applied in the prevention of scurvy in a way that would have satisfied Lind

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IN 1949 a committee of the Scottish Health Service Council was set up, under the chairmanship of Mr Alexander Cunningham to review provision for child health in the country The committee has now reported,[1] and it suggests that the position should again be surveyed at the end of the first decade of the National Health Service

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production of keratohyalin, and the "hard keratin" which results has physical and chemical peculiarities. The distal nail-bed as well as the matrix has no granular layer, and unless it were "onychogenic" one would expect to find it giving rise to parakeratotic horn, which is friable. The enlargement and disappearance of these spots are less easily explained if they are due to structural changes in the nail, since one must then assume that fully formed nail is still alive. If the white spots were due to foci of parakeratosis it seems most improbable that this could be altered to give rise to normal nail.

White spots are common in normal people but are apparently confined to the finger-nails. They may be congenital and affect a single nail or part of a nail. Disorders to which leukonychia has been ascribed include psoriasis, leprosy, fevers, arsenic and thallium poisoning, fluorosis, and trichinosis. The common disorders of the nails—psoriasis, eczema, and fungus infections—usually discolour the nails yellow, brown, or black. With subungual hæmorrhage the nail is blue or black. An unfamiliar cause of such hæmorrhage is epidermal hypersensitivity provoked by "undercoats" applied to render nail-varnish more permanent. Argyria causes bluish-violet coloration of the nails; and a fixed drug eruption due, for example, to phenolphthalein may appear in the nail-bed as a dusky erythematous patch. Violaceous bands have been seen in congenital syphilis; and those who served in the Far East in the late war became accustomed to a purplish discoloration of the nail-bed in men who were taking mepacrine prophylactically. Green nails have been attributed to infection with common skin fungi or to superinfection with *Pseudomonas aeruginosa*. Heller [4] lists as occupational stigmata green nails in pea-shellers, red nails in vineyard workers, and black nails in feltmakers; and he has seen blackish-brown nails in April to June, due to exposure to formic acid, in "seekers after ants' eggs."

ASSESSMENT OF LEUCOTOMY

Prefrontal leucotomy should be a convenient meeting-ground for clinician and experimental psychologist. By providing what is practically an experimental incision into the frontal lobe it has challenged the ingenuity of the research-worker to uncover the functions of a part of the brain of which little is known with precision. At first this ingenuity was limited to speculation, and "a skyscraper of theory was erected on an unstable foundation of insufficient fact" [5]; but when the experimental psychologist entered the field, the ingenuity was extended to method. One American worker, who had complained that "not a single patient has been adequately studied," [6] produced a book [7] in which mathematical treatment ran riot; and the same line of approach is taken in an article by Le Beau and Petrie.[8] Giving brief statistical conclusions from the application of ten or more tests to 35 patients, who among them had some twelve different operative lesions, this work adds to the number of combinations of cuts, tests, and patients which Mrs. Petrie described previously.[9] The risk in such work, however, is that zeal for objectivity may lead to a preoccupation with technique. The clinician, at least, is likely to find himself less interested in the test data than in the authors' observation (mentioned almost as an afterthought) on the patients' attitude to time. We know that after leucotomy some patients have an altered appreciation of time, and this is something not yet analysed. In relation to pain, Le Beau and Petrie say there is increased orientation to the present, as opposed to the past and future; the leucotomised patient contends with present pain only, thus making a long-continued pain more bearable. This touches one of the clinician's topical interests, and is the kind of observation that could be followed by an empirical investigation along traditional lines.

"Science," says Professor Zangwill, "aims at a quantitative treatment of its data, but the scientist should never allow himself to become bemused by the prestige of numbers." [10] "In studying problems of temperament," he continues, "it may well turn out that the descriptive method, despite its notable lack of precision, has the greater value. Empirical science is not in the first place a technique: it is an attitude of mind." To the clinician it must seem that what is needed for the assessment of leucotomy is the use of established case-history methods, but in a more controlled fashion than is commonly needed in clinical practice, combined (where appropriate) with a more generous and flexible use of psychometric tests.

TOXICITY OF CHLORAMPHENICOL

Administration of chloramphenicol may result in aplastic anæmia [11] or other side-effects, including anaphylactic reactions, cutaneous eruptions, moniliasis, and irritation of the mucous membranes. Lasky et al. [12] describe a case of bacterial endocarditis in which administration of 6 g. of the drug daily for six weeks led to severe anæmia followed by retinal hæmorrhages and bilateral optic neuritis. After the chloramphenicol was discontinued the anæmia disappeared, but the vision remained seriously and permanently affected. This report should not deter doctors from using chloramphenicol; for the dosage was very large, and the drug was given for a long period. It is well known that compounds containing a benzene ring with a nitro-group attached—as in chloramphenicol—are potentially toxic. In moderate dosage, and for short-term administration, chloramphenicol is safe enough; but the use of other antibiotics should always be considered if medication has to be long continued.

COUNTING BACTERIA

In microbiology it is often necessary to determine the number of living or dead bacteria contained in a fluid—for example, milk or a bacterial vaccine. The number of living organisms is usually estimated by counting the number of colonies which develop after a known volume of the fluid has been spread over a solid medium; while total bacteria, living or dead, are usually enumerated by comparing the fluid with tubes of standard opacity. Both these techniques are subject to various errors, and their use in assessing the proportion of living bacteria in a fluid is liable to be fraught with inaccuracy. Valentine and Bradfield [13] have now described an elegant and accurate method for determining the number of living and dead bacteria simultaneously. The method depends on the fact that 3% urea inhibits cell-division of certain organisms but does not affect cell-growth, so that living bacilli develop into long filaments, which can easily be distinguished microscopically from the normal-sized dead bacilli.

By this method a collodion film, supported on a stainless-steel specimen grid, is laid on to nutrient agar containing 3% urea. A drop of the fluid in which the bacteria are to be enumerated is placed on the collodion and the whole is incubated at 37°C for 3 hours. The grid is then fixed in osmium tetroxide or formalin vapour, washed in distilled water, dried, and examined with an electron microscope. The proportion of living organisms

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medical services, including maternity. His application named his residence as the place where he would attend for treating health service patients and stated his proposed hours for the purpose. In the following month he was accordingly placed on the list, and he so continued, except that in November, 1951, his name was (by agreement) omitted from the separate part of the list which contains the names of those undertaking to provide maternity medical services. In the same month of November he notified the council of a change in his hours for treating patients which does not appear material to the findings. In June, 1949, he asked the council's permission for a grant for training Dr. P. as an assistant. This was sanctioned. From June to October he employed Dr. P. as his paid assistant. From Aug. 2 she was in effect conducting the practice at his residence by herself; on that date he took a whole-time appointment at the X hospital where he continued to serve (full time) till March 2, 1952. The tribunal found that he had at one stage suggested to Dr. P. that she should become his trainee assistant, but she never acted as such. He filled up a form (E.C. 45) stating that she so acted from July 1 to Sept. 30, and claiming £191 2*s.* with £40 19*s.* for boarding expenses. He asked Dr. P. to sign the form; she refused and sent the form unsigned to the council. Dr. M. and Dr. P. had a difference of opinion about his conduct of the practice, and in October he dismissed her from his service.

In November Dr. M. engaged Dr. W. as a trainee assistant and informed the council that he had done so. During 1950 he completed four quarterly claims for training grant, signing them and obtaining Dr. W.'s countersignature; on these claims he drew sums totalling £697 4*s.* 4*d.* From Oct. 10 to February, 1952, he employed her as an ordinary assistant. Dr. W. told the tribunal that she discussed cases with Dr. M. in the evenings (like Dr. P. she lodged in the house of Dr. and Mrs. M.), that she learnt a good deal from him, and that he did his best to supervise and train her. The tribunal has found, however, that he neither gave, nor was in a position to give, any sufficient training to Dr. W., as he was already employed in a whole-time hospital appointment elsewhere. The tribunal has no doubt that he committed a serious fraud upon the council by claiming and receiving sums of money, as he did, for training Dr. W. when he was engaged whole time at a hospital a considerable distance away from the place where the trainee assistant was employed.

The council received information from the Ministry of Health in November, 1951, about Dr. M.'s hospital appointment. His reply to the council's consequent inquiry referred to "my letter of the 7th October, 1950, explaining the position." As no such letter could be traced he was asked for a copy of it. The copy which he furnished stated that as from Oct. 10 Dr. W. would be acting as his full-time assistant, and that, unless he heard to the contrary, he would assume that the consent given for her to act as his trainee assistant would continue for her new status. The tribunal observed that a year earlier (and two months after the date of the missing letter) the council had asked Dr. M. to complete a return on which questions were asked as to his employment of an assistant and as to his own effective service under the National Health Service. Receiving no answer, the council drew his attention to his omission to complete the form and sent him a further questionary asking (among other things) if he employed an assistant and, if so, whom, and whether he was substantially employed on other work and, if so, what. To this he replied on Dec. 30, 1950, that he proposed to retire from the service on March 31, 1951; he asked that this letter should be accepted as notice of his intention.

The tribunal found no evidence that Dr. M. had written the letter of Oct. 7, 1950. They consider it quite untrue, and quite untrue to his knowledge, that he ever sent such a letter. They find that Dr. M. has "over a substantial period of time committed serious breaches of his terms of service . . . and has carefully taken deliberate steps to deceive [the council] as to the true state of affairs." He has "perpetrated a gross financial fraud" upon the council. Four witnesses, it is stated, were tendered to the tribunal by the complainant council; Dr. M. was present at the hearing but neither gave evidence himself nor called any witnesses.

While the onus must be upon the complainants to prove allegations which, if established, will affect the livelihood of a practitioner, it is difficult to see on what grounds the Minister could have reversed the tribunal's decision.

Parliament

Processed Foods

IN the House of Lords on June 10, Lord TEVIOT called attention to the high proportion of processed and chemically treated foods now consumed, and urged the Government to do everything possible to increase the availability of fresh food in the interests of public health. He said he was a trustee of what was perhaps the biggest clinic in the country and the number of people who came in for special diet there was very large. In the rise of agene, and other so-called improvers of bread, was to be found one of the great dangers to the general health of the people. He hoped that the Zuckerman Committee would go into the question whether poisonous sprays used on crops infiltrated into the human body. He had seen people who had eaten fruit that had been sprayed and who had undoubtedly been poisoned thereby. The late Sir Jack Drummond had once told him that if the people of this country could be fed on fresh home-grown and home-killed food he believed that in twenty years the hospitals would be nearly empty. It would be an advantage if school-children were told what they should eat and how they should eat it, instead of being lectured on sex. The degradation of our daily bread had reached a stage which made it vital that a halt should be called at once: the wheat germ and wheat-germ oil should never be taken out of bread. Summing up, Lord Teviot said that the comfort of our "tummies" greatly affected our point of view and attitude to everyday problems. In nearly every hotel in the country could be seen slot-machines containing stomach powders, aspirin tablets, and purgatives. Properly fed people did not need these drugs. Far too many people were making fortunes out of tampering with natural food, and there were far too many people making vast sums out of the antidotes to eating these bad foods.

THE DEBATE

Lord HANKEY, who had a motion on the paper urging the Government to reconsider the use of agene in flour for human consumption, explained that he would not move it until after the debate if necessary. In support of Lord Teviot's motion, he said that agene was a by-product of the white-bread complex which for 200 years had been the cause of much adulteration of food. It was not until the early 18th century that the popular craze for white food became serious. Until then it had been the luxury of the rich and the new craze started mainly in the towns; but, as the wheat crop was often insufficient to supply the need, the adulteration of bread followed. Alum, the principal improver for 100 years or more, was a double sulphate of aluminium and potash. It was found to be harmful to the internal organs and the townsfolk became afflicted by chronic dyspepsia, while their children were described as "pale, puny, lingering and sickly." But despite their sufferings, the warnings of doctors and scientists, and the repeated efforts of Parliament between 1750 and 1800 to foster the sale of standard bread, our people clung to their adulterated white bread as obstinately as they did today. What else could have been expected? There was no established principle to guide Governments. But in the 1850s, thanks largely to *The Lancet* and *Punch* (whose editors Lord Hankey hoped would take note)—*The Lancet* had already broken a lance on agene—the Government was goaded into action. After an official inquiry by a select Parliamentary Commission, remedial legislation was enacted, but often rather feebly administered. About the year 1877 a new trouble arose through the introduction of steel rollers to replace the old grindstones. The result was what the late Sir Jack Drummond called "poverty bread" because it had been robbed of its essential vitamins and minerals. Though it may have made fortunes for the trade, it completed the ruin of the nation's teeth. The tragedy of this "poverty bread" was that its dangers were unsuspected and were only discovered some 50 years later, about 1925, after the establishment of the Medical Research Council.

But the health aspect of white bread was still disregarded and, in spite of the improvement inaugurated by Lord Woolton during the war, the country was now is readily determined by a differential count of the numbers of filamentous and normal cells.

The method appears to give accurate results within the limits of normal sampling errors. It has its disadvantages, however. The use of an electron microscope is perhaps not essential, though it seems to provide the only reliable means of distinguishing between very short bacilli and particles of medium or detritus. Electron microscopy is also necessary if lysed cells are to be included in the count. The main disadvantage of the technique is that it cannot be used to count cocci, which do not develop into giant forms in the presence of urea, or organisms which normally contain filamentous cells. The organisms which have been counted successfully are various strains of bacterium, chromobacterium, pseudomonas, and a paracolon bacillus.

The usefulness of this method in routine work is clearly limited, but it may find a place in the armamentarium of the research-worker. Valentine and Bradfield have applied it successfully to the study of the resistance of bacteria to drying and also of the effects of radiations on bacterial cells.

MALIGNANT SYNOVIOMA

TUMOURS arising from synovial membrane were first described in 1910 by Lejars and Rubens-Duval.[1] Not all tumours in synovial tissue, however, are synoviomas; and de Santo et al.[2] have for this reason criticised the use of the term. Today "synoviomas" are known to fall into two groups—the malignant and the benign. Harkness,[3] Hale,[4] and others have emphasised that at operation the former may appear innocent.

In 47 examples of malignant synovioma collected by Wright,[5] close on three-quarters of the patients died of generalised metastases, with an average survival-time of twenty-three months. 10 are still alive today: 2 have survived twenty-four and thirteen years, while 4, though still alive after nine years, have had recurrences of the tumour. The findings of King[6] in a smaller series are substantially similar. The majority of the malignant tumours studied by Wright were devoid of giant-cells, but even in the most malignant of them synovial characters were recognisable: they were, therefore, essentially mixed tumours, and either the endothelial or the sarcomatous element preponderated—usually the former. In the well-differentiated and sometimes encapsulated forms of malignant synovioma, cavity formation was conspicuous; and then, but for the fact that the lining cells had no true border but merged imperceptibly with the diffusely arranged surrounding cells, their differentiation from true epithelial cells became somewhat difficult. The first of the 2 cases described by Harkness,[3] for instance, distinctly resembles a spheroidal-cell carcinoma of the breast, as also does the original case figured by Lejars and Rubens-Duval. Haagensen and Stout[7] illustrate in their series well-differentiated columnar cells. Carcinomatoid features in the malignant synovioma are paralleled in certain inflammatory states of synovial membrane by an exuberance of the endothelium with groups of spheroidal cells resembling epithelium. In the well-differentiated forms of malignant synovioma, sarcomatous and endothelial elements are usually equally prominent, the former being mainly spindle-cells with varying amounts of collagen. Mucin production is usual. Giant cells are occasionally seen in malignant synoviomas, and confusion may then arise with the benign variety; in Wright's experience, however, the malignant tumours are the more cellular and show fairly numerous foci of necrosis, mitoses, and a tendency to form synovial cavities. The only giant-cell synovial tumours which metastasised were distinctly anaplastic, and for that reason were readily recognised. Infiltration of muscle, however, was noted in one of the well-differentiated giant-cell tumours, so that their malignant character cannot be doubted.

Fisher,[8] de Santo et al.,[2] and King[6] have all built up their histological classifications on slightly different lines; but they recognise the essential unity of the malignant synovioma. King remarks that in assessing the malignancy of any particular tumour it is necessary to consider the characters of any group of rapidly growing cells rather than the general degree of differentiation found throughout the tumour. Metastases may be confined to the regional lymph-nodes but are apt to be widespread: the lungs and the bones are evidently common sites. Cases have been recorded where metastases developed seven, ten, and twelve years after amputation. Of Wright's series a definite history of local injury was obtained in 28%; but in only 1 of the 17 cases reported from the Massachusetts General Hospital by Hale[4] was there a reliable history of trauma. de Santo and his co-workers concluded that trauma occasionally initiated symptoms but by no means produced the tumour. Rarely, they thought, a chronic bursitis might predispose to the onset of a synovial sarcoma.

The commonest site of this tumour seems to be the lower limb, especially in the region of the knee. Fisher[8] drew attention to tumours histologically of the same pattern but occurring in the limbs outside joints and not in relation to bursæ or tendon-sheaths; while Haagensen and Stout[7] emphasised that often the tumour does not arise in actual synovial membrane. King[6] believes that, given the appropriate stimulus, connective-tissue cells anywhere are capable of the particular kind of differentiation found in synoviomas. The tissue-culture studies of Vaubel[9] show the potentialities of embryonic synovial tissue, especially histiocytic.

The radiographic findings are fairly characteristic but not diagnostic. A soft tissue mass in or near a joint, lobulated, often with a fine speckled type of calcium, and sometimes associated with periosteal proliferation, is suggestive of this disease.[4] For the encapsulated uniformly well-differentiated growths, Wright[5] regards local excision as adequate but in the poorly differentiated tumour amputation offers the only hope—and it is not a good one. The prognosis apparently depends more on histological structure than on the mode of surgical treatment. It is a disease more of the young than the old, the average age of the patients being lower than that of those with fascial and related sarcomata.[6] It has been recognised in a nine-month-old child in whom the history dated back to the age of two months.[10] In the Boston series females were more commonly affected than males; but in most other series males have predominated.

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which may also be refractory to treatment—which showed the highest percentages of patients receiving both forms of treatment Patients with illnesses which Western medicine has shown that it can control are thus placed in the care of Western practitioners, where such a superiority on the part of Western medical science has still to be conclusively proved to the layman, then help from the traditional Ayurvedic system is sought (One possible and interesting exception to this is the observation that Ayurvedic practitioners treated more accident cases than did the Western practitioner)

It may, of course, be argued that the Ayurvedic practitioner treats more illnesses of doubtful ætiology because his lack of skill in modern diagnostic methods prevents his making a precise and understandable diagnosis This may be true, but it cannot be proved from the data provided by this survey For example, as many cases of ill defined cause were treated by Western as by Ayurvedic doctors (These illnesses with an ill-defined cause would include those sicknesses the cause of which the interviewed persons could not remember, as well as undiagnosed or not yet diagnosed cases)

Another factor which may influence the choice of treatment is the relative availability of the different practitioners On estates, where dispensers are stationed, these practitioners treat most of the illnesses Western doctors tend to be concentrated in urban areas, whereas in the rural areas, treatment by the Ayurvedic physician and the apothecary predominates

The lower the family income, too, the higher the proportion of cases treated by Ayurvedic practitioners This may be a direct influence of poverty or, it may be claimed, an indirect effect of the ignorance which is often associated with poverty

The type of medical attention received also varies to some extent with the duration of the illness (and therefore, as noted, with the cause of illness) The proportion of cases treated by Western practitioners increases with duration of illness up to 3 months and then decreases, Ayurvedic practitioners treat progressively smaller proportions of cases as duration of illness increases up to 28 days and then more of the longer duration cases receive this system of treatment This may be due to patients with different illnesses seeking different methods of treatment or may indicate a transference of the patient from Western to Eastern practitioner as the disease becomes chronic The latter explanation is supported by the fact that as duration of illness lengthens so the proportion of patients receiving attention from both Western and Ayurvedic practitioners progressively increases

As the age of the patient increases, so the proportion of illnesses receiving attention from Western practitioners or apothecaries or dispensers decreases, while relatively more illnesses are treated by Ayurvedic or by both Ayurvedic and Western practitioners This may be due to a combination of circumstances Older people may prefer the traditional Ayurvedic system or, because the incidence of chronic illness increases with age, more old patients seek Ayurvedic treatment

During infancy the majority of cases, irrespective of the duration of illness, are treated by Western practitioners, although as the duration increases so the proportion receiving skilled treatment decreases and the proportion treated only by relatives increases (Which is the cause and the effect in the latter is not certain)

During the pre school years again, Western practitioners are the most favoured with all durations of illness, although as the duration increases so relatively more cases are treated by Ayurvedic or both Ayurvedic and Western practitioners

For illnesses among school children Western practitioners treat the greater proportion for durations up to 3 months after which Ayurvedic treatment is the more readily sought

During the early and mid adult age periods, Ayurvedic practitioners are favoured for illnesses of short duration (7 days and less) The proportions of illnesses treated by relatives or by Western practitioners increase as the duration of illness increases, and the reverse is true for Ayurvedic practitioners

In the late adult and old ages as illness duration lengthens so more patients treat themselves or seek Ayurvedic or both Ayurvedic and Western treatment, and Ayurvedic is preferred irrespective of the duration of illness

The Future

On the whole the Ceylonese shows a reasonably intelligent approach to the new ideas of Western medicine He has accepted and demands those therapies which are known to be effective, for the rest he still turns to his traditional, conservative Ayurveda The expansion of international health services since the war has introduced modern medical techniques from the West into regions where only the ancient systems of medicine have been previously known The new ideas will be accepted only if and when they prove more efficacious than the old In addition there may be religious and cultural barriers to be overcome

It is difficult to assess the value of the indigenous systems or to compare them with Western medicine Many inhabitants of Ceylon have great faith in them, and there seems recently to have been a considerable increase in the number of patients seeking these forms of treatment The Indigenous Hospital in Colombo for example, has increased the number of outpatients attending per year by over 500% since 1942

The Ayurvedic system does not recognise surgical methods of treatment but many practitioners do not hesitate to prescribe and to dispense the latest synthetic drugs from the West Others have faith only in the ancient remedies, though all are handicapped by the difficulties of obtaining these in sufficiently large quantities and by the lack of an Ayurvedic pharmacopœia

These ancient arts cannot be ignored, indeed, where there are so few Western-trained practitioners, the indigenous systems may have to be supported and integrated into the over all system of medical care Some attempt to do this has been made in Ceylon There, in 1928, a Board of Indigenous Medicine was established by the government for the purpose of controlling and developing the local systems of medicine To date about 5000 applications for registration have been made A College of Indigenous Medicine, a hospital, a pharmacy, and a dispensary are also now maintained as government institutions Many local authorities and organisations have also established and financed Ayurvedic dispensaries It is the eventual hope to combine the best in all systems—to mix the East with the West It is an ambitious ideal that should not be confined solely to the arts of medicine

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Medicine and the Law

Fraud by Practitioner

It is not often that a National Health Service tribunal makes such findings of deliberate fraud on the part of a medical practitioner as were pronounced in the case of Dr M on the representation of the *London Executive Council* As the result of its inquiry the tribunal directed that his name be removed from the council's medical list and not included in any corresponding list kept by other councils and it ordered him to pay the costs of the hearing *The Minister of Health* has subsequently dismissed Dr M's appeal and has forbidden the inclusion of his name in any medical list till the tribunal or the Minister otherwise directs

The findings of the tribunal may be summarised as follows

In May, 1945 Dr M applied to be included in the council's medical list of practitioners undertaking to provide general

Special Articles

THE SLOUGH EXPERIMENT

A Comprehensive Industrial Health Service on Trial

THOSE not engaged in industrial medicine are apt to think of industry as conducted in large well-lit factories, equipped with specially designed machinery and echoing to the strains of *Music While You Work.* In fact, however, a good deal of industry is done with home-made equipment in small factories, some of which are cramped and dirty, having a random, back-kitchen sort of air. Into such unsuitable quarters a new process may be introduced which gives rise to potentially dangerous fumes or dust; and indeed even a large modern factory may develop unrecognised hazards when a new process is introduced. It is not at all easy to assess the degree of risk to health in such cases. An industrial doctor can give an opinion; and with some hazards he can measure by physiological methods the effects on individual workers, once these have developed; but what he really needs, in order to prevent illness, are means of measuring the concentration of toxic or dangerous substances at various places in the factory, and reliable standards of safety against which to check them. American practice is far ahead of us in this matter, as Dr. Peter Nash has pointed out in our columns.[1]

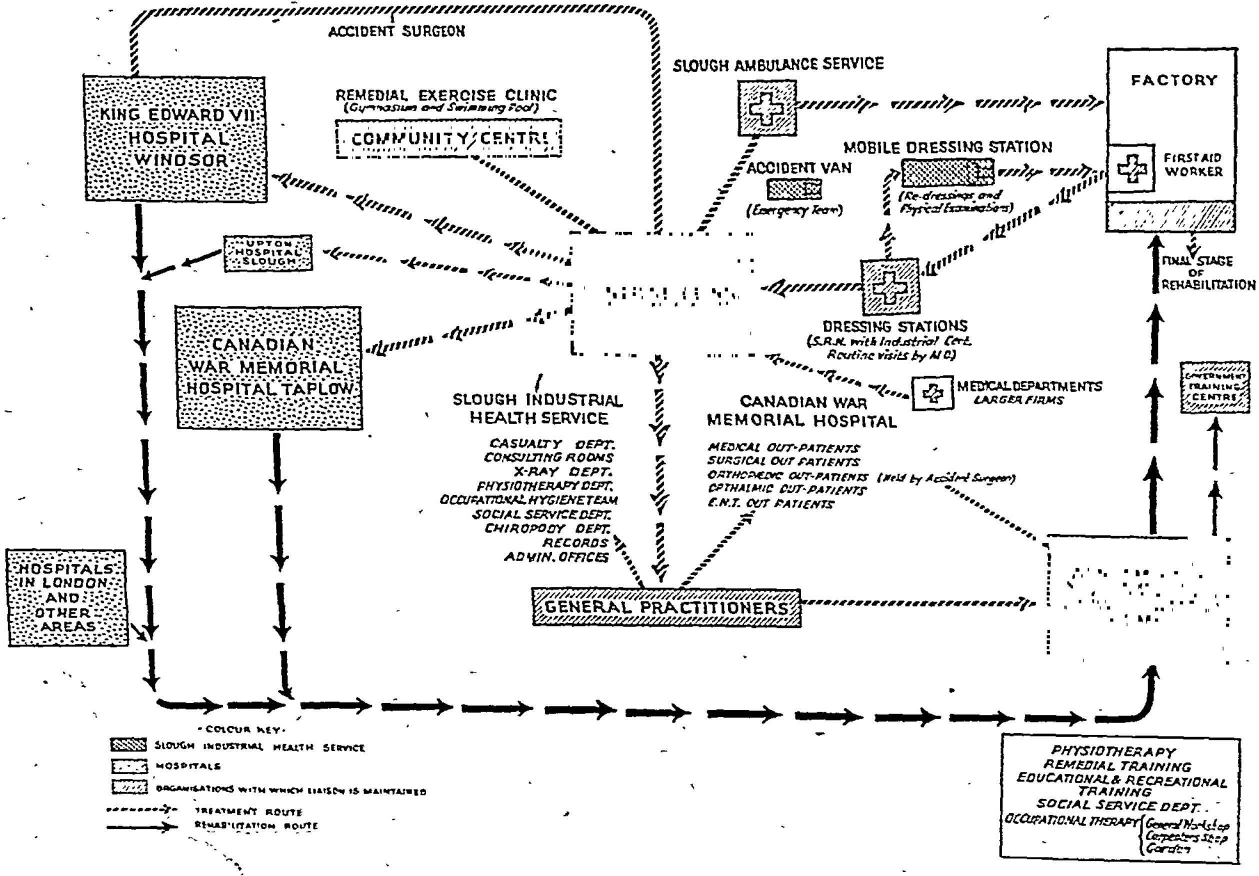
In America many States have set up divisions of industrial hygiene, usually as branches of their public-health departments. When a hazard is suspected the industrial hygiene laboratory examines air samples taken from various points in the factory, and supplies quantitative evidence of contamination. Moreover, the laboratory is staffed not only with doctors and chemists, but with engineers trained in industrial hygiene, whose task it is to recommend protective devices and to make sure that they are effective when installed.

We have no such pattern over here; but the Slough Industrial Health Service has established a pioneer occupational hygiene unit which is demonstrating what can, and should, be done.

THE OCCUPATIONAL HYGIENE TEAM

This service was founded in 1947, with the help of the Nuffield Foundation and the Nuffield Provincial Hospitals Trust, which between them granted £30,000 towards equipment and running expenses during the first five years. The aim was to promote the health and welfare of workers in local industry; and local firms were invited to become members of the service, paying a per-caput subscription (14s. at the outset, now 16s.) for their employees. Initially, 52 firms, employing 6324 workers, joined; and in five years these numbers have risen to 143 firms, with 15,175 employees. There are some 300 firms in the area, and though some of those not belonging to the service offer their own industrial health care, most of them do not provide for the care of their employees while at work. The service has thus still much opportunity to grow.

The occupational hygiene team was set up only three years ago. At the head of it is Dr. Nash, quoted above, who trained at the Harvard School of Public Health under Prof. Philip Drinker. He is assisted by Mr. R. J. Sherwood, an engineer, who has also trained in industrial hygiene under Professor Drinker, the Nuffield Foundation having sent him to Harvard for the purpose, and Miss Joan Bedford, a chemist, who has been provided with a laboratory in the London School of Hygiene and Tropical Medicine. All three members of the team hold joint appointments in the school and the Slough Industrial Health Service. They help to train students for the diploma in public health of London University, with which they thus provide a close bond.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SLOUGH INDUSTRIAL HEALTH SERVICE
HOSPITALS
ORGANISATIONS WITH WHICH LIAISON IS MAINTAINED
TREATMENT ROUTE
REHABILITATION ROUTE
PHYSIOTHERAPY
REMEDIAL TRAINING
EDUCATIONAL & RECREATIONAL TRAINING
SOCIAL SERVICE DEPT.
OCCUPATIONAL THERAPY
General Workshop
Carpenters Shop
Garden

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[1] *Lancet,* 1952, ii, 478.

for special needs. Food in its natural state was the proper food for mankind. But in civilised conditions the food of city-dwellers had to be processed and preserved. They had to see to it that none of these processes or preservatives caused illness. He had great faith in the Ministry of Health and in the Medical Research Council who, he believed, kept all the necessary factors in view. He was not unduly alarmed by some things that had been said in the debate. He agreed with Lord Horder that it was dangerous to correlate these things without full information. It was true that certain cardiac diseases had increased, but the health of the people of this country had enormously improved since the 1920s. They should beware of too easy generalisations in this matter and not reach conclusions until the subject had been thoroughly investigated. The proper people to investigate it were disinterested people able to put forward the facts and to act upon them. Two things were important: the wartime policy should be continued and foods of special nutritive value should be made available to the poorest persons; and we should produce more of our own fresh food. In a world of great uncertainty, in peace or in war, we were still importing more than half the food we ate. He suggested that an attempt should be made to set the target at 75% healthy home-produced foods instead of only 60% above the pre-war figure by 1956.

Lord JESSEL pointed out the importance of matured flour in producing a stable dough which would make a good loaf under predetermined conditions. It was commercially impracticable for millers and bakers to provide the enormous storage facilities needed for maturing all the flour consumed in this country, and it was for this reason that improvers, which achieved the same results as storage in regard to the baking qualities and colour of the flour, were introduced. From all he had read, he could see no evidence that bread made from agenised flour had had any harmful effect on human beings; but he felt sure that the milling industry was more than willing to follow official recommendations as to what types of improvers they should use.

Lord SEMPILL urged the acceptance of Sir Edward Mellanby's advice that "no use of chemicals should be countenanced if they have harmful effects on animals," as agene had been shown to have.

THE GOVERNMENT REPLY

Lord CARRINGTON, replying for the Government, said there was every prospect that the Government's aim to increase production of food to 60% above the pre-war level by 1956 would be achieved. We must continue to rely on imports for a large part of our food-supply, and these were preserved or processed by methods which had little or no effect on the nutritive value of the food. As regards improvers in breadmaking, the Government had no intention of belittling or ignoring the evidence of the effect of agene on animals, or the other medical evidence which had been mentioned in the debate. It had been decided to abandon agene as soon as a suitable substitute could be found. They did not think, however, that the evidence so far available justified them in preventing the use of agene without knowing what would be the probable effects of the several substitutes which could be used. The only evidence the Ministry of Food had of any ill effects was the one case referred to in *The Lancet* last March. He would like to emphasise that in the 30 years during which agene had been widely used in this country this was really the only authenticated case of human allergy associated with agene or chlorine dioxide. He did not think this case should be considered a cause for alarm, and the Government did not intend to allow it to force them to take precipitate action. That point was also made in *The Lancet's* leading article. Investigations were now proceeding into the various alternatives to agene, conducted by the Ministries of Food and Health and the Medical Research Council, in collaboration with the research associations of the milling and baking industries. These investigations were designed to assess the relative suitability of the various improvers which included agene, chlorine dioxide, vitamin C, and a recently developed aeration process in which improvement was effected by high-speed mixing. The investigations included studies of any chemical changes produced in the flour's constituents, the effects on the health and growth of experimental animals of feeding them with the treated flours, and assessment of the quality of the breads made from treated flours. They also included both small-scale and commercial trials of the vitamin C and aeration processes. The work was being pushed on as fast as possible, but there were difficult problems involved, and, if they were to be adequately examined, a quick answer could not be expected. The Government had in mind the need to ensure a supply of bread which would meet the nutritional needs of the nation. Lord Carrington said he felt there was no need for additional inquiry into the matter. He was inclined to be cautious of the words "artificial" and "poisonous" which had been used in the debate. Poisonous was a dramatic word, but it could be misleading. The addition of some chemicals was necessary if 50 million people were to be fed in this country and, with safeguards, there was no cause for disquiet.

Lord TEVIOT's motion was withdrawn, and Lord HANKEY said that although he was not entirely satisfied, he would not move his motion that day.

Medical Services in the Gas Industry

In the House of Commons on June 9, Mr STEPHEN SWINGLER said that the Gas Council, almost alone today among national boards and national councils of industries, had not established on a national scale an industrial medical service for their workers, yet the gas industry had special medical problems and the Medical Research Council had recently decided to undertake long-term research into the incidence of lung cancer among gas-workers. It was, therefore, disappointing to find that only 4 out of the 12 area boards in the gas industry had full-time medical staffs. Mr Swingler believed that the Minister of Fuel and Power was not entirely convinced that the present medical arrangements in the industry were satisfactory, and he hoped that if the Minister could not persuade the council to establish an occupational health service he would use his powers of direction under the Act.

Dr BARNETT STROSS suggested that if the Government held it desirable to have a comprehensive health service for the country as a whole, it should start with those industries where the risks of accident or occupational disease were greatest. It was unlikely that the Medical Research Council would complete their investigation into the incidence of lung cancer among gas-workers under two or three years, and the Ministry should urge that the service given to gas-workers should at least be evened up to the best level in any area in the country.

Mr L. W. JOYNSON-HICKS, parliamentary secretary to the Ministry of Fuel and Power, feared that there was no hope of getting results from the M.R.C. investigations even in two or three years, but he did not think that the fact that there were only 4 permanent medical officers of the boards had any effect on this issue. Turning to the points raised by Mr Swingler, he said that it was not the job of the Gas Council to set up a medical service for the industry. That was a matter for each area board to do for itself in the light of their local experience. When the industry was nationalised the Government of the day appointed a committee on industrial health services—the Dale Committee—and shortly afterwards development in industrial medical services was held up pending the committee's report. Early in 1951 the ban was removed and the committee's recommendations were referred to the National Joint Advisory Council. Replies had now been received from the British Employers' Federation and from each of the nationalised industries, but no reply had yet been received from the T.U.C. Consequently, action on these recommendations could not be taken. In the meantime, the Ministry were determined to progress. Some of the area boards were reluctant, or had been so in the past, for many good reasons. One was the question of expense, for to set up these medical services was costly. Moreover, the boards had been heavily occupied in general reorganisation. The Minister did not think that there was a case here for direction. If there was to be a successful permanent medical service, When a request comes from a firm for the investigation of a suspected hazard—say from fumes or dust—Dr. Nash first looks over the factory and examines those likely to have been affected, sending physiological samples for examination, or arranging radiography or blood-counts as necessary. Mr. Sherwood then visits the factory, takes samples of air at likely danger-points, and examines existing protective devices. All the medical and engineering findings are combined into a report which notes any damage to health and sets the quantitative results of air analyses against the proportion of a particular contaminant considered dangerous by the Medical Research Council and by American authorities. If the proportion of contaminant has proved to be too high for safety, the report concludes with some clear proposals for improving matters—usually by arranging for better exhaust ventilation, or other protective devices; photographs and illustrations are included if necessary. Neatly bound copies of the report are sent to the firm, and as a result the necessary changes are usually made.

The annual report of the Slough Industrial Service for 1951–52 notes that in a study made for one firm, which casts a lead-antimony alloy, no lead hazard was discovered but undesirable concentrations of antimony were present. Recommendations were made for preventing this. In another factory a risk from asbestos dust has been removed by local exhaust ventilation, installed on the team's advice; the workers here were all examined radiographically. Ten reports were made to firms using toxic substances, and advice for improving conditions given to 6. An outbreak of dermatitis among packers exposed to liquid paraffin has been brought to an end; and the medical officer of health of a large London borough has been assured that a chromium-plating factory, about which local residents were complaining, is doing no harm.

The work of the team, in their first three years, has grown so fast that they are unable to cope with all the requests reaching them. These include invitations to examine the dust hazards for workers in the whole of the diamond cutting and polishing industry, and in a large grinding-wheel and abrasives factory. In fact this pioneer unit, the only one of its kind in the country, has demonstrated conclusively the need for others—perhaps a dozen scattered up and down the United Kingdom, like the public-health laboratories.

THE ROUTINE SERVICE

The occupational hygiene team, however, is doing only a relatively small—though highly important—part of the work of the service as a whole. Under the medical direction of Dr. A. Austin Eagger, the service provides casualty care for workers from all the member firms, industrial nursing, physiotherapy, remedial gymnastics, social services, and recuperative treatment in a residential centre at Farnham Park nearby.

The central clinic is quartered in a solid square building, part of the Slough Community Centre. It contains, besides a large casualty department, rooms where clean dressings are done (no-touch technique is used), a room for the trained social worker, a chiropodist's surgery, administrative and record rooms, consulting-rooms where members of the staff of the Canadian Red Cross Memorial Hospital hold outpatient sessions, and an X-ray department shared by these hospitals, and of course by the clinic. This liaison with the local hospitals and their consultants has been of the greatest value. It means that a difficult or serious case can—with the consent of the general practitioner—be seen on the spot by an appropriate specialist, and if necessary the patient can be admitted to one of his hospital beds. Continuity of treatment is thus the rule rather than the exception, and this appeals to the patient as much as the doctor. Moreover the arrangement is doing much to win the confidence of local general practitioners who at the outset were somewhat suspicious of the service. Most of them are now on good terms with Dr. Eagger and his staff, and refer cases to the centre on their own initiative, well aware that in this way they can count on getting a consultant's opinion at once when necessary. Two orthopædic clinics are held weekly, and the consultant orthopædic surgeon of the area is also a paid member of the clinic staff. The X-ray department examines some 14 cases a day—mostly bone injuries, but also some cases of suspected tuberculosis or other chest conditions.

MINOR INJURIES

The clinic staff deal with about 3 serious accidents a month, most of which require hospital care; but their major concern is with minor accidents, of which some 500 daily come their way. Such things as foreign bodies or splashes in the eye, and damaged fingers or hands respond quickly to effective treatment at the outset. Neglected, they may mean great discomfort as well as loss of time. The finger which has gone septic can keep a man anchored to the hospital casualty department for many hours a day. At Slough he can be treated first at the centre, and afterwards by the team of the mobile dressing-station which travels round the member firms every morning for this very purpose. The patient leaves his job when the van arrives, and may be back at work in ten minutes. The mobile dressing-station is staffed by a State-registered nurse, who does the dressings, and a doctor who pays routine visits, in the afternoons, to examine personnel at the various factories. There is also an accident van with an emergency team of doctor and nurse, which goes to the scene of an accident as soon as a call comes in to the centre. Seriously injured patients are brought in by ambulance; and thanks to the close liaison between the centre and the Emergency Bed Service it is always possible to get a bed for anyone who needs it.

The records of minor accidents kept at the centre are of a time-saving pattern, but very full and informative. An average of 50 eye injuries—mostly due to foreign bodies or splashes—are seen weekly. More than once it has been possible to point out to a firm that they are getting a high incidence of accidents of a certain type, and that these are preventable; with the result that the firms have asked the occupational hygiene team for advice on ways of preventing them.

Each firm, of course, has its own first-aid team, manned by volunteers. At one time volunteers were hard to find, because time spent in learning first-aid reduced the bonus for the group in which the volunteer worked. The firms were asked to adjust this difficulty, and did so; and as a result volunteers have come forward to take the course of training organised by the service. The standard of first-aid has risen rapidly, and now these lay helpers are able to deal with 60% of minor casualties. These various arrangements, it is estimated, save 2000 man-hours a month.

ANCILLARY SERVICES

It often happens that a patient recovering from an injury, or suffering from a rheumatic or other affection of the joints or muscles, needs remedial exercises or physiotherapy; but to get this at hospital he may have to spend hours away from work. The physiotherapy department of the centre is housed in an adjoining building, and is very active. Patients come by appointment, and are away from their work only for as long as their treatment requires. The community centre swimming-bath can be used by those who need to do water-borne exercises. The chiropodist employed by the centre holds two sessions a week.

RECUPERATION AT FARNHAM PARK

A well-run and very agreeable course of reablement is offered at Farnham Park to those patients who need it. They go either as residents or outpatients to this fine house with wide gardens, where they work hard at recovery every day until 4·30 P.M. They may be sent either to the workshops, where there are plenty of ingenidrifting back towards "poverty bread." As though more than 200 years of "improving" flour, first by the addition of alum and other whiteners and later by the abstraction of the essentials of health, were not enough, in 1921 agene was introduced so surreptitiously that it was not even mentioned in the first edition of *The Englishman's Food*, and Lord Hankey, who was watching these things closely because he was horrified by the fact that 60% of our would-be recruits for the Army were being rejected, had never heard of agene until 1946 when Sir Edward Mellanby showed that agenised flour produced nervous disorders in dogs and, if continued, canine hysteria and eventually death. In 1950, after the usual haggling between the trade and the scientists, the Government at last decided to ban agene but to permit chlorine dioxide which they said it would take a long time to provide. So long had it taken that seven years after Mellanby's warning the banned and discredited agene was still in general use and chlorine dioxide was suspect.

In support of the technical case against agene, Lord Hankey referred to the experiments in 1940 by Dr. Coghlan, of Hull, Dr. Pollak, the physician in charge of the allergy clinic at the Middlesex Hospital, and the paper by Dr. Sheldon and Dr. Yorke published in *The Lancet* on March 21, 1953. To the layman Dr. Coghlan's letter to the *Medical Press* on April 2, 1952, provided presumptive evidence of a tendency for agene to induce coronary thrombosis and other diseases of the heart and circulatory system and also suggested that certain reactions set up ideal conditions for ulcer formation. This disturbing indictment was supported by official statistics. But heart and vascular diseases were not the only complaints in respect of which agenised flour was suspect. Dr. Pollak, in a report to the *Medical Press* in July, 1950, showed that there were many people who, while tolerant of flour made from the wheat berry, had allergic symptoms on eating bread made from agenised flour. The experiments of Dr. Sheldon and Dr. Yorke led to the unescapable conclusion that chemically treated flour was the cause of serious skin disorders associated with loss of appetite and mental depression. Agene was the original cause of the trouble but chlorine dioxide was found to produce the same symptoms.

Summarising the case against agene, Lord Hankey said that there was no dispute that it was injurious to dogs and some other animals. Secondly, many of the nations which consumed mainly white bread had prohibited agene, and France, which did not permit its use, seemed, prima facie, to have suffered much less severely than we had from some of the more serious diseases which agene was suspected of promoting. Thirdly experts had warned us that agene might promote tendencies towards coronary thrombosis and other heart and vascular diseases, ulcers, skin diseases, and lack of appetite, and the list in Dr. Franklin Bicknell's book, *The English Complaint*, was even longer. But he did not claim that the case against agene as he had presented it provided proof, as a whole or in part, that agene was deleterious. Here Lord CARRINGTON, parliamentary secretary to the Ministry of Agriculture, interjected: Neither does *The Lancet*. Lord Hankey said that was perfectly true, but there were a great many other things in the leading article in *The Lancet* which he dare say he could quote. The governments of the United States and Canada had found the evidence sufficient to justify their banning agene, and no one had been able to prove that agene was not as dangerous as the "poverty bread" to the teeth of the nation. If he were responsible for the decision, he would want to be convinced of some overwhelming health advantage in agene before he permitted its continuance for a single day.

Turning to the supposed advantages of agene, Lord Hankey recalled that, in 1951, Major Lloyd George, Minister of Food, said:

> Flour treated with agene yields a dough which has more uniform baking qualities and is more easily handled by the baker; the resulting loaf is whiter and of superior lightness and texture. Agene treatment has no effect on the keeping quality of the flour.

But Lord Hankey thought that the implication that agene was necessary to obtain these qualities was illusory. In France, where agene was banned, the bread had all these qualities, and was much more palatable than ours. It could not be said that the health of the consumer had been considered first in this matter; the only people who got any benefit were possibly the millers and certainly the "other interests" who supplied the unnecessary agene and the other chemical improvers and emulsifiers.

Lord HORDER said that last year, when this matter was under debate, he had drawn attention to the frequency with which that very common fallacy of non sequitur seemed to arise in this matter. For example, Lord Teviot had mentioned cancer. With what causative agent could they associate the incidence of that disease? They would be only too pleased to get that information. Again, Lord Hankey had asked, if the increase in the incidence of coronary thrombosis was not due to agene what was it due to? He wished he knew. These statements really did require checking. In New Zealand agene had never been used in the preparation of bread, and the incidence of coronary thrombosis in New Zealand was exactly comparable with its incidence in this country. To quote part of what *The Lancet* said and not all was not quite fair. The purpose of improvers in flour was to make the bread acceptable to the senses—to the palate, to the eye, and to the smell—as well as nutritious. There were two very simple desiderata: bread, being the staple article of diet of 50 million people in the islands, must be nutritious up to the limit of scientific knowledge of nutrition today, and it was a Governmental responsibility to see that it was. Next autumn cereals were to be decontrolled and he shared the anxiety which had been expressed as to whether the Government were going to see that the minimum of nutritional ingredients were preserved in the whiter loaf. He understood that was their intention. He strongly opposed the introduction, even the availability, of this whiter bread unless that safeguard was assured.

Agene was given up by America rather more than two years ago and there coronary thrombosis had increased still further during that period. He was not one of those who had been convinced that agene had produced any illness in human beings. He knew of no series of nervous complaints which even suggested that they were produced by the same reagent as in the case of canine hysteria produced by agene. Both the doctors who reported the case of the lady with the peculiar skin in *The Lancet* were fair enough to raise the question whether this was a rare, an isolated, case or whether it was opening up a new field on the nervous side of disease—something that had not been met before. Lord Hankey preferred the second conclusion because it fitted his thesis, but Lord Horder said that he, with no less knowledge, chose the first. He thought the Government were justified in going on with agene until an improver could be introduced which cut out the chemical altogether. We should not hurry the change from one chemical to another as the Americans had done. The chemical improver to which they had switched was not known to be either better or worse than the original one. The bakers and the millers should work at this problem and, as soon as might be, change over from a chemical improver to a physical one.

Viscount BLEDISLOE said that about 30 years ago Lord Horder, as his medical adviser, had advised him not to take medicines unless absolutely necessary and to give Nature a chance. In carrying out Lord Horder's advice, we should also give the products of Nature a chance without undue adulteration. There should be an impartial investigation into this problem so that both the medical profession and the Government could speak with greater assurance on the subject than they could today.

Lord BOYD-ORR said that nutrition was by far the most important factor in health. A great improvement had been achieved in the health of the women and children of this country today compared with the pre-war years. It was interesting and important to note that that improvement was made during the war amid a food shortage and when the enemy was at our gates. The Government of that time ensured proper food priorities ous devices to keep particular muscle-groups exercised, or to the warm plunge-bath, where physiotherapists exhort and persuade the gaily clad bathers to achieve the next stage of activity, or to the gymnasium, where the instructor notes with pride the gain in power of limbs impaired by poliomyelitis or other disorder. From 4·30 to 9.30 P.M. the patients are off duty. They can have tea in the handsome lounge, rest and read in the quiet room, chat or play games in the common-room, walk in the grounds, go out and visit friends, or join in the programme arranged by their own entertainments committee. On three evenings a week the education and recreation department provides programmes of documentary and instructional films, or arranges discussions, games, or plays by local amateur dramatic societies or by the patients themselves. All the patients have physical disabilities. Treatment for industrial patients with neuroses is, of course, available at Roffey Park, near Horsham. The average stay at Farnham Park is four weeks—the longest ten weeks. The food is very good, and so is the morale of the patients; perhaps the two are linked.

The Slough Industrial Health Service is thus a comprehensive scheme for the welfare of workers in industry, and has already shown its member firms a good return in the saving of working-time. The workers themselves at first regarded it with the customary scepticism of the British working man, who is always wary of institutions outspokenly designed to do him good. Gradually, however, they have come to recognise the value of the service, and now make full use of it.

SCURVY

The Edinburgh Meeting

As already recorded in these pages, the Royal College of Physicians of Edinburgh and the Nutrition Society combined during the weekend of May 22 to celebrate in Edinburgh the bicentenary of the publication of Lind's *Treatise of the Scurvy*.[1]

The proceedings opened with a "special graduation ceremonial" at which the Vice-Chancellor (Sir Edward Appleton, F.R.S.) conferred the honorary degree of doctor of laws upon Surgeon Vice-Admiral Sir **Sheldon Dudley**, F.R.S. In a fighting speech Sir Sheldon said that the medical officer in the Royal Navy must educate his executive superior in practical hygiene, and that the importance of this subject was so great that there should be a health officer on the Board of Admiralty. There was, he declared, no such entity as subclinical scurvy, and he believed that less than 15 mg. daily of ascorbic acid was a maintenance dose although during the war dietitians had tried to persuade him that the figure was 300 mg. At the conclusion of the ceremony a bronze plaque commemorating Lind was unveiled, the gift of the Sunkist Growers of Citrus Fruit in California and Arizona. Later in the day another formal speech was made—this time by Prof. V. P. **Sydenstricker** (Augusta, Georgia), who gave the Sydney Watson Smith lecture in the Royal College of Physicians on the Impact of Vitamin Research on the Practice of Medicine.

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The scientific meetings of the Nutrition Society were opened by Sir **Edward Mellanby**, F.R.S., who stated that Lind was the first to introduce the experimental method into medicine. He cruised in safer waters when he came to contemporary history and reminded us of the service Sir Sheldon Dudley had performed in establishing the Royal Naval Personnel Research Committee, and of the careful researches on nutrition of Dame Harriette Chick over many years; he and she were the only two surviving members of the original Accessory Food Factors Committee set up jointly in 1917 by the Medical Research Committee and the Lister Institute. Dame **Harriette Chick** then reviewed the early investigations of scurvy and incidentally differed from Sir Sheldon in affirming the existence of the prescorbutic state. Later in the symposium a paper on authors on scurvy before Lind was read on behalf of Mr. A. J. **Lorenz**.

Perhaps the most important contribution of the session was given by Mr. C. G. **King**, PH.D. (Nutrition Foundation, New York City), who by labelling compounds with ^{14}C has indicated how L-ascorbic acid is formed in the body of the rat from D-glucose, D-glucuronic acid being an intermediate. He has also made the interesting observation that with deficiency of ascorbic acid there is an increased formation of cholesterol from acetate; but, although he is a champion of high human allowances of ascorbic acid, he was careful not to claim that ingestion of the vitamin would decrease atherosclerosis.

This relation to cholesterol metabolism is possibly related to one of the most interesting aspects of ascorbic acid, its connection with the adrenal cortex. Ascorbic acid may form as much as 4% of the dry weight of the adrenal cortex, and the vitamin was of course initially isolated from adrenals by Szent-Györgyi in 1927. Sayers[2] and his colleagues have shown that adrenal ascorbate is reduced by corticotrophin (A.C.T.H.) or by various stresses. It is possible that an oxidation product of ascorbic acid is required for the synthesis of adrenal cortical hormone from cholesterol, and it may be that corticotrophin promotes the oxidation of ascorbic acid; Cornforth and Long[3] have suggested that cortisone promotes the peripheral oxidation of ascorbic acid.

Prof. R. M. **Kark** (Chicago) reviewed the relation of ascorbic acid to scurvy, corticotrophin, and surgery: he claimed that there was no evidence that cold or adrenal cortical activity increases the human requirement of ascorbic acid, and he did not believe that ascorbic acid or a derivative of it is used in synthesising adrenal hormones.

The Lind tradition of experimental work on man was upheld by papers from Dr. J. H. **Crandon** (Boston) and Prof. H. A. **Krebs**, F.R.S. Dr. Crandon described the now classical experiment[4] in which he subsisted for six months on a diet containing no vitamin C; subsequently he has investigated the relation of ascorbic acid to surgery. Professor Krebs described the similar experiment later conducted in Sheffield on conscientious objectors.[5] In the latter experiment a supplement of 10 mg. of ascorbic acid daily was found to cure clinical scurvy in all six volunteers and protected three volunteers from scurvy for 424 days; this figure of 10 mg. was somewhat arbitrarily trebled to arrive at a figure which would satisfy "ill-defined additional needs and to allow a margin of safety." Even this figure of 30 mg. is of course very much lower than that required for saturation: in a delightful paper Prof. **Gounelle**, of Paris, informed the meeting that he had found that tuberculous prisoners-of-war did not become saturated until they were given 300 mg. daily. The question whether saturation is desirable or necessary was taken up by Dr. King in the discussion at the end of the sessions when he defended the daily allowance of 75 mg. of ascorbic acid recommended by the National Research Council. Mr. L. J. **Harris**, SC.D., had suggested that the question of requirement was one that needed discussion, and, after pronouncing himself in favour of saturation, he called on Dr. King. Dr. **King** said that 75 mg. gave only half-saturation; the guineapig allowed to choose its diet kept itself saturated, and animals that synthesised their own ascorbic acid were saturated; it could be shown that guineapigs survived diphtheria toxin better on high levels (5–10 mg. daily) than on lower levels (2–5 mg.), even though these lower levels completely protected for special needs Food in its natural state was the proper food for mankind But in civilised conditions the food of city-dwellers had to be processed and preserved They had to see to it that none of these processes or preservatives caused illness He had great faith in the Ministry of Health and in the Medical Research Council who, he believed kept all the necessary factors in view He was not unduly alarmed by some things that had been said in the debate He agreed with Lord Horder that it was dangerous to correlate these things without full information It was true that certain cardiac diseases had increased but the health of the people of this country had enormously improved since the 1920s They should beware of too easy generalisations in this matter and not reach conclusions until the subject had been thoroughly investigated The proper people to investigate it were disinterested people able to put forward the facts and to act upon them Two things were important the wartime policy should be continued and foods of special nutritive value should be made available to the poorest persons . and we should produce more of our own fresh food In a world of great uncertainty in peace or in war, we were still importing more than half the food we ate He suggested that an attempt should be made to set the target at 75% healthy home-produced foods instead of only 60% above the pre-war figure by 1956

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[1] *Lancet*, May 16, 1953, p. 988.

[2] Sayers, G. *Physiol. Rev.* 1950, 30, 241.

[3] Cornforth, J. W., Long, D. A. *Lancet*, Jan. 24, 1953, p. 160.

[4] Crandon, J. H., Lund, C. C., Dill, D. B. *New Engl. J. Med.* 1940, 223, 353.

[5] *Lancet*, 1948, i, 853.

Lord **JESSEL** pointed out the importance of matured flour in producing a stable dough which would make a good loaf under predetermined conditions It was commercially impracticable for millers and bakers to provide the enormous storage facilities needed for maturing all the flour consumed in this country, and it was for this reason that improvers, which achieved the same results as storage in regard to the baking qualities and colour of the flour, were introduced From all he had read, he could see no evidence that bread made from agenised flour had had any harmful effect on human beings; but he felt sure that the milling industry was more than willing to follow official recommendations as to what types of improvers they should use

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THE GOVERNMENT REPLY

Lord **CARRINGTON**, replying for the Government said there was every prospect that the Government's aim to increase production of food to 60% above the pre-war level by 1956 would be achieved We must continue to rely on imports for a large part of our food-supply, and these were preserved or processed by methods which had little or no effect on the nutritive value of the food As regards improvers in breadmaking the Government had no intention of belittling or ignoring the evidence of the effect of agene on animals or the other medical evidence which had been mentioned in the debate It had been decided to abandon agene as soon as a suitable substitute could be found. They did not think, however, that the evidence so far available justified them in preventing the use of agene without knowing what would be the probable effects of the several substitutes which could be used The only evidence the Ministry of Food had of any ill effects was the one case referred to in *The Lancet* last March He would like to emphasise that in the 30 years during which agene had been widely used in this country this was really the only authenticated case of human allergy associated with agene or chlorine dioxide He did not think this case should be considered a cause for alarm, and the Government did not intend to allow it to force them to take precipitate action. That point was also made in *The Lancet*'s leading article Investigations were now proceeding into the various alternatives to agene, conducted by the Ministries of Food and Health and the Medical Research Council, in collaboration with the research associations of the milling and baking industries These investigations were designed to assess the relative suitability of the various improvers which included agene chlorine dioxide, vitamin C, and a recently developed aeration process in which improvement was effected by high-speed mixing The investigations included studies of any chemical changes produced in the flour's constituents the effects on the health and growth of experimental animals of feeding them with the treated flours, and assessment of the quality of the breads made from treated flours They also included both small-scale and commercial trials of the vitamin C and aeration processes The work was being pushed on as fast as possible but there were difficult problems involved, and, if they were to be adequately examined a quick answer could not be expected The Government had in mind the need to ensure a supply of bread which would meet the nutritional needs of the nation Lord Carrington said he felt there was no need for additional inquiry into the matter He was inclined to be cautious of the words "artificial" and "poisonous" which had been used in the debate. Poisonous was a dramatic word but it could be misleading The addition of some chemicals was necessary if 50 million people were to be fed in this country: and, with safeguards, there was no cause for disquiet

Lord **TEVIOT**'s motion was withdrawn, and Lord **HANKEY** said that although he was not entirely satisfied, he would not move his motion that day

Medical Services in the Gas Industry

In the House of Commons on June 9, Mr **STEPHEN SWINGLER** said that the Gas Council almost alone today among national boards and national councils of industries, had not established on a national scale an industrial medical service for their workers, yet the gas industry had special medical problems and the Medical Research Council had recently decided to undertake long-term research into the incidence of lung cancer among gas-workers It was, therefore disappointing to find that only 4 out of the 12 area boards in the gas industry had full-time medical staffs Mr Swingler believed that the Minister of Fuel and Power was not entirely convinced that the present medical arrangements in the industry were satisfactory, and he hoped that if the Minister could not persuade the council to establish an occupational health service he would use his powers of direction under the Act.

Dr **BARNETT STROSS** suggested that if the Government held it desirable to have a comprehensive health service for the country as a whole it should start with those industries where the risks of accident or occupational disease were greatest It was unlikely that the Medical Research Council would complete their investigation into the incidence of lung cancer among gas-workers under two or three years and the Ministry should urge that the service given to gas-workers should at least be evened up to the best level in any area in the country

Mr **L W. JOYNSON-HICKS**, parliamentary secretary to the Ministry of Fuel and Power, feared that there was no hope of getting results from the M R C investigations even in two or three years, but he did not think that the fact that there were only 4 permanent medical officers of the boards had any effect on this issue Turning to the points raised by Mr Swingler, he said that it was not the job of the Gas Council to set up a medical service for the industry That was a matter for each area board to do for itself in the light of their local experience When the industry was nationalised the Government of the day appointed a committee on industrial health services—the Dale Committee—and shortly afterwards development in industrial medical services was held up pending the committee's report. Early in 1951 the ban was removed and the committee's recommendations were referred to the National Joint Advisory Council Replies had now been received from the British Employers' Federation and from each of the nationalised industries but no reply had yet been received from the T U C Consequently action on these recommendations could not be taken. In the meantime the Ministry were determined to progress Some of the area boards were reluctant, or had been so in the past. for many good reasons One was the question of expense for to set up these medical services was costly Moreover the boards had been heavily occupied in general reorganisation The Minister did not think that there was a case here for direction. If there was to be a successful permanent medical service

When a request comes from a firm for the investigation of a suspected hazard—say from fumes or dust—Dr. Nash first looks over the factory and examines those likely to have been affected, sending physiological samples for examination, or arranging radiography or blood-counts as necessary. Mr. Sherwood then visits the factory, takes samples of air at likely danger-points, and examines existing protective devices. All the medical and engineering findings are combined into a report which notes any damage to health and sets the quantitative results of air analyses against the proportion of a particular contaminant considered dangerous by the Medical Research Council and by American authorities. If the proportion of contaminant has proved to be too high for safety, the report concludes with some clear proposals for improving matters—usually by arranging for better exhaust ventilation, or other protective devices; photographs and illustrations are included if necessary. Neatly bound copies of the report are sent to the firm, and as a result the necessary changes are usually made.

The annual report of the Slough Industrial Service for 1951–52 notes that in a study made for one firm, which casts a lead-antimony alloy, no lead hazard was discovered but undesirable concentrations of antimony were present. Recommendations were made for preventing this. In another factory a risk from asbestos dust has been removed by local exhaust ventilation, installed on the team's advice; the workers here were all examined radiographically. Ten reports were made to firms using toxic substances, and advice for improving conditions given to 6. An outbreak of dermatitis among packers exposed to liquid paraffin has been brought to an end; and the medical officer of health of a large London borough has been assured that a chromium-plating factory, about which local residents were complaining, is doing no harm.

The work of the team, in their first three years, has grown so fast that they are unable to cope with all the requests reaching them. These include invitations to examine the dust hazards for workers in the whole of the diamond cutting and polishing industry, and in a large grinding-wheel and abrasives factory. In fact this pioneer unit, the only one of its kind in the country, has demonstrated conclusively the need for others—perhaps a dozen scattered up and down the United Kingdom, like the public-health laboratories.

THE ROUTINE SERVICE

The occupational hygiene team, however, is doing only a relatively small—though highly important—part of the work of the service as a whole. Under the medical direction of Dr. A. Austin Eagger, the service provides casualty care for workers from all the member firms, industrial nursing, physiotherapy, remedial gymnastics, social services, and recuperative treatment in a residential centre at Farnham Park nearby.

The central clinic is quartered in a solid square building, part of the Slough Community Centre. It contains, besides a large casualty department, rooms where clean dressings are done (no-touch technique is used), a room for the trained social worker, a chiropodist's surgery, administrative and record rooms, consulting-rooms where members of the staff of the Canadian Red Cross Memorial Hospital hold outpatient sessions, and an X-ray department shared by these hospitals, and of course by the clinic. This liaison with the local hospitals and their consultants has been of the greatest value. It means that a difficult or serious case can—with the consent of the general practitioner—be seen on the spot by an appropriate specialist, and if necessary the patient can be admitted to one of his hospital beds. Continuity of treatment is thus the rule rather than the exception, and this appeals to the patient as much as the doctor. Moreover the arrangement is doing much to win the confidence of local general practitioners who at the outset were somewhat suspicious of the service. Most of them are now on good terms with Dr. Eagger and his staff, and refer cases to the centre on their own initiative, well aware that in this way they can count on getting a consultant's opinion at once when necessary. Two orthopædic clinics are held weekly, and the consultant orthopædic surgeon of the area is also a paid member of the clinic staff. The X-ray department examines some 14 cases a day—mostly bone injuries, but also some cases of suspected tuberculosis or other chest conditions.

MINOR INJURIES

The clinic staff deal with about 3 serious accidents a month, most of which require hospital care; but their major concern is with minor accidents, of which some 500 daily come their way. Such things as foreign bodies or splashes in the eye, and damaged fingers or hands respond quickly to effective treatment at the outset. Neglected, they may mean great discomfort as well as loss of time. The finger which has gone septic can keep a man anchored to the hospital casualty department for many hours a day. At Slough he can be treated first at the centre, and afterwards by the team of the mobile dressing-station which travels round the member firms every morning for this very purpose. The patient leaves his job when the van arrives, and may be back at work in ten minutes. The mobile dressing-station is staffed by a State-registered nurse, who does the dressings, and a doctor who pays routine visits, in the afternoons, to examine personnel at the various factories. There is also an accident van with an emergency team of doctor and nurse, which goes to the scene of an accident as soon as a call comes in to the centre. Seriously injured patients are brought in by ambulance; and thanks to the close liaison between the centre and the Emergency Bed Service it is always possible to get a bed for anyone who needs it.

The records of minor accidents kept at the centre are of a time-saving pattern, but very full and informative. An average of 50 eye injuries—mostly due to foreign bodies or splashes—are seen weekly. More than once it has been possible to point out to a firm that they are getting a high incidence of accidents of a certain type, and that these are preventable; with the result that the firms have asked the occupational hygiene team for advice on ways of preventing them.

Each firm, of course, has its own first-aid team, manned by volunteers. At one time volunteers were hard to find, because time spent in learning first-aid reduced the bonus for the group in which the volunteer worked. The firms were asked to adjust this difficulty, and did so; and as a result volunteers have come forward to take the course of training organised by the service. The standard of first-aid has risen rapidly, and now these lay helpers are able to deal with 60% of minor casualties. These various arrangements, it is estimated, save 2000 man-hours a month.

ANCILLARY SERVICES

It often happens that a patient recovering from an injury, or suffering from a rheumatic or other affection of the joints or muscles, needs remedial exercises or physiotherapy; but to get this at hospital he may have to spend hours away from work. The physiotherapy department of the centre is housed in an adjoining building, and is very active. Patients come by appointment, and are away from their work only for as long as their treatment requires. The community centre swimming-bath can be used by those who need to do water-borne exercises. The chiropodist employed by the centre holds two sessions a week.

RECUPERATION AT FARNHAM PARK

A well-run and very agreeable course of reablement is offered at Farnham Park to those patients who need it. They go either as residents or outpatients to this fine house with wide gardens, where they work hard at recovery every day until 4·30 P.M. They may be sent either to the workshops, where there are plenty of ingenithe Ministry must carry both sides of the industry with them Progress had been made The Scottish Board had agreed to a permanent medical service The Gas Council as a council had also agreed and their views were shared by the Minister But some of the boards were in a special category For instance Mr Joynson-Hicks did not think it would ever be the best thing for the Wales Gas Board to have a permanent medical service They had a different set-up and different problems The Northern Board also had different circumstances By and large, it was reasonable to expect that the remaining boards would be taking action, and therefore they had achieved a considerable step towards getting a permanent medical service for the gas industry He hoped it would not be long before that service was available

QUESTION TIME

The Guillebaud Inquiry

Replying to questions Mr J Stuart Secretary of State for Scotland said an experienced officer of the Department of Health for Scotland was being specially appointed to the secretariat of the committee of inquiry into the National Health Service to assist on matters specially affecting Scotland It was for the committee themselves to decide having regard to their terms of reference, the nature and scope of their review As to the question of the protection of the Scottish people in this matter, he understood that the committee had invited memoranda from Scottish bodies and intended to hear oral evidence in Scotland, so that they would become fully aware of the Scottish needs and circumstances He had no doubt they would have due regard to the Highlands and Islands

Mr Hector Hughes In view of the widespread alarm which the appointment of this committee has caused in Scotland could the Minister give an assurance that the advantages which the Scottish people have enjoyed for the last six years will be in no way imperilled ?

Mr Stuart I can only draw the attention of the hon Member to the terms of reference which end by saying ' while providing for the maintenance of an adequate service " That is our intention

B C G Vaccine in the Army

Replying to a question Mr A Head, Secretary of State for War, said that B C G vaccine was not under test but was already in use by the Army Members of the Royal Army Medical Corps and Queen Alexandra's Royal Army Nursing Corps who, on testing by the Mantoux technique appeared to be susceptible to tuberculosis were offered this form of vaccination and might not be employed in a tuberculosis ward or laboratory unless, following the treatment a further test gave a satisfactory reaction

Medical Examination of National Service Recruits

Replying to a question Sir Walter Monckton, Minister of Labour and National Service, said that the study undertaken by the London School of Hygiene and Tropical Medicine into the results of examinations of men called up for National Service was a statistical survey of some aspects of the medical conditions of a limited number of men The Ministry of National Service made available some data, but the inquiry was not made on their behalf nor had he any responsibility for its conclusions

Mr D L Donnelly asked whether it was not a fact that the inquiry had been widened and would not the Minister who had been approached by the London School of Hygiene and Tropical Medicine give full consideration to such an inquiry, as this was one of the rare occasions when full data of the nation's health could be collected

Sir Walter Monckton said this was a pilot inquiry and dealt with one medical board and one place only A wider inquiry was now thought necessary and if it went forward the Ministry of National Service would provide data as they had done before

Hospitals and the Bread Subsidy

Replying to a question Dr Charles Hill, parliamentary secretary to the Ministry of Food said the proposal to give a subsidy to hospitals in respect of bread which they baked for their own use had been considered but the Minister did not think that such a widening of bread subsidy payments would be justified

In England Now

A Running Commentary by Peripatetic Correspondents

If you accept the self-demand principle in infant feeding, you cannot make a diagnosis of "overfeeding" can you ? The infant's demand is your guide He may be underfed if he is not getting enough, but he cannot "overfeed" himself Here on the Pacific Coast the self-demand method is well-entrenched. The mothers like it The babies like it Early mixed feeding is the rule A baby of two months, amply breast-fed, will take daily half a banana, two ounces of 'Pablum,' and half a can of peach custard He may look pale and obese, but that is irrelevant If you are following the self-demand method, other standards—æsthetic or avoirdupois—do not apply

But what troubles me is this. when do you begin to diagnose obesity ? Ten million people in North America are said to suffer from it It afflicts children as well as adults A 12-year old schoolgirl weighs 200 lb If you didn't diagnose that as obesity, you would have to use some other term meaning the same thing But to put it crudely, obesity is usually due to overfeeding and when do you begin to diagnose overfeeding We have agreed that there is no such thing in infants And everybody knows (or should know) that you respect the dietary inclinations of the toddler Overfeeding of a toddler is just unthinkable Would you then concede obesity in the nursery school ? In the 5-year-old ? When does appetite cease to be a standard and begin to be a menace ? We shall have to make up our minds soon, because these self-demand-fed expansive infants will soon be turning up in the schools and will have to be put on a Wetzel grid

Dietary regimentation is going to be tough for these uninhibited youngsters "Not at all," you will hear some expert say, "Just the reverse It was all that restrictive feeding-by-the-clock and frustration of the infants' hunger that produced the ten million insatiable adults If you allow the self-demand principle in infancy, the children will grow up to be emotionally more stable, less demanding, and generally better controlled "

O K Then in a few years there won't be any obesity I, for one, am quite prepared to wait and see if the proof of the pudding is in the eating

* * *

All good general practitioners are ready-witted and resourceful, and it is my secret sorrow that the years have taught me the right things to say and do—always about a day too late Except once

In my practice in the country I used to reserve a quiet hour or two on Sunday mornings for benevolent but time consuming procedures, one of which was tapping hydroceles A village ancient arrived for the biennial removal of his half pint and, as an old customer, fetched his basin and perched on the stool Always tender hearted, I inserted the smallest possible trocar and left him to drain as usual

I lived then in a big rabbit warren of a house with a large garden and orchard behind it It was a lovely morning in early summer so I wandered into the garden to while away the necessary ten or twenty minutes The air was fresh and sweet, and the sun was drying the dew on the petals of my roses My lovingly nursed rhododendrons gave promise of a wondrous beauty I found a rare catch of earwigs in the traps on my dahlia stakes, and there was a purposeful hum about my beehives A garden offers much to tempt the mind and I mused my way round the orchard and thought of many things Everything in fact except what I ought to have thought of

I was jerked back to the rude earth by an alarmed wife with a tale of a strange man wandering round the house calling for me in a loud voice Like a schoolboy who has overstayed his playtime, I hastened guiltily back meeting on the garden path the ancient who by this time had rambled through the house and discovered the back door He held the trocar in place with one hand and did his best to support his trousers with the other, and he moved with a gait undescribed in any textbook Then it was that for once in my life my grey cells worked at speed Tut tutting impatiently, I hustled him back to his stool where I made him perch another few minutes while the last few, but most important, drops of fluid came resumed virus origin. In the two years there were nfections with *Leptospira icterohæmorrhagiæ* and 12 h *L. canicola*. No other strain has been identified in at Britain.

he figures included under mumps in table II refer only patients who were negative in the other tests, who had history of mumps, and in whom a pair of sera were ted. It does not include sera in which there was an changing titre in two specimens which made accurate erpretation impossible. Great difficulty can arise ring the poliomyelitis "season" if mumps-meningitis curs without parotitis. Sera may be obtained too late the illness to demonstrate a rising titre; and. until itable tests for poliomyelitis are available, it will be possible to make a certain diagnosis in such cases ith a high but unchanging titre of mumps antibodies. e have also received sera from a patient with menin-tis who was a household mumps contact but was roved to be a case of leptospirosis (*L. canicola*).

In 1949 there were no rising titres for mumps virus in atients without parotitis. In 1950 only 2 of 73 had ising titres. These were in children aged five years with lnesses in June and July. In addition there were 4 atients with positive sera who had a history of mumps rom seven to fourteen days before admission with meningitis.

In both the L.C.M. and the leptospiral groups the roportion of positive results was four or five times greater in paired sera than in the single convalescent specimens. This suggested that pairs of acute and convalescent sera were collected more often from the more typical cases, whereas the single specimens were from cases in which the diagnosis "virus" was an afterthought.

In virus infections involving the central nervous system recent, past but recent, or simultaneous infection with two or more viruses, or with viruses and leptospira, are liable to cause considerable difficulty in diagnosis. Thus, mumps may occur in a household with a dog excreting *L. canicola*: poliomyelitis may occur in a similar household: poliomyelitis and Coxsackie viruses have often been found together in fæces as well as a rise in titre of antibodies to both viruses at the same time. A precise diagnosis may be virtually impossible in such cases.

SUMMARY

The results of the use of serological tests in the diagnosis of suspected virus diseases in 1660 patients with affections of the respiratory tract, and 334 with affections of the central nervous system in 1949–51, are briefly described.

As has often been emphasised in other similar reports, two samples of serum showing a rising titre of antibodies are essential for a definite diagnosis of the current illness.

The largest proportion of sera examined were from patients with presumed virus infections of the respiratory tract, mainly pneumonia. The results indicate that the sera from such patients with suspected virus infection in Great Britain, should be tested for antibodies to *Strep. M.G.*, influenza viruses, the psittacosis-L.G.V. group of viruses, and *R. burneti*.

Suspected virus infections of the central nervous system can be investigated for antibodies to mumps and L.C.M. viruses and leptospires. Serological tests for poliomyelitis will probably be available in the near future. If these tests give negative results, tests for herpes virus and toxoplasmosis may help the diagnosis.

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NEW YEAR HONOURS

The list of honours published last week contains the names of the following members of the medical profession:

Order of Merit

Wilder Graves Penfield, C.M.G., M.D. Johns Hopkins, D.SC. Oxfd, F.R.C.S., F.R.S.
Professor of neurology and neurosurgery, McGill University, Montreal.

K.C.M.G.

Eric Denholm Pridie, C.M.G. D.S.O., O.B.E., M.B. Lond.
Chief medical officer, Colonial Office.

K.B.E. (Military)

Lieut.-General Frederick Harris, C.B., C.B.E. M.C., M.B. Dubl., Q.H.S.
Director-general, Army-Medical Services.
Surgeon Vice-Admiral Kenneth Alexander Ingleby MacKenzie, C.B., B.M. Oxfd.
Medical director-general, Royal Navy.

Knights Bachelor

Vincent Zachary Cope, M.D., M.S. Lond., F.R.C.S.
Consulting surgeon to St. Mary's Hospital, London.
Arthur William Mickle Ellis, O.B.E., D.M. Oxfd, F.R.C.P.
Emeritus regius professor of medicine, University of Oxford; consulting physician to the London Hospital.
Norman McAlister Gregg, M.C., CH.M. Sydney, F.R.A.C.S.
Ophthalmic surgeon, Royal Prince Alfred Hospital, Sydney.
Edmund Britten Jones, M.A. Oxfd, M.B. Adelaide, F.R.C.P.
Consulting physician. Adelaide Children's Hospital.
Peter MacCallum, M.C., M.A.N.Z., M.D., M.SC. Melb., F.R.A.C.P., M.R.C.P.E.
Formerly professor of pathology and dean of the faculty of medicine, University of Melbourne.

C.B. (Military)

Major-General Arthur Joseph Beveridge, O.B.E., M.C., M.SC., M.B. N.U.I., Q.H.P.
Surgeon Rear-Admiral Thomas Norman D'Arcy, C.B.E., L.R.C.P.I.
Air Vice-Marshal Edward Demetrius Dalziel Dickson, C.B.E., M.D. Edin., F.R.C.S.E., Q.H.S.
Consultant in otorhinolaryngology, R.A.F.
Major-General Frank Kingsley Norris, C.B.E., D.S.O., M.D. Melb.
Director-general of Medical Services. Australian Military Forces.

C.M.G.

Alfred Edward Rowden White, M.D. Melb., F.R.A.C.P.
Consulting physician, St. Vincent's Hospital, Melbourne.

C.M.G. (Honorary)

Samuel Layinka Ayodeji Manuwa, O.B.E., M.D. Edin., F.R.C.S.E.
Inspector-general of Medical Services, Nigeria.

C.B.E. (Civil)

Ivor Jones Davies, M.D. Lond., F.R.C.P.
Consulting physician, Ministry of Pensions Hospital, Rookwood, Cardiff.
John Lowe, M.D. Birm., M.R.C.P.
Senior specialist, Nigeria Leprosy Service.
Robert Alexander McCance, M.D. Camb., F.R.C.P., F.R.S.
Professor of experimental medicine, University of Cambridge.
Charles Lindsay Sutherland, O.B.E., M.D. Glasg.
Senior medical officer, Ministry of National Insurance.
Arnold Learoyd Walker, M.B. Camb., F.R.C.S., F.R.C.O.G.
Chairman, Central Midwives Board.
Robert Weaver, M.D. Belf.
Senior medical officer, Ministry of Education.

O.B.E. (Military)

Lieut.-Colonel Morris Sutherland Worgan Bisdee, M.R.C.S., R.A.M.C.

O.B.E. (Civil)

Reginald Norris O'Connell Blanc, M.B. N.U.I.
Senior medical officer, Colonial Medical Service, Tobago.
Eric Lauder Caldwell-Smith, M.B. Camb.
Chief medical officer, Shipping Federation Ltd.
John Singleton Darling, M.B. Belf., F.R.C.S.
Surgical specialist, Overseas Food Corporation.

TABLE I—DISTRIBUTION OF POSITIVE SERA AMONG ONLY THOSE PATIENTS FROM WHOM ADEQUATELY PAIRED WERE OBTAINED AND A FOURFOLD OR GREATER RISE IN TITRE DEMONSTRATED

Diagnosis	Influenza			Q fever	Psittacosis	Strep M G	Negative	T
	A	B	Total					
"Influenza" "Febrile catarrh" "Acute bronchitis"	34	18	52 (39%)	1 (0 7%)	0	3 (2%)	76	1
Lobar pneumonia	7	1	8 (10%)	0	1 (1%)	2 (2%)	72	[illegible]
Bronchopneumonia	3	1	4 (7%)	0	1 (2%)	1 (2%)	47	[illegible]
Virus or primary atypical pneumonia	11	8	19 (8%)	22 (9%)	2 (1%)	38 (16%)	160	[illegible]
P U O	0	3	3 (7%)	2 (5%)	1 (2%)	1 (2%)	35	[illegible]
Total			86 (16%)	25 (6%)	5 (1%)	45 (8%)	390	[illegible]

infective agent or may have been examples of aspiration pneumonia Of the patients diagnosed as having influenza, bronchitis, or febrile catarrh, about 39% had evidence of infection with influenza virus A or B These positives were confined to times of epidemic prevalence Evidence of infection with influenza virus was distributed fairly generally among diagnoses other than "influenza" and similarly confined to the epidemic period The incidence of Q fever was highest in the groups diagnosed initially as virus pneumonia or pyrexia of unknown origin By contrast, the incidence of infection with the psittacosis-L G V group of viruses, as determined serologically, was fairly evenly distributed between clinical diagnoses The incidence of *Strep M G* reactions was greatest (16%) in the group diagnosed clinically as virus or atypical pneumonia (Tests for cold agglutinins were usually made by the laboratory forwarding the sera, the Virus Reference Laboratory made these tests on only a small proportion of sera received direct from practitioners)

The influenza cases occurred, as already stated, during certain limited periods of three or four months in the two winters Cases of infection with the psittacosis-L G V group of viruses and with *R burneti* were distributed fairly evenly throughout the period Infection with agents causing illness characterised by the presence of cold hæmagglutinins or agglutinins to *Strep M G* was detected throughout the year but was more prevalent during the late summer and the winter months

It is obvious that, by chance, dual or even triple infection with these agents could take place, especially during the epidemic prevalence of influenza or of infection by *Strep M G* Thus, a resident in an area where there are cows or other animals infected with *R. burneti* might keep pigeons with ornithosis and himself be exposed to influenza Such a patient was seen at the beginning of May, 1950 This man, employed at a glass works, experienced on May 10 a cold and slight fever from which he recovered in two days On May 19 he became ill with severe headache, shivering, sweating, and pyrexia, clinically typical of Q fever Serological investigation of sera showed the following results

*Day**	*Complement fixation tests*				*Agglutination to Strep M G*
				Psittacosis	
7	<4†	32	<8	<10	<10
14	<4	32	32	20	<10
23	<4	32	256	20	<10

*From onset of second illness † Reciprocates of the titre

The rising titre of *R burneti* antibodies indicates that this patient had Q fever, which diagnosis was supported by the finding of two other cases of Q fever in the household Possibly the influenza-B antibodies were due to upper respiratory infection on May 10 If the tests had only been made for influenza, post-influenzal pneumonia might have been diagnosed The slight rise in titre to the psittacosis-L G V group of viruses possibly represents an anamnestic reaction, since the patient had kept pigeons in the past

Two cases of glandular fever with pneumonia were diagnosed during the period One had been diagnosed clinically as Q fever

CENTRAL NERVOUS SYSTEM

Most viruses are known to be able to cause vari degrees of infection of the central nervous syste particularly meningitis or meningo-encephalitis, but on a few of those viruses for which tests are available hav been shown to be responsible for a significant percenta of these cases During the period from January, 194 to December, 1950, it was possible to make compleme *fixation tests only for L C M and mumps and agglutinatio* tests for leptospires as a routine in cases diagnosed a benign aseptic meningitis, virus meningitis, meningo-encephalitis, or non-paralytic or abortive poliomyelitis A few patients were also tested for influenza, psittacos herpes, and Q-fever antibodies with negative results, and these tests are not included in table II Tests for thre strains of Coxsackie-A viruses were also made in some patients diagnosed as having aseptic meningitis o abortive poliomyelitis Complement fixing antibod were present in some sera to Dalldorf's group A, typ 1 and 2, and Melnick's High Point strain, but no new titres were found Neutralisation tests for Coxsackie viruses were not made in this period No satisfactory serological tests for poliomyelitis were available then

The results of tests on 138 patients in 1949 and 19 in 1950 from whom satisfactory samples of serum wer obtained are seen in table II They include results o patients from whom paired sera or one or more conva*lescent specimens* were received The sera were tested first for leptospires and L C M, and the negative ones the tested for mumps, so the latter series is smaller

There is no obvious explanation for the rise in the percentage of L C M *positives* in 1950 over 1949 other *than a possible increasing interest in the diagnosis* of L C M on the part of physicians The 19 patients in 1950 with either a rising titre (13) or positive convalescent serum suggesting recent infection with this virus cam from nineteen different localities, but 1 came from th same street as one of the 1949 cases

The proportion of leptospiral infections in 1950 (4·0%) was lower than in 1949 (7 7%) This may be due partly to the increasing recognition by doctors of the possibility of this organism being responsible for this type of meningitis with the result that many more sera were sent direct to Dr Broom and did not first pass through our hands as specimens from lymphocytic meningitis

TABLE II—RESULTS OF SEROLOGICAL INVESTIGATIONS FOR MUMPS, L C M, AND LEPTOSPIRAL ANTIBODIES IN PATIENT WITH SUSPECTED VIRUS INFECTION OF CENTRAL NERVOU SYSTEM OF UNKNOWN ÆTIOLOGY

Year	No examined	Mumps		L C M		Leptospirosi	
		No tested	No positive	No tested	No positive	No tested	No positive
1949	138	51	0	132 [134]	3* (2 2%) [5† (3 7%)]	130	10 (7 7%)
1950	196	73	2 (2 7%)	185 [191]	13* (7 3%) [19† (10 0%)]	196	8 (4 0%)

* Number with rising titres in two or more sera
† Total no of positives including single specimens or unchangin titres in paired sera

away. He was apologetic. He didn't know, perhaps I had forgotten—more tut-tutting from me—anyway, he meant no harm.

To those of ready wit and resource it would have been a trifle. But to me, with my moss-grown mentality, that little episode represents the red-letter day when I finished master of the situation.

* * *

Do you remember the story of the old Negro slave apprehended for having run away? "I can't understand you," said the judge petulantly: "you had a good master, plenty of food, a bed to sleep in." "Well, boss," retorted the Negro, "the situation's still open if you want it." And therein I think he epitomised the whole philosophy of living. How easy it is to make rules for other people. In the same way we contemplate with surprise the dissatisfaction of those who seem to have everything that anyone could wish. Probably they have everything except the one thing that they really desire. A nobleman with wealth, intellect, physical beauty, good health, charm, and apparently domestic happiness craved for one thing and would be satisfied with only that—to win the men's singles at Wimbledon. Could I help him, physically, psychologically, any way? Only after years of disappointment did he admit the impossibility, and it will be a poignant regret for the rest of his life. The richest man in our profession was disgruntled because he failed to secure a large consulting practice. A great lawyer whose success was the envy of all his professional brethren, whose ability to sway by his eloquence ought to have given him the most wonderful sense of power, fumed and fretted at his inability to lower his golf handicap below 14.

The more one is admitted to the secret ambitions of the great, the less one finds to envy, the more one realises the profundity of the banal truism that it is not what you have but what you are satisfied with that really counts.

* * *

A junior colleague of ours was recently assigned to the tropics, and the veterans among us gave him the usual hints and tips. Most of us knew there was a medical school out there, though none of us had seen it. Exact information could, of course, have been found in the *Universities Yearbook*, but being doctors we didn't know it existed. And so, when our friend said he was taking them a current textbook of medicine, we agreed it was a kindly thought, and that the East would know how to value this fraternal gesture from the West. Indeed it did, as we learned on our colleague's return at the end of the session. He was bronzed and fit, but much quieter than he used to be—not quite the debonair Empire-builder we had said goodbye to. "Well, what sort of a joint was it?" we asked. "A swell set-up—in fact they're better equipped than we are. New buildings, you know, with first-class research facilities, and all sorts of gadgets and fittings that this university's never heard of." "But surely the staff must be rather mothy?" "Mothy? They're all two-fellowship men." "You mean Eng. and Ed.?" "No, Lond. and Eng.—you can't tell the physicians from the surgeons." "And what about the book?" "They were quite nice about it, but a consignment of it had got there before I did. 'If you don't want your copy,' they said, 'it would be appreciated by the Women's Institute—they're all medicine-minded now, and like to catch the radio and television doctors out. Or there's the grammar school—they'd welcome it, since we gather that medicine is soon to be recognised as a G.C.E. subject.' 'Thanks for these happy suggestions,' I replied, 'but I think I'd better read it myself.'"

Our general conclusion is that the Empire, far flung though it be, is now (culturally speaking) a built-up area, and that there's really no place like home.

* * *

Overheard at a forensic examination

Examiner: Dissertate on this rag.
Candidate: It's bloodstained, Sir.
Examiner: Good. How old is the stain?
Candidate: A little over six months, Sir.
Examiner: Very good, but how do you know that?
Candidate: You showed me the same rag six months ago, Sir.

Letters to the Editor

THE NURSE'S RESPONSIBILITY

SIR,—May I comment on your leading article of June 6? With reference to the disaster you cite, I cannot believe that anyone in the medical-nursing team can be exonerated from blame for failure to read and understand the label of any container of drugs or products to be administered to a patient. The fact that the responsibility of administration ought not to have been delegated does not lessen the blame for the omission. It would seem to be almost as fundamental to expect that enough of the drug or medicament required should be available before the treatment is begun.

The estimation of blood-pressure has for some time been included in the course of training for pupil-midwives, whether registered nurses or not (C.M.B. rules B 36 (*d*)). The syllabus of subjects for examination for the certificate of general nursing requires "taking and recording blood pressure" (G.N.C. England and Wales, 1952, final examination VII). Preparation for intravenous injection is also to be taught. As long ago as 1937 a doctor writing in the *Nursing Times* (Dec. 25) criticised the training of English nurses and pointed out that in France intravenous injections are generally given by the nurse, rarely by the doctor.

This raises the question of the proper duty of the nurse. Obviously a nurse in training should be taught only those skills and techniques ordained by the registering body and should never be asked to perform as an employee what she may not be taught as a student. But once the nurse is trained and registered it would be difficult to agree that she should never undertake what she did not learn while training, or any technique not mentioned in a syllabus which may have been drawn up years ago. The essential requirements seem to be: (1) that the decision to permit a nurse, or other person in the ward team, to perform a procedure shall be a result of deliberate policy, arrived at by discussion between all the persons concerned, including the body having ultimate responsibility; (2) that the technique must have been thoroughly learned and practised until the requisite skill is attained and is known to have been attained; (3) that whenever it is foreseen that a nurse or other person, who does not normally apply a particular technique, may be called on to apply it in an emergency, or in the absence of the person who usually undertakes it, she must have received the necessary training. Otherwise an emergency may become a disaster.

Drugs, procedures, skills, and techniques are changing and developing so rapidly that it would seem imperative that the nursing councils should have permanent curriculum committees, whose business it would be to issue from time to time "addenda" on training between the periodical reviews of the entire curriculum and syllabus.

Edinburgh. G. B. CARTER.

SIR,—I read with interest and concurrence your leading article, and I also read a reply last week by Dr. R. E. Smith.

We, in the nursing profession, do realise how busy the house-physicians and house-surgeons are, and we would help in all possible ways to lighten their load provided this does not entail neglecting nursing duties. The State-registered nurse not only nurses her patients but also helps in the training of the student nurse, and I feel that the satisfactory fulfilment of these duties constitutes a full-time job.

Who will be held responsible if a patient develops a bedsore? The nurse, because she has failed to carry out her nursing procedures adequately, or the doctor, because he has prevented her from so doing by adding

HEADACHE AND HYPERTENSION

I McD G Stewart
M D Lond , M R C P

MEDICAL REGISTRAR UNITED BRISTOL HOSPITALS ,
UTOR IN MEDICINE UNIVERSITY OF BRISTOL

nt years fresh efforts have been made to treat ion by arbitrary reduction of the blood-pressure , and indeed with some success By sympathectomy, or treatment with drugs, not only has it proved possible to lower the pressure, at least temporarily, but also left ventricular failure has been observed to recover, heart size to diminish, fundal changes to regress and electrocardiographic abnormalities to return to normal At the same time paroxysmal breathlessness has been overcome and vision improved These are substantial benefits Unfortunately they are seldom achieved Many claims to success have been based upon less substantial grounds They have derived solely from the alleged cure of symptoms. But of what exactly, had these patients complained ? What are these "symptoms of hypertension" ? Do they indeed exist apart from those disorders of organs which accompany or complicate the course of hypertensive disease ?

Clearly some doctors believe that they do The most highly accredited symptom is "headache" Others widely acknowledged include "dizziness" "lack of energy," and "lack of concentration" The cure of such complaints has often been taken to prove the worth of a treatment More than one remedy has claimed support solely on the strength of its reputed efficacy in the "relief of symptoms"—the particular ills so ameliorated remaining unspecified

This kind of language has appeared repeatedly in the medical literature during the past few years Even Smithwick (1940), who first popularised splanchnic sympathectomy, scarcely defined the "symptomatic relief" which he designated one of the important objects of surgery , admittedly his main intent was to offer an improvement in survival-rate Many of his followers have been less restrained

For example, no misgiving prevented FitzGerald (1950) from proclaiming his view that "symptomatic relief is one of the greatest blessings conferred by sympathectomy symptoms determine the operability one frequently operates for their alleviation alone This is a simple but well proven maxim" He did not define these symptoms His contention, in common with that originally put forward by Smithwick (1948) was that operation should be undertaken early Clearly, therefore, they could not have been caused by heart failure, uræmia, or hypertensive retinopathy such are late events in the disease

"Shortness of breath. intellectual decline, and irascibility " were said by Atkins (1950) to have been evident among his hypertensive patients, many of whom, nevertheless, "complained mainly of headache" Hammarström and Bechgaard (1950) defined a group of hypertensives in whom there were "marked subjective symptoms but without signs of myocardial damage", on the strength of this criterion these hypertensives were subjected to surgery Yet the symptoms thus held to have been so significant could scarcely have included paroxysmal dyspnœa or visual disability, since pulmonary œdema consequent on hypertension, and retinal changes sufficient to affect vision, are, again, virtually always accompanied by the appearances of myocardial strain or failure

Chris (1951) accepted "severe headaches" as one of the most important of "definite symptoms referable to hypertension," thereby constituting an indication for sympathectomy Allen (1952), however, has reported that American surgeons have recently lost some of their enthusiasm for sympathectomy as a means of dealing with "hypertensive headache"

Most of the physicians who have conducted trials with the new methonium drugs have written in similar vein.

Thus Murphy (1951) reported that "symptomatic improvement was impressive" in most of his cases, while Mackey and Shaw (1951) maintained that "of all the manifestations of hypertension headache is the most easily relieved"

Smirk and Alstad (1951) were satisfied about the benefit to "headache, dyspnœa, and vertigo" A few months later Smirk (1952) gave as the main hope offered by prolongation of the action of hypotensive drugs the prospect that more relief might be afforded to the 10% of hypertensive patients whose headaches are at present insufficiently relieved"

Much the same type of claim has been advanced on behalf of the rice diet treatment originally suggested by Kempner A report published by a committee of the Medical Research Council (1950) included the sentence "Of 33 patients with symptoms referable to hypertension 25 (75%) obtained relief Headaches, which were present in 26, disappeared in *all but 4, often within a few days of starting the diet*"

It cannot be denied that people who have hypertension are liable to complain of headache, to experience dizziness and shortness of breath, even to lose their tempers Such distresses, however, are not unusual It does not follow that the blood-pressure is in any way to blame To establish a sequence of cause and effect more evidence is required Can there be demonstrated any clear relation with hypertension ? Is there, perhaps, a type of headache that is characteristic of hypertensive disease ?

Despite the confident assertions that have been quoted these are disputed questions

For example, Russell Brain (1952) writes "High blood-pressure causes paroxysmal, throbbing or 'bursting' headaches," and Platt (1950) asserts that "true hypertensive headache may be frontal or occipital and is usually most prominent in the early morning" Alexander (1948), in common with many other writers, has drawn attention to a parallel with migraine

Symonds (1946), however, contents himself with the more cautious statement that "headache is a common but inconstant symptom of arterial hypertension," while making the reservation that he is excluding from consideration the "relatively rare condition known as hypertensive encephalopathy" Wood (1950a) goes further and declares roundly that "it is doubtful whether any symptoms can be ascribed to high blood pressure itself" Others have agreed with this view

It was in an attempt to clarify this association between high blood-pressure and the symptoms that so often accompany it that the following clinical study was undertaken Particular attention was paid to the significance of headache

Scheme of Investigation

The study was made upon 200 consecutive cases of severe hypertension and upon a number of controls All the patients were interviewed and examined by me Among the hypertensives the only criterion of selection was the height of the diastolic blood-pressure The standard adopted was a minimum of 120 mm Hg, measured with the patient recumbent, after ten minutes' rest in that position Whenever a reading had been made previously by another observer, the level then noted had nearly always been considerably higher than that obtained by this routine technique Occasionally the pressure was found at a subsequent examination to have fallen below 120 mm Hg Unless there had been obvious cause for this—e g , intervening cardiac infarction—all record of the patient was expunged from the survey. It was thought best to abide by the blood-pressure alone as a standard for inclusion in the series Inevitably, however, this led to the omission of a few patients who, though clearly severely hypertensive, never presented a sufficiently high diastolic level, because when they were first seen, they had cardiac failure, recent infarction, or some similar complication

The following points were determined

(1) Whether or not the patient was aware of the raised blood pressure

(2) The volunteered symptoms, if any, in the order in which they were volunteered

special techniques to her already over-full programme? It is a question not only of legal responsibility—although this is a serious consideration—but of allowing the nurse to nurse her patients. She does not want to become a technician.

The nurse is adequately equipped to take her place after registration in a surgical or medical ward. She will increase her value to her patients and to the senior staff when she gains experience in that particular ward or department, but I deprecate the suggestion that she should specialise and be expected to carry out special procedures.

If the time is ripe, as Dr. R. E. Smith suggests, for another Commission on Nursing, let this be set up by the nurses of the country.

South Devon and East Cornwall Hospital, Plymouth. ANN G. NOTMAN Sister Tutor.

TUBERCULOSIS IN GLASGOW

SIR,—Dr. Paul's letter last week does not contain any convincing evidence that social improvements can eradicate tuberculosis. In 1950 over 14,000 people in England and Wales died of tuberculosis: if this death-rate was one-tenth of the death-rate a hundred years previously, it does not demonstrate a satisfactory position in 1950, but emphasises how dreadful tuberculosis was in 1850. Any complacency, therefore, is Dr. Paul's, not mine.

It is from the behaviour of the tuberculosis death-rate in the past five years, however, that the most valuable lessons can be learned. In Northern Ireland, where the trend has been similar to that in the rest of the United Kingdom, this rate was 73 per 100,000 in 1947. In 1952 it was approximately 30 per 100,000. In the intervening five years as much had been achieved in reducing tuberculosis mortality as in the previous forty years. Furthermore, the reduction in the number of deaths has been accompanied by a reduction in the number of new cases which are being discovered. The present position is directly related to the vigorous efforts of the Northern Ireland Tuberculosis Authority since 1947 to provide for the diagnosis and treatment of tuberculosis in the Province, and we are now in a position to measure our progress towards eradication not in generations and centuries but in single years. It is quite true that for many of our patients the new drugs have postponed death and that tuberculous lesions can relapse; but life for all of us is a postponement of death, and if, after treatment, a tuberculous patient can be restored to normal health, it is not of great importance whether we say that his death has been postponed or that his life has been saved.

I am not as ignorant of the epidemiology of tuberculosis in other countries as Dr. Paul might think. The high standard of living in Scandinavia has been accompanied by a high rate of hospital building, and as far as I know there has never been a waiting-list for Scandinavian chest hospitals. While the new drugs have made the treatment of tuberculosis infinitely more efficient, it was far from being ineffective before. The countries, therefore, in which the isolation and treatment of the majority of their infectious cases of tuberculosis have always been possible are certain now, with the addition of modern discoveries, to have less tuberculosis than elsewhere.

It is not possible here to explore the vast subject of the immunology of tuberculosis. It should scarcely be necessary to remind Dr. Paul that measures which are effective in abolishing one infectious disease are not necessarily effective against another, and that the tubercle bacillus shows certain important differences from the diphtheria bacillus. The majority of deaths from tuberculosis occur in those sections of the population which contain the largest numbers of positive reactors to tuberculin, and if a positive tuberculin test as a indication of acquired resistance is compared to a negativ Shick test, this would mean that the greatest number o deaths from diphtheria should occur amongst thos groups containing the largest numbers of negativ Schick-reactors, which is obviously absurd. The mechanism of acquired resistance to tuberculosis, therefore is quite different from that of any other disease, and I share Dr. Paul's appreciation of the irony of injectin live tubercle bacilli into the non-tuberculous subject of civilised nations. I can give details to Dr. Paul, if he would like to have them, of other civilised nations in which tuberculosis is being controlled by the isolatio and treatment of infectious cases, in which a positiv tuberculin reaction is regarded as a danger and no a blessing, and in which the complete eradication o tuberculosis is already in sight.

I have not been trailing my coat, and there wa nothing particularly astonishing about my previou letter. It could provoke only those who have not realised yet that there has been a scientific revolution in the treatment of tuberculosis. This revolution demands a new approach to the disease and a re-examination of previous theories, however sanctified they may have become by the passage of time and the prestige of those who hold them. It is clear to me, as it is to any clinician who pauses to look around him, that we have within our hands the means of abolishing tuberculosis and of making a tremendous contribution to human happiness. But we must not be obstructed. If we are given the tools we can finish the job.

Dungannon Chest Hospital, co. Tyrone. E. F. JAMES.

MITRAL STENOSIS

SIR,—In their very interesting and inspiring paper (May 30) Mr. Logan and Dr. Turner do not mention simple venesection in the treatment of acute pulmonary œdema. In my experience withdrawal of 300 ml. of blood is the quickest and safest way of bringing out of immediate danger a patient with acute pulmonary œdema.

Municipal Hospital, Aalborg, Denmark. CARL SCHWENSEN.

PHARMACEUTICAL ADVERTISEMENTS

SIR,—Much of the costly advertising matter which is causing so much concern to your readers must be regarded as a direct consequence of the N.H.S., which has attracted into the so-called "ethical" pharmaceutical trade a great number of firms with no real roots in the industry. Thus there are makers of various useful household goods and foods who are exploiting commonplace preparations of well-known drugs with the simple ferocity with which they would otherwise be marketing furniture-polish or stocking dyes. To make a nationally advertised nostrum acceptable for N.H.S. prescribing, all that need be done is to register another trade mark and suitably adjust the package.

Another contributory factor is the fact that many minor firms of wholesale druggists, who formerly reaped a comfortable but unspectacular revenue from materials for medical dispensing (e.g., mist. expectorans 1-8), have had this relatively harmless activity dislocated by the N.H.S. and have had to buy a battery of tablet-machines and the services of an advertising agent to make up for the consequent loss of trade.

Prescribers sometimes seem to me to take an irrational pride in their ignorance of the composition of the preparations they prescribe; they should, at least, attempt to learn a little about the status and antecedents of their manufacturers. For example, Megatherium Pharmaceuticals (1947) Ltd. undoubtedly spend a great deal of money on research—*market* research. Their most highly paid technician is the sales manager, who is *often* director of pharmacological research as well. His chief reason for

Faculty of Radiologists

The annual meeting of the faculty will open at the Royal College of Surgeons, London, at 9 30 A M on Friday, July 3, and will continue on July 4

Lady Tata Trust

The trustees of this fund announce that they have made the following awards for research on leukæmia and allied diseases, in the year beginning next October

Grants for research expenses or for scientific assistance—Dr Astrid Fagraeus and Dr Bo Thorell (Stockholm), Dr Clarence Mershey (Cape Town), Prof. Charles Oberling (Paris), Dr C C Ungley (Newcastle upon Tyne), Dr Jo Nordmann (Paris)

Part time personal grant—Dr J B G Dausset (Paris)

Scholarships—Dr Ragna Rask Nielsen (Copenhagen) Dr Roger Robineaux (Paris), Dr Flemming Kissmeyer Nielsen (Aarhus, Denmark), Dr N A Stenderup (Aarhus, Denmark)

Senior Research fellowships—Dr A R. Gopal Ayengar (India) for work at the Royal Cancer Hospital, Dr Jorgen Kieler (Denmark) for work at the Fibiger Laboratories Copenhagen

A special scholarship awarded to Dr Gavino Negroni (Italy), for work at the Imperial Cancer Research Fund Laboratories, will continue until April 30, 1954

Beit Fellowship for Medical Research

The following awards have been made

Fourth-year Fellowship

JOAN E KEILIN MA, MB, PHD Camb To investigate the catalytic activity of hæmatin compounds and the effect of oxidising agents on hæmatins Also to investigate the properties of purified helicorubin and its relationship to other natural hæmoproteins and to investigate the reactions of hæmatins with proteins and their constituent amino acids and peptides to gain more information as to the structure of the hæmoglobin molecule and the link between the hæm and globin and to use hæmatin as a reagent for the study of other biologically important proteins At the Department of Biochemistry, Cambridge

Junior Fellowships

J R. CANNON, M.SC, Sydney To continue the study of the chemical structure of Vitamin B_{11} At University Chemical Laboratories, Cambridge

G P LEWIS B PHARM Wales To study the relationship between structure and action of drugs particularly of antagonists of histamine, acetylcholine adrenaline and noradrenaline, to examine how far ionisation of a drug or its receptor modifies drug action At the National Institute for Medical Research, Mill Hill London

W L NICHOLAS, B SC Lpool To investigate the determination of the growth requirements of free living and parasitic nematodes in chemically defined media with a view to its possible application to the chemotherapy of nematode infections At the Department of Zoology, Liverpool University

EVELYN E B SMITH, B.SC PH D Glasg To investigate the enzymic mechanisms of transfer reactions involving uridine pyrophosphate compounds containing glucose, glucuronic acid, and N-acetylglucosamine and the biosynthesis of glucuronic acid, glucuronides, and oligosaccharides containing glucuronic acid, using carbon and phosphorus isotopes At the Department of Biochemistry, Glasgow University

South Western Regional Hospital Board

The Minister of Health has appointed Sir Havergal Downes Shaw, O B E, to be chairman of this board Sir Havergal Downes Shaw, a former departmental manager of the Imperial Tobacco Company, has been a member of Bristol City Council since 1931 and an alderman since 1946

Society for Relief of Widows and Orphans of Medical Men

This society s annual meeting was held on June 10, with Sir Robert Young, the president, in the chair Members of the society number 198, and at the end of 1952 there were 35 widows in receipt of grants Widows over 65 receive £75, and those under that age £60 a year In addition a present of £30 was made at Easter, and again at Michaelmas The total amount distributed in 1952 was £4525 Sir Ernest Rock Carling, the treasurer, reported that during the year income exceeded expenditure by £723 The address of the society is 11, Chandos Street, London, W 1

Institute on Œsophageal Speech

An institute on teaching and improving œsophageal speech will be held on Aug 10–16 at the Cleveland Hearing and Speech Center, Cleveland, Ohio This institute is being sponsored by the American Cancer Society, the National Cancer Institute of Institutes of Health the Office of Vocational Rehabilitation, the Cleveland Otolaryngological Society, the Cleveland Academy of Medicine, and the Western Reserve University School of Medicine Non speaking laryngectomised persons may attend without charge They may be sent by surgeons, cancer societies, societies for crippled persons, and rehabilitation services Surgeons speech pathologists, and laymen are also invited to attend the sessions Application must be made by July 15 to Warren H Gardner, PH D program chairman 11206 Euclid Avenue, Cleveland 6, Ohio

Royal Medical Benevolent Fund

At the annual meeting, held on June 9, honorary of were re elected as follows president, Lord Webb-John treasurer, Mr F A Juler, secretary, Dr R Cove Smith

International Hæmophilia Society

A meeting of this society is to be held at Seymour H London, W 1, on Sunday, June 21, at 2 P M The Lond Group will meet at the society's offices, 94, Southwark Brd Road, S W 1, on Wednesday, July 1, at 6 30 P M

Visitor in Lunacy

The Lord Chancellor has appointed Dr R G Ander a commissioner of the Board of Control, to be a medical v in the place of Dr A E Evans who is retiring

Oxford Graduates Medical Club

The summer dinner will be held in the Queen's Colle Oxford, on Friday, July 10, at 7 for 7 30 P M Dr C G Douglas, F R S, will preside Tickets (£2 2s inclusive) m be had before July 4 from Mr Selwyn Taylor, F R C S, Roedean Crescent, London, S W 15

Diary of the Week

JUNE 21 TO 27

Monday, 22nd

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 1
4 P M Dr W Ritchie Russell Poliomyelitis

Tuesday, 23rd

SOCIETY FOR ENDOCRINOLOGY
5 30 P M (1, Wimpole Street W 1) Dr Charles Hug (Chicago) Prostatic Glands as Targets for Steroids.

Wednesday, 24th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr E F Gale Mode of Action of Antibacterial A (First of two lectures)
INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle St W C 2
5 30 P M Dr H Haber Parapsoriasis, Poikiloderma Mycosis Fungoides
BRITISH ASSOCIATION OF SPORT AND MEDICINE
5 P M (Westminster Hospital Medical School Horseferry Road S W 1) Sir Adolphe Abrahams, Dr A McEldowney Doping of Athletes
BIRMINGHAM MEDICAL INSTITUTE 154, Great Charles Stre Birmingham 3
8 P M *Section of Psychiatry* Dr W Mayer Gross Problem of Symptomatic Psychoses.

Thursday, 25th

ROYAL COLLEGE OF SURGEONS Lincoln s Inn Fields, W C 2
5 P M Prof Arnold Sorsby New Antibiotics
UNIVERSITY COLLEGE Gower Street, W C 1
4 45 P M Prof J H Quastel D SC, F R S (Montreal) Act of Drugs on Enzyme Systems
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Colonel W R M. Drew Recent Advances in Malar Problems
INSTITUTE OF CHILD HEALTH The Hospital for Sick Childre Great Ormond Street, W C 1
5 P M Dr W C Davison (Duke University, North Carolina Childhood Cancer
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Subcutaneous Mycotic Infec
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray s Inn Road, W C 1
5 30 P M Prof B Gusic (Zagreb) Pathological Chang Blood vessels and Nerves of Œsophagus Due to Corro
BRITISH ASSOCIATION OF UROLOGICAL SURGEONS Home and Overseas
11 A.M (General Infirmary, Leeds) Short papers
2 P M Professor Huggins Adrenal in Cancer

Friday, 26th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr C E Dent Diagnosis of Hyper parathyroidis
4 P M Prof L J Witts Splenomegaly and Splenectomy
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3 30 P M Mr Anthony Radcliffe Chronic Rhinitis
BRITISH ASSOCIATION OF UROLOGICAL SURGEONS Home an Overseas
9 30 A M Mr J Cosbie Ross Mr J G Gow Dr J Col Mr M I Nicholls Urinary Tuberculosis

Saturday, 27th

UNIVERSITY OF CAMBRIDGE
10 30 A [illegible] Hospital (Cambridge) [illegible] of the ear nose, and throat

BRITISH ASSOCIATION OF UROLOGICAL SURGEONS Home a Overseas
9 30 A M Short papers and films

including some new component in a remedy may be to give his advertisement copywriters something to work on.

It would be, of course, both impracticable and undesirable to try to enforce any kind of closed shop in the pharmaceutical industry. Only an undischarged bankrupt is at present restricted from evolving some new formula of analgesics and sedatives and launching it on to the nation's drug bill with costly advertising. But prescribers should learn to recognise the comparatively few drug firms which make a real contribution to medicine through original research, and adjust their prescribing habits accordingly—and Megatherium Pharmaceuticals (1947) Ltd. should return to their shoe-polish, home perms, or whatever their proper line of country may be.

London, W.5. JOHN LOTHIAN.

BARBITURATES AND ALCOHOL

SIR,—In your annotation of June 6 you ask whether simultaneous intake of barbiturates and alcohol involves a grave risk of fatal poisoning, or whether the two fatal cases reported are merely examples of particular idiosyncrasies.

A comprehensive series of investigations into this question has been made here. We concluded, from clinical data and chemical analyses, that intake of relatively moderate doses of barbiturates and relatively large doses of alcohol may prove fatal, and that accordingly administration of barbiturates, especially intravenously, to severely intoxicated persons is extremely dangerous. This empirical material will be published later.

Further, we have shown that intake of alcoholic drinks by persons with chronic bromism may lead to death.

Even more important from a clinical point of view is our demonstration that injection of therapeutic doses of morphine salts (15–30 mg.) or of morphine-scopolamine in persons with 0·18–0·2% or more alcohol in the blood effects an often fatal poisoning with all the signs and symptoms of severe morphine poisoning. Within the past few years we have examined 16 fatal cases of this type. In several instances the drugs had been given as sedatives to persons who had been violent owing to alcohol intoxication.

A paper on our experiences concerning morphine in association with alcohol, published in Danish in December, 1952,[1] has been accepted for publication in the *Bulletin of Narcotics* United Nations, New York).

Department of Pharmacology,
University of Copenhagen. KNUD O. MOLLER.

EFFECT OF GLUTAMIC ACID ON THE COMA OF HEPATIC FAILURE

SIR,—I read with great interest the account by Dr. Walshe of the treatment of hepatic coma with intravenous sodium glutamate (May 30). This is undoubtedly of the greatest importance, especially as it applies to a group of cases with which my own régime[2] has not proved very successful. Like Karl et al.[3] I have seen only one recovery after coma due to hepatic cirrhosis.

Although sodium glutamate will be a welcome addition to our therapeutic weapons, I should like to emphasise that in the type of hepatic coma which we have been treating at Newcastle it will still be necessary to continue with a régime of the kind I have described. As your leading article (June 6) clearly states, the liver cells in acute necrosis are suffering from the effects of some acute noxa which does not persist. This almost certainly means that they require supportive therapy during the period of recovery.

Your article also lays stress on the importance of electrolytes in therapy. With this I fully agree. Not only is there the question of electrolyte disturbance owing to intravenous glucose, &c., but I have also on several occasions seen cases of postoperative liver-failure associated with biliary drainage, which had low serum levels of sodium and chloride, and which responded dramatically to the administration of hypertonic saline.

As the Newcastle series increases, the mortality-rate still remains somewhere between 10 and 20%. I believe that this is a distinct improvement on previous forms of therapy, especially as care is now being taken to include for statistical evidence only those cases in which massive amino-aciduria has been demonstrated by paper chromatography. The régime has been slightly modified in that after the first few days $^1/_5$ normal, and not normal, saline is now used. Gamma-globulin is also given in those cases where the hepatitis virus may still be active.

The therapy is still proving useful for liver-failure in obstetrics and in the preparation of patients for operation in the presence of jaundice. Other centres seem to be having similar success with both medical and surgical patients.

It is a pleasure once again to thank colleagues at the Royal Victoria Infirmary who have helped in this work.

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Newcastle upon Tyne. A. L. LATNER.

TRANSPLANTATION OF HUMAN TUMOURS

SIR,—I was very interested to read of H. W. Toolan's success in transplanting human tumours into cortisone-treated weanling rats.[1]

Since October of last year I have been engaged in work under the direction of Prof. R. W. Scarff on heterologous tumour transplants, using various sites in mice and rats including the peritoneum, the anterior chamber of the eye, and the lens. The brain has also been used in adult irradiated and non-irradiated animals, and in these cases it soon became apparent that fibrous tissue appeared to grow down the needle track and surround the graft.

During discussions with my colleague Dr. J. B. Walter, it was agreed that corticotrophin and cortisone might inhibit the last reaction to the implant. Only a small quantity of cortisone was available, and therefore investigations were limited to a few animals.

The tumour used was a subcutaneous secondary "oat-cell" carcinoma removed by Mr. W. Grundill, at Harefield Hospital. Cortisone by subcutaneous injection was started three days before inoculation or implantation and continued daily. In a case where a small portion of tissue was implanted directly into the brain (using a technique similar to that of H. S. N. Greene[2]) the malignant and the fibrous tissue of the graft remained viable with little surrounding inflammatory reaction. This was twenty-six days after implantation.

In cases where cortisone was not started until five days after implantation the tumour showed almost complete regression after eleven days with marked surrounding cellular reaction.

In one case, where scrapings from the cut surface of the tumour were inoculated through the skull without drilling, there was histological evidence of vascularisation and invasion by tumour showing mitoses, some of which were aberrant. There was very little cellular reaction to the tumour in this case. The animal died on the thirteenth day after tumour inoculation.

Naturally, the significance of these isolated cases is impossible to assess, but in view of these and H. W. Toolan's work further investigation will be undertaken when cortisone is available. It may well be unnecessary to use weanling animals. The mice I used were thirty-four days old at the start of the experiments.

Other effects (presumably due to the cortisone) were a decrease in the total white-cell count with lymphopenia,

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[1] *Ugeskr. Læg.* 1952, 114, 1785.
[2] Latner, A. L. *Brit. med. J.* 1950, ii, 748.
[3] Karl, M. E., Howell, R. A., Hutchinson, J. H., Catanzaro, F. G. *Arch. intern. Med.* 1953, 91, 159.

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[1] See *Proc. Amer. Ass. Cancer Res.* 1953, 1, 56; *Lancet*, May 16, 1953, p. 982.
[2] *Cancer Res.* 1951, 11, 529.

HEADACHE AND HYPERTENSION

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nt years fresh efforts have been made to treat ion by arbitrary reduction of the blood-pressure , and indeed with some success By sympathectomy, or treatment with drugs, not only has it proved possible to lower the pressure, at least temporarily, but also left ventricular failure has been observed to recover, heart size to diminish, fundal changes to regress, and electrocardiographic abnormalities to return to normal At the same time paroxysmal breathlessness has been overcome and vision improved These are substantial benefits Unfortunately they are seldom achieved Many claims to success have been based upon less substantial grounds They have derived solely from the alleged cure of symptoms. But of what, exactly, had these patients complained ? What are these " symptoms of hypertension " ? Do they indeed exist apart from those disorders of organs which accompany or complicate the course of hypertensive disease ?

Clearly some doctors believe that they do The most highly accredited symptom is " headache " Others widely acknowledged include " dizziness," " lack of energy," and " lack of concentration " The cure of such complaints has often been taken to prove the worth of a treatment More than one remedy has claimed support solely on the strength of its reputed efficacy in the " relief of symptoms "—the particular ills so ameliorated remaining unspecified

This kind of language has appeared repeatedly in the medical literature during the past few years Even Smithwick (1940), who first popularised splanchnic sympathectomy, scarcely defined the " symptomatic relief " which he designated one of the important objects of surgery , admittedly his main intent was to offer an improvement in survival rate Many of his followers have been less restrained

For example, no misgiving prevented FitzGerald (1950) from proclaiming his view that " symptomatic relief is one of the greatest blessings conferred by sympathectomy symptoms determine the operability one frequently operates for their alleviation alone This is a simple but well proven maxim " He did not define these symptoms His contention, in common with that originally put forward by Smithwick (1948), was that operation should be undertaken early Clearly, therefore, they could not have been caused by heart failure, uræmia or hypertensive retinopathy such are late events in the disease

" Shortness of breath, intellectual decline, and irascibility " were said by Atkins (1950) to have been evident among his hypertensive patients, many of whom, nevertheless, " complained mainly of headache " Hammarström and Bechgaard (1950) defined a group of hypertensives in whom there were " marked subjective symptoms but without signs of myocardial damage " , on the strength of this criterion these hypertensives were subjected to surgery Yet the symptoms thus held to have been so significant could scarcely have included paroxysmal dyspnœa or visual disability, since pulmonary œdema consequent on hypertension, and retinal changes sufficient to affect vision, are, again, virtually always accompanied by the appearances of myocardial strain or failure

Chris (1951) accepted " severe headaches " as one of the most important of " definite symptoms referable to hypertension," thereby constituting an indication for sympathectomy Allen (1952), however, has reported that American surgeons have recently lost some of their enthusiasm for sympathectomy as a means of dealing with " hypertensive headache "

Most of the physicians who have conducted trials with the new methonium drugs have written in similar vein

Thus Murphy (1951) reported that " symptomatic improvement was impressive " in most of his cases, while Mackey and Shaw (1951) maintained that " of all the manifestations of hypertension headache is the most easily relieved "

Smirk and Alstad (1951) were satisfied about the benefit to " headache, dyspnœa, and vertigo " A few months later Smirk (1952) gave as the main hope offered by prolongation of the action of hypotensive drugs the prospect that ' more relief might be afforded to the 10% of hypertensive patients whose headaches are at present insufficiently relieved "

Much the same type of claim has been advanced on behalf of the rice diet treatment originally suggested by Kempner A report published by a committee of the Medical Research Council (1950) included the sentence " Of 33 patients with symptoms referable to hypertension 25 (75%) obtained relief Headaches, which were present in 26, disappeared in all but 4, often within a few days of starting the diet "

It cannot be denied that people who have hypertension are liable to complain of headache, to experience dizziness and shortness of breath, even to lose their tempers Such distresses, however, are not unusual It does not follow that the blood pressure is in any way to blame To establish a sequence of cause and effect more evidence is required Can there be demonstrated any clear relation with hypertension ? Is there, perhaps, a type of headache that is characteristic of hypertensive disease ?

Despite the confident assertions that have been quoted these are disputed questions

For example, Russell Brain (1952) writes " High blood-pressure causes paroxysmal, throbbing, or ' bursting ' headaches," and Platt (1950) asserts that " true hypertensive headache may be frontal or occipital and is usually most prominent in the early morning " Alexander (1948), in common with many other writers, has drawn attention to a parallel with migraine

Symonds (1946), however, contents himself with the more cautious statement that " headache is a common but inconstant symptom of arterial hypertension," while making the reservation that he is excluding from consideration the " relatively rare condition known as hypertensive encephalopathy " Wood (1950a) goes further and declares roundly that " it is doubtful whether any symptoms can be ascribed to high blood pressure itself " Others have agreed with this view

It was in an attempt to clarify this association between high blood pressure and the symptoms that so often accompany it that the following clinical study was undertaken Particular attention was paid to the significance of headache

Scheme of Investigation

The study was made upon 200 consecutive cases of severe hypertension and upon a number of controls All the patients were interviewed and examined by me Among the hypertensives the only criterion of selection was the height of the diastolic blood-pressure The standard adopted was a minimum of 120 mm Hg, measured with the patient recumbent, after ten minutes' rest in that position Whenever a reading had been made previously by another observer, the level then noted had nearly always been considerably higher than that obtained by this routine technique Occasionally the pressure was found at a subsequent examination to have fallen below 120 mm Hg Unless there had been obvious cause for this—e g , intervening cardiac infarction—all record of the patient was expunged from the survey It was thought best to abide by the blood-pressure alone as a standard for inclusion in the series Inevitably, however, this led to the omission of a few patients who, though clearly severely hypertensive, never presented a sufficiently high diastolic level, because when they were first seen, they had cardiac failure, recent infarction, or some similar complication

The following points were determined

(1) Whether or not the patient was aware of the raised blood pressure

(2) The volunteered symptoms, if any, in the order in which they were volunteered

which was used to some extent as a guide to effective dosage. At necropsy there was enlargement of the liver with marked fatty change in the mid-zones and, to a certain extent, the peripheral zones. No increase in glycogen was observed in histological preparations of the liver.

In five weanling rats which are being used for the first passage of a human tumour the two cortisone-treated animals bearing subcutaneous transplants weigh 10 and 11 g. at twelve days as against the 32 g. of each of the three controls. In the absence of distinct infection in the mice or the transplants this inhibition of growth is presumably due to depression of the pituitary by the cortisone.

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F. C. CHESTERMAN.

THE CLIMBING OF EVEREST

SIR,—In connection with your annotation last week, one of the most interesting features of Colonel Hunt's account (*Times*, June 12) was the fact that three out of the five Sherpas chosen to do the final carrying at high altitudes were unable to, owing to altitude sickness, and that, in fact, much of the ultimate carrying over 27,000 feet was done by Europeans of the expedition. The courage and tenacity of the Sherpas as a group cannot be doubted, and their opportunities for acclimatisation one would assume to be greater than the Europeans'. Colonel Hunt's account therefore leaves us with a most interesting problem of the fundamental causes of high altitude sickness.

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NICHOLAS MARTIN.

JUNIOR RESIDENT STAFF

SIR,—We were disappointed in the letters which have appeared in your recent issues, commenting on our article of May 23.

Can we make it clear at the outset that we attempted to look at this problem from a national point of view and made an effort to put forward suggestions which in our opinion may ease the situation ? The observations made by your correspondents were only on limited aspects of the problem: they pin-pointed weaknesses without putting forward suggestions to improve the position.

To deal with the three points raised by "Filius Terræ" (June 6):

(*a*) "Cheap labour and no more." Is it not reasonable to expect that a graduate obtaining a teaching hospital appointment would be prepared to make a small monetary sacrifice as compared with the training facilities in a peripheral hospital? Is it not also fair to point out that newly qualified doctors working in hospitals are trainees not remunerated *according* to value of service, since they are gaining experience and some are trainee specialists ?

(*b*) Inducements of accommodation and facilities are no substitute for instruction and opportunity. Here we venture to suggest it should be the aim of all hospital managements to give resident medical staff the best possible accommodation and facilities, without in any way detracting from the value of supervision, instruction, and opportunity for self-improvement.

(*c*) After reading the quoted article by the committee of the American Medical Association on "The Essentials of an Approved Internship," we cannot accept the view that the training of doctors comes before the care of the patients. The two must proceed side by side.

We accept entirely the first point made by Dr. J. Greenwood Wilson—that working conditions in industry have to some extent permeated the hospital service. We regret that the old idea of a vocation is slowly passing. We compliment Dr. Greenwood Wilson on his outlook but must remind him that conditions have changed substantially since the days of which he speaks.

We can assure "Ex-House-officer" that in this area there is no lack of understanding of the junior medical officers' side of the problem: the consultants and the administration do everything in their power to assist house-officers in every possible way. "Ex-House-officer," we hope, does appreciate that certain regulations must be observed by everybody in a well-run organisation, but we can only assume that his experience has been unfortunate in connection with petty restrictions. When he implies there is no shortage of doctors for hospitals, he presumably shares the view of Mr. F. R. Zadik who in his letter of May 23 refers to a maldistribution of doctors; and it would have been helpful to hear how "Ex-House-officer" would have solved this problem.

We like Mr. Zadik's suggestions (May 23), although we feel there is a definite place for general practitioners in the hospital service as clinical assistants, even where a continuous emergency service is required. In this connection, we would point out that there are several acute general hospitals in this country with busy casualty departments where no house-officers are employed and where excellent service is given by general practitioners.

We only wish that consideration could be given to the employment of registrars at non-teaching hospitals as suggested by Mr. Zadik, and the possibility of introducing a new category of S.H.M.O. casualty officer could be investigated.

Replying to Dr. C. D. Needham (June 13), we would say that most of the junior housemen of our experience have completed twelve months' hospital service before entering upon their service with the Forces. This we believe to be general; so Dr. Needham's point upon the effect of service in the Forces would not be the great influencing factor he suggests. His statistical data are interesting and we note that the Medical Register has increased by some 27,000 names in nineteen years, a yearly average of about 1420, the average number during the last six years being approximately 1270, showing a definite falling off in the latter years. While we disagree with some of Dr. Needham's statements, we support wholeheartedly his view that it is high time that the medical man-power position be investigated as a comprehensive whole.

Dr. Needham asks: "Are lay administrators really the right people to advise on these matters ?" We are not seeking to advise: we are only seeking to focus a spotlight on an increasingly serious problem which has shown no improvement with the passing of each year of life of the "National Sickness Service." The hospital administrator must view the hospital service in all its branches, of which the medical services (though most important) form but one part. Our suggestions were simply meant to offer possible lines of inquiry, not advice.

Dr. Needham points out that barely half of the 83,914 registered doctors are occupying permanent established medical posts. If he could give us details of the disposition of the other half we might find ourselves much nearer to getting over our difficulties.

Finally may we reiterate that the junior medical staffing of hospitals is a national problem which needs early attention by all concerned if a partial breakdown in the service is to be avoided. If teaching hospitals and certain favoured peripheral hospitals have no problem, we suggest that they should come to the rescue of the less fortunate hospitals.

We have been most impressed by last week's article on this subject by Dr. R. M. Forrester and hope it receives the consideration it deserves. We hope to give it detailed study and would welcome an opportunity of offering further comment at a later date.

T. W. HURST
C. B. LINFOOT
T. K. WOODHOUSE.

Wigan and Leigh
Hospital Group.

(3) The presence or absence of headache, whether volunteered or elicited.

(4) The nature of any headache admitted—in particular, its site and distribution, how long suffered in its present form, any previous migraine or tendency to have been a "headachy person," whether the pain was tending to get better or worse, its character, its duration, any precipitating or relieving factor, any history of past head injury, and any other possible cause of headache apart from hypertension.

(5) The patient's age on first interview, age on identification as hypertensive, present blood-pressure, cardiac rhythm, retinal appearances, electrocardiograms, and left ventricular size estimated radioscopically.

In pursuing these inquiries care was taken to avoid suggestion. Many patients began at once, early in the first consultation, to talk spontaneously of their "blood-pressure." If they did so, the subject was at this stage brushed aside. Instead they were asked what had first induced them to visit their own doctor, and whether they had now any symptoms. Later the blood-pressure was taken. At this point, if the patient had so far said nothing to show that he was already aware of his condition, his attention would be drawn to the sphygmomanometer. As if the aim were to make conversation, a casual question would be put asking whether he had "ever seen one of these things before." Sometimes the answer would be crisply to the effect that he had seen one only too often, ever since they had found out about his "blood-pressure." On the other hand, there might be no flash of recognition, the reply coming only in vague terms such as "Isn't it the thing you take blood-pressures with?" Exchanges of this kind invariably provided the clue to the patient's knowledge or ignorance of his hypertension without telling him anything, and without, apparently, evoking his curiosity.

A similar care was exercised in seeking to elicit the symptom of headache if it were not volunteered. Thus, for instance, the only spontaneous complaint might be of pain in the chest. If nothing more were forthcoming, there would then be addressed to the patient some such seemingly routine question as this: "You're all right in every other way, I suppose—no reason why you shouldn't be. You've not lost any weight? No cough? Or headache? No pains in the legs?" If the word "headache" were seized on, that was taken as evidence of the presence of this symptom on elicitation. Before its acceptance as significant it was further pointed out that of course, everyone gets headaches from time to time, the present concern was only with something definite.

Findings

Of the 200 hypertensives 93 were men and 107 women. The average diastolic pressure of the whole series was 136 mm Hg. All but 5 were in normal rhythm. Headache was volunteered by 57 patients, with men and women in about equal proportion; two thirds of these women were of menopausal age. The average diastolic pressure of all those volunteering headache was 145·5 mm Hg. From a further 31 patients the symptom was elicited. Thus the total number of patients laying claim to headache was 88, leaving 112 unaffected in this way. Further investigation was made into factors which, it was thought, might throw light on the relationship between such headache, or its absence, and the hypertension.

SEVERITY OF HYPERTENSION

The standards of severity adopted were four—the height of the diastolic pressure, the retinal appearances judged by the grading of Keith et al. (1939), the electrocardiograms, and the size of the left ventricle estimated on radioscopy. The interpretations that may be put on abnormalities presenting in these last two investigations are of course often highly debatable. In this survey only unequivocal electrocardiographic changes, for which hypertensive "strain" seemed overwhelmingly the most likely cause, were accepted as significant.

TABLE I—RELATION BETWEEN PRESENCE OF HEADACHE AND SEVERITY OF HYPERTENSION

Category	No of patients	Average diastolic B P (mm Hg)	E C G indications of L V strain	Fundi of hypertensive grade II or more	Hypertensive L V change on radioscopy
Headache	88	140·8	52%	51%	78%
No headache	112	133·6	69%	36%	60%

Patients with and without headache were compared (see table I). This shows that the average diastolic pressures of the two main groups were fairly close to each other, being respectively 140·8 and 133·6 mm Hg. In both groups the scatter was wide. Thus 3 of the 4 highest values in the whole series, all higher than 180 mm Hg, were found in patients who would admit to no headache. Of the other indications of severity radioscopic enlargement of the left ventricle favoured the group with headache, although not very much. By contrast electrocardiographic changes were seen slightly more often in the group with no headache. These differences were insignificant. Relative diminution in the calibre of the retinal arteries did, however, show an apparently significant tendency to be more severe in the patients with headache—51% against 36%. Moreover, as Pickering (1942) has found, the diastolic pressure tended to be highest among the patients with papillœdema—the criterion of so-called "malignant" disease. There were 18 such patients. Their average diastolic pressure was 159 mm Hg. Of these, 11 had headache. Apart from this it was at once evident that the severity of the hypertension gave no indication as to whether or not any individual patient might complain of headache.

TABLE II—RELATION OF HEADACHE TO KNOWLEDGE OF HYPERTENSION WITHIN PARALLEL GROUPS OF DIASTOLIC PRESSURE

Diastolic B P (mm Hg)	Aware of hypertension		Unaware of hypertension	
	Headache	No headache	Headache	No headache
–120	■■□■ □■	+ + +	□□□ □□	+ +
125	■■■■ ■■■	+ + + +	□□□	+ + + + + + + + + + + +
130	■■□■■ ■■□■	+ + +	□■	+ + + + + + + + + + + + + + +
135	■□■ ■□	+	□	+ + + + + + + +
140	■□■■■□■□ ■■■■■■■	+ + + +	□□	+ + + + + + + +
145	■■□■	+		+ +
150	□■■□■■	+ + + +	□□	+ +
155	□□■■□	+	■	+
160	■■■■■□	+ + +		+
165	■	+		+ +
170	■■■■□		■	+ +
175	■			
180				+
185				+ +
190				
195				
200	■			
Total	71 (74%)	25 (26%)	17 (16%)	87 (84%)

■ Headache volunteered □ Headache elicited + No headache

HOSPITAL COSTING

SIR,—I pay tribute to Dr. A. F. Mohun's thoughtful article of May 16 upon hospital costing and its importance to the doctor. Few better services could be rendered to the cause of hospital efficiency than that of introducing the aims of departmental accounting to those from whom stem the specific application of most hospital activities. Much of the sage advice he gives—for example, on the vital importance of distributing the costs of "overhead" services—epitomises the findings of the three reports to which he refers. As further supporting comment upon these matters of common-agreement would be superfluous, I shall, if I may, draw attention to those features of the article which are, in my opinion, serious and even dangerous weaknesses.

The assiduity with which Dr. Mohun has so obviously analysed and dissected the theory of his subject unfortunately leaves him unaware not only of the lessons of practical accounting but also of the important psychological advantages that can flow from purposeful accounting in terms of individual responsibility.

By over-simplified examples, and by insistence upon probing the ultimate meaning of such accepted phrases as "objective accounting" and "subjective accounting," he leads himself to an unwitting yet fundamental contradiction. "My object in writing this article is to provide a corrective to any too-enthusiastic adoption of detailed schemes," he says (an object incidentally, which is at variance with the title of his article), and yet he advocates an approach to a scheme which in practice would involve hospitals in accounting intricacies of unlimited dimensions. It is easy to give a statement with six subjective and four objective headings, but it is fatally superficial to deduce therefrom that all that is involved in costing is "an extension of the present analysis." Regional treasurers insist upon more than forty subjective headings! Combine these by "extension" to each of the many departments of a hospital and to groups of hospitals, and we have a book-keeper's paradise but an accountant's nightmare. These practical accounting issues, part and parcel of an accountant's training and judgment, must inevitably influence such theorising, and an intensive programme of weeding out those innumerable accounts of no significance is clearly vital to the success of any scheme of costing. Failure to do so will assuredly prove Dr. Mohun correct in his opinion that a costing system "will itself cost money," just as it will confound the contrary view of those who have actually practised sensible departmental accounting. If only your contributor had drawn deeper upon his source of business accounting experience, he would have found that to accent the objective classification of expenditure does amount to a fresh outlook; and that one of the biggest obstacles that had to be overcome in business was the nostalgia for detailed expense classification by type.

His article deserves a much more intensive study of the many fields entered upon, but I must content myself with comment on just three other points.

An interesting contribution is made on the subject of statistical statements, but the suggestion that these should be adapted to varying needs of the several tiers of administration would have carried more weight if the individual hospital—still the only natural unity in hospital practice—had been accorded even a mere mention. Actual samples of such graded statements are given in the reports of the Nuffield Trust and the King's Fund, but neither body would legislate on this but would rather leave their selection to the independent judgment and requirements of each hospital.

The section of the article devoted to the "limitations of the costing system" turns out to be a somewhat platitudinous general warning against the misuse of costing material—no doubt much needed, but also applicable to almost every instrument used by human beings. A rather naïve example of this abuse of costs is left as though the fallacy arises from the costing system itself, whereas it derives from the clumsy application of a cost, produced for a particular purpose, to an entirely different set of circumstances in which a marginal cost was obviously required.

Finally, I consider it to be most regrettable that, in an otherwise excellent article, the author should summarise with the cliché of "the wholesale application of an elaborate conventional costing system." Without specific explanation, such phrases are meaningless; being negative, they are even more dangerous than the "slogans" against which Dr. Mohun warns his readers. It is to be devoutly hoped that in the practice of his own professional arts he does not allow himself to be fobbed off with inferior equipment—a child's spyglass, for example, in lieu of his microscope! Moreover, that he does not insist upon using the wrong end for fear of otherwise being thought conventional, and that essential lenses are not discarded merely to avoid the charge of being a "whole-hogger."

ADMINISTRATOR.

CATION-EXCHANGE RESINS

SIR,—I read with interest your leading article last week.

With diets low in Na the amount of Na taken up by a sulphonated exchange resin is low—less than 1 m.eq. per g. of resin.[1] We have now confirmed that the uptake of K is inversely related to that of Na; with diets low in Na it exceeds 2 m.eq. per g. Even if the resin is given partly in the K form, K may be removed from the body, and there is a danger of K depletion.

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PAUL FOURMAN.

THE EXPERT WITNESS

SIR,—Dr. Wells (May 30) raises a point of the utmost importance, subversive as it is of the whole principle of British justice.

Common Law in England is based upon the experience of some thousand years, and on the integrity and common sense of the layman. The McNaughten rules are objected to by psychiatrists because they take no account of emotional disturbance. The provision of a panel of psychiatrists, or of a single *amicus curiæ*, to assist the court in assessing the emotional factor, might have far-reaching effects. Obviously, any, to the layman, "sane" person who commits a crime is suffering from emotional disturbance, and to take this into account would ultimately lead to the acquittal of any person accused of any illegal act.

In a volume of the Notable British Trials series (*The Trial of John George Haigh*), the editor, Lord Dunboyne, who has achieved a masterly introduction, nevertheless falls into error in stating (p. 41) that the McNaughten Rules are the yardstick determining whether capital punishment shall be inflicted. This is not the case. The protection of the insane person is a defence in depth. The first line of defence is entrenched in the McNaughten rules, by which it must be shown that the accused was, at the time of the crime, suffering from such a defect of reason due to disease of the mind either that he did not know what he was doing, or that he did not know that it was wrong. Surely this is a fair decision for a jury of laymen. Having decided this point, there is yet another line of defence, which is best illustrated in the case of Ronald True.

There was no doubt that True was insane; his defence of insanity failed because it was equally obvious that he knew what he was doing at the time he committed the murder, and there was evidence to show that he knew that it was wrong. However, the defence having been one of insanity, the Home Secretary was, by statute provided, forced to appoint a committee of specialists to decide on True's sanity. This committee came to the conclusion that True was insane, and execution was therefore respited.

This is a sensible compromise, removing nothing from the jurisdiction of the Court, but preventing the inhumanity

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1. Fourman, P. *Brit. med. J.* March 7, 1953, p. 544.

KNOWLEDGE OF HYPERTENSION

Of the 88 patients with headache 71 (81%) were aware of their raised blood-pressure, whereas of the 112 patients who had no headache only 25 (22%) realised that their blood-pressure was in question, many of them had been sent to the outpatient department because of some complaint unconnected with the cardiovascular system Since there was no great difference in the average severity of disease between those with headache and those without it, this definite tendency of headache to appear more often among those aware of their condition might be taken to suggest that such knowledge had predisposed to headache Cause and effect could not be directly demonstrated, but there appeared a correspondence which might be significant Such a suggestion must be modified by the admission that a few patients in the survey maintained that they had learnt of their hypertension only after visiting their family doctor because of headache It was, of course, impossible to judge such a story with accuracy On close questioning, however it seemed unlikely that more than a very few of these people had, in fact, originally sought advice because of unexplained headache

TABLE III—ANALYSIS OF SYMPTOMS OF 25 PATIENTS WITHOUT HEADACHE THOUGH AWARE OF HYPERTENSION

Organic symptoms with hypertensive association	No of cases	Organic symptoms of unassociated disease	No of cases	Symptoms coupled with ' blood pressure " and suggesting anxiety	No of cases	No symptoms	No of cases
Anginal pain	5	Symptoms associated with carcinoma	4	Dizziness,' &c	1	No symptoms	1
Cardiac asthma	1	Melæna (peptic ulcer)	1	" Nerves " &c	1		
Visual difficulties	3			" Weakness, ' &c	1		
Effort dyspnœa	3			' Fainting attacks " &c	1		
" Fits " (hypertensive encephalopathy)	1			' Stuffed-up feelings ' &c	1		
				" Heart bulging out ' &c	1		
Total	13		5		6		1

Investigation from the opposite standpoint precluded exposure to this type of error (table II) There were 96 patients who were aware of their hypertension Of these, 71 (74%) complained of headache Yet of the 104 patients who did not know of their raised blood-pressure only 3 (less than 3%) volunteered that they had headache The symptom was elicited from a further 14 (bringing the total to 16%), of whom 12 were women, about half of them of menopausal age The remaining 87 (84%) denied headache These 87 were all, nevertheless, severely hypertensive Their average diastolic pressure was 135 mm Hg—only a millimetre less than the mean for the whole series Electrocardiograms suggesting left ventricular " strain " were found in 77% of them, and in 56% radioscopy revealed left ventricular enlargement Again the retinal damage was relatively less, being of grade II or more severity in only 27%

The relation between headache and knowledge of hypertension within parallel groups of diastolic pressure is demonstrated in table II The tendency of headache to appear in conjunction with knowledge of hypertension persists uniformly through the whole range By contrast, among patients unaware of their hypertension the paucity of headache is striking In this group the numbers tail off symmetrically upwards through the pressure gradient This accords with the casual pick-up of an abnormality occurring on a correspondingly diminishing scale of frequency On the other hand, most of the patients aware of their hypertension were regular attendants at a cardiological outpatient clinic, they thus formed a selected hypertensive sample of the population

Patients without Headache though Aware of Hypertension

The 25 out of 96 patients who escaped headache, though aware of their hypertension, did not do so because of any relative sparing of their cardiovascular systems Analysed separately the average diastolic pressure of these patients was 140 mm Hg, retinal changes of grade II or more were found in 52%, electrocardiographic changes of left ventricular strain in 89%, and radioscopic left ventricular enlargement in 92%—findings which indicate a severity well above the average for the whole series

All the same these patients, though aware of their hypertension, did not complain of headache At first sight this fact might be taken as evidence against any view that the symptom, when found among hypertensives, is commonly psychogenic

To investigate this point the case histories of these 25 patients were examined in detail They fell into four groups (table III)

(1) Patients whose attention was centred on some disorder which could be recognised as associated organically with the hypertension—e g, anginal pain or visual difficulties for which good cause could be found in the fundi

(2) The victims of severe incidental disease usually malignant The people in these two groups did not attach any importance to their blood-pressure, they had something else to worry about

(3) Mostly women whose symptoms, and the manner of their expression, suggested anxiety They complained of " weakness " or " blackouts " or " dizziness " which was neither rotatory nor related to posture They referred repeatedly to their " blood pressure " The impression was gained that these patients, knowing their blood pressure to be raised, found themselves afflicted by symptoms which they subconsciously felt to be appropriate to that disorder While others might seize upon ' headache " they, quite unwittingly, chose something else

(4) One stalwart avowed that he felt perfectly fit

Thus, of 96 hypertensives aware of their condition 71 complained of headache, 18 complained, with abundant organic justification, of something else, 6 produced symptoms which bore all the hallmarks of anxiety, and only 1 pronounced himself fit

Patients with Headache but Unaware of Hypertension

It seemed that a characteristic " hypertensive headache," if indeed such a thing should exist, might certainly be expected to show itself among the patients who complained of headache, without other evident cause, while unaware of their hypertension It has been pointed out that only 17 of 104 came into this category, a mere 3 complaining of headache spontaneously The severity of the hypertension affecting these 17, estimated by the usual criteria, was comparatively slight, with an average diastolic pressure of only 131 mm Hg, this being well below the average for the series Retinal changes of grade II were found in only 3, while less than half showed minor electrocardiographic and radioscopic abnormalities

The ages showed a wide scatter Nevertheless all members of the group were suffering much the same sort of headache Three-quarters of them had first noticed it within the previous three years, about half of them within eighteen months Most of them declared that the trouble had been bad but was now getting better They did not make a great deal of it Only 1 gave a history of previous migraine The pain was usually referred to one part of the head—front, back, or either side It might simulate migraine both in this localisation and in its liability to be precipitated by worry, activity, or excitement But there was never an aura The sensation might be described as " thumping," " bumping," or " bursting," the periodicity thus suggested being sometimes related to the pulse rate Transient faintness might accompany it Several patients confined their description to " just an ache " It was often at its worst in the early of the execution of an insane person, because, as Sir Edward Coke said, it lies beyond conscience to execute a man who cannot make his peace with God.

I have diffidence in penning this letter as I am neither a psychiatrist nor a barrister. As a member of the medical profession who has been interested in matters criminous for some time, I feel it my duty to express the frank opinion of one who has no axe to grind.

The confusion in the lay mind, and apparently among many psychiatrists, concerning the function of these two lines of defence seems to have caused unnecessary concern. The liberty of the subject, in the first instance in England, and ultimately, we may hope, in the whole world, depends upon the integrity of British Law. Any attempt to alter the existing constitution of our Courts of Criminal Law by the introduction of psychological advisors, financial advisors, political agents, or what-have-you is bound, sooner or later, to react with profound detriment to mankind. Unfortunately, no system is absolutely perfect, but hard cases make bad law. The McNaughten Rules and the provision for the respiting of an insane, but guilty, person provide an admirable compromise, and the public can remain assured that with such a system in operation injustice will be done in the minimal number of cases.

Newcastle upon Tyne. M. H. ARMSTRONG DAVISON.

ERYTHEMA MULTIFORME AND A.C.T.H.

SIR,—The cases of Stevens-Johnson syndrome treated with A.C.T.H., reported by Dr. Caldwell and by myself (June 6), strongly suggest that this condition is allergic in origin. Antibiotics definitely appear to be ineffective and may even be dangerous at times owing to monilial infection.[1]

Various cases supporting an allergic ætiology have been reported.

Ashby and Lazar[2] reported a case where the patient developed angioneurotic œdema following aspirin therapy, but they favoured an infective agent as the cause of this syndrome. Straus[3] and Thomas[4] both described patients who relapsed after the administration of sulphonamides; and a history of asthma or eczema has been reported.[5]

When A.C.T.H. is given, aureomycin should be given also as a prophylactic measure to prevent secondary infection of the skin lesions due to the lowering of the body's resistance by the action of A.C.T.H.[6]

Dr. Caldwell suggests that the use of A.C.T.H. in further cases of Stevens-Johnson syndrome would give a clearer picture of its value. I have seen 2 cases treated with A.C.T.H., and the accompanying photographs show the boy described in my letter. The lips are characteristic of erythema multiforme (fig. 1); œdema of the forehead and chemosis is predominant, and a diffuse coalescent maculopapular rash can be seen on the legs (fig. 2). He was completely cured with A.C.T.H. and aureomycin. In all, 6 cases have been reported in which A.C.T.H. has been used, and excellent responses have been noted. The search for an infective agent has proved negative,[7] and I think that the syndrome is definitely allergic in origin, sensitisation playing an important part.

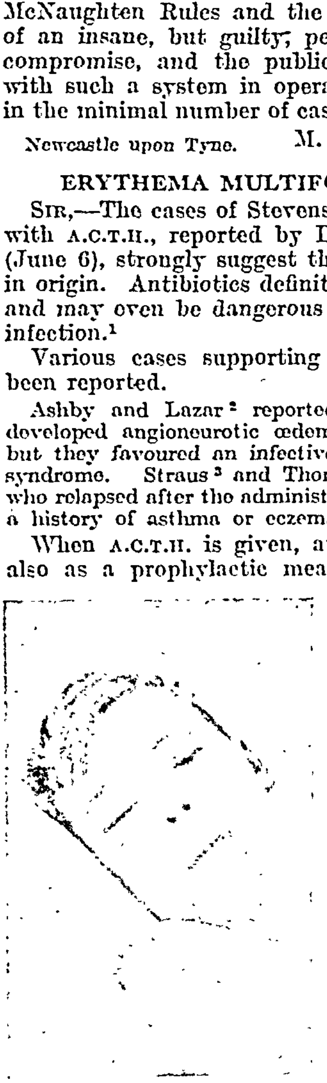

Fig. 1—Boy, aged 9, with Stevens-Johnson syndrome.

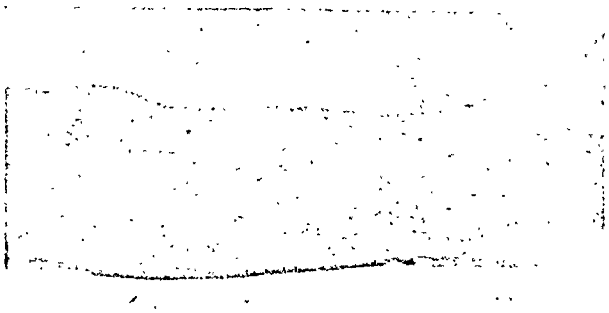

Fig. 2—Maculopapular rash on legs.

Whittington Hospital,
London, N.19. DEREK H. CLARK.

SIR,—Severe cases of erythema multiforme (Stevens-Johnson syndrome) are not common enough for controlled trials of treatment to be easily possible, but I feel that, since the condition is a self-limiting one, a very critical approach to therapeutic successes should be adopted. Of the four cases recorded in your issue of June 6, Dr. Davies makes no claim that his case recovered as a result of treatment; but Dr. Caldwell, Dr. Grant, and Dr. Clark ascribe recovery in their cases to the treatment used. Dr. Stephen Gold[8] has recently drawn attention to this uncritical attitude in respect of another case.[9]

I have perhaps seen more than my fair share of these cases, and in 1947 described six.[10] All these cases recovered completely in under four weeks, and a dramatic improvement took place 7–10 days from the onset of the illness. Dr. Caldwell's and Dr. Clark's patients did not begin treatment with A.C.T.H. until at least 6 days after the onset, and though it is quite likely that the beneficial response to treatment was a result of the treatment it is also possible that a natural remission was due to occur.

Most large centres will deal with two or three such cases a year, and it would appear practicable to treat every other case with A.C.T.H. early in the illness and to treat the remainder with antibiotics. Within a few years sufficient data would be gathered to settle this problem.

Rupert Hallam Department of
Dermatology, Royal Infirmary, Sheffield. I. B. SNEDDON.

TREATMENT OF HEPATIC COMA

SIR,—In your leading article of June 6 you cite a paper by Karl et al.[11] The implication of your remarks is that their 58 cases were treated on the regimen they recommend and despite this only 1 survived.

I read the paper differently, though my first interpretation was the same as yours.

To quote: "58 cases of cirrhosis complicated by hepatic coma were selected from the records of the St. Louis City Hospital. All but one of the patients had died. *Nearly* all had been observed by one of us." (*N.B.*, past tense.) The authors do not say how many years were covered by the series, though this is likely to be several and is important. They then survey the mode of presentation and pathological findings.

Under the heading "Management" they state that, because of the poor results in these cases "it seemed desirable to review the treatment used, and to search the literature for any theoretical or clinical studies that might suggest better methods of therapy." They go on to list the types of treatment but do *not* state how many of their patients had all or some of this treatment. The rest of the paper is a review of reports on the various therapeutic measures that have been used. There is little original contribution or critical

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1. *Lancet*, 1951, ii, 532.
2. Ashby, D. W., Lazar, T. *Ibid*, 1951, i, 1091.
3. Straus, D. A. *New Engl. J. Med.* 1948, 239, 956.
4. Thomas, B. A. *Brit. med. J.* 1950, i, 1393.
5. Schwartz, M. H., Brainerd, H. D. *J. Pediat.* 1946, 29, 512.
6. Billow, B. W., Lowen, H. J. *Arch. intern. Med.* 1952, 90, 310.
7. Murphy, R. C. *New Engl. J. Med.* 1944, 230, 69.
8. *Brit. med. J.* May 16, 1953, p. 1111.
9. Romer, C. *Ibid*, April 4, 1953, p. 768.
10. *Ibid*, 1947, i, 925.
11. Karl, M. E., Howell, R. A., Hutchinson, J. H., Catanzaro, F. G. *Arch. intern. Med.* 1953, 91, 159.

(3) The presence or absence of headache, whether volunteered or elicited.

(4) The nature of any headache admitted—in particular, its site and distribution, how long suffered in its present form, any previous migraine or tendency to have been a "headachy person," whether the pain was tending to get better or worse, its character, its duration, any precipitating or relieving factor, any history of past head injury, and any other possible cause of headache apart from hypertension.

(5) The patient's age on first interview, age on identification as hypertensive, present blood pressure, cardiac rhythm, retinal appearances, electrocardiograms, and left ventricular size estimated radioscopically.

In pursuing these inquiries care was taken to avoid suggestion. Many patients began at once, early in the first consultation, to talk spontaneously of their "blood-pressure." If they did so, the subject was at this stage brushed aside. Instead they were asked what had first induced them to visit their own doctor, and whether they had now any symptoms. Later the blood pressure was taken. At this point if the patient had so far said nothing to show that he was already aware of his condition, his attention would be drawn to the sphygmomanometer. As if the aim were to make conversation, a casual question would be put asking whether he had "ever seen one of these things before." Sometimes the answer would be crisply to the effect that he had seen one only too often, ever since they had found out about his "blood pressure." On the other hand, there might be no flash of recognition, the reply coming only in vague terms such as "Isn't it the thing you take blood-pressures with?" Exchanges of this kind invariably provided the clue to the patient's knowledge or ignorance of his hypertension without telling him anything, and without, apparently, evoking his curiosity.

A similar care was exercised in seeking to elicit the symptom of headache if it were not volunteered. Thus, for instance, the only spontaneous complaint might be of pain in the chest. If nothing more were forthcoming, there would then be addressed to the patient some such seemingly routine question as this: "You're all right in every other way, I suppose—no reason why you shouldn't be. You've not lost any weight? No cough? Or headache? No pains in the legs?" If the word "headache" were seized on, that was taken as evidence of the presence of this symptom on elicitation. Before its acceptance as significant it was further pointed out that, of course, everyone gets headaches from time to time, the present concern was only with something definite.

Findings

Of the 200 hypertensives 93 were men and 107 women. The average diastolic pressure of the whole series was 136 mm Hg. All but 5 were in normal rhythm. Headache was volunteered by 57 patients, with men and women in about equal proportion; two-thirds of these women were of menopausal age. The average diastolic pressure of all those volunteering headache was 145·5 mm Hg. From a further 31 patients the symptom was elicited. Thus the total number of patients laying claim to headache was 88, leaving 112 unaffected in this way. Further investigation was made into factors which, it was thought, might throw light on the relationship between such headache, or its absence, and the hypertension.

SEVERITY OF HYPERTENSION

The standards of severity adopted were four—the height of the diastolic pressure, the retinal appearances judged by the grading of Keith et al. (1939), the electrocardiograms, and the size of the left ventricle estimated on radioscopy. The interpretations that may be put on abnormalities presenting in these last two investigations are of course often highly debatable. In this survey only unequivocal electrocardiographic changes, for which hypertensive "strain" seemed overwhelmingly the most likely cause, were accepted as significant.

TABLE I—RELATION BETWEEN PRESENCE OF HEADACHE AND SEVERITY OF HYPERTENSION

Category	No. of patients	Average diastolic B.P. (mm Hg)	E.C.G. indications of L.V. strain	Fundi of hypertensive grade II or more	Hypertensive L.V. change on radioscopy
Headache	88	140·8	52%	51%	78%
No headache	112	133·6	69%	36%	60%

Patients with and without headache were compared (see table I). This shows that the average diastolic pressures of the two main groups were fairly close to each other, being respectively 140·8 and 133·6 mm Hg. In both groups the scatter was wide. Thus 3 of the 4 highest values in the whole series, all higher than 180 mm Hg, were found in patients who would admit to no headache. Of the other indications of severity radioscopic enlargement of the left ventricle favoured the group with headache, although not very much. By contrast electrocardiographic changes were seen slightly more often in the group with no headache. These differences were insignificant. Relative diminution in the calibre of the retinal arteries did, however, show an apparently significant tendency to be more severe in the patients with headache—51% against 36%. Moreover, as Pickering (1942) has found, the diastolic pressure tended to be highest among the patients with papillœdema—the criterion of so called "malignant" disease. There were 18 such patients. Their average diastolic pressure was 159 mm Hg. Of these, 11 had headache. Apart from this it was at once evident that the severity of the hypertension gave no indication as to whether or not any individual patient might complain of headache.

TABLE II—RELATION OF HEADACHE TO KNOWLEDGE OF HYPERTENSION WITHIN PARALLEL GROUPS OF DIASTOLIC PRESSURE

Diastolic B.P. (mm Hg)	Aware of hypertension		Unaware of hypertension	
	Headache	No headache	Headache	No headache
•120	■■□■ □■	+++	□□□ □□	++++++++ ++++++++ ++++++++ +++++++
125	■■■■ ■■■	++++	□□□	++++++ ++++++
130	■■□■■ ■■□■	+++	□■	++++++++ +++++++
135	■□■ ■□	+	□	++++ ++++
140	■□■■■□■□ ■■■■■■■	++++	□□	++++ ++++
145	■■□■	+		++
150	□■■□■■	++++	□□	++
155	□□■■□	+	■	+
160	■■■■■□	+++		+
165	■	+		++
170	■■■■□		■	++
175	■			
180				+
185				++
190				
195				
200	■			
Total	71 (74%)	25 (26%)	17 (16%)	87 (84%)

■ Headache volunteered. □ Headache elicited. + No headache.

observation in this section; probably neither was intended. As a result of this review they then suggest a suitable regimen to follow in the future. There is no suggestion that it was in fact tried in their 58 cases.

I draw attention to what is, I think, a misinterpretation in your leading article as it may mislead readers to conclude that it is useless to treat hepatic coma from cirrhosis by any of the present methods. Indeed, this may be true, but this paper does nothing to prove it.

Ipswich. J. W. PAULLEY.

HEALTH OF A TROPICAL PEOPLE

SIR,—At the end of his interesting article last week Dr. Cullumbine gave a list of so-called diseases of civilisation.

The meaning of the word civilisation may be differently interpreted, but, as regards disease, it falls roughly into two eras: before and after the introduction of public health in general and of environmental and personal hygiene in particular.

People living in England, for example, in the reign of Queen Elizabeth I, paid their penalties for an over-indulgence in meat. An amount equal perhaps to about ten weeks of our ration might be scoffed at one meal! At a cost of what? About 2*d.*! They suffered from surfeit diseases and not inconsiderably, too, from their treatment. They suffered far more, though, from lack of sanitation, plague, and infectious diseases; and scabies was, I believe, almost universal. But circulatory and respiratory diseases are not particularly noted. In those days amenities were few, aids or replacements were few, and the average person had to use his body and his limbs to get about, to work, and to get his food—though they moved less, no doubt, than our more remote ancestors.

In this middle period of the 20th century, in the reign of Queen Elizabeth II, we enjoy immeasurable benefits from public-health services. On the other hand, owing to a vast increase in amenities, a large number of people are scarcely using their bodies at all and spend the day and evening sitting, standing, and being carried, while at work their bodies and limbs are being steadily replaced by machines. Surely a penalty is being paid in the silting up of the body tissues, varying in degree and in the site of manifestation. Shall we say diseases of "disuse"?

A failure of adaptation is now regarded as a starting-point for a number of functional failures leading to structural changes. Adaptation is mainly, however, a protective policy of living matter with which the human being has been trying to catch up, maybe ever since he stood directly upright. But the factors involved are largely beyond individual control. Disuse of the body should be open to correction.

London, W.1. F. D. SANER.

HAZARD OF FOG

SIR,—Although the Meuse Valley fog episode in 1930 appears to have been the first epidemic fog incident recorded,[1] the hazard of fog to sufferers from chest diseases was apparently well known as long ago as the 18th century. Thomas Percival, M.D., in his report to the Manchester Board of Health in 1796 refers to the problem thus:

> "I have computed that three hundred tons of coal are every day consumed in the winter season at Manchester. The factitious gas generated by its combustion must amount at least to one-third of this quantity; it is probable that the smoke proceeding from it constitutes another third part, and both together are capable of occupying a space of very wide extent. Now if it were not for the dispersion of these vapours by wind, the precipitation of them by rain, and the influence of other causes, which restore salubrity to the air, respiration could not be carried on under such circumstances. And we may observe that frosty weather, which is generally serene and without wind, always proves extremely oppressive, and sometimes even fatal to asthmatic patients in great cities. Indeed the rate of human mortality bears a pretty near proportion to their magnitude and population."

It is therefore particularly fitting that the centre of Manchester is one of the first places to be declared a smokeless area.

Windsor, Berks. ROBERT PIPER.

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[1] See Logan, W. P. D. *Lancet*, Feb. 14, 1953, p. 336.

THE INCONTINENT WOMAN PATIENT

SIR,—I read with interest Dr. Brocklehurst's letter last week. Retention of a patient immobile over a receptacle offends against nursing principles; and I should like to recommend a different approach to the problem of the incontinent patient.

I look after a psycho-geriatric unit of 320 beds for frail patients over 70 years. There are no bedridden patients. The helpless ones are dressed and placed in sling armchairs built to retain an inert patient in a sitting position. The helpless, from a sitting position, watch and join in the social life of the ward. The sitting position prevents bedsores and pulmonary congestion, and patients can feed themselves much more readily.

There are 38 incontinent patients. These are dressed in towelling nappies and waterproof knickers to prevent soiling of furniture and clothing. Their cleanliness is ensured with mobility; the weak patients can be exercised, and the helpless ones can be dressed warmly. Urine rashes do not occur any more frequently. The saving in laundry and nurses' time is enormous.

No patient needs to be retained in bed because of mental apathy or paralysis.

Anyone with a young baby will be amazed that this idea has not been generally adopted.

Middlewood Hospital,
Sheffield.

G. I. TEWFIK
Assistant psychiatrist.

TREATMENT OF WHOOPING-COUGH WITH ANTIBIOTICS

SIR,—It is with diffidence that I offer criticism of the findings of the M.R.C. subcommittee which evaluated the effectiveness of chloramphenicol and aureomycin in the treatment of whooping-cough. Having been interested in the use and abuse of chloramphenicol particularly in relation to dosage, I feel impelled to offer a few comments.

In the subcommittee's trial reported in your issue of June 6, the drug was given twice a day in equally divided doses. I assume that the time-interval was 12 hours; and approximately 85% of an ingested amount of chloramphenicol is excreted during this period.[1] It can thus be reasonably argued that as the cumulative effect is minimal the therapeutic action depends on the amount given in this single 12-hourly dose.

Instead of treating each patient on the basis of tissue mass the subcommittee have chosen age. This adds to the difficulty in determining the amount given per kg. body-weight. By assuming, however, that the children were all mesomorphs (which is unlikely) and relating weight to age, the following would appear to be the approximate amount of chloramphenicol given per kg. per dose: 6 months, 65 mg.; 9 months, 55 mg.; 11 months, 50 mg.; 1 year, 75 mg.; 18 months, 65 mg.; 2 years, 62·5 mg.; $2^{1}/_{2}$ years, 55 mg.; 2 years 11 months, 52·5 mg.; 3 years, 70 mg.; $3^{1}/_{2}$ years, 65 mg.; 4 years, 60 mg.; $4^{1}/_{2}$ years, 57 mg.; 5 years 11 months, 55 mg.

For the assessment of results the cases were grouped into three categories and two divisions: early, middle, and late and severe or mild. The cases were partitioned without relation to age, and therefore weight. It would thus appear that no allowance was made for the possible effect of varying dosage levels in any given group, nor for the possibility that the groups might be unbalanced because the chance distribution of weights was erratic. Alternatively, the subcommittee may have

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[1] Glazko, H. J., Wolfe, L. M., Dill, W. N., Bratton, H. C. *J. Pharmacol.* 1949, 96, 445.

KNOWLEDGE OF HYPERTENSION

Of the 88 patients with headache 71 (81%) were aware of their raised blood-pressure, whereas of the 112 patients who had no headache only 25 (22%) realised that their blood pressure was in question, many of them had been sent to the outpatient department because of some complaint unconnected with the cardiovascular system Since there was no great difference in the average severity of disease between those with headache and those without it, this definite tendency of headache to appear more often among those aware of their condition might be taken to suggest that such knowledge had predisposed to headache Cause and effect could not be directly demonstrated, but there appeared [illegible] which might be significant Such a [illegible] modified by the admission that a few patients in the survey maintained that they had learnt of their hypertension only after visiting their family doctor because of headache It was, of course, impossible to judge such a story with accuracy On close questioning, however, it seemed unlikely that more than a very few of these people had, in fact, originally sought advice because of unexplained headache.

TABLE III—ANALYSIS OF SYMPTOMS OF 25 PATIENTS WITHOUT HEADACHE THOUGH AWARE OF HYPERTENSION

Organic symptoms with hypertensive association	No of cases	Organic symptoms of unassociated disease	No of cases	Symptoms coupled with "blood pressure" and suggesting anxiety	No of cases	No symptoms	No of cases
Anginal pain	5	Symptoms associated with carcinoma	4	'Dizziness,' &c	1	No symptoms	1
Cardiac asthma	1	Melæna (peptic ulcer)	1	"Nerves," &c	1		
Visual difficulties	3			"Weakness," &c	1		
Effort dyspnœa	3			'Fainting attacks," &c	1		
"Fits" (hypertensive encephalopathy)	1			'Stuffed-up feelings" &c	1		
				"Heart bulging out' &c	1		
Total	13		5		6		1

Investigation from the opposite standpoint precluded exposure to this type of error (table II) There were 96 patients who were aware of their hypertension Of these, 71 (74%) complained of headache Yet of the 104 patients who did not know of their raised blood-pressure only 3 (less than 3%) volunteered that they had headache The symptom was elicited from a further 14 (bringing the total to 16%), of whom 12 were women, about half of them of menopausal age The remaining 87 (84%) denied headache These 87 were all, nevertheless, severely hypertensive Their average diastolic pressure was 135 mm Hg—only a millimetre less than the mean for the whole series Electrocardiograms suggesting left ventricular "strain" were found in 77% of them, and in 56% radioscopy revealed left ventricular enlargement Again the retinal damage was relatively less, being of grade II or more severity in only 27%.

The relation between headache and knowledge of hypertension within parallel groups of diastolic pressure is demonstrated in table II The tendency of headache to appear in conjunction with knowledge of hypertension persists uniformly through the whole range By contrast, among patients unaware of their hypertension the paucity of headache is striking In this group the numbers tail off symmetrically upwards through the pressure gradient This accords with the casual pick-up of an abnormality occurring on a correspondingly diminishing scale of frequency On the other hand, most of the patients aware of their hypertension were regular attendants at a cardiological outpatient clinic, they thus formed a selected hypertensive sample of the population

Patients without Headache though Aware of Hypertension

The 25 out of 96 patients who escaped headache, though aware of their hypertension, did not do so because of any relative sparing of their cardiovascular systems Analysed separately the average diastolic pressure of these patients was 140 mm Hg, retinal changes of grade II or more were found in 52%, electrocardiographic changes of left ventricular strain in 89%, and radioscopic left ventricular enlargement in 92%—findings which indicate a severity well above the average for the whole series

All the same these patients, though aware of their hypertension, did not complain of headache At first sight this fact might be taken as evidence against any view that the symptom, when found among hypertensives, is commonly psychogenic

To investigate this point the case histories of these 25 patients were examined in detail They fell into four groups (table III)

(1) Patients whose attention was centred on some disorder which could be recognised as *associated organically with the* hypertension—e g, anginal pain, or visual difficulties for which good cause could be found in the fundi

(2) The victims of severe incidental disease, usually malignant The people in these two groups did not attach any importance to their blood pressure, they had something else to worry about

(3) Mostly women whose symptoms, and the manner of their expression, suggested anxiety They complained of 'weakness," or 'blackouts," or "dizziness" which was neither rotatory nor related to posture They referred *repeatedly to their "blood pressure"* The impression was gained that these patients, knowing their blood pressure to be raised, found themselves afflicted by symptoms which they subconsciously felt to be appropriate to that disorder While others might seize upon 'headache" they, quite unwittingly, chose something else

(4) One stalwart avowed that he felt perfectly fit

Thus, of 96 hypertensives aware of their condition 71 complained of headache, 18 complained, with abundant organic justification, of something else, 6 produced symptoms which bore all the hallmarks of anxiety, and only 1 pronounced himself fit

Patients with Headache but Unaware of Hypertension

It seemed that a characteristic "hypertensive headache," if indeed such a thing should exist, might certainly be expected to show itself among the patients who complained of headache, without other evident cause, while unaware of their hypertension It has been pointed out that only 17 of 104 came into this category, a mere 3 [illegible] headache spontaneously The severity [illegible] affecting these 17, estimated by the usual criteria, was comparatively slight, *with an average* diastolic pressure of only 131 mm Hg, this being well below the average for the series Retinal changes of grade II were found in only 3, while less than half showed minor electrocardiographic and radioscopic abnormalities

The ages showed a wide scatter Nevertheless all members of the group were suffering much the same sort of headache Three quarters of them had first noticed it within the previous three years, *about half of them* within eighteen months Most of them declared that the *trouble had been bad* but was now getting better They did not make a great deal of it Only 1 gave a history of previous migraine The pain was usually referred to one part of the head—*front*, back, or either side It might simulate migraine both in this localisation and in its liability to be precipitated by worry, activity, or excitement But there was never an aura The sensation might be described as "thumping," "bumping," or "bursting," the periodicity thus suggested being sometimes related to the pulse-rate Transient faintness might accompany it Several patients confined their description to "just an ache" It was often at its worst in the early decided that a dose-spread of approximately 20 mg. per kg. body-weight was of little experimental importance.

To me, there are three dominant factors to be considered in evaluating the effect of an antibiotic dose: the resistance of the organism, the patency of the vascular tree supplying the tissue under treatment, and the concentration of the antibacterial substance achieved per unit of pathological tissue. The acquisition of some knowledge of the first two is not difficult, but as far as I can determine there is very little known of the last. With this question in mind I have been collecting suitable necropsy material over the last eighteen months and subjecting it to chloramphenicol estimations, with some surprising results:

Case 1.—Weight 1·9 kg. Dose 50 mg. per kg. body-weight every 3 hours; last dose given about 4 hours before death.

Concentration of chloramphenicol per g. wet-weight lung tissue = 7μ.

Concentration of chloramphenicol per g. wet-weight brain tissue = 30μ.

Case 2.—Weight 2 kg. Dose 50 mg. per kg. body-weight every 6 hours. Last dose given 3 hours before death.

Concentration of chloramphenicol per g. wet-weight lung tissue = $7{\cdot}7\mu$.

Concentration of chloramphenicol per g. wet-weight brain tissue = $19{\cdot}8\mu$.

Case 3.—Weight 2·3 kg. Dose 50 mg. per kg. body-weight every 4 hours. Last dose given 50 minutes before death.

Concentration of chloramphenicol per g. wet-weight lung tissue = 12μ.

Concentration of chloramphenicol per g. wet-weight brain tissue = $2{\cdot}2\mu$.

This child died of widespread thromboses of the cerebro-vascular tree.

These three cases demonstrate that: (1) at any given time the chloramphenicol concentration varies from tissue to tissue; (2) vascular obstruction coincides with very low amounts of antibiotic; and (3) in the uninflamed human lung chloramphenicol is removed with some rapidity.

We know that *Hæmophilus pertussis* is markedly sensitive to chloramphenicol, but what we do not yet know is the amount of antibiotic that must be given in order to produce an optimum concentration in the diseased tracheobronchial mucosa invaded by this organism. It is obvious from what has been said that the various stages of the illness will require increasing dosages of chloramphenicol to bring about the same effects.

This thesis cannot be fully expanded within the confines of a letter, but I feel that its substance suggests that it would have been advisable for the subcommittee to have qualified their findings by relating them only to the dosage system tried.

London, S.W.9.

J. D. GRAY.

Public Health

World-wide Poliomyelitis

POLIOMYELITIS was often described in the past as a disease of temperate climates; but *nowadays* there is good evidence to show that few parts of the world are free from poliomyelitis viruses. Indeed, one view is that they originated in the tropics.[1] The World Health Organisation has now published[2] a survey of the attacks made by the disease during 1952, and the figures from 113 countries and territories show how widespread they were. In North America there was more poliomyelitis than ever before: in the United States more than 57,000 *cases* were *notified*—twice as many as in 1951 and more than in any year since notification began: and in Canada the number of notifications for both August and September exceeded the annual totals for the majority of the preceding 28 years. "A veritable wave" spread over Europe, involving particularly Denmark, Western Germany, and Belgium. Provisional figures for England and Wales show an increase from 3095 cases in 1951 to 4475 in 1952; but, the report observes, "the notifications do not show such a regular and, one might almost say, inexorable tendency to rise during the last 20 years as is the case in the United States." On the other side of the world, there was a serious new outbreak in New Zealand, the Hawaiian Islands, and the Gilbert and Ellice Islands; but in Australia and Japan the number of cases reported showed a definite decrease. And 1952 was also quite a good year in Africa, where recorded cases fell by 25%, though in Kenya and Tanganyika "notifications exceeded all figures recorded since 1945." For the fourth time since 1934, there was a sharp outbreak in the island of Mauritius. As the report points out, the total number of notifications from tropical countries is still low, but there are relatively few doctors to detect the disease in these areas, and the indication is that poliomyelitis "remains or is becoming a threat of world-wide significance."

Obituary

GEORGE WILLIAM RIPPON

M.B. Sheff.

Dr. Rippon, consultant anæsthetist to the United Sheffield Hospitals, died on June 1 in Sheffield, where he had spent the whole of his medical career from student to consultant. After graduating as M.B. at the University in 1925 he held house-appointments at the Royal Infirmary and the Jessop Hospital before settling in general practice at Abbeydale. As the years passed his growing interest in anæsthetics absorbed more and more of his time and finally led to his appointment to the staff of the United Sheffield Hospitals.

R. P. writes: "George Rippon was an exceptionally good doctor; indeed, it was difficult to see patients with him, for he always knew so much more about them and their illnesses than the consultant whose advice he appeared to be seeking, and there was always the likelihood that a sudden devastating comment from George, uttered in the kindest and gentlest of tones, would come dangerously near to upsetting any dignity or solemnity which had been assumed for the occasion. He had wit and erudition and his friends all had a warm affection for him as well as a great respect for his judgment. I should guess that he had no enemies, for his comments on the pompous and self-opinionated were framed in terms which they would not comprehend. I know few men who come anywhere near to his standards of doctoring and it is the greatest pity that we should lose him so soon. Nevertheless I find it almost impossible to feel solemn about George. He just wouldn't like it."

Dr. Rippon leaves his widow with a son and two daughters.

Appointments

ARRATOON, LILY, M.R.C.S., M.R.C.O.G.: asst. M.O., child health and maternity services, West Ham.

BENNETT, P. A., M.B. Brist.: principal M.O. (mental health service), Middlesex County Council.

CLARK, A. S., M.B. Lond., D.P.M.: psychiatrist, public-health department, London County Council.

GLANCY, B. P., M.B. Belf., D.P.M.: psychiatrist (S.H.M.O.): Northern Ireland Hospitals Authority special care service.

GRAY, I. G., M.B. Lond.: appointed factory doctor, Acle, Norfolk.

JACKSON, C. R. S., M.A., B.M. Oxfd, F.R.C.S.E.: asst. ophthalmic surgeon, Edinburgh Royal Infirmary.

LUDLOW, JOYCE, M.B.E., M.B. Lond., F.R.C.S.: asst. county M.O., N.E. Kent area.

MURPHY, J. H., M.D. Dubl.: appointed factory doctor, Biddulph, Staffordshire.

NEYLON, J. P., M.B. N.U.I.: asst. M.O.H. and asst. school M.O., Barnsley.

SHEARER, C. W., M.B. Edin., D.P.H.: deputy to the M.O.H. and school M.O., Swindon, Wiltshire.

Eastern Regional Hospital Board:

ADAMSON, D. G., M.D. St. And., M.R.C.P.: asst. physician (consultant), Dundee Royal Infirmary.

BURKE, N. H. M., M.R.C.S., D.P.M., D.M.R.E.: psychiatrist, public-health department, London County Council.

CLEMENTS, P. A. H., surgeon lieut.-commander, M.R.C.S.: deputy group medical superintendent, Dundee general hospitals.

DAVIDSON, W. A., M.D. St. And., D.P.H.: group medical superintendent, Dundee general hospitals.

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1. Lépine, P. *An. Inst. Med. trop., Lisb.* 1951, 8, 483.
2. *Epidem. vital Statist. Rep.* 1953, 6, 87.

morning; this, however, was by no means constant or predictable. When it was severe, nothing short of complete rest and analgesics would relieve it.

MALIGNANT HYPERTENSION

There were 18 patients who had entered the so-called "malignant" phase, in virtue of the development of papillœdema superimposed upon the primary retinal vascular changes. The average diastolic pressure was 159 mm. Hg. A detailed examination was made of this group. To 6 of them the nature of their illness remained unknown. Of these, only 1 complained of headache. On the other hand, 10 of the remaining 12, all aware of their hypertension, complained of this symptom. It thus seems possible that, even with this degree of hypertension, auto-suggestion may sometimes play a part in the production of headache. Again, about half of those who complained of it maintained that it was becoming less. None of them had previously experienced migraine. The average age at onset of the symptom was 40 in men and 33 in women.

The headache endured by these victims of malignant hypertension proved recognisable as a fairly clear-cut entity. It had never been present for long. Very commonly it was referred to one eye, often to the "back" of an eye, or it might be described in terms such as a "pulling of the eye." In addition there might be episodes of transient impairment of vision in addition to a recent progressive deterioration. Usually it was unilateral. It might affect any part of the head. It was often described as "thumping" or "bursting," but again it was evident that these sensations did not always bear a relation to the pulse-rate. Sometimes the pain, for so long as it was present, was "continual." It seldom lasted for more than a few hours at a time. Perhaps its most constant feature was its association with nausea, if not with vomiting. It was evident that to these patients the headache was only a part, and it might be a relatively trivial part, of their affliction. Rarely did it dominate and absorb them, as so often happens with the headache of a space-occupying intracranial lesion. Even without the complications of congestive failure, pulmonary œdema, or uræmia, these unfortunate people felt wretched in a way which they found difficult to define. "I just feel thoroughly miserable" was an expression several times heard. Two of the patients in this "malignant" group might have been said to be experiencing "hypertensive encephalopathy" in that spasmodic headache was accompanied on occasion by transient palsies or by fading of consciousness.

FACTOR OF ANXIETY

It has been pointed out that 104 of the patients in this survey did not know that their blood-pressure was abnormal. Of these 87 would admit no headache. On the other hand, all but one of those who had learnt of their condition offered symptoms of some kind, those with headache numbering 71 out of 96. These headaches, however, were seldom described in terms bearing any resemblance to those used with a readily appreciable uniformity by the few patients who protested headache while ignorant of their disease. Obviously the fact that a patient may have discovered that he has hypertension gives him no exemption from any organic symptom which that disorder may induce. Yet in fact, most of these 71 patients gave the clear impression that their symptoms stemmed from anxiety consequent on that knowledge.

Those so affected included many elderly women. The ubiquitous 'blackout' figured prominently in their stories. 'Dizziness' was mentioned specifically by 23 of them; only 5 made this complaint while ignorant of their hypertension. Of the whole 200 no more than 4 or 5 had experienced true vertigo without evident cause in a labyrinth or elsewhere. It then seemed that such vertigo might have an organic origin in the cerebral cortex, analogous to that occasionally presenting in migraine. Usually, however, the complaint of dizziness did not suggest an organic basis.

The headaches of these 71 patients, it was at once evident, had nearly all begun soon after the victims had first learnt of their hypertension. The reality of the complaint was seldom in doubt; but it was described in terms characteristic of anxiety. Commonly it was said to be "continual," in the sense of never ceasing for a moment. Activity, nevertheless, or inert tablets might relieve it. Sometimes it was "bad in the morning." Above all it was evident that "headache" and "blood-pressure" were regarded as a virtually inseparable combination. One lady expressed it: "But I thought blood-pressure *was* headache." A second remarked, perhaps more significantly than she realised: "Before I knew I had this blood-pressure I didn't have any headaches." To all of them it seemed natural and indeed inevitable that, if their blood-pressure was raised, they must have headaches. Many of the people in this survey used the terms "blood-pressure" and "headache" as if they were interchangeable.

CONTROLS

Patients who had complained of headache without any evidence of organic illness were questioned. A neurologist (Dr. A. M. G. Campbell) had judged the background to be one of anxiety. These people often volunteered that their headaches were worse in the early morning. Such timing is, of course, also characteristic both of migraine and of space-occupying intracranial lesions. Moreover, transient indisposition of many kinds can produce, in otherwise normal people, a "hangover" type of morning headache. Such a sensation may, perhaps, become exaggerated, as part of a neurosis, and be experienced daily. Many of these controls complained also of "dizzy feelings." Their symptoms were, in fact, indistinguishable from those offered by most of those hypertensives who had headache while aware of their high blood-pressure.

A further 3 controls had complained incidentally of long-standing headache, for which no reason could be found, after admission to hospital for abdominal surgery. It was suggested to them that the surgical treatment would in all probability achieve the happy additional effect of curing this headache. Six months later all 3 declared their headaches to be much less severe.

Discussion and Conclusions

This survey seems to show that headache can result directly from hypertension. Such headache is rare, but it bears the stamp of an organic symptom. In character it closely resembles migraine. Reasonably, perhaps, it may be supposed that its origin is similar—that it is due, in fact, to intermittent stretch of the cerebral arterial walls, and is analogous to that produced experimentally with histamine by Pickering (1933), Graham and Wolff (1938), and others. Such is the view of Symonds (1946), who holds that a few of the headaches that accompany arterial hypertension appear to have "much the same basis as those of migraine."

On the other hand, it seems to be indisputable that in association with hypertension a second type of headache occurs very often. This headache derives from anxiety. Platt (1950) has said that "very many hypertensive subjects . . . have been given an anxiety neurosis by the discovery of their high blood-pressure. It would not be far from the truth to say that the majority of symptoms of hypertension are iatrogenic." The conclusion to be drawn from the present investigation reinforces that assertion. Supporting evidence was obtained from several sources. Thus of the 104 patients unaware of their hypertension only 3 volunteered that they had headache, a further 14 admitting it, the tendency for headache to be absent persisted symmetrically

Notes and News

RECIPROCAL SOCIAL INSURANCE

The Under-Secretary for Commonwealth Relations announced in the House of Commons last week that an agreement on social security between the Government of the United Kingdom and the government of Australia was signed by the Prime Minister and the prime minister of Australia on June 8. The agreement covered retirement pensions and widows' benefits, unemployment and sickness benefits, and family allowances on the United Kingdom side, and the corresponding benefits of the Australian social services scheme. It was hoped that the agreement would come into operation early next year; and the full text will be published shortly as a white paper.

A similar reciprocal agreement between the United Kingdom and Italy has now been brought into force.[1] The agreement covers retirement pensions, widows' benefits and guardian allowances, unemployment, sickness and maternity benefits, and all industrial injuries benefits. The agreement also provides for each country to take account of insurance contributions paid in the other country so that people who go from one country to the other will not lose their benefit rights. Employed persons who are sent to Italy by their employers in Great Britain for short periods will, in future, remain fully insured under the British National Insurance and Industrial Injuries schemes while in Italy.

University of Oxford

On June 6 the following degrees were conferred:

D.M.—R. R. de Mowbray, R. A. Sladden, E. M. Vaughan Williams.

University of Cambridge

Mr. H. U. Willink, master of Magdalene College, has been elected to the office of vice-chancellor for the academical year 1953–54, in succession to Sir Lionel Whitby.

On June 6 the following degrees were conferred:

M.D.—R. E. Church, *R. J. Dickson, H. G. Dowler, R. D. Eastham, J. W. Fawcett, John Foley, D. K. Ford, Gordon Wetherley-Mein, D. B. B. Whitehouse.

* By proxy.

University of London

The following have been successful in the examination for part I of the diploma in psychological medicine:

J. E. A. Bartlet, Valerie A. Cowie, L. A. Hersov, S. G. E. Laverty, I. J. MacDonald, A. A. Reid, M. J. Rosenthall.

University of Birmingham

The council has approved a recommendation that undergraduates of all faculties should be X-rayed at the beginning of each year of their course.

The title of reader in systematic bacteriology has been conferred on Dr. K. A. Bisset, lecturer in bacteriology; the title of reader in social medicine on Dr. R. G. Record, lecturer in social medicine; the title of honorary lecturer in radiology in the department of surgery on Dr. C. G. Teall, university clinical lecturer in radiology; the title of university research fellow on Dr. W. Taylor, part-time lecturer in medical statistics, during his tenure of a Rockefeller fellowship; and the title of university clinical lecturer on Dr. J. F. K. Hutton (radiology).

Professor C. H. Pae, of the department of pharmacology of the University of Taegu, South Korea, will work in the department of pharmacology for a year from Oct. 1, 1953.

The Barling scholarship, for postgraduate work in surgery, has been awarded for 1953 to J. M. Small, university clinical lecturer in neurosurgery.

University of Edinburgh

Dr. D. J. A. Kerr has been appointed to the regius chair of forensic medicine in succession to Sir Sydney Smith, who is retiring.

Dr. Kerr, who is 58, was educated at St. Paul's School, London, and Edinburgh University, where he is at present a lecturer in forensic medicine. He graduated M.B. in 1920, and took the D.P.H. two years later. After holding a resident post at the Fife and Kinross District Asylum he was appointed assistant pathologist to the Edinburgh Royal Infirmary. In 1927 he became F.R.C.P.E., and graduated M.D. with commendation. Since 1929 he has been police surgeon and medical referee to the City of Edinburgh. He sits on the General Medical Council as the representative of the Royal College of Physicians of Edinburgh. His textbook on *Forensic Medicine* first appeared in 1935 and is now in its fourth edition.

University of Glasgow

The diploma in public health has been awarded to the following:

G. G. Browning, Helen W. Greenlees, H. M. Macfarlane, Sheenah J. M. Russell, L. G. Samuel, Richard Short, R. S. Sloan, Elizabeth Stewart, Norval Watson.

Royal College of Surgeons of England

At a meeting of the council on June 11, with Sir Cecil Wakeley, the president, in the chair, the following were coöpted to the council for the year 1953–54 representing various branches of practice:

Dr. O. C. Carter (general practice), Prof. A. M. Claye (gynæcology and obstetrics), Mr. M. L. Formby (otolaryngology), Dr. B. R. M. Johnson (anæsthetics), Mr. A. B. Nutt (ophthalmology), Sir William Kelsey Fry (dental surgery).

The following examiners were appointed for the ensuing year:

[illegible] E. A. Blake Pritchard. Anatomy: Th [illegible] Mary F. Lucas Keene, Lambert Ro [illegible] and Pathology: D. T. Harris, Theodore Crawford, Geoffrey Hadfield, Albert Hemingway.

Diploma of L.R.C.P., M.R.C.S.—Elementary Biology: A. G. Hamilton, C. C. Hentschel. Anatomy: Thomas Nicol, E. W. T. Morris, A. J. Heriot. Physiology: C. C. N. Vass, Esther M. Killick. Midwifery: R. K. Bowes, D. M. Stern, R. G. Maliphant, W. R. Winterton. Pathology: Sir Ernest Finch, L. E. C. Norbury, Joseph Bamforth, A. C. Cunliffe.

Diploma in Public Health.—Preliminary: Arthur Massey. Final: Stanley King.

Diploma in Tropical Medicine and Hygiene.—P. C. C. Garnham, A. W. Woodruff.

Diploma in Ophthalmology.—R. C. Davenport, A. B. Nutt, T. Keith Lyle, A. G. Cross, A. M. Reid, Eugene Wolff, E. F. King.

Diploma in Psychological Medicine.—Part I: Louis Minski.

Diploma in Laryngology and Otology.—Part I: G. H. Livingstone, F. C. W. Capps. Part II: W. A. Mill.

Diploma in Medical Radio-Diagnosis.—Part I: F. W. Spiers. Part II: Hugh Davies.

Diploma in Medical Radiotherapy.—Part I: F. W. Spiers. Part II: J. A. C. Fleming.

Diploma in Child Health.—G. H. Macnab, D. F. Ellison Nash, W. F. Gaisford.

Diploma in Physical Medicine.—Part I: E. J. Crisp, Leon Gillis. Part II: Philip Wiles, W. S. Tegner.

Diploma in Industrial Health.—L. G. Norman.

Diploma in Pathology.—J. H. Dible, Theodore Crawford.

Diploma in Anæsthetics.—Surgery: C. E. Shattock. Anæsthetics: W. Alexander Low.

Mr. R. Danbury (Royal Free) was presented with the Begley prize.

Diplomas of fellowship were granted to the following:

R. L. Rees, D. G. B. Bennett, R. A. J. Baily, R. L. A. Gouges-d'Agincourt, J. R. Dyer, R. L. Batten, J. G. Kendall, †Robert Pracy, Geoffrey Mizbah, R. W. Povey, A. H. M. Littlewood, C. S. Kirkham, C. F. Noon, D. B. Leaming, P. W. Seargeant, D. C. Stevenson, E. C. Edwards, Phyllis A. George, D. B. J. Wardle, F. G. Ellis, E. A. Badoe, Fida Mohamad Khan, I. B. Speight, †Ben Cohen, *Brojo Mohan Chatterjee, Anil Krishna Barat, R. D. Venn, K. J. Watson, W. G. Davidson, Parimal Chandra Ghosh, E. O. Williams, D. S. Kidd, W. P. Crone, Ralph Ger, J. R. Kenyon, †F. D. Martinson, J. P. Swain, W. N. Coombes, *J. S. Groves, J. M. Mynors, Daphne M. Scott, *Jack Swartz, H. T. Thompson, Paul Abbey, H. H. Francis, *Irene D. R. Gregory, E. F. Shanahan, N. D. Ashe, H. J. Bagnall, †R. J. Bennett, Ram Prosad Chakrabarty, M. W. Falloon, J. M. Hay, Robert Jacobs, Allan Kelly, L. E. Neri, Jamnadas Narottam Ravalia, E. L. Angliss, Jean-Jacques Brossy, J. V. L. Colman, †D. F. Cossar, D. G. L. Davies, *R. F. Elliott, Dinshaw Jamshedji Ghadialy, J. K. Henderson, A. F. Hunter, Pearse O'Donoghue, O. E. Owen, *I. W. Payne, Philip Rhodes, Vasant Kanaiyalal Vani, A. J. C. Allison, J. K. Clarebrough, *R. H. L. Ferguson, †H. J. Groves, P. J. Heery, Joseph Jaconelli, Geoffrey Slaney, G. C. Slee, J. G. Watson, M. E. E. White, Ismail Ahmed Agjee, Nirmalchandra Rochiram Amesur, Muhammad Ismet Khurshid Anwar, G. B. Cavaye, Subir Kumar Chatterjee, J. A. Hanley, C. Q. Henriques, J. T. Hueston, G. J. Kane, P. A. King, E. R. McKenzie, C. P. Mills, J. K. M. Quartey, M. W. Reece, N. A. Stephens, C. H. Talbot, A. W. R. Williamson, R. E. Candlin, D. S. Cole, K. J. Coleman, R. D. Cundall, M. B. O'Donnell, D. A. Simpson, R. H. Thorlakson, W. J. D. Bradfield, B. S. Pearson, R. J. M. Whittle.

* In ophthalmology. † In otolaryngology.

Diplomas of membership were granted to G. P. Lowther and B. K. A. Muller.

Royal Medico-Psychological Association

The following have been successful in the association's examinations for the diploma in psychological medicine:

Part I.—R. E. Brandon, N. C. Connell, F. H. Corbitt, W. Johnston, R. E. Lovelace, J. Mukerjee, Elizabeth Shoenberg, D. C. V. Stewart.

Part II.—Ruth Hoffman, N. B. Jetmalani.

Medical Insurance Agency

At the annual meeting of the Medical Insurance Agency, held on June 11 with Dr. James Fenton in the chair, Sir John McNee, Mr. R. L. Newell, Dr. Henry Robinson, Sir Arnold Stott, and Dr. E. R. C. Walker were re-elected to the committee, and Dr. Janet Bottomley was elected for the first time. Dr. Fenton was re-elected as chairman and Dr. Robinson as secretary.

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[1] The National Insurance and Industrial (Reciprocal Agreement with Italy) Order, 1953; S.I. 1953, no. 884. 6*d.*

through all grades of diastolic pressure Yet the symptom was complained of usually in terms strongly suggesting neurosis by 71 out of 96 comparable hypertensives who knew the nature of their illness It had then nearly always appeared shortly after their acquisition of that knowledge Moreover most of the 25 remaining out of this 96 had excellent organic cause for concentrating their attention on something else Only 1 declared himself to feel well On the strength of these findings it seemed virtually impossible for a patient to remain symptom-free after being told of his raised blood-pressure.

How are the organic and anxiety types of headache to be distinguished? Features which have been widely held to indicate typical "hypertensive" headache—e g exacerbation in the early morning—seem after all, to be of little diagnostic value There are however, better points of distinction, they are summarised in table IV

On the whole, the organic type of headache has seldom been present for more than a few months It declares itself soon after the pressure begins to rise either for the first time, or after a period of stability following an initial increase The severity of the hypertension, shown by the diastolic pressure and the state of the left ventricle, plays no direct part in its production. In the late stages however, there is a tendency for advanced retinal changes to be associated with it It is likely to resemble migraine in its unilateral localisation and in liability to be precipitated by worry or excitement, but there is no aura Transient faintness, occasionally true vertigo, may accompany it It seldom lasts for more than a few hours at a time While severe it responds only to complete rest or powerful analgesics After a time it tends to become less The victim is unlikely to be of more than middle age He is often unaware that his blood-pressure is in question

By contrast, the onset of the anxiety type of headache follows closely on the patient's first learning of his "blood-pressure". The sufferer may be beyond middle age, commonly an elderly woman Bizarre complaints, typical of anxiety, accompany the headache, which tends to be perpetual. Suggestion, however may bring relief

TABLE IV—COMPARISON OF FACTORS CHARACTERISTIC OF ORGANIC AND ANXIETY HEADACHE FOUND IN ASSOCIATION WITH HYPERTENSION

Organic	Anxiety
Rare	Common
Seldom found over middle-age in women often at menopause, sometimes much younger	Any age, common in the elderly, particularly women
Often no knowledge of disease	Always knowledge of "blood-pressure"
Short history of headache	Headache dates from the time of acquiring knowledge of 'blood pressure'
Severity of hypertension tends to be: (1) comparatively slight, or (2) malignant (state of left ventricle of no account)	Severity (measured by any standard) of no account
Retinal changes often severe in later stages of hypertension	Severe retinal changes relatively uncommon
Headache often "bad in the morning"	Headache often 'bad in the morning
Headache made worse by worry and activity	Headache made worse by worry, may be lessened by activity
Headache often tending to get less	Little spontaneous relief inert tablets may be effective
Headache like migraine, but no aura: vertigo occasionally faints more common, in malignant" phase eye pain, nausea and feeling of wretchedness	Headache bizarre typical of neurosis accompanied by or alternating with, black-outs' dizzy turns' &c, faints rare, no nausea no vertigo

Headache of the type which can be supposed organic was found in three main groups of hypertensives

(1) *Menopausal women* —Two-thirds of the women volunteering that they had headache were of menopausal age The symptom may be caused at this period of life by associated organic changes, which are probably vascular

(2) *With early benign hypertension* —The average severity of hypertension among the 17 patients who complained of headache while unaware of their hypertension was much below the average for the rest of the series Moreover three quarters of these patients had developed their headache comparatively recently, more than half of them declaring that there had already been considerable improvement Lovibond (1949) has suggested that headache may result, in hypertension, from the first rise in pressure

(3) *With malignant hypertension* —Such patients fall into a separate category, which has been described Deep eye pain, nausea, and severe general malaise are almost constant accompaniments of the headache.

These organic varieties of headache are rare Should they present in a menopausal woman, or in a patient whose blood-pressure has lately begun to rise, they can confidently be expected to vanish spontaneously particularly on rest, within an hour or two, and to exhibit a general tendency, over a longer period to disappear of their own accord It follows that successful treatment of organic headache caused by benign hypertension can never be identified with certainty In fact, whatever may be the evidence of success in combating this form of hypertension, the alleviation of headache can never, logically, be part of it

Nearly all the headaches presenting during the course of benign hypertension are due to anxiety They are thus likely to respond favourably to any form of treatment that promises benefit It has been shown by Friedman et al (1949) that the degree of the response is likely to vary directly with the impressiveness of the treatment adopted Sympathectomy seems to be well qualified in this respect

With malignant hypertension the problem is different In this condition organic headache presents fairly often, even if submerged among other symptoms Sympathectomy seems to be effective in reducing it It may be noted, however, that according to Wood (1950b) a mere 0 2% of persons with simple hypertension pass into the malignant phase

Today there is some hope of cutting short the sinister, and still unexplained rise in blood-pressure that occurs in hypertension In particular the new hypotensive drugs show promise Already it seems that on occasion, cardiac failure may be postponed visual difficulty improved. and life prolonged. The future is hopeful Yet it would be a pity if a confusion of premises should lead to false optimism Certainly it would be well to remain unimpressed with any measure that bases its claims upon the relief of headache.

Summary

A survey was made of 200 consecutive patients with severe hypertension The average diastolic pressure measured under standard conditions of rest, was 136 mm Hg

Assessment was made of the symptom of headache, whether spontaneous or elicited by an interrogation technique designed to avoid suggestion.

Those patients who were aware and those unaware of their hypertension were compared. The severity of disease was found to be roughly the same in the two groups estimated by diastolic level, electrocardiograms, and radioscopic appearances of the left ventricle Retinal changes were somewhat greater in those with headache

Of the 104 patients unaware of their hypertension 87 would not admit to having headache This tendency for headache to be absent persisted symmetrically through all grades of diastolic pressure The symptom was volunteered by only 3 of these patients, being elicited from the remaining 14 Of 96 patients

Faculty of Radiologists

The annual meeting of the faculty will open at the Royal College of Surgeons, London, at 9.30 A.M. on Friday, July 3, and will continue on July 4.

Lady Tata Trust

The trustees of this fund announce that they have made the following awards for research on leukæmia and allied diseases, in the year beginning next October:

Grants for research expenses or for scientific assistance.—Dr. Astrid Fagraeus and Dr. Bo Thorell (Stockholm); Dr. Clarence Merskey (Cape Town); Prof. Charles Oberling (Paris); Dr. C. C. Ungley (Newcastle upon Tyne); Dr. Jo Nordmann (Paris).

Part-time personal grant.—Dr. J. B. G. Dausset (Paris).

Scholarships.—Dr. Ragna Rask-Nielsen (Copenhagen); Dr. Roger Robineaux (Paris); Dr. Flemming Kissmeyer-Nielsen (Aarhus, Denmark); Dr. N. A. Stenderup (Aarhus, Denmark).

Senior Research fellowships.—Dr. A. R. Gopal-Ayengar (India) for work at the Royal Cancer Hospital; Dr. Jørgen Kieler (Denmark) for work at the Fibiger Laboratories, Copenhagen.

A special scholarship awarded to Dr. Gavino Negroni (Italy), for work at the Imperial Cancer Research Fund Laboratories, will continue until April 30, 1954.

Beit Fellowship for Medical Research

The following awards have been made:

Fourth-year Fellowship

JOAN E. KEILIN, M.A., M.B., PH.D. Camb. To investigate the catalytic activity of hæmatin compounds and the effect of oxidising agents on hæmatins. Also to investigate the properties of purified helicorubin and its relationship to other natural hæmoproteins; and to investigate the reactions of hæmatins with proteins and their constituent amino-acids and peptides to gain more information as to the structure of the hæmoglobin molecule and the link between the hæm and globin and to use hæmatin as a reagent for the study of other biologically important proteins. At the Department of Biochemistry, Cambridge.

Junior Fellowships

J. R. CANNON, M.SC., Sydney. To continue the study of the chemical structure of Vitamin B_{12}. At University Chemical Laboratories, Cambridge.

G. P. LEWIS, B.PHARM. Wales. To study the relationship between structure and action of drugs, particularly of antagonists of histamine, acetylcholine, adrenaline, and noradrenaline, to examine how far ionisation of a drug or its receptor modifies drug action. At the National Institute for Medical Research, Mill Hill, London.

W. L. NICHOLAS, B.SC. Lpool. To investigate the determination of the growth requirements of free-living and parasitic nematodes in chemically defined media, with a view to its possible application to the chemotherapy of nematode infections. At the Department of Zoology, Liverpool University.

EVELYN E. B. SMITH, B.SC., PH.D. Glasg. To investigate the enzymic mechanisms of transfer reactions involving uridine pyrophosphate compounds containing glucose, glucuronic acid, and N-acetylglucosamine; and the biosynthesis of glucuronic acid, glucuronides, and oligosaccharides containing glucuronic acid, *using carbon and phosphorus isotopes.* At the Department of Biochemistry, Glasgow University.

South Western Regional Hospital Board

The Minister of Health has appointed Sir Havergal Downes-Shaw, O.B.E., to be chairman of this board. Sir Havergal Downes-Shaw, a former departmental manager of the Imperial Tobacco Company, has been a member of Bristol City Council since 1931 and an alderman since 1946.

Society for Relief of Widows and Orphans of Medical Men

This society's annual meeting was held on June 10, with Sir Robert Young, the president, in the chair. Members of the society number 198; and at the end of 1952 there were 35 widows in receipt of grants. Widows over 65 receive £75, and those under that age £60 a year. In addition a present of £30 was made at Easter, and again at Michaelmas. The total amount distributed in 1952 was £4525. Sir Ernest Rock Carling, the treasurer, reported that during the year income exceeded expenditure by £723. The address of the society is 11, Chandos Street, London, W.1.

Institute on Œsophageal Speech

An institute on teaching and improving œsophageal speech will be held on Aug. 10–16 at the Cleveland Hearing and Speech Center, Cleveland, Ohio. This institute is being sponsored by the American Cancer Society, the National Cancer Institute of Institutes of Health, the Office of Vocational Rehabilitation, the Cleveland Otolaryngological Society, the Cleveland Academy of Medicine, and the Western Reserve University School of Medicine. Non-speaking laryngectomised persons may attend without charge. They may be sent by surgeons, cancer societies, societies for crippled persons, and rehabilitation services. Surgeons, speech pathologists, and laymen are also invited to attend the sessions. Application must be made by July 15 to Warren H. Gardner, PH.D., program chairman, 11206, Euclid Avenue, Cleveland 6, Ohio.

Royal Medical Benevolent Fund

At the annual meeting, held on June 9, honorary offi were re-elected as follows: president, Lord Webb-Johns treasurer, Mr. F. A. Juler; secretary, Dr. R. Cove-Smith.

International Hæmophilia Society

A meeting of this society is to be held at Seymour H London, W.1, on Sunday, June 21, at 2 P.M. The Lond Group will meet at the society's offices, 94, Southwark Brid Road, S.W.1, on Wednesday, July 1, at 6.30 P.M.

Visitor in Lunacy

The Lord Chancellor has appointed Dr. R. G. Anders a commissioner of the Board of Control, to be a medical visit in the place of Dr. A. E. Evans who is retiring.

Oxford Graduates Medical Club

The summer dinner will be held in the Queen's Colle Oxford, on Friday, July 10, at 7 for 7.30 P.M. Dr. C. G Douglas, F.R.S., will preside. Tickets (£2 2*s*. inclusive) ma be had before July 4 from Mr. Solwyn Taylor, F.R.C.S., 3 Roedean Crescent, London, S.W.15.

Diary of the Week

JUNE 21 TO 27

Monday, 22nd

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.1
4 P.M. Dr. W. Ritchie Russell: Poliomyelitis.

Tuesday, 23rd

SOCIETY FOR ENDOCRINOLOGY
5.30 P.M. (1, Wimpole Street, W.1.) Dr. Charles Hu (Chicago): Prostatic Glands as Targets for Steroids.

Wednesday, 24th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. E. F. Gale: Mode of Action of Antibacterial Ag (First of two lectures.)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Str W.C.2
5.30 P.M. Dr. H. Haber: Parapsoriasis, Poikiloderma Mycosis Fungoides.
BRITISH ASSOCIATION OF SPORT AND MEDICINE
5 P.M. (Westminster Hospital Medical School, Horsefer Road, S.W.1.) Sir Adolphe Abrahams, Dr. McEldowney: Doping of Athletes.
BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles Str Birmingham, 3
8 P.M. *Section of Psychiatry.* Dr. W. Mayer-Gross: Problem of t Symptomatic Psychoses.

Thursday, 25th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Prof. Arnold Sorsby: New Antibiotics.
UNIVERSITY COLLEGE, Gower Street, W.C.1
4.45 P.M. Prof. J. H. Quastel, D.SC., F.R.S. (Montreal): Acti of Drugs on Enzyme Systems.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Colonel W. R. M. Drew: Recent Advances in Malari Problems.
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Childr Great Ormond Street, W.C.1
5 P.M. Dr. W. C. Davison (Duke University, North Carolina) Childhood Cancer.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. W. Riddell: Subcutaneous Mycotic Infectio
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Roa W.C.1
5.30 P.M. Prof. B. Gusic (Zagreb): Pathological Change Blood-vessels and Nerves of Œsophagus Due to Corro
BRITISH ASSOCIATION OF UROLOGICAL SURGEONS HOME A OVERSEAS
11 A.M. (General Infirmary, Leeds.) Short papers.
2 P.M. Professor Huggins: Adrenal in Cancer.

Friday, 26th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. C. E. Dent: Diagnosis of Hyper-parathyroidism.
4 P.M. Prof. L. J. Witts [illegible] Splenectomy.
INSTITUTE OF LARYNGOLOG [illegible]
3.30 P.M. Mr. Anthony [illegible]
BRITISH ASSOCIATION OF [illegible] HOME A OVERSEAS
9.30 A.M. Mr. J. Cosbie Ross, Mr. J. G. Gow, Dr. J. Colqu Mr. M. F. Nicholls: Urinary Tuberculosis.

Saturday, 27th

UNIVERSITY OF CAMBRIDGE
10.30 A.M. (Addenbrooke's Hospital, Cambridge.) Postgradu symposium on diseases of the ear, nose, and throat a diseases of the eye.
BRITISH ASSOCIATION OF UROLOGICAL SURGEONS HOME A OVERSEAS
9.30 A.M. Short papers and films.

aware of their hypertension 71 complained of headache, most of them in terms characteristic of anxiety On analysis of the remaining 25 it was found that 18 had good organic cause for complaining of something else, and 6 offered symptoms characteristic of anxiety

From these and other findings, together with evidence afforded by the examination of controls, it was concluded that the headache which so often accompanies hypertension is usually a product of anxiety Moreover it seems almost impossible for a patient who has been told of his "blood-pressure" to remain symptom-free

It appeared further that hypertension might occasionally produce headache as an organic symptom It was most likely to do so in menopausal women, during the early stages of benign hypertension, or, as a relatively insignificant feature, within the syndrome of malignant hypertension

Analysis was made of factors which serve to distinguish this rare organic headache from the common one which is due to anxiety

Attention is drawn to the fallacy of acclaiming any treatment of hypertension in virtue of its alleged cure of headache

This survey was made at the instigation, and with the advice, of Dr D H Davies Most of the patients concerned were under his care A few, however, were under the care of other members of the consultant staff of the Bristol Royal Infirmary, to whom, therefore, I should like to express my thanks

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INTRA-ARTERIAL TRANSFUSION

THE POTASSIUM HAZARD

D G Melrose
B M Oxfd
ASSISTANT LECTURER

A O Wilson
B Sc, M B Edin
REGISTRAR

DEPARTMENT OF SURGERY, POSTGRADUATE MEDICAL SCHOOL OF LONDON

The replacement of blood with the least possible delay is now regarded as fundamental in the prevention and treatment of shock Blood may be replaced rapidly either by the intravenous or the intra-arterial route The pros and cons of intra-arterial transfusion have been discussed by Seeley and Nelson (1952) in a review of most of the pertinent literature and it may be said that such transfusions can be a life-saving measure and are often the method of choice The extreme case of resuscitation of the clinically dead has been reported by Negovsky (1945) and Gold et al (1949) have reported dramatic results in patients with complete circulatory collapse

The mode of action of such transfusions seems to be that the intra-aortic pressure is rapidly raised to a level sufficient to revoke the intense vasoconstriction previously initiated by the pressoreceptors in the aortic arch and carotid sinus, and hence to promote restoration of normal vascular tone, which in turn permits normal perfusion of the capillary networks, particularly those of the heart and brain, which may even be perfused directly by the ingoing infusion

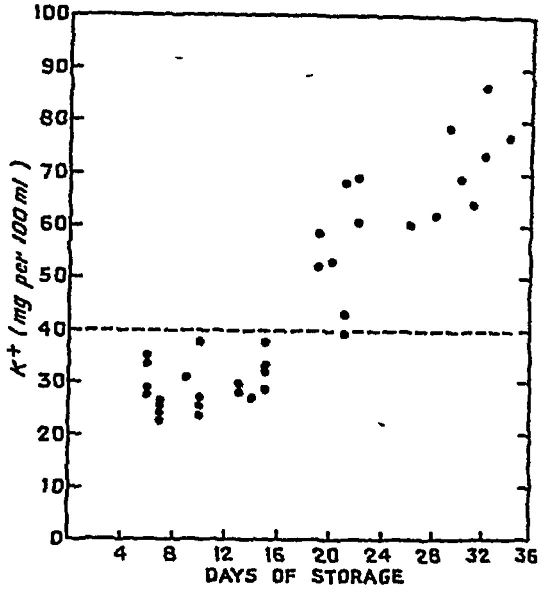

Fig 1—K+ values of samples from plasma-cell interface of bottled blood.

POTASSIUM IN STORED BLOOD

Intra-arterial transfusions are generally given in emergencies and often in large amounts, and therefore stored blood must usually, if not always, be used This raises the possibility of adverse effects due to the altered chemical composition of stored blood Crafoord (1948) expressed a preference for fresh blood when large amounts are to be given rapidly, but did not refer to the question of the chemical composition of the blood

Mainwaring et al (1940) and De Gowin et al (1940) have drawn attention to the rapid release of potassium from the red cells during the storage of blood, and we have confirmed their results (fig 1) Potassium was determined by means of an internal standard flame photometer based on that described by Berry et al (1946) Our figures tend to be lower, possibly because of improved methods of storage and because our samples were collected from the region of the plasma-cell interface Nevertheless plasma-potassium levels of 35 mg or more per 100 ml are not uncommon in blood stored for up to three weeks This figure of 35 mg of potassium per 100 ml of plasma is just below the fatal concentration in man, which is about 40 mg of potassium per 100 ml

The danger of giving potassium-containing solutions intravenously has been much emphasised (Fenn 1940, Hoffman 1950), and for administration by this route at a rate not exceeding 2 or 3 ml per minute a safe potassium concentration is about 200 mg per 100 ml (50 m eq per litre) This would be diluted to give a rise in plasma-potassium level of only about 0·25 mg per 100 ml (0·06 m eq per litre) per minute, provided the blood volume was normal and all the potassium remained in the plasma Wright (1952) states "The high plasma K+ concentration of stored blood must be borne in mind as K+ in excess has toxic effects on the circulation these may be avoided if the transfusion is performed at rates not exceeding 40 cc per minute"

In the same context Blixenkrone-Moller (1949) advises against the use of stored blood if many transfusions are to be given in quick succession, even by the intravenous r Law" (*British Medical Journal* 1909). This was view of doctors in private practice, and there were ications that at that time many of them would have n prepared to accept a salary for part-time public vice.

he full implementation of either of these proposals ght have prevented the division between the preventive d curative personal services. For the medical staff of gressive public-health authorities were then extenely engaged in treatment as well as prevention of sease, and had both been sanctioned by Parliament it n hardly be doubted that a unified service would have own up—no doubt with serious effects upon private actice. Alternatively, had general practitioners been rmitted to undertake the work in schools, and later child-welfare clinics, it is also possible that the division ight have been avoided. In this case the attitude of octors to local-authority administration and payment by lary might later have been different from what it was. he Education Act, 1907, and the Maternity and Child Velfare Act, 1918, effected a compromise, by assigng the preventive personal services to public-health uthorities, while curtailing treatment in deference to he wishes of private doctors. This in effect made revention a public responsibility, and left treatment a rivate one. The National Health Service Act removed his distinction, but left the machinery of administration f the personal health services essentially unchanged.

Against this background we turn to an examination f the work done at child-welfare clinics today, and to onsideration of their future organisation.

Material of Study

We collected our data by investigation of work done at child-welfare clinics in Birmingham (population 1,112,340), and Coseley (an urban district in the administrative county of Stafford, population 34,414).

In Coseley there is only one welfare centre, a well-equipped modern building designed for the purpose. School, antenatal, postnatal, and child-welfare clinics are held in this centre. There are no special sessions for toddlers, and the obstetrician responsible for the combined antenatal and postnatal clinics does not examine infants; consequently the child-welfare sessions, held twice a week, cater for preschool children of all ages. The medical officer who holds these clinics (J. T. A. G.) is also medical officer of health for Coseley. Two qualified health visitors attend each session.

In Birmingham, child-welfare clinics are held at 33 different centres. Of these, 2 (a church hall and a Friends' meeting-house) are in part-time use by the local authority; 31 are full-time child-welfare centres. Of the latter, 13 were designed and built as clinics; the remaining 18 originally served some other purpose (private residence, municipal house, public house) and were adapted by more or less extensive structural alterations for use as children's clinics. Some of these buildings are unsatisfactory, and but for building restrictions during and since the war would have been replaced.

In Coseley all child-welfare services, including immunisation against diphtheria, are provided at the same clinic session. In Birmingham, although all children under 5 years old may attend, the children's clinics are mainly concerned with the supervision of children between 3 and 18 months of age. Mothers with babies under 3 months are encouraged to attend special postnatal clinics, mothers with older children (18 months to 5 years) are given quarterly appointments for toddlers' clinics, and immunisation against diphtheria is offered at special immunisation sessions. The 33 welfare centres provide 64 children's clinics a week, and employ fifteen full-time and twenty-six part-time medical officers, of whom all but four are women. At each session two, occasionally three, health visitors are in attendance.

After a pilot survey conducted at Coseley two record cards were designed. The first was completed by a social worker, who interviewed mothers in reasonable privacy as they arrived at the clinic and recorded their reasons for attending on that particular day. The second card was completed in Coseley by the clinic medical officer (J. T. A. G.), and in Birmingham by one of two medical observers (J. T. A. G. or C. R. L.) who sat in with the clinic medical officer. Data recorded were: sex, age, and birth rank of each child; the reason for medical consultation; and the type of service or services given by the doctor. Direct questioning of the mother was usually unnecessary, since most of the information was available in clinic records or from the mother's conversation with the medical officer. The work of the health visitors at the clinics was not examined in detail.

In the pilot survey the health visitor recorded the reason for attendance at the clinic. This proved unsatisfactory, because health visitors were already fully occupied and because consultations were usually within earshot of those waiting. This part of the inquiry was therefore conducted by a social worker in Birmingham; it was omitted in Coseley.

The Coseley data were collected at 62 consecutive sessions at the child-welfare centre between the end of July, 1951, and the beginning of May, 1952; the Birmingham data were obtained by a single visit, between Feb. 11 and May 12, 1952, to a children's clinic at each of the city's 33 centres. At Coseley the same child was often seen at more than one attendance. In Birmingham, as the postnatal and toddler sessions were excluded, the material is weighted in favour of children between 3 and 18 months of age. Of children referred to medical officers, the proportions under 3 months were 48% and 17% in Coseley and Birmingham respectively. Neither of these features seriously affects the results of our analysis, which is concerned primarily with the work of the clinics and not with the children attending.

Results

REASONS FOR ATTENDING THE CLINIC

The reasons given for attending were to have the child weighed, to obtain advice from the health visitor or doctor on some specific problem, and to purchase proprietary foods (table I). On the recommendation of the medical officer proprietary foods are available at wholesale prices, and whatever the official view mothers evidently consider this function of the clinic important. Nearly half of them (44%) gave food purchase as a reason for attending, 19% gave it as the only reason, and 15% had not brought the child with them. (In principle mothers are not allowed to buy food unless the child has been seen within the preceding fortnight.) In addition, an average of 51 mothers per clinic session attended for the sole purpose of shopping at the branch food offices established at 26 of the 33 Birmingham centres. These mothers, who came without children, did not enter the clinic proper, and are excluded from all tables.

REASONS FOR REFERRING CHILDREN TO THE MEDICAL OFFICER

The proportions of children referred by health visitors to the medical officers were 39% and 27% in Birmingham and Coseley respectively (table II); the average numbers

TABLE I—REASONS GIVEN BY BIRMINGHAM MOTHERS FOR ATTENDING CLINIC

Mothers accompanied by children					Mothers not accompanied by children	Total
Routine weighing	Specific advice	Purchase of proprietary foods			Purchase of proprietary foods	
		Only	And routine weighing	And specific advice		
39·4% *(650)*	16·9% *(278)*	4·3% *(71)*	21·2% *(349)*	3·3% *(55)*	14·9% *(245)*	100% *(1648)*

Alfred Charles Fisher, M D Brist, F R C S
For medical services and welfare work in Northern Rhodesia

Simon Reginald Gunewardene, M B Lond
Medical superintendent, State Home for the Aged, Koggala, Ceylon

Arthur Kidd, M B N.Z
Medical practitioner at Waipiatu Sanatorium, Otago

William Steele Mitchell, M R C S
Acting Government medical officer, Grenada, Windward Islands

Wilfrid Raffle, M B Camb
Principal medical officer, Ministry of Pensions

Theodore Howard Somervell, M B Camb, F R C S
Associate professor of surgery, Christian Medical College, Vellore, Madras

Leonard Boole Stott, M C, M B Lpool
Chief medical officer, Papworth Village Settlement

M B E (Military)

Major **Percy Lionel George Cole**, L S A, F A M C

M B E (Civil)

Lucien Noel Bartholomeusz, F R C S
Visiting surgeon, General Hospital, Colombo

James Gerrard Clearkin, M B Belf
Health officer, West Pahang, Federation of Malaya

Al Haj Mohamed Purvis Drahaman
Medical practitioner, Ceylon

Eric Parry, M B Lpool, F R C S E
Chief medical officer to the Kuwait government

Richard Henry Barter Snow, M B Camb
Chief medical officer to the Bahrain government

Bertram Alfred Wood Stone, M B Oxfd
Admiralty surgeon and agent, Southsea

Public Health

AN EXAMINATION OF THE WORK OF LOCAL-AUTHORITY CHILD-WELFARE CLINICS

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M B Birm, D P H
ASSISTANT COUNTY MEDICAL OFFICER, STAFFORDSHIRE

C R Lowe
M D, Ph D Birm, D P H
LECTURER IN PUBLIC HEALTH, UNIVERSITY OF BIRMINGHAM

Thomas McKeown
M D Birm, Ph D McGill, D Phil Oxfd, M R C.P
PROFESSOR OF SOCIAL MEDICINE IN THE UNIVERSITY OF BIRMINGHAM

The traditional services provided by local health authorities were designed to meet circumstances which existed during the 19th and early 20th centuries, in particular the high incidence of infectious disease and the absence of a generally available personal medical service During recent years the incidence of infectious disease has been greatly reduced, and since 1948 personal medical attention has been provided through a national service Yet except for the transfer of hospitals to regional hospital boards, there has been no major change in the organisation of the local-authority services, some of which overlap the general-practitioner and consultant services, while others are unsatisfactorily separated from them A re examination of the work of local health authorities against the background of the National Health Service is clearly necessary, and it is the purpose of the present communication to consider the work done by the child-welfare clinics provided under schemes for maternity and child welfare

HISTORICAL BACKGROUND

The traditional child-welfare service consists essentially of four features

Food Distribution—The distribution of cheap and safe milk to women who could not breast-feed their babies was introduced in France and England at the end of the 19th century The service was later extended to include dietetic supplements, and a National dried milk scheme was added during the last war

Advisory Service—Systematic instruction of working-class mothers by women with some knowledge of hygiene began in Manchester in 1862 as a voluntary service In time it was taken over by local authorities, and trained nurses (health visitors) were appointed, whose primary duty was the education of the mother at home and in clinics on all matters related to the care of her child

Routine Examination—In response to widespread concern about the health of young people, systematic medical inspection of school-children was recommended in the report of the Inter-Departmental Committee on *Physical Deterioration of 1904*, and was provided fo the Education Act, 1907 Regular examination later included among services for the preschool cl but is even now irregularly applied many authori insist on only one medical examination (at the postn clinic, or at the first visit of the child to a welfare cent others aim at examinations at the 1st and 3rd birthda while in some cases an attempt is made to exan children at three-monthly intervals throughout presc life

Medical Service—Free medical attention was off at infant clinics in France at the end of the 19th cent and in England at the beginning of the 20th This ser originally comprised both prevention and treatmen disease, but treatment was later curtailed Neverthe a considerable amount of treatment, mainly of a m kind, is still given at the clinics

The child-welfare service of today is composed of t diverse elements They were derived in part from 19th-century environmental services, but resulted ma from extension of local authority interest to pers services which had formerly been the concern of poor-law authority and voluntary agencies T development was ultimately responsible for the separat of the preventive from the curative personal serv and the reasons for it are of considerable histor importance

Local authorities entered the field of personal he service because of the inadequacy of existing provis for the care of children, of which there was evidenc the high infant-mortality rate (154 in 1900), and high proportion of recruits considered unfit for milit service (40% in 1901–02) For those unable to for treatment, the alternatives at the beginning of century were the medical services of the poor law o voluntary agencies But although it was generally agr that some extension of the public service was nee and that the medical branch of the poor-law was unsatisfactory means of providing it, how it should administered was for many years in dispute Broadly may be said that there were two proposals, and service which eventually emerged was a comprom between them

The first was the proposal that there should be a unif State medical service, based on public health princip and organised in local areas This was recommend to the Royal Commission on the Poor Laws (1905–09) by the heads of the four Government medical depart ments, who undoubtedly expressed the views of mo doctors in the public service

The alternative proposal was that the additional public medical services should be given by doctors in private practice According to the medico political committee of the British Medical Association " the most satisfactory provision for the treatment of children whose parent cannot afford to pay for it is to place them under the care of private practitioners, who should be adequately remunerated out of public funds independently of th route. Trumper (1951) has made similar observations on the use of plasma obtained from stored blood in the treatment of burns, and our measurements of the potassium level in twelve samples of plasma withdrawn from 1000-donor pools (fig. 2) confirms that values above 40 mg. per 100 ml. are common. Trumper also drew attention to the fact that, in shock, oliguria and a decreased cardiac output obviously potentiate the effect of any increase in plasma-potassium level, and these same factors operate in the similar but smaller changes in cardiac output and renal function occurring in all surgical patients.

The danger to the patient is largely the effect on the cardiac musculature of too high a concentration of potassium. It *may* be that another determining factor operates—i.e., the rate at which the cells can take up the excess of circulating potassium. Nevertheless a raised plasma-potassium level produces extrasystoles and ultimately death from cardiac arrest in diastole (Best and Taylor 1950).

REDUCTION OF POTASSIUM LEVEL

Since stored blood may contain a high level of potassium, attempts were made to reduce this by various means, so as to make the blood safer for rapid and massive intra-arterial transfusion. Maizels (1949) reinvestigated Harris's (1941) observation that incubation of stored blood at 37°C for a few hours in the presence of glucose causes cation distribution to return to normal. He found, however, that potassium did not return to the cells until after eight hours, the pH and other factors being of great importance in determining the rate. Thus the ideal method of restoring the composition of the blood is unfortunately impracticable.

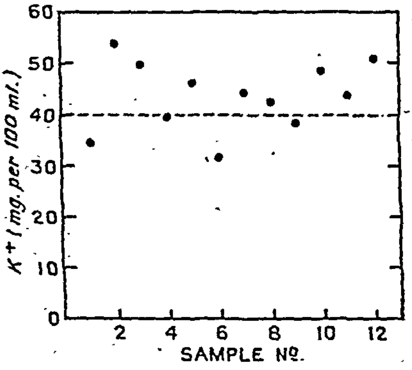

Fig. 2—K+ values of twelve samples of plasma from 1000-donor plasma pool.

Much of the potassium which has diffused out of the red cells may be removed by decanting the plasma from stored blood and reconstituting with physiological saline solution or better, with salt-free dextran, since this would obviate the risks attached to the administration of large amounts of sodium chloride to patients many of whom would be suffering from cardiac disease. It may be argued that this is inadequate since the plasma-potassium level round the sedimented red cells is higher than in the supernatant fluid. The volume of plasma remaining between the cells is, however, relatively small. This method proved to be a useful means of reducing the potassium level, a reduction of over 40% being obtained after replacement of the supernatant plasma by saline solution. Fig. 3 shows the reduction of potassium level in 13 samples of bank blood stored for more than twenty-one days. The cells and saline solution had been gently mixed and the potassium level determined on the "plasma" after centrifuging.

CARDIAC EFFECTS OF EXCESSIVE POTASSIUM

Attempts were also made to demonstrate in the dog the danger of intra-arterial transfusions of blood containing high levels of potassium by studying the effects of these on the electrocardiogram. Though slight changes were noted, no unequivocal evidence was obtained. Nevertheless these changes were probably significant in view of the fact that the fatal potassium level is higher in the dog than in man, and the total amount of potassium given was less than a quarter of that required by Winkler et al. (1938) to produce changes in the electrocardiogram after slow intravenous infusion.

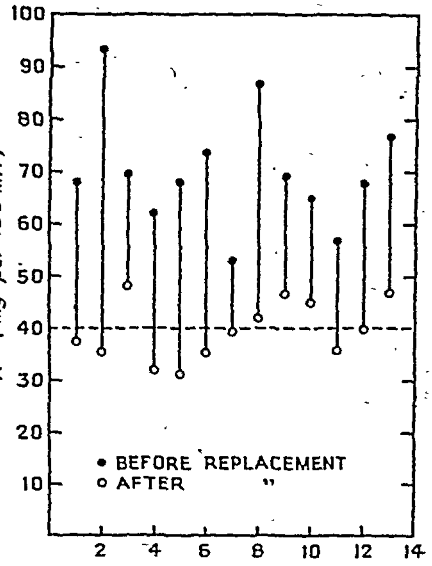

Fig. 3—K+ values of thirteen samples before and after replacement of plasma by isotonic saline solution.

Three important considerations govern the effect of potassium solutions, given intra-arterially on the heart. These are the direction of flow of the transfusion, the extent to which it is diluted in its passage to the heart, and the immediate state of potassium metabolism in the recipient. According to the site of infusion and the existing cardiac output, the bulk of the entering blood will go either with the normal stream away from the heart or in a retrograde direction into the coronary vessels. Where the output of the heart is very low a large proportion of the entering blood must go into the coronary vessels, regardless of the site of infusion, and in the stopped heart this undoubtedly happens (Smirenskaia and Maksimishina 1951). Jones et al. (1950) showed that 35% 'Diodrast' injected into the femoral artery of the dog passes directly into the coronary vessels if the systolic blood-pressure is less than 50 mm. Hg. It has further been demonstrated that, even in the presence of a normal cardiac output, the infused fluid may enter the coronary vessels if given into the aorta (Steiner 1952, Page 1946).

If mixing is instantaneous and complete, it is theoretically possible to give with safety a transfusion of 500 ml. of blood a minute, with a plasma-potassium level of as much as 100 mg. per 100 ml. (25·6 m.eq. per litre); for, even if the cardiac output is as low as 2 litres a minute, the level of potassium in the mixed blood reaching the heart should not exceed 36 mg. per 100 ml.—a safe level. In practice it is unlikely that mixing is complete and instantaneous, and the possibility exists that dangerous amounts of potassium may be *forced into* the heart although the output is not seriously reduced. In those instances where the output is less than 2 litres a minute, and it is under just such conditions that intra-arterial transfusions are particularly indicated, dilution may not reduce to a safe level the amount of potassium in the plasma of stored blood when this is given at an adequate rate. Especially is this likely in operations on the heart, where the output may temporarily fall to nil, and it must be assumed, and indeed is hoped, that the infused blood passes directly into the coronary vessels.

RESUSCITATION

In such circumstances it is essential to have available a simple method of resuscitation. Experience with a modified Henri-Jouvelet rotary pump suggests that it is the ideal device for rapid transfusion into either artery or vein. In use the tube connecting the blood reservoir of corticosteroids can be estimated without the usual unsatisfactory hydrolysis and extraction procedures

The term "17-ketogenic steroids" will be used here to denote corticosteroids bearing the side-chains III, IV, or V—i.e., those converted by bismuthate (and not by periodate) into 17-ketosteroids

Method

24 hour urine specimens are collected without preservative, made up to 2 litres with distilled water, and stored in a refrigerator Each specimen is assayed, in duplicate, concurrently for 17 ketosteroids (17-K.S.) and for "total 17 K.S." (after bismuthate oxidation) The difference between the two measurements represents the 17 ketosteroids formed from 17 ketogenic steroids on oxidation This figure is designated '17 K.G.S.' On a molar basis, and subject to the limitations inherent in the colorimetric determination of 17 K.S., it is a direct measure of the assayed 17 ketogenic steroids If, as is customary, the figures for 17 K.S. and "total 17 K.S." are expressed in weight units, the resulting values of 17 K.G.S. are about 20% lower than the actual quantities of the estimated 17 ketogenic steroids

Estimation of 17-K.S.

The following procedure is adapted from the method of Drekter et al (1952) 12 glass stoppered centrifuge tubes of about 30 ml capacity are held by spring clips in an H-shaped metal frame From each of six specimens two 8 ml aliquots are placed in the tubes, and 2 ml glacial acetic acid and 3 ml concentrated hydrochloric acid are added to each tube The rack of tubes is kept in a boiling water bath for 10 minutes, then cooled in cold water, to each tube 10 ml ethylene dichloride (purified by shaking with concentrated sulphuric acid and redistilled) is added, the tubes are stoppered and shaken mechanically (in the rack) for 15 minutes The stoppers are now removed, the tubes centrifuged, and the aqueous phases removed with suction The ethylene dichloride extracts are shaken firstly with 2·5 ml distilled water for 2 minutes and then with 2·5 ml 3N sodium hydroxide solution for 5 minutes, after each wash the layers are separated by centrifuging and the upper phases removed by suction The washed extracts are filtered through fluted paper into test-tubes, and from each filtrate two aliquots of 2·5 ml are transferred into smaller test tubes (5 × ½ in.), evaporated on a water-bath kept just below boiling, and finally brought to dryness in vacuo and assayed by the Callow Zimmermann method (Callow et al 1938), as modified by Zygmuntowicz et al (1951), a colour correction (Talbot et al 1942a and b, Medical Research Council 1951) is applied The colorimetric estimation is made on batches of twelve extracts, with each batch two standards of 20 µg dehydroepiandrosterone are included, and the 17-K.S. content of the extracts is calculated from the average standard value The conversion factor from µg per aliquot into mg 17 K.S. per 24 hours is 1·0

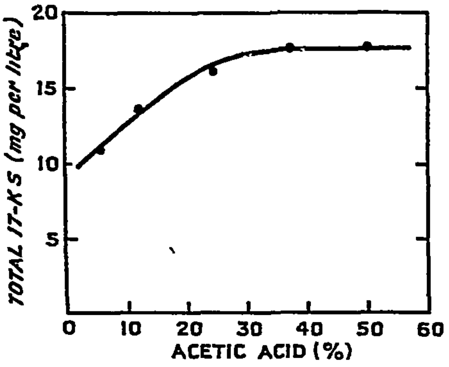

Fig 3—Relation between concentration of acetic acid and assayed "total 17-K S"

TABLE I—COMPARISON OF ORIGINAL AND MODIFIED METHOD

Experimental detail	'Total 17 K.S. (mg per litre)	d_{520} d_{430}
Treatment with NaOH pellets (Original method)	11·2 11·8 8·8 9·3 14·1 12·8	1·0 1·0 1·0 0·9 1·1 1·1
As above with added $NaHSO_3$	16·4 14·7	1·2 1·1
Treatment with aqueous alkali	9·8 8·7 8·4 10·3 9·7	1·5 1·6 1·5 1·7 1·5
As above with added $NaHSO_3$ (Present method)	16·8 16·6 18·0 16·4 16·2	2·2 2·0 2·0 1·8 1·9

Estimation of "Total 17 K.S."

As in the estimation of 17-K.S. two 8 ml aliquots are taken from each specimen and all following operations carried out on a batch of 12 tubes To each tube 8 ml glacial acetic acid and 2 g sodium bismuthate ('Analar') are added The mixtures are shaken mechanically for half an hour with exclusion of direct daylight The stoppers are removed and the tubes centrifuged for 5 minutes at a moderate speed From each supernatant aliquots of 10 ml are transferred into large centrifuge tubes (approximate capacity 50 ml), to each tube five drops of a 5% sodium hydrogen sulphite solution and 10 ml distilled water are added, the mixtures are stirred with a glass rod, treated with 6 ml concentrated hydrochloric acid, and stirred again The hydrolysis and all following operations are performed as in estimating 17 ketosteroids, but using 20 ml ethylene dichloride for extraction and 5 ml water and 5 ml 3N sodium hydroxide solution for washing Of the final extracts two aliquots of 5 ml are taken for the colorimetric estimations The conversion factor into mg "total 17 K.S." per 24 hours is 1·6

VARIATION OF EXPERIMENTAL CONDITIONS

Quantity of Sodium Bismuthate

Apart from corticosteroids other urinary constituents—e.g., sugars—must be expected to react with sodium bismuthate, hence a large excess of the reagent will be necessary for the quantitative oxidation of urinary corticosteroids in situ Fig 1 clearly shows that, for the investigated urine specimen, the quantity of sodium bismuthate used in the standard procedure is in fair excess of that necessary

TABLE II—RECOVERY OF MODEL SUBSTANCES ADDED TO URINE

Type (a)	Substance added (b)	µg of (b) per ml (c)	17 ketosteroid formed (d)	Colour equiv of (d) (e)	Increase of "total 17-K.S." (µg per ml)		% recovery (i)
					Calc (f)	Found (g)	
III	17α 20β 21 Trihydroxypregn 4-en 3 one	14·5	Androst 4 ene 3 17 dione	119	14·1	13·3	94
IV	17α Hydroxy 11 dehydrocorticosterone (cortisone)	15·4	Androst 4-ene 3 11 17 trione	93	12·0	9·5	79
IV	17α-Hydroxycorticosterone (Kendall's Compound F)	12·5	11β Hydroxyandrost-4-ene 3 17 dione	66	6·9	5·8	84
V	3α 17α 20β Trihydroxypregnan 11-one	14·7	3α Hydroxyetiocholane 11 17 dione	118	15·1	12·8	85

Column (e) expressed in µg dehydroepiandrosterone per 100 µg 17 ketosteroid

Column (f) calculated value $= \dfrac{\text{molecular weight of (d)} \times (c) \times (e)}{\text{molecular weight of (b)} \times 100}$

to the cannula is simply clamped within the pump, the stationary eccentric roller adjusted to act as a tap, and the usual rate of infusion at about 60 drops a minute may be obtained. To increase the rate of delivery the handle driving the roller is turned manually. No other adjustment is required. Flow-rates of about 400 ml. a minute may easily be achieved by using standard transfusion tubing with pump rotation speeds of 60 a minute. This rate has been found to have of itself no undesirable effects in patients (Melrose and Shackman 1951); and, so far as is known, the only other reference to such rates of administration by the intra-arterial route in man is that of Hitchcock et al. (1952). The danger of gas embolism is very remote with this method, and no demonstrable alteration of the blood is brought about during one passage through the pump.

In intra-arterial transfusions it is inadvisable to inject in any quantity anything but blood. Particularly must dextrose solutions be avoided. A small area of skin adjacent to the site of cannulation into the radial artery is often perfused directly during transfusion into this artery. If saline solutions or dextrose is used, the area becomes totally anoxic and may slough; when blood alone is used, this disturbing side-effect is avoided. There is in fact little justification for giving fluids other than blood by the intra-arterial route, since they possess no oxygen-carrying power and the stay of glucose and saline solution within the circulation is evanescent.

At present there is insufficient experience of intra-arterial transfusions to solve all the problems involved. The best rate of administration is not yet known, although it seems probable that the higher rates of about 300 ml. a minute are better. If blood-transfusion is required at lower rates than this, it is generally possible to give it by the intravenous route rather than by the more complicated intra-arterial infusion. The general trend seems to be towards unnecessarily complex machines, even though a simple pump system is adequate.

Fortunately it is becoming appreciated that blood is the only fluid suitable for administration by the intra-arterial route, but we still have insufficient knowledge of the immediate fate of the blood in the circulation, and the advantages and disadvantages of this method of therapy have yet to be assessed.

SUMMARY

Intra-arterial transfusion may be needed to save life.

Blood alone should be used.

If stored blood is used, precautions should be taken that the plasma-potassium level is not dangerously high.

The plasma-potassium level of stored blood increases with length of storage and may exceed 40 mg. per 100 ml. (10 m.eq. per litre)—a concentration which is lethal to man.

Simple decanting of plasma and reconstituting with saline solution or with dextran will lower the plasma-potassium to safer levels.

Rapid transfusions, both intravenous and intra-arterial, are safely and easily given with a simple rotary pump.

We are indebted to Miss M. McKay, Blood Group Reference Laboratory, Chelsea, London, for the samples of pooled plasma.

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POLIOMYELITIS FOLLOWING INOCULATION

A SURVEY OF 29 CHILDREN

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DURING September, 1949, one of us (D. G.) becam aware of an association between immunisation agai diphtheria and/or whooping-cough and the incidence o paralytic poliomyelitis; accordingly a preliminary repor on the subject was sent to the Chief Medical Officer Ministry of Health, and the Medical Officer of Health fo the County of London.

This association between poliomyelitis and inoculatio appeared to apply chiefly to the use of a diphtheria pertussis combined prophylactic; as a result its use i London was discontinued in the following month.

The matter was submitted to Prof. A. Bradford Hil and Dr. J. Knowelden, who concluded that, in the 194 epidemic of poliomyelitis in this country, cases o paralysis were occurring which were associated with inoculation carried out within the month preceding the recorded date of onset of the illness (Hill and Knowelden 1950). At about the time this matter was made public (Geffen 1950) other reports confirmed these findings, both in this country (Martin 1950) and in Australia (McCloskey 1950).

In 1949 it seemed that this association between inoculation and poliomyelitis was possibly confined to Britain and Australia, for, in correspondence with American authorities, one of us (D. G.) was informed that similar occurrences had not been noted in U.S.A., where both the rate of immunisation and the incidence of poliomyelitis are very high. However, in 1951 Anderson and Skaar, of Minneapolis, published a paper on poliomyelitis occurring after injections of antigen. Their report was based on data collected in 1946. They came to the following conclusions:

> (1) In poliomyelitis patients who had received some antigen in the previous month there was a high degree of correlation between the site of paralysis and the site of injection.
>
> (2) Such cases tended to show a different distribution of paralysis, with more severe involvement, than did comparable children immunised from two to six months previously, in previous years, or not at all.

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to complete the oxidation With other urines we have repeatedly observed that the use of larger quantities of the reagent (over 2 g) does not significantly affect the results of the estimations

Time of Reaction

Fig 2 shows the relation between the reaction time and the assayed "total 17 K S" 30 minutes appears to be a suitable reaction time for the standard procedure

Concentration of Acetic Acid

While pure 17 ketogenic steroids are quantitatively convertible to 17 ketosteroids on oxidation with sodium bismuthate in 1–5% acetic acid (Brooks and Norymberski 1952), it appears that the oxidation in situ of urinary corticosteroids requires a much higher concentration of acetic acid (see fig 3) Furthermore, we find that in the presence of 10% acetic acid only 60% of added dehydroepiandrosterone is recovered from urine submitted to treatment with sodium bismuthate, whereas in the presence of 50% acetic acid the recovery exceeds 90% These observations may be explained if it is assumed that steroids are adsorbed on the surface of sodium bismuthate At low concentrations of acetic acid, and in the presence of large quantities of the reagent, necessary for the oxidation in situ but not for the oxidation of pure substances, the quantity adsorbed can be expected to increase

Other Changes of Experimental Conditions

The estimation procedure in initial experiments (Norymberski 1952) differed in two respects from that now reported (1) the ethylene dichloride extracts were treated with sodium hydroxide pellets as recommended by Drekter et al (1952), (2) no sodium hydrogen sulphite was added after oxidation and before hydrolysis For a time the original method was considered satisfactory, judging by the agreement between separate estimations and by the ratios of optical densities (d) at wave lengths 520 mμ and 430 mμ (Talbot et al 1942a) Occasionally, however, a series of estimations was found to give results which, by both criteria, were unsatisfactory Furthermore, when it became possible to calculate more accurately the recoveries of pure 17 ketogenic steroids added to urine, the recovery figures were found to be rather low The source of the erratic results was finally traced to the treatment with sodium hydroxide pellets and to the presence of an oxidising agent in the supernatant of the urine/acetic acid/bismuthate mixture By substituting for the pellet treatment a conventional aqueous alkali wash, and by reducing the soluble oxidant with sodium hydrogen sulphite, the following improvements were achieved (1) more consistent results of separate estimations (2) increased ratios of d_{520}/d_{430} and (3) higher values for estimated "total 17 K S" Table I illustrates these improvements in a series of experiments which by the original method gave particularly bad results Similar, though less striking, improvements were observed in other experiments designed to compare the original with the present method The greater efficacy of the latter is further demonstrated by the improved recoveries of corticosteroids added to urine

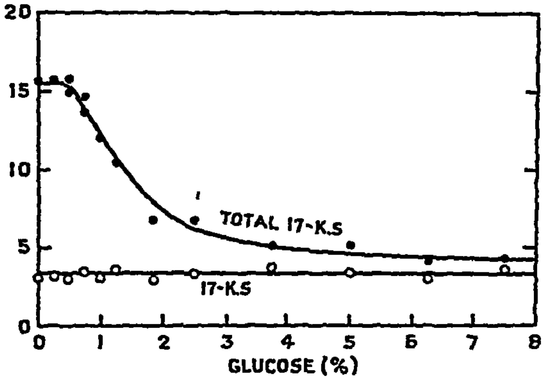

Fig 4—Inhibition by glucose of oxidation of urinary 17 ketogenic steroids

RECOVERY OF 17 KETOGENIC STEROIDS ADDED TO URINE

Norymberski (1952) recorded the recoveries of corticosteroids representing types III, IV, and V Since then the technique of the estimation has been improved and Zimmermann colour equivalents have been determined for 17 ketosteroids derived from model substances used in the recovery experiments We have therefore repeated the recovery experiments (table II)

Wilson (1950) has previously shown that individual 17 ketosteroids can differ considerably in the colour intensities developed with the Zimmermann reagent It was necessary to repeat this work because (1) our colorimetric technique differs from that employed by Wilson, and (2) the colour equivalents of several substances relevant to our work were not recorded Apart from the colour equivalents listed in table II, column (c), those of various other ketosteroids have been determined and will be reported elsewhere

TABLE III—EXCRETION OF 17 K S AND 17 K G S IN NORMAL ADULTS AND CHILDREN

Subject	Sex	Age (yr)	mg per 24 hr	
			17 K S	17 K G S
ST/1	M	24	18 2	9 6
ST/2			15 4	9 7
BR	M	25	15 0	15 6
CR	M	25	19 2	19 2
NW	M	36	14 0	15 7
MF	M	51	10 2	10 0
HW	M	5[illegible]	14 6	13 2
SQ	M	61	15 3	12 2
WH	F	19	14 6	9 4
KP	F	19	8 0	7 0
MD	F	19	9 8	10 0
GR	F	26	15 6	4 6
CS	F	39	12 6	7 4
CR	F	44	5 2	7 8
RH	F	51	4 8	12 8
MR	F	51	5 6	13 4
GR	F	53	4 8	7 6
FM	M	6	1 3	2 9
WL	M	6	0 9	2 3
JH	F	6	1 1	2 3
DD	F	6	0 9	3 4
FM	F	8	1 4	2 8
WS	F	11	3 5	3 8

INHIBITION BY GLUCOSE

The experimental conditions laid down in the preceding paragraphs have been found satisfactory in over 200 urinary assays, many of which were checked by the recovery of added pure 17 ketogenic steroids or by varying the quantity of sodium bismuthate Occasionally, however, it may be necessary to assay a specimen with an abnormally high glucose content which could vitiate the determination To test the extent of such interference estimations of 17 K S and "total 17 K S" were carried out on a specimen to which glucose had been added in quantities varying from 0 25 to 7 5% The results, recorded in fig 4, show that with more than 0 5% glucose the estimated "total 17 K S" are significantly decreased It is therefore important to test for

TABLE IV—EXCRETION OF 17 K S AND 17 K G S IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, OR STILL'S DISEASE

Subject	Sex	Age (yr)	Disease	mg per 24 hr	
				17 K S	17 K G S*
KN	M	27	Ank spond	7 0	6 2
HW	M	37	"	10 0	6 1
FH	M	45		21 1	12 8
BR*	M	38	Rh arth	7 1	[illegible]
SN*	M	52	" "	7 1	[illegible]
HL	M	55		7 6	[illegible]
HR	M	60	"	4 8	[illegible]
SN	F	22	" "	10 4	10 9
BR	F	31	" "	7 3	[illegible]
SM	F	39		4 6	[illegible]
DN	F	43	"	6 6	[illegible]
BI	F	46	" "	16 8	[illegible]
MR	F	47		6 1	[illegible]
CI	F	51	"	[illegible]	[illegible]
PR	F	54		5 2	[illegible]
CT 1	F	[illegible]	"	4 0	[illegible]
CT 2*				1 [illegible]	[illegible]
SC*	F	59		1 8	[illegible]
HW 1	F	60		16 1	[illegible]
HW 2				19 7	[illegible]
WH	F	[illegible]		4 [illegible]	[illegible]
WH	F	3	Still's	6 [illegible]	[illegible]
TP	F	12		1 5	

* On phenylbutazone treatment

(3) The interval between injection and the subsequent onset of poliomyelitis suggested some relationship other than chance.

More recently Korns et al. (1952) have studied the association between poliomyelitis and parenteral injections of all kinds by collecting data from 2137 poliomyelitis patients in 1950, from 6055 members of the patients' households, and from 14,710 other controls living in adjacent houses.

They found that their poliomyelitis cases had had twice as many injections of all kinds in the two months before the onset of poliomyelitis than had the controls of similar age, and they conclude that their data tend to indicate that the risk of poliomyelitis is doubled during the two months following an injection of an immunising substance, penicillin, or other materials. In addition, like the workers previously mentioned, they found a positive correlation between the site of paralysis and the site of injection. They state that, although the cases are few, it may be worth recording that in their study the mean interval between immunising injections in the arm and paralysis was twenty-three days, whereas for injections in the leg it was thirty days. They noted that paralysis tended to be slightly more severe after injections than where there had been no injections.

The main aim of our survey reported here was to assess the amount of subsequent recovery in the children who were the subject of a previous report (Geffen 1950).

McCloskey (1952) has also compared the recovery of 25 children whose poliomyelitis had followed recent inoculation (upon whom he had reported in 1950) and 65 children in whom there was no such history. The inoculated groups contained a higher proportion of cases of severe paralysis; but, when cases of equal initial severity were compared, the residual paralysis after eighteen months was not significantly different in the two groups.

Observations

In the earlier report (Geffen 1950) reference was made to 37 children, of whom 30 had developed poliomyelitis within a month of immunisation, the site of paralysis being the site of injection. None of these subsequently died, and we have seen and examined 27 of these 30 children some two years later. Of the other 3, we have full hospital records of the illness and present condition of 2 (cases 2 and 12), but 1 (case 9) remains untraced, though there is no reason to doubt that he is alive.

In order to get a comparison of the extent of recovery, we also obtained the history and examined another 23 children who had not had any recent injection but who had developed poliomyelitis at about the same time in London in 1949, who were of approximately the same age, and in 21 of whom an upper limb was one of the limbs affected.

In the course of examining these children we came across one child (case 28) who had developed paralytic poliomyelitis affecting the left upper arm, the onset of illness being fourteen days after an injection of pertussis vaccine. We have therefore transferred this child to the survey of recovery of children who suffered from post-inoculation paralytic poliomyelitis. We also had referred to us another child (case 29) who received an injection of alum-precipitated toxoid (A.P.T.) on Oct. 5, 1949, in the left arm and developed paralytic poliomyelitis affecting the left upper arm on Oct. 15, 1949, and we have included this child as well.

We have omitted 2 of the original cases for the following reasons:

(1) In one case the interval between injection and paralysis was about a month; but, though the child was injected in

TABLE I—INOCULATED CASES

Case no.	Sex	Age at onset of illness	Reagent	Limb of injection	Interval between injection and onset of poliomyelitis (days)	Maximum paralysis	Present state
1	F	9 mths	*Combined	L. arm	14	L. arm severe R. leg slight	L. arm slight R. leg nil
2	M	10 mths	Combined	L. arm	12	L. arm very severe L. leg ,, ,, R. leg moderate	L. arm very severe L. leg ,, ,, R. leg nil
3	F	11 mths	Combined	L. arm	21	L. arm very severe	L. arm severe
4	M	1 yr 5 mths	Combined	L. arm	12	L. arm severe	L. arm slight
5	F	9 mths	Combined	L. arm	12	L. arm very severe R. arm ,, ,, R. leg moderate L. leg slight	L. arm very severe R. arm severe R. leg moderate L. leg slight
6	F	2 yrs 10 mths	Combined	R. arm	16	R. arm very severe	R. arm severe
7	M	1 yr 3 mths	Combined	L. arm	10	L. arm very severe	L. arm severe
8	F	10 mths	Combined	L. arm	12	L. arm very severe	L. arm moderate
9	M	1 yr 11 mths	Combined	L. arm	15	L. arm very severe	L. arm severe
10	M	10 mths	Combined	L. arm	26	L. arm very severe R. arm ,, ,, R. leg severe	L. arm very severe R. arm ,, ,, R. leg severe
11	M	10 mths	Combined	R. arm	8	R. arm very severe L. leg moderate	R. arm severe L. leg slight
12	F	10 mths	Combined	R. and L. thighs	15	L. leg very severe R. leg severe	L. leg severe R. leg slight
13	M	11 mths	Combined	L. thigh	22	L. leg very severe	L. leg severe
14	M	2 yrs 3 mths	†A.P.T.	L. arm	9	L. arm very severe R. leg moderate	L. arm very severe R. leg slight
15	F	1 yr 7 mths	A.P.T.	L. arm	7	L. arm moderate	L. arm slight
16	M	1 yr 1 mth	A.P.T.	L. arm	24	L. arm very severe	L. arm moderate
17	F	1 yr 2 mths	A.P.T.	L. arm	11	L. arm very severe	L. arm severe
18	M	9 mths	Combined	L. arm	5	L. arm very severe	L. arm severe
19	M	1 yr 1 mth	Combined	L. arm	16	All 4 limbs very severe	All 4 limbs severe
20	M	1 yr	Combined	L. arm	12	All 4 limbs very severe	L. arm very severe R. arm severe R. leg slight L. leg nil
21	F	1 yr	Combined	L. arm	8	L. arm very severe	L. arm moderate
22	F	4 yrs 6 mths	A.P.T.	L. arm	11	L. arm very severe	L. arm severe
23	F	11 mths	A.P.T.	L. arm	9	L. arm very severe	L. arm very severe
24	M	1 yr 3 mths	A.P.T.	L. arm	8	L. arm very severe	L. arm moderate
25	F	10 mths	A.P.V.	L. arm	8	L. arm very severe	L. arm moderate
26	M	1 yr	Combined	L. arm	36	L. arm severe	L. arm moderate
27	F	1 yr 11 mths	Combined	L. arm	9	L. arm very severe	L. arm moderate
28	M	4 yrs 11 mths	‡A.P.V.	L. arm	16	L. arm severe	L. arm severe
29	M	10 mths	A.P.T.	L. arm	10	L. arm very severe	L. arm very severe

* Combined diphtheria—pertussis prophylactic.
† A.P.T. = alum-precipitated toxoid (diphtheria).
‡ A.P.V. = ,, ,, vaccine (pertussis).

the presence of glucose (e g, with Benedict s solution) before carrying out the estimation of 17-K G S The problem of assaying specimens with a high glucose content may be approached either by increasing the amount of sodium bismuthate or by attempting to remove the glucose prior to estimation

Results of Assays

Some of the results given here can be confidently accepted for interpretation, while others require additional data to make statistically sound generalisations possible Whenever several specimens of one subject were assayed, estimations of creatinine were carried out as well The latter are recorded only for the one case in which they were found erratic

Normal Adults and Children

From the figures in table III no relation is apparent between the excretion of 17-K G S and the age of the adults There seems to exist however a difference between the 17-K G S levels of men and women, the latter being, on the average, about 30% lower

TABLE V—EXCRETION OF 17-K S AND 17 K G S IN VARIOUS CONDITIONS

Subject	Sex	Age (yr)	Condition	mg per 24 hr	
				17 K.S	17 K G S
			Pregnancy		
CR	F	24	4th month	11 3	6 4
ML	F	20	7th ,,	10 3	8 9
CD	F	20	9th	16 0	8 2
MN	F	28	5th month plus Addison s dis	3 2	3 2
			Operation		
FX/1	M	71	Before (*a*)	6 0	20 2
FX/2			After	11 6	55 2
BC/1	M	56	Before (*b*)	10 8	15 8
BC/2			After	16 0	20 8
BT/1	M	47	Before (*c*)	6 8	6 8
BT/2			After	13 6	14 6
PR/1	F	49	Before (*d*)	4 4	1 8
PR/2			After	7 8	26 2
SH	F	66	Simmonds s dis	nil	2 0
CH	F	65	Cushing's syn	9 3	14 8

(*a*) Prostatectomy (*b*) Excision of sacrococcygeal sinus
(*c*) Partial gastrectomy (*d*) Partial colectomy

Rheumatoid Disease and Ankylosing Spondylitis

Patients with rheumatoid arthritis or ankylosing spondylitis show considerably lower 17-K G S levels (average about 40%) than normal adults (table IV) Whether this finding is characteristic of these diseases or is simply due to the inactivity that they impose remains to be shown Within this group, as among normal adults, the same relation is discernible between excreted 17-K G S and the sex of the subjects Treatment with moderate doses of salicylate or phenylbutazone does not appear to affect the output of 17-K G.S

Other Conditions

In three cases of pregnancy the 17-K G S figures were found to fall within the normal range (table V) This is of some interest since (1) amelioration of rheumatoid arthritis during pregnancy (Hench 1938) could tempt one to postulate an increased adrenal output of 17α hydroxycorticosterone (Kendall's Compound F) in this condition, and (2) Venning (1946) reported an increased excretion of corticoids (assayed by the liver glycogen test) in pregnancy Urines from patients after operation show, as expected, greatly increased 17-K G S values

Treatment with Cortisone Acetate

The excretion of 17-K S and 17-K G S in a normal male aged 42 was estimated at short intervals for 24 hours before and after a single oral dose of 100 mg cortisone acetate The excretion-rate is graphically recorded in fig 5 The output of 17-K G S returns to normal after 16 hours, about 50% of the total increase is excreted within the first 4 hours, and about 75% within 8 hours This rate of excretion roughly corresponds to the commonly observed period of clinical effectiveness of a single large oral dose

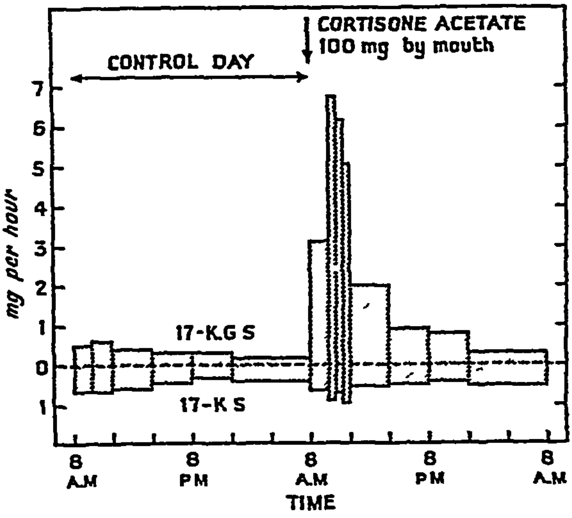

Fig 5—Excretion-rate of 17-K.G.S and 17 K.S after administration of cortisone acetate by mouth

Results of assays on patients receiving between 12 5 mg and 100 mg cortisone acetate daily clearly show proportionality between dose and 17-K G S levels (table VI) The graphic representation (fig 6) exhibits, for doses over 37 5 mg, a straight line passing through the origin We tentatively conclude that oral doses of about or above 37 5 mg cortisone acetate can almost completely suppress the endogenous production of 17-ketogenic steroids It is interesting to note that this figure corresponds with the minimum dose that produces benefit in rheumatoid arthritis

TABLE VI—EXCRETION OF 17-K.S AND 17-K G.S IN PATIENTS UNDER TREATMENT WITH CORTISONE ACETATE

Subject	Sex	Age (yr)	Disease	Day of treatment	Cortisone acetate by mouth (mg per day)	mg per 24 hr	
						17-K.S	17-K.G S
BV/1	M	45	Rh arth	52	75 0	6 8	30 2
BV/2				60	75 0	9 6	31 4
BV/3				73	75 0	8 0	28 8
BV/4				101	75 0	6 6	32 0
BV/5				111	75 0	6 4	29 8
BV/6				125	75 0	7 0	28 2
BV/7				143	75 0	6 2	23 2
LM/1	M	30	Ank spond	74	75 0	8 6	27 4
LM/2				97	75 0	10 2	29 2
LM/3				101	75 0	8 2	28 0
ES	M	36	Rh arth.	113	75 0	10 4	35 6
SP	F	40		30	75 0	5 4	24 4
MR/1	F	26	Ank spond	365	62 5	4 4	24 4
MR/2				374	62 5	3 2	24 8
TT	F	29	Rh arth.	39	62 5	5 2	19 6
RB	F	37	,,	729	62 5	4 0	28 6
PR	F	52		46	50 0	6 2	19 0
RG	F	47		276	50 0	4 6	18 6
PR	F	52		23	37 5	5 2	14 4
TR	F	12	Still s	2	37 5	5 0	14 0
BR/0	F	31	Rh arth.	0	0 0	8 2	6 2
BR/1				1	12 5	8 0	8 8
BR/2				2	12 5	7 6	9 4
BR/3				3	25 0	7 0	12 8
BR/4				4	25 0	8 8	11 6
BR/5				5	37 5	5 8	13 4
BR/6				6	37 5	9 0	15 1
BR/7				7	50 0	5 0	19 2
BR/8				8	50 0	6 3	21 7
BR/9				9	50 0	6 8	22 2
BR/10				10	62 5	6 4	26 8
BR/11				11	75 0	7 4	30 2
BR/12				12	75 0	8 4	29 6
BR/13				13	87 5	7 0	37 8
BR/14				14	87 5	4 9	33 9
BR/15				15	87 5	5 0	30 8
BR/16				16	100 0	4 6	39 2
BR/17				17	87 5	5 0	35 0

the left arm, it was the right shoulder and left leg which were mainly affected.

(2) In another case the interval was about a month, but there was no definite information about the site of the inoculation.

Originally some doubt was expressed as to whether the paralysis ensuing on inoculation in these and similar children was in fact due to poliomyelitis. As it is now generally accepted that this is so, we shall not discuss the matter in detail; but it is of interest that MacCallum (1950) isolated poliomyelitis virus from the stools of 2 of our children who had been inoculated in the subsequently paralysed limb eleven and twelve days previously. Further, 26 of our 29 inoculated children had a lumbar puncture in the acute stage of their illness, and the cerebrospinal fluid was characteristic of poliomyelitis.

Table I relates to 29 children who developed poliomyelitis in 1949 following recent inoculation, the limb of inoculation becoming subsequently the limb of major paralysis or one of the parts maximally involved. The extent of paralysis at the height of the illness and about *two years later (" present state ") was assessed in accordance* with the following scale, which is similar to that adopted by McCloskey (1952):

Very Severe.—Flaccid paralysis involving the major part of an extremity.

Severe.—Paralysis of at least one muscle group.

Moderate.—Partial paralysis of at least one muscle group.

Slight.—Slight paralysis involving a muscle group.

Nil.—No detectable weakness.

TABLE II—CONTROLS

Case	Sex	Age at onset of illness	Maximum paralysis	Condition 2 years *later*
A	M	1 yr 7 *mths*	L. arm very severe	L. arm severe
B	F	7 mths	L. arm slight L. leg very severe R. leg ,, ,,	L. arm nil L. leg severe R. leg ,,
C	M	2 yrs 6 mths	R. leg very severe	R. leg very severe
D	F	2 yrs	R. arm moderate L. arm slight L. leg moderate	R. arm moderate L. arm nil L. leg slight
E	F	5 mths	L. arm very severe L. leg ,, ,, R. leg ,, ,,	L. arm very severe L. leg ,, ,, R. leg ,, ,,
F	M	8 mths	L. arm moderate R. arm ,, L. leg ,, R. leg very severe	L. arm nil R. arm ,, L. leg ,, R. leg very severe
G	F	1 yr 11 mths	R. arm very severe R. leg moderate	R. arm severe R. leg nil
H	M	3 yrs 6 mths	R. arm severe	R. arm severe
I	M	2 yrs 3 mths	R. arm very severe L. arm ,, ,, R. leg severe L. leg ,,	R. arm very severe *L. arm nil* R. leg moderate L. leg ,,
J	M	2 yrs 10 mths	L. arm very severe R. arm severe	L. arm very severe R. arm nil
K	F	3 yrs 6 mths	L. arm moderate R. arm slight	L. arm slight R. arm nil
L	M	1 yr 4 mths	L. arm slight L. leg ,, R. leg ,,	L. arm nil L. leg ,, R. leg slight
M	M	1 yr	L. arm very severe	L. arm severe
N	M	1 yr 8 mths	R. leg severe L. leg moderate	R. leg moderate L. leg nil
O	F	1 yr	R. arm severe	R. arm moderate
P	F	1 yr 11 mths	L. arm severe L. leg ,, R. leg moderate	*L. arm nil* L. leg moderate R. leg slight
Q	F	2 yrs	L. arm very severe	L. arm severe
R	M	2 yrs 9 mths	L. arm severe	L. arm severe
S	M	3 yrs	R. arm severe R. leg moderate	R. arm moderate R. leg nil
T	F	1 yr 6 mths	L. arm very severe L. leg severe	L. arm severe L. leg nil
U	F	3 yrs	R. arm moderate	R. arm nil
V	M	4 mths	L. arm moderate L. leg ,, R. leg ,,	L. arm nil L. leg moderate *R. leg nil*
W	M	1 yr	L. arm moderate R. arm ,, R. leg ,,	L. arm nil R. arm slight R. leg moderate

TABLE III—AGE AND SEX DISTRIBUTION OF THE INOCULATED AND CONTROL GROUPS

Age at onset (mths)	Inoculated			Controls		
	Males	Females	Total	Males	Females	Total
Less than 12 ..	6	7	13	2	2	4
12–23	8	4	12	5	4	9
24–35	1	1	2	4	2	6
36 or more ..	1	1	2	2	2	4
Total ..	16	13	29	13	10	23

CONTROLS

For purposes of comparison we obtained details of 23 children who had acute poliomyelitis in the same epidemic and in the same city (London) as did our inoculated cases. We have also examined them recently—*i.e., from two to two and a half years later.* Their particulars are set out in table II. These children were about the same age as the inoculated children, and in 21 of them an upper limb was one of the limbs affected.

Unfortunately we were not able to match the two groups accurately in respect of these factors, but in respect of age all but 27 of the 29 inoculated children and 19 of the 23 controls were aged less than 3 years when they contracted poliomyelitis. The sex-distribution was about the same. Table III summarises the age and sex distribution in the two groups.

INTERVAL BETWEEN INOCULATION AND ONSET OF POLIOMYELITIS

Table I shows that the interval between the last injection and the onset of poliomyelitis was from five to thirty-six days. Here a difficulty arises because in some cases the first day of the disease is reported as the day the first symptoms were noticed—often diarrhœa and vomiting, restlessness, or the like—whereas in other cases the first day of illness obviously refers to the time when *paralysis became evident.*

We have carefully examined the cases where the incubation periods are twenty-one or more days, and we find the position to be as follows:

Case 3.—Here the interval was twenty-one days between immunisation and onset of poliomyelitis, and there was flaccid paralysis of the left upper arm by the time the child had been admitted to hospital. The onset was said to have been sudden, but there is a history that the child had diarrhœa, passing five or six greenish stools, three or four days previously.

Case 10.—Here the interval was twenty-six days, and the child had been treated at home with *sulphonamides* for tonsillitis two weeks before the mother noticed that he could not sit up or use his arms.

Case 13.—Here the interval was twenty-two days between injection and the day on which stiffness of the neck and spine, with commencing paralysis, came on.

Case 16.—Here the interval was twenty-four days. There were two notes: a statement, made by the mother two years later, that the child had had an injection a week before he *was taken to hospital; and a note in the hospital records* to the effect that the child had been immunised two weeks before admission. The official date, however, given us for the last injection by the medical officer of health of the district in which the child was resident, was Aug. 16, 1949, twenty-four days before the onset of poliomyelitis.

Case 26.—Here the interval was thirty-six days, and poliomyelitis was *not diagnosed* before the boy was taken to hospital by his mother because he was not using *his left arm.* On admission there was complete flaccid paralysis of this limb. There is no history of illness before this, but possibly there were preparalytic symptoms which escaped recognition.

It is not surprising that in many cases the diagnosis rests on the presence of gross paralysis, because the patients were mostly of an age at which minor illness would not be associated in the mother's mind with the onset of poliomyelitis. Further, it *is of course* quite that it is thyroid deprivation, and not a toxic effect of the drug, which harms the fœtus They concluded that if the mother's metabolic rate is kept within normal limits the fœtus should be unharmed, but that if the mother becomes myxœdematous, the fœtus will share the same fate In pregnancy the metabolic rate remains at the normal level until the sixth month, and may then rise as high as +25% Therefore, when a woman in late pregnancy is receiving thiouracil, her metabolic rate should not be allowed to fall to normal, for the mild hypothyroidism induced may result in a deficient supply of thyroid hormone to the fœtus On the basis of experimental work, the human fœtus and suckling infant might be expected to suffer if thiouracil and related drugs are administered during pregnancy Several reports have been published on the offspring of mothers who received thiouracil or a derivative for the whole or part of pregnancy

PREVIOUS REPORTS

Williams (1946) treated 5 women, including 1 with a twin pregnancy The 6 infants were healthy at birth and none had a goitre Astwood and Vander Laan (1946) treated 3, Reveno (1948) 3, Sexton (1946) 2, Trotter (1951) at least 4, and Rose and McConnell (1944), Vogt (1946), Carns and Poser (1946), Caren (1949), Bain (1947), and Eisenberg (1950) each treated 1 case, and all these babies were normal Palmer (1945) treated 3 women, and the only infant on which she reported fully was normal

Whitelaw (1947) described 3 cases only 2 carried to term, and 1 baby was normal, the other was an anencephalic monster The weight, iodine content, and histological appearance of its thyroid gland were within normal limits

Lahey and Bartels (1947) treated 8 pregnant women, and Mussey et al (1948) 1, by partial thyroidectomy following preparation with an antithyroid drug Each patient delivered a normal infant at term Bell (1950) treated 21 pregnant women in the same way 10 of his patients were delivered at term of 11 normal infants, who developed normally while under observation for periods ranging from eleven months to five years, 6 women had not reached term when the report was written, and 1 woman aborted There were 2 premature deliveries, 1 of the babies being macerated, while the other was deformed and died in four hours Another baby died at birth, and another, delivered by cæsarean section, died at six hours The condition of the thyroid glands of these infants was not reported

10 cases have been reported in which abnormality in the fœtus or infant was considered to be due to the passage of thiouracil through the placenta

Davis and Forbes (1945) described the case of a woman who was taking 0 2 g of thiouracil daily when she became pregnant After the diagnosis of pregnancy in the second month she took 0 2 g on alternate days until the sixth month when she died suddenly, her death being unexplained The fœtus had a hyperplastic and hypertrophied thyroid gland the histological appearance being similar to that found by Donald and Dunlop (1945) in an adult receiving too much thiouracil Davis and Forbes ascribed the effect to the direct action of thiouracil on the fœtal thyroid gland, rather than to lack of maternal thyroxine for the mother was not myxœdematous Freiesleben and Kjerulf-Jensen (1947) treated a pregnant patient with methylthiouracil until the fifth month, when the fœtus was removed because the pregnancy was complicated by heart failure The fœtal thyroid gland was hyperplastic Eaton (1945) reported 2 cases in which thiouracil was given during pregnancy The first patient began with thiourea in the third month and this was later replaced by thiouracil which was continued until four weeks before term The baby was healthy The second patient was receiving thiouracil (600 mg daily) when she became pregnant, and took this dose throughout the first month and from the third to the fifth months The dose was reduced to 400 mg daily for another month and then to 200 mg daily until delivery which was by cæsarean section because of placenta prævia Three months before delivery the mother's basal metabolic rate was + 5% The baby had an enlarged thyroid gland but was otherwise normal The enlargement had subsided after three months, and growth had been normal

Frisk and Josefsson (1947) described the case of a woman who was taking methylthiouracil (100–200 mg daily) when she became pregnant The dose was increased to 200 mg daily after three months Treatment was stopped for six and a half weeks but 300 mg was given daily for the last seven weeks The patient never had signs of myxœdema and the basal metabolic rate was usually +10% with a minimum of +5% Uterine myomata necessitated delivery by cæsarean section two weeks before term The baby was in fairly good general condition, and the thyroid gland was not clinically or radiologically enlarged, but X ray examination of bones showed retarded development of centres of ossification, the appearance being that of an eight month fœtus The serum cholesterol was 145 mg per 100 ml The baby was not breast fed, and during the first month there was no obvious abnormality in the general condition or behaviour, apart from moderate hypochromic anæmia In the second month she became agitated and developed exophthalmos Spontaneous improvement began after two months, and in three months the child seemed normal for her age, apart from the exophthalmos which subsided by the eighth month The authors explanation is that thiouracil blocked fœtal synthesis of thyroxine resulting in increased activity of the hypophysis Maternal thyroxine prevented myxœdema in the fœtus and suppressed thyrotropic activity, but when the drug was withdrawn, pituitary hyperfunction persisted

Keynes (1952) described a baby, whose mother received methylthiouracil and sodium thyroxine throughout pregnancy, who, at delivery, had partly obstructed breathing due to a large thyroid swelling which regressed over the next nine days X ray examination showed delayed ossification He also recorded the condition at birth of 19 infants whose mothers had received thiouracil compound during pregnancy 12 mothers had received the drug for a short time only, and the babies were normal 6 had received it for a longer period Premature twins were born to 1 mother 2 other babies were cretinous with swollen necks, 1 was cretinous without goitre, and 2 had goitres 1 of the cretinous babies with a goitre was the case described below, and Keynes gives the baby's history in the mother's own words

No case has been reported of a mother taking thiouracil who breast fed her baby

The following case is described because a search of the literature has revealed no other report of an infant, whose mother was treated with thiouracil during pregnancy, who besides having a large thyroid gland, showed clinical signs of hypothyroidism at birth and failed to develop normally

CASE RECORD

Mrs A, aged 29, was first seen in the antenatal clinic on May 2, 1950, when she was four and a half months pregnant She had 2 normal children, aged 5 and 2 She had severe thyrotoxicosis, the symptoms having begun thirteen months previously Treatment with methyl thiouracil (200 mg twice daily) was begun on May 25 and was continued throughout pregnancy and the puerperium At term there was no evidence of thyrotoxicosis apart from exophthalmos Hydramnios developed, and artificial rupture of the membranes was performed at term on Oct 5 1950 fourteen pints of liquor being withdrawn The baby was delivered spontaneously on Oct 8 after a labour complicated by uterine inertia Her colour was good, and she cried at once Her weight was

The baby on the fourteenth day

possible for a parent to miss paresis or paralysis when a baby is ill, listless, and apathetic, and has to have everything done for it. The preparalytic symptoms observed in our cases are discussed below.

Fig. 1 is based on the intervals stated in table I, and shows that the average interval was about thirteen and a half days, being twelve days in 5 cases, from five to eleven days in 13 cases, and from fourteen to thirty-six days in 11 cases. In 24 cases (more than 82%) it was from five to sixteen days. We doubt whether some of the longer intervals are correct. The point is important because in a district where poliomyelitis is present, the medical officer of health and the physicians practising there are anxious to know the maximum duration of the period of risk in this connection. It is also important in differential diagnosis. Hill and Knowelden (1950) say:

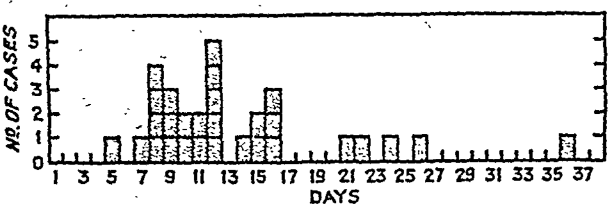

Fig. 1—Number of days between injection and onset of symptoms of poliomyelitis.

> "There is no evidence whatever that inoculations carried out in the more distant past have any effect at all upon the incidence or localization of paralysis. These effects appear to be confined to injections given within about a month of the onset of poliomyelitis, and after that interval from inoculation has elapsed no risk need be envisaged."

While agreeing entirely with this statement we think that the period of risk can be further shortened. Taking into consideration the possibility that some mothers have not sought medical advice until such time as illness is acute or paralysis is present, it is probably fair to say that, if a child shows no signs of illness distinguishable by a medical practitioner within two or three weeks of injection, the period of risk has passed.

PREPARALYTIC DISTURBANCES

In table IV the preparalytic symptoms and signs recorded in the inoculated and control groups of children are summarised. These are in almost every instance such that it would be difficult for a layman to associate them with poliomyelitis. In both the inoculated and control groups the commonest manifestations are fever, vomiting, drowsiness, and injected fauces. Most of our children were too young to complain of headache; those that did were aged 2 years or more.

TABLE IV—PREPARALYTIC SYMPTOMS AND SIGNS IN 29 CHILDREN WHO DEVELOPED POLIOMYELITIS AFTER INOCULATION AND IN 23 CONTROLS

Symptom or sign	Inoculated group	Controls
Fever	20 (*69%*)	16 (*70%*)
Vomiting	17 (*58%*)	9 (*39%*)
Drowsiness	16 (*56%*)	9 (*39%*)
Injected fauces ..	13 (*45%*)	5 (*22%*)
Anorexia	8 (*28%*)	3 (*13%*)
Diarrhœa	6 (*21%*)	2 (*9%*)
Headache	3 (*11%*)	2 (*9%*)
Coryza	0 (*0%*)	4 (*18%*)

Clearly the numbers are too small to allow any conclusions to be reached about any significant differences in the preparalytic symptoms in the two groups. In any case it has already been seen that the inoculated children were somewhat younger than the controls, a factor which might well influence their preparalytic signs and symptoms.

TABLE V—PARALYSIS IN INOCULATED LIMBS OF 29 CHILDREN

Initial paralysis and no. of cases		Residual paralysis			
		Very severe	Severe	Moderate	Slight
Very severe	24	8	11	5	..
Severe ..	5	..	..	2	3
Moderate..	1	..	..	..	1
Slight ..	..	..	..	..	..

One child was inoculated in both thighs.

EXTENT OF RECOVERY

Tables I and II reveal the degree of recovery in approximately two years in the inoculated limbs in our 29 patients with post-inoculation poliomyelitis and in the most severely affected limbs in the 23 controls.

Tables V and VI summarise this information for purposes of comparison between the two groups. They show, as one might expect, that the degree of recovery in either group is related to the severity of the original paralysis. In addition, however, they show that, whereas the paralysis in the inoculated limb was nearly always initially severe or very severe, the limb of major paralysis in the controls was not uniformly seriously affected.

The state of all four extremities in both groups is summarised in tables VII and VIII, where the degree of initial involvement is contrasted with the residual state found some two years later. It will be seen that in the series of 29 inoculated children 46 out of 116 limbs (39·7%) were involved; the comparable figures for the controls being 49 out of 92 (53·3%). This difference tends to confirm our clinical impression that the paralysis of post-inoculation poliomyelitis, though severe, was more limited in extent than in comparable uncomplicated cases. The initial paralysis was severe or very severe in 39 limbs of the injected children, and in 27 cases (69·2%) remained so two years later. A similar state was found in the controls, the comparable figure being 64%. It therefore seems that the difference in recovery in limbs affected to a more or less equal extent in the inoculated and control groups is not of significance.

TABLE VI—PARALYSIS IN MAXIMALLY AFFECTED LIMBS OF 23 CONTROL CHILDREN

Initial paralysis and no. of cases		Residual paralysis				
		Very severe	Severe	Moderate	Slight	Nil
Very severe ..	11	6	5	..	..	..
Severe	6	..	2	4	..	..
Moderate ..	5	..	..	1	1	3
Slight	1	..	..	..	1	..

Discussion

PROPHYLACTIC AGENT

Table I shows that a combined diphtheria-pertussis prophylactic was used in 19, A.P.T. in 8, and pertussis vaccine alone in 2 of our 29 children who subsequently developed paralytic poliomyelitis. Unfortunately we do not know the over-all proportion of children immunised

TABLE VII—STATE OF ALL LIMBS IN 29 INOCULATED CHILDREN

Initial paralysis	No. of extremities	Residual paralysis				
		Very severe	Severe	Moderate	Slight	Nil
Very severe ..	33	9	17	5	1	1
Severe	6	..	1	2	3	..
Moderate ..	5	..	..	1	3	1
Slight	2	..	..	..	1	1
Nil	70	..	..	..	..	70
Total ..	116	9	18	8	8	73

6 lb 7 oz She was œdematous all over but no more so than some healthy infants The anterior and posterior fontanelles were widely open The eyes appeared widely spaced and the bridge of the nose was depressed (see figure) The thyroid gland was diffusely enlarged Breast-feeding was not allowed.

During the next twenty-four hours other abnormalities became apparent The baby was very lethargic, she cried and moved infrequently, and her muscle tone was poor There was persistent cyanosis of the extremities and the skin felt cool Attempts at sucking were feeble and feeds were taken very slowly For the first few days the rectal temperature never rose above 97 2°F, and the pulse rate varied between 100 and 110 per minute Apart from further enlargement of the thyroid gland her condition remained stationary for several days after which she improved in every way

On the fifteenth day when she was discharged, she was still lethargic and hypotonic but sucked strongly, and crying was infrequent but lusty The skin felt warmer and there was only occasional peripheral cyanosis The thyroid swelling was subsiding Rectal temperature was 98°–98 4°F and the pulse rate 110–120 The serum cholesterol level was 130 mg per 100 ml on the thirteenth day Although this level was within normal limits, it is not considered to invalidate the diagnosis of hypothyroidism. for there was considerable clinical improvement by the thirteenth day, and in young untreated cretins the serum cholesterol level may be within normal limits (Bruch and McCune 1944, Topper 1951, Wilkins and Fleischmann 1941)

Owing to domestic difficulties, Mrs A failed to keep appointments, and the baby was not seen again until June, 1951 when she was eight months old She had followed a light with her eyes at two months, and had smiled at four months She had always been lethargic, and had only recently begun to kick her legs or hold up her head She was plump and hypotonic, and still had the strange naso-orbital configuration She smiled and took notice of what was going on but did not reach out to grasp objects, kicked feebly, and could only lift up her head momentarily The pulse rate was 110 and the skin was warm and pink. No thyroid enlargement was detected No other abnormalities were found and there was no evidence of hypothyroidism.

Two weeks later a lower central incisor erupted, and at nine months she could kick vigorously, hold up her head and sit up with slight support, though she could not pull herself up X-ray examination of the carpus showed centres of ossification for the os magnum and unciform bones on both sides, and diaphyseal dysgenesis was not present

From Sept 5 until Oct 3, 1951, thyroid was given (the dose is unknown), but it was stopped because it was considered to be unnecessary The mother noticed no change during this period.

Her subsequent progress has been disappointing The mother reported at seventeen months that the baby was lively and contented, but backward. She could pull herself up into a sitting position but could not sit or stand without support, and had made no attempt to crawl She had spoken no intelligible words, and played with toys like a much younger child She was neither clean nor dry The anterior fontanelle had almost closed She had twelve teeth Her weight was 22 lb, and her height 33 in

DISCUSSION

Thyroid enlargement in the infant of a mother who received methylthiouracil during pregnancy, and its disappearance after withdrawal of the drug at birth is to be expected in the light of experimental work (Hughes 1944 Goldsmith et al 1945 Freiesleben and Kjerulf-Jensen 1946) although few cases have been reported

The hypothyroidism exhibited by this baby is not difficult to explain On the thirteenth postpartum day her mother's basal metabolic rate was —5%, and the serum-cholesterol level was raised to 375 mg. per 100 ml As treatment had been unchanged, she had probably been mildly myxœdematous during the latter part of pregnancy The fœtus whose own thyroid function was depressed by thiouracil must therefore have been receiving insufficient thyroid hormone After withdrawal of the drug at birth the infant's thyroid gland recovered quickly and produced enough thyroid hormone to cure the hypothyroidism and prevent its recurrence

At nine months mental development was retarded, although physical and skeletal development were satisfactory, and there was no evidence of hypothyroidism Mental retardation may occur in congenitally hypothyroid children in spite of apparently adequate therapy (Aldrich 1936, Bruch and McCune 1944, Lewis 1937, Wilkins and Fleischmann 1941), and Topper (1951) and Bruch and McCune (1944) consider that cerebral damage is the factor which prevents satisfactory mental progress Lotmar (1929) found histological changes in the brain cells of cretins after death which he thought to be due to the effect of thyroid deficiency. Tredgold (1929) believed that there were two types of cretin · in one type mental and physical retardation were due to hypothyroidism. and the child became normal under treatment, in the other, the essential condition was primary amentia, the hypothyroidism being a complication, and the child remained mentally defective in spite of treatment

In the case reported here, it is not possible to tell whether prenatal lack of thyroid is the sole cause of backwardness, or whether primary amentia exists as well The strange facial appearance, which is unlike that of a cretin or of any named condition, makes the child appear defective It is not likely that better progress would have been made if thyroid had been given, for recovery from the early hypothyroidism took place spontaneously There is evidence that thyroid hormone may impair mental capacity when given to cretins in amounts greater than those required for satisfactory physical growth (Bruch and McCune 1944), although Aldrich (1936) advocated giving the largest dose of thyroid tolerated by the patient, in case more thyroid were needed to produce normal mental development than to provide satisfactory physical growth

This case is reported in order to draw attention to the fact that the administration of thiouracil to a pregnant woman may give rise not only to thyroid hyperplasia, but also to hypothyroidism and permanent damage in the fœtus The danger could be minimised by careful control of the dosage, so that the mother is not allowed to become myxœdematous In view of Keynes's report that the babies of mothers who had received the drug for a short time only were healthy, and that 5 out of 7 whose mothers had received it for a longer time were abnormal, it is clearly advisable to give it only for short periods

SUMMARY

Experimental work on animals has shown that the administration of thiourea or its derivatives to pregnant animals may lead to thyroid hyperplasia and cretinism in the young animal

Only 10 cases of abnormality ascribed to thiouracil in the human fœtus or newborn infant have been reported These are described

A baby girl, whose mother received thiouracil during pregnancy, had hypothyroidism at birth She recovered spontaneously, but her mental development was subsequently retarded

The cause of the hypothyroidism and mental retardation is discussed

I wish to thank Dr Simon Yudkin for his help and encouragement in the preparation of this paper.

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TABLE VIII—STATE OF ALL LIMBS IN 23 CONTROLS

Initial paralysis	No. of extremities	Residual paralysis				
		Very severe	Severe	Moderate	Slight	Nil
Very severe	15	7	7	..	..	1
Severe	10	..	2	6	..	2
Moderate ..	17	..	..	3	4	10
Slight	7	..	..	..	1	6
Nil	43	..	..	..	..	43
Total ..	92	7	9	9	5	62

with a combined reagent, compared with A.P.T. and pertussis vaccine in the areas whence these children came in 1949. Such a small series would render invalid any attempt at assessing the relative danger incurred in using any particular type of prophylactic in these circumstances. Yet it is generally agreed that the combined prophylactic was implicated in that year more often than would have been explained by the frequency with which it was used. Perhaps it is significant that, since the use of this vaccine in London clinics was discontinued in October, 1949, very few cases of post-inoculation poliomyelitis have occurred in the London area, although due allowance must be made for the fact that in the subsequent two years far fewer cases of poliomyelitis were notified in the age-groups concerned.

To reduce the local reaction following the inoculation Bousfield (1950) advises subcutaneous instead of intramuscular injection of the reagent. We do not know whether this would have a significant effect on the issue, for we have no information about the depth of the inoculations given in our series or in other children of the same age so protected at that time.

AGE OF INOCULATED CHILD

Bousfield (1950) has also suggested that immunisation during the first few months of life would minimise the risk of post-inoculation poliomyelitis. This may be true to some extent, but it is clear that poliomyelitis may give rise to paralysis in even the youngest infants. Smallpeice and Ounsted (1952) described 3 such cases in infants aged 7, 3, and 2 weeks. Wright and Owen (1952) recorded 3 similar examples of early infantile poliomyelitis. Logan (1952) published figures showing the incidence of poliomyelitis in England and Wales in 1950 for children aged less than 1 year: 254 such children were notified as having paralytic poliomyelitis. Of these, 10% were aged less than 3 months and 18% between 3 and 6 months; hence 72 (28%) of these children had paralytic poliomyelitis before they were 6 months old. It therefore seems unlikely that earlier immunisation would effectively prevent this serious complication.

POST-INOCULATION POLIOMYELITIS AND ANTI-DIPHTHERIA CAMPAIGN

The association between injections and poliomyelitis has naturally received some publicity in the lay press as well as in medical journals, and many medical writers have suggested that this has been unfortunate in that it has given rise to public alarm which has been both unnecessary and out of proportion to the actual situation. It has been argued, for example, that the recent reduction in the number of children immunised against diphtheria is due to this cause, although Gray and Cartwright (1952) have recently concluded that the fear of contracting poliomyelitis after immunisation does not at present constitute a factor of importance in the immunisation campaign. So far as our experience is concerned, we are in agreement with them, having questioned mothers whose children contracted poliomyelitis in 1949 in these circumstances, and who have since had another child.

If the incidence in London of diphtheria and poliomyelitis in recent years (*fig. 2*) is *considered*, it is easily seen that the public in this city has every reason to be more worried about poliomyelitis than diphtheria, no only because the case-incidence and death-rate of polio myelitis are higher but also because the crippled stat of some of the survivors of acute poliomyelitis contrast forcibly with the present rarity of serious diphtheriti sequelæ.

We believe that the public is entitled to know th facts of the situation. These should be put before then fairly and without exaggeration, for in our experience a well-informed public can assess the situation and mak a wise decision.

Summary

A report is presented showing the extent of recovery of 29 London children who developed paralytic poliomyeliti in 1949 after a recent inoculation. Comparison is made with 23 children of about the same age who had not had a recent inoculation but had developed paralytic poliomyelitis during the same epidemic, and in 21 of whom *an upper limb* was affected.

There was no fatality in the 29 inoculated children.

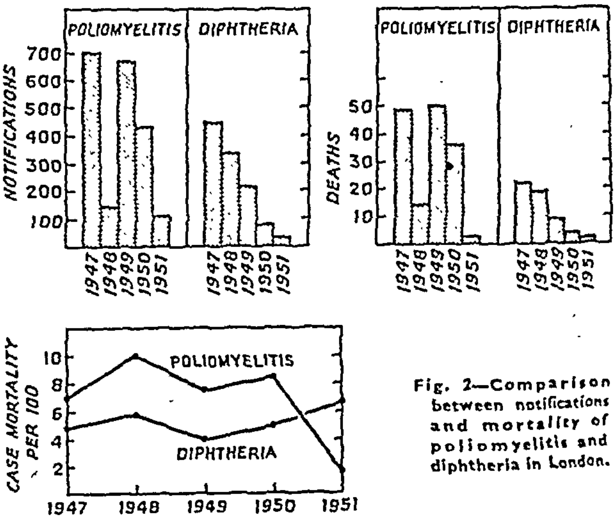

Fig. 2—Comparison between notifications and mortality of poliomyelitis and diphtheria in London.

The average interval between inoculation and the onset of poliomyelitis was thirteen or fourteen days; in over 80% of cases it was between five and sixteen days. It is probable that three weeks after inoculation the *period of risk* has passed.

The preparalytic symptoms recorded in the 29 inoculated children were in the main similar to those observed in the controls.

The paralysis of poliomyelitis following recent inoculation appears to be relatively limited in extent. When paralysis occurs in an inoculated limb, such paralysis is nearly always severe. Recovery of a limb appears *to depend on the initial severity of the paralysis, irrespective* of whether the limb has been inoculated or not. The extent of recovery which took place in two and a half years *in both the inoculated and control groups* was *related to the severity* of the *original* paralysis.

In the 29 inoculated children there was *no information* that the inoculations were intramuscular rather than subcutaneous.

It is considered doubtful if immunisation at an earlier age would prove effective in avoiding post-inoculation poliomyelitis.

It has not been proved that lay publicity on post-inoculation poliomyelitis is the reason for recent reduction in the number of *children immunised* against diphtheria. We are of opinion that the public is entitled to have the facts put before them clearly.

This work was done with the support and help of a grant from the Medical Research Council.

References at foot of next column

(1) ladder climbing (figs 2 and 3), (2) holding leads from a fearsome looking X ray switch panel with suggestion of increasing current as switches are pressed and knobs turned, although no current is passed at all (fig 4), (3) locked up in a small dark room, (4) making a public speech, (5) balancing at a height, and (6) fire extinguishing drill (fig 5)

Muscle action potential can also produce a β frequency in the E E G, but this artefact is excluded by voluntary test movements before the exercises.

(1) Failure to produce β by voluntary muscular effort Frowning, looking surprised, head-turning teeth-clenching arm raising, walking, arm-straining leg-raising, leg-straining

(2) Where possible, repetition of the test in absence of anxiety without occurrence of β For example, ladder-climbing may be done repeatedly without production of β and then show β when situations are altered to produce anxiety on climbing

(3) Absence of β during similar active movement when there is absence of β-productive situation—i e, a quiet base line except during the anxiety situation.

β frequency is the term applied to rhythm at 14–25 cycles per sec It is especially seen in the frontal areas and is thought in some cases to be associated with anxiety. For example, it was noticed in one exercise that in four different men β rhythm occurred when they reached the middle of an extension ladder (fig 6) This *appeared* on inspection to be associated with either increased sway in the middle of the ladder or a rope knot at this point requiring careful negotiation No conclusions are intended from this particular illustration, but one may speculate whether the instrument could be used in this way to indicate the points of irritation or special attention in performance of a given task—e.g, routine factory job—and perhaps lead to elimination of points of difficulty in the job performance, or as objective evidence of acquisition of confidence during learning of a particular act Perhaps we have a machine here which will give us objective evidence of anxiety as opposed to subjective

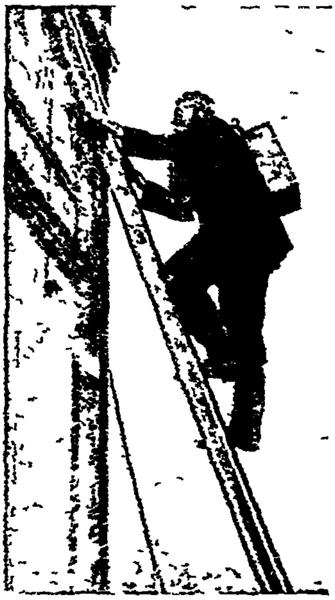

Fig 3—Man climbing ladder while wearing apparatus for recording E.C.G and E.E.G

A further point which has arisen in our initial tests is that the prefrontal cortex is relatively quiescent for considerable periods during continuous recording For example, in one subject there was no great activity throughout a game of deck tennis and "shooting in" at football, whereas in the same subject β activity is easily provoked by anxiety situations of a particular kind It also seems from our initial tests that different people exhibit β in anxiety situations peculiar to themselves—e g, climbing a ladder might never produce β in one person but being shut up [illegible] dark room would [illegible] In one test a fireman got stuc [illegible] underside of a ladder at roof height when the [illegible] ught in the ladder rungs This gave him "a ve [illegible] moments" and was reflected in the E E G as [illegible] burst of high voltage β activity (fig 7) [illegible] ies the spontaneity of the situations which [illegible] ing, be so different from the normal E.E G, taken at rest

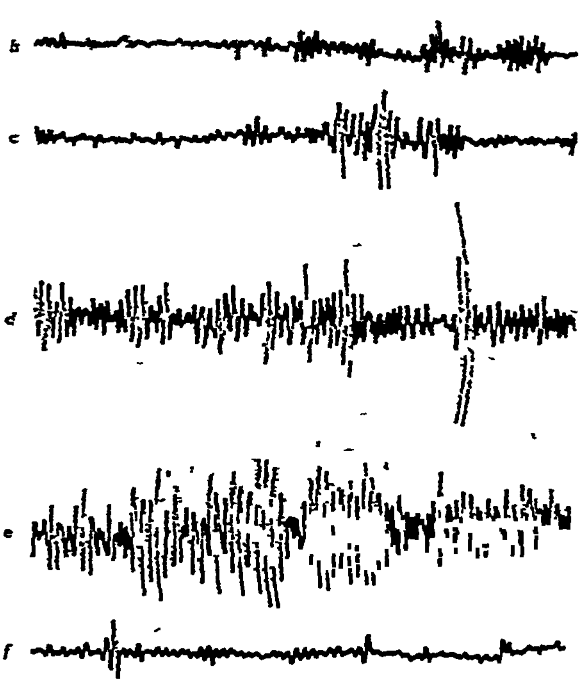

Fig 4—E.E.G of person, holding leads from electric switch panel who has been told that he will feel increased current when switches are pressed and knobs turned, although no current is passed at all a before test b, while test is being explained, c while knobs are being turned, d, when big switch is pressed, e, when 'full power' has supposedly been turned on f, after test. Note increasing β activity while switch panel is being manipulated

One of the probable reasons why the E.E G has been of less immediate clinical application in psychiatry than might have been thought is that recording has hitherto had to be done with the subject at rest This portable apparatus now enables us to study the E E G in everyday situations

Fig 8 compares an ordinary direct E E G recorded simultaneously with a radio E.E G

The Apparatus

The design of a suitable radio transmitter presented many difficulties, the main requirements being economical operation to restrict weight of batteries or other power supply, small size, and an almost infinite capacity to withstand rough usage during the tests (fig 9)

Fig

A METHOD OF TREATMENT FOR VARICOSE VEINS

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THE method of treatment described here has been used in 50 cases at the Bristol Royal Infirmary with encouraging results.

There is general agreement that when the internal saphenous vein is incompetent and varicose the first step in treatment is its ligation at the point of entrance into the femoral vein. But usually this does not suffice for cure, and many different procedures have been introduced to deal with the residual varicosities in the leg:

Excision of the vein through a long incision (Madelung 1884) is a major procedure which is very occasionally necessary but leaves an unsightly scar. The vein may be removed through small incisions with Mayo's (1906) stripper or Babcock's (1907) acorn-tipped guide. Both these methods tear across tributaries and may cause hæmatomata.

Sclerosants may be injected to obliterate the vein either after operation (Tavel 1904) or at the same time (Schiassi 1908). A ureteric catheter may be used to make the injection (Unger 1927). Disadvantages of the use of sclerosants are the production of thrombosis in the deep veins (Atlas 1943), damage to valves in the deep veins (Kinmonth 1948), and, if the injection is made at the time of operation, a painful leg which tends to discourage early ambulation.

Electrocoagulation as an alternative or an adjuvant to the use of sclerosants by passing a cystodiathermy electrode along the vein was suggested by Smith (1944), but there is difficulty in passing the electrode along tortuous veins and in regulating the current. All these methods of inducing clotting in the veins may be followed by recanalisation.

Multiple ligature of the internal saphenous vein is now the most popular method of dealing with varicosities, and the tendency is to tie the vein in more places. Sclerosants are being reserved to obliterate what varicosities remain after multiple ligature and for minor varicosities of the calf without demonstrable incompetence of the main saphenous trunk.

McElwee and Maisel (1947), following on the work of Moore and Knapp (1942) at the New York Hospital, have compared the results obtained in five different methods used unselectively, and placed them in the following order: (1) multiple ligation; (2) high ligation and retrograde injection; (3) high ligation and stripping; (4) high ligation and excision; and (5) high ligation alone. In all cases postoperative injections were given to complete the obliteration. Although McElwee and Maisel concluded that multiple ligature (with an average of four ligatures) gave the best results in their follow-up (average of eighteen months), they record that an average of 3·4 injections was required later to complete the obliteration, and that minor wound sepsis and delayed healing were troublesome.

The more ligatures, within reason, that are used at the primary operation, the fewer injections are needed later and the better the end-results should be; but as the operation becomes more lengthy and severe, the patient becomes less willing to be ambulant immediately afterwards. Also the incidence of minor wound troubles is higher, and an operation which may have been performed largely to remove unsightly veins may substitute unsightly scars.

A method which can increase the number of permanent interruptions of the veins and at the same time abolish the incisions down the leg would have obvious advantages over those discussed hitherto. Goldstone (1943) suggested, as a substitute for high ligation, the passage of a ligature round the upper part of the saphenous vein by a neat trick in which only two punctures are made, the ligature remaining in situ under the skin. As a substitute for a formal high ligation this is unacceptable; but, if a non-absorbable ligature material, such as braided 'Nylon' is used, it is an effective means of applying multiple ligatures. It is done quickly—a dozen ligatures can be placed in as many minutes—and leaves practically no trace. Consequently a larger number of points can be reasonably ligated, and all the varicosities can usually be completely obliterated at the primary operation. This is the basis of the method described here.

Other percutaneous methods, notably those of Davat (1837) and Schede (1877), have been described; but they are not comparable, because the ligature was tied outside the skin and removed later.

In Davat's method a needle was passed through the skin under the vein and left there while a figure-of-eight ligature was tied tightly round its protruding ends. In Schede's method the ligatures were tied over a rubber tube. In both methods the object was to induce thrombosis and perhaps to cut through the vein. Neither method was very successful; both are crude and have long been obsolete.

Technique

Preliminary Marking

The marking out of the veins before operation is of great importance because it is then that the situation and numbers of ligatures to be used are decided. Hartley's ink * is suitable for this purpose; it produces a deep black mark which does not wash off when the skin is "sterilised" at operation. The incompetent internal saphenous vein is marked off at intervals of 2–4 in. wherever it can be seen or palpated; varicose tributaries are also marked off and at shorter intervals if necessary. Where a large varix is very close to the skin and appears to be adherent to it, ligatures are placed above and below. It is probably better to avoid tying veins immediately over the subcutaneous border of the tibia, especially if the patient is thin.

A suitable method of marking is to place a dot where the punctures will be made, on either side of the vein and about $^3/_4$ in. away from it, so that the two dots are about $1^1/_2$ in. apart with a dash between to link them (fig. 1). If there are large blow-outs that need excision, a line is placed over them.

In some cases it is helpful to have an infra-red photograph of the leg beforehand. This helps one to understand the pattern of the varicosities and is also a permanent record (fig. 2). The results are somewhat variable and depend on the thickness of the patient's skin and the amount of subcutaneous fat.

Operation

Under general anæsthesia the skin of the whole leg is cleaned; the foot is towelled separately, so that the whole leg can be freely moved and veins on the back of the calf reached without turning the patient over.

For the high ligation a transverse incision is preferred to the vertical one, which, though affording better access

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* Hartley's ink is one of a number of inks sold for marking garden labels. It produces a thick black mark that is insoluble in water or in spirit. Dr. W. A. Gillespie, who kindly carried out some bacteriological tests, found it sterile on culture on aerobic and anaerobic blood-agar and in broth.

DR. GEFFEN AND OTHERS: REFERENCES

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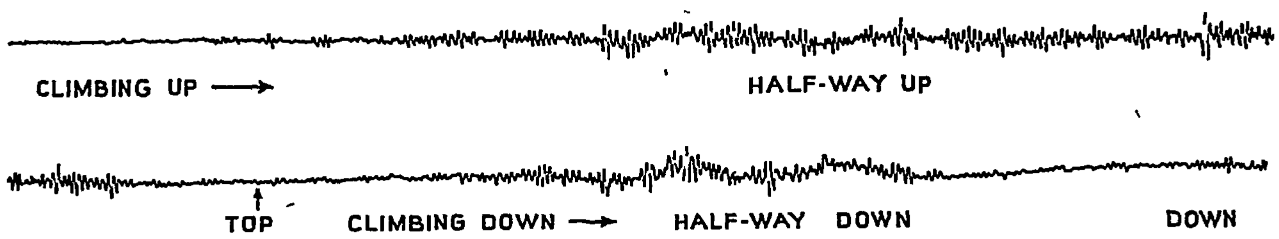

Fig 6—E E G of man climbing up ladder and down again , note β activity when he is half way up and again when he is half way down

It was anticipated that, during exercise, the patient's movements would cause variation in the strength of the signal, owing to changes in the standing wave pattern and to reflections from nearby buildings, lampposts, drain pipes, and other metalwork in the vicinity

Since the wave length allocated is just below two metres (158 75 megacycles per sec), the probability was that such variations would occur at frequencies falling within the low-frequency band required for electroencephalography and interfere with the record Tests proved such fears to be well founded

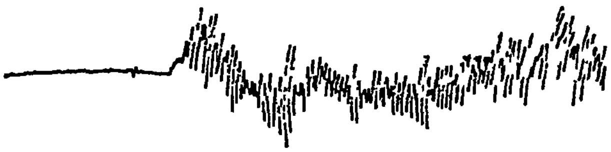

Fig 7—E E G of man climbing ladder who accidentally slipped off rungs and swung from underside of ladder, showing burst of β activity

It was apparent that, if amplitude modulation were applied to the carrier wave, some form of automatic volume control would also be required at the receiving end , and, as a quick response would be necessary, the time constants of such a device would be short enough to permit distortion of lower E E G frequencies But Canadian workers seem to have attempted amplitude modulation (Glasscock and Holter 1949), though later they used frequency modulation (Glasscock and Holter 1952)

Full consideration of alternative methods appeared to indicate that the use of frequency modulation (F M) would offer the greatest chance of success since, owing to limiter action and other reasons a F M receiver is relatively insensitive to amplitude variations, at least within certain limits

For preliminary tests a small F M transmitter was built Seven valves, of indirectly heated subminiature type, were used in a circuit embodying master oscillator and frequency multiplying stages with integral head-amplifier and reactor stages

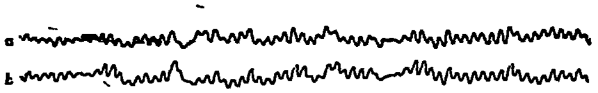

Fig 8—Simultaneous records of E E G from same electrodes in a child aged 12 years *a*, radio , *b*, direct.

The apparatus was fitted in a light copper box measuring 6 × $3^1/_2$ × $3^1/_2$ in and, although it was fairly successful in use, operation was rather difficult owing to frequency drift caused by temperature rise This produced a change in the recording base line necessitating frequent retuning of the receiver

Further tests indicated that if the instrument was to be of clinical value, the use of a free running oscillator could not be justified, and that apparatus built for permanent use would have to be crystal controlled This would ensure a steady basic frequency and permit the use of a crystal controlled receiver, thus eliminating all tuning adjustments during operation, allowing undivided attention to recording

The use of crystal control is not without difficulty, since phase modulation is also implied, leading to a loss of gain equal to 6 db per octave as the frequency of the modulating source is reduced , hence, at frequencies common in E E G work, an inordinate amount of amplification would be required, together with the use of an amplifier having a rising characteristic with reducing frequency

The apparatus in use at present was designed to overcome the difficulties described and has proved to be satisfactory in service

Construction was undertaken in two stages A conventional crystal controlled transmitter, with phase modulation, was built on one chassis, this being bolted to a second and similar chassis carrying the head amplifier and an oscillator capable of reasonably pure output at a frequency of 5 kc per sec

After amplification the E E G wave form is applied to the suppressor grid of the 5 kc oscillator producing an amplitude-modulated tone, which is then coupled, via a suitable transformer, to the control grids of the phase modulator valves

With the head electrodes short circuited the carrier wave will be deviated to a predetermined degree at the rate of 5 kc per sec The arrival of an E E G signal then causes a change in the extent to which the carrier wave is deviated

Fig 9—Apparatus in position

At the receiver the signal is reproduced as a 5 kc tone with the E E G wave form superimposed thereon, and it is a simple matter to demodulate this, to remove the 5 kc component, and to restore the E E G to a form suitable for amplification to the desired level for recording

It will be obvious that, by the addition of other tone generators operating at suitable frequencies, each connected to its own amplifier, a number of channels could be accommodated for the simultaneous transmission of other physiological data—pulse rate, electrocardiogram, &c —the information being extracted at the receiver by passing the output through filter units

As the transmitter was built for test purposes, no attempt was made to achieve minimum size , and, as ordinary valves were used in most of the stages, power-supply requirements are rather heavy Fortunately a new light-weight accumulator of the silver zinc type is now generally available enabling a small rotary convertor for ligation of tributaries, does not heal well. The internal saphenous vein is divided and tied flush with the femoral vein. Its terminal tributaries are sought and divided.

Ligatures are now placed down the leg at the points previously marked. Braided nylon is most suitable for this purpose, because it is non-absorbable and produces no reaction in the tissues. It is softer than monofilamentous nylon and leaves a knot which is in most cases impossible to feel under the skin later. "Six-pound" braided nylon used double is sufficiently strong.

A nick is made in the skin through two companion dots with a tenotome or narrow-ended blade such as the standard no. 11 blade. If the axis of the nick is made along Langer's lines it remains almost invisible, but it may gape if made at right-angles to it. A large $^1/_3$-circle needle—e.g., Bonney's no. 1—is threaded with braided nylon and held on a strong needle-holder (fig. 3). It is now passed, blunt end first, through one nick, under the vein, and out of the other nick, leaving the ligature in its track. It is then reinserted, blunt end first, through the second nick and passed, under the skin but over the vein, to emerge through its original point of entry, from which the two ends of the ligature are now left protruding. These are pulled backwards and forwards once or twice to enable the ligature to slip through the fat close to the vein—if it is not round the vein it will slip out altogether—and tied tightly with three hitches. The ends are cut off with a knife close to the knot. This leaves the skin puckered up, with the knot just below the puncture. If this pucker is now straightened out by stretching the skin, the knot disappears under the skin and the vein resumes its previous position half-way between the two dots. Occasionally a vein may be torn in this process and blood oozes from a puncture; this is controlled with digital pressure and ceases when the next ligature has been tied. The average number of ligatures used per limb in 50 cases was 11, and the largest number 28.

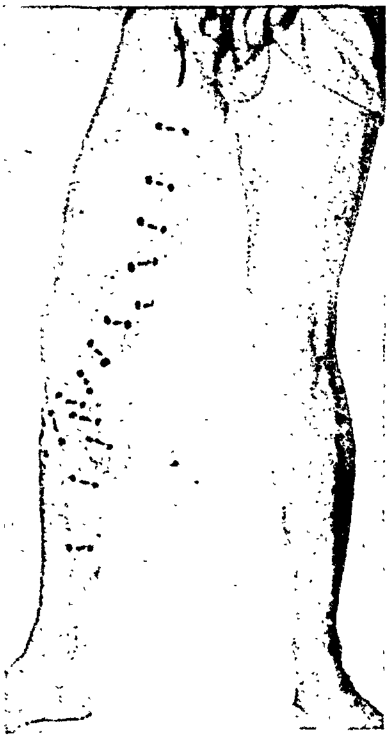

Fig. 1—Infra-red photograph showing method of marking veins. (Varicose anterior femoral cutaneous vein was missed.)

No dressings are needed except in the groin, and a sterile crêpe bandage is applied to the leg.

Results

Two or three days after the operation a clot can be felt in most cases in the isolated segments of the vein between the ligatures. Patients are ambulant from the start and are usually fit to go home the day after operation; but in the present series they were kept in hospital longer for close observation. Occasionally a mild inflammation has developed round a knot but in no case has this been severe, and the great majority of patients have no reaction beyond a vague tenderness, a little local œdema, and perhaps bruising.

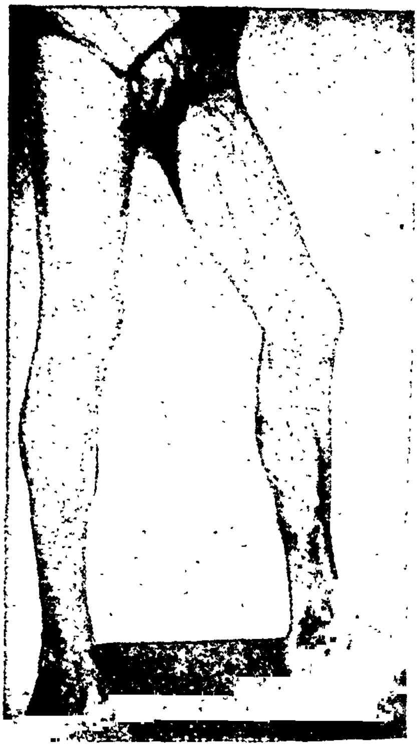

Fig. 2—Pattern of varicose veins elucidated by infra-red photography.

Degree of Obliteration Achieved

In 64% the primary obliteration was regarded as complete without the help of any injections—i.e., all visible varices had disappeared.

In 30% slight varicose veins remained; in half they were negligible, and in half injections were needed to complete the obliteration.

In 6% (3 cases) the varicosities remaining when seen fourteen, thirteen and five months after operation were more than could be obliterated by injections alone. However, the patients were symptomatically relieved, and no further treatment was advised. It must also be said that 2 of the 3 in this group were in the first 5 to be treated; had they appeared later in the series, the veins would have been ligated at more points, perhaps with better results.

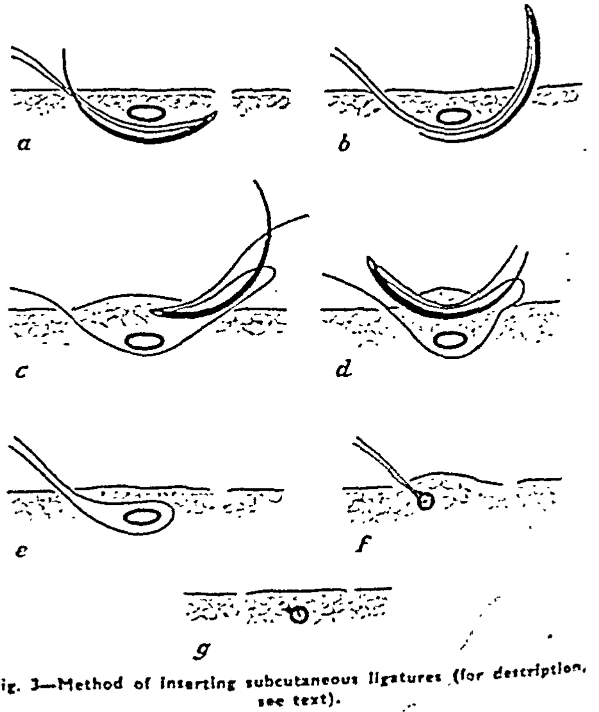

Fig. 3—Method of inserting subcutaneous ligatures (for description, see text).

to be used for high-tension supply, providing a useful recording time of about four hours

Conclusions

We are concerned in this article merely with describing the apparatus and its possible applications, and the tests mentioned are not intended to indicate any conclusions but simply mode of use of the apparatus and possible lines of research with it

The E E G and E C G have so far been mentioned, but, of course, any physiological phenomenon which can be expressed electrically could be studied in the same way with this apparatus—e g, radio tracer work, muscle action potentials, and electrical activity of mucosa No doubt other workers will see applications to their own especial field

There are many uses for this apparatus For example, the phonocardiogram could probably be studied in this way, giving records of the heart sounds during everyday and unrestricted activity Again, the apparatus might be usefully adapted to animal experiments where freedom of movement in the animal is desired

Our thanks are due to Dr A R Grant medical superintendent, Whittingham Hospital, for his most helpful encouragement

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Medical Problems in Korea

THE United Services section of the society met on June 10, with Sir Stanford Cade, the president, in the chair

Lieut Colonel R L MARKS described the medical picture in Korea as he had seen it from January, 1952, to January, 1953, when he was commanding a field ambulance in the Commonwealth Division At this time the division held a static position and there was constant patrolling, shelling, and occasional attacks by both sides Enemy air activity was virtually nil and this had influenced forward medical arrangements, particularly evacuation by helicopter There had been a steady trickle of casualties, with some increase after an attack—the greatest number at any one time was 76 The terrain consisted of small hills, scrub, ploughed fields, and paddy fields, the earth roads were dusty in the summer and a sea of mud after rain The front line was reached by travelling in a jeep to company level, and then walking forward in gradually deepening trenches which eventually were about eight feet deep Off these were a number of two to four man dugouts, lit by candles and heated by stoves, in which the men lived

The R M O was situated near battalion headquarters Five miles back was a field ambulance which had two casualty-clearing posts, two miles behind the front-line A field dressing station of 120 beds, with a surgical team and psychiatrist, was ten miles farther back, and on one flank an American M A S H (mobile army surgical hospital), the main centre for surgery, was situated From the M A S H cases were evacuated by train to Seoul, and, if necessary, Commonwealth casualties went by air from Seoul to Kure in Japan and the Americans to Tokyo Cases not likely to recover within three weeks were not kept in Korea The advanced dressing station held cases for up to seven days, and a reserve field ambulance of 100 beds held cases likely to recover within three weeks Because of the static nature of the war and the absence of enemy air activity, the policy was to hold the sick as far forward as possible

With the help of a helicopter, a casualty could be in the hands of the surgeon forty-five minutes after reaching the R M O Some revision of the policy on morphine administration was therefore necessary to prevent cases arriving at the M A S H too heavily drugged Only the R M O gave morphine, and he also gave penicillin and set up dextran drips when needed Medical conditions were mostly seasonal in the winter there were colds, influenza, and a very few cases of frostbite, in summer the main cause of disability was skin diseases and, to a lesser extent, malaria and intestinal infections From May until November there were sporadic cases of hæmorrhagic fever The incidence of gonorrhœa and chancroid was appreciable, and there was some non specific urethritis, but no syphilis Initial diagnosis and treatment (lasting two days) of venereal diseases was carried out at the advanced dressing station, and continuation treatment by the R M O There were few psychiatric casualties Road accidents and burns from stoves accounted for the considerable number of accidental injuries

Major F J INGHAM, introducing the subject of Army health, said that in Korea malaria was endemic, intestinal diseases and tuberculosis were common, and typhus and relapsing fever occurred On the whole, the health of the Army had been good

The climate was extreme, and temperatures lower than 11°F and as high as 95°F were encountered For the winter, special clothing had been provided, including a string vest, combat jacket and trousers, a lined parka coat, special boots, and three pairs of gloves Slacks, a flannel shirt, and ammunition boots were worn in summer The ration per day was 5100 calories in winter and 4500 in summer Water was available at three fixed water points in the divisional area In some areas a tributary of the Imjin river was used The bunkers in which the front line troops lived were infested with rodents which were a menace to the troops 'Warfarin' was successful in controlling the rodents, and D D T powder dealt with the lice D B P and D M P were used as insect repellents Korea was a fairly large reservoir of *Plasmodium vivax*, but the incidence of malaria in the U N Forces was kept low by suppressive proguanil ('Paludrine') (100 mg daily) Civilians were given mepacrine In the Commonwealth division there had been 94 cases of hæmorrhagic fever, with 3 deaths Infection was localised to the forward areas, especially rat infested or swampy regions To protect against the vectors of the disease clothing was impregnated with D B P and antirodent measures were carried out There were not many flies in the forward areas and very few clinical cases of dysentery

Major-General A G HARSANT spoke of the development of the Commonwealth Division in Korea American Headquarters were at Tokyo, where they had their main hospital The Commonwealth hospital was at Kure, where there were 1000 beds The director of medical services for Korea and the consultants in medicine and surgery (all of whom are American) were at Seoul

At the M A S H primary surgery was carried out on battle casualties, who were then evacuated by air or train to Seoul where secondary suture might be carried out Men not retained in Korea were flown from Seoul to Iwakuni by R A A F Dakotas, and thence by train or launch to Kure or, if they needed special surgical treatment, they were flown direct to the American hospital in Tokyo, where there were specialist surgical teams—e g, maxillofacial, thoracic, and neurosurgical teams All neurosurgical cases were treated by the Americans, who had two neurosurgical teams at M A S H.s in Korea and a base unit in Tokyo, and casualties from the whole front were flown by helicopter to one or other of these

In only 6 of 47 patients whose veins have been satisfactorily obliterated was it necessary to inject sclerosants.

Death from Pulmonary Embolus

It must be recorded that there was 1 death from pulmonary embolus. This occurred on the sixth post-operative day. Clotting had taken place in all the varices and had extended from one on the back of the calf, along a communication through the soleus muscle to the posterior tibial vein, and thence to the popliteal and femoral veins.

The possibility of this catastrophe seems inseparable from the intentional clotting of blood in the veins of a patient's legs. Nevertheless it seems to happen more often with some methods than with others, and retrograde injections of large amounts of sclerosants and extensive operations seem to carry the greatest risk. Thus Faxon and Barrow (1938) record 3 pulmonary emboli, 2 of which were fatal, in 228 cases of high ligation with retrograde injection; and Moore and Knapp (1942) reported 2 fatalities from this cause in 88 cases in which excisions had been done.

Whether the present method will be found to carry an undue liability to pulmonary embolus remains to be seen. On theoretical grounds it should not, because the use of sclerosants at operation is avoided and the patients can be fully ambulant immediately after operation. A patient in a hospital ward, though officially ambulant, has nothing to do to keep him on the move, and, though not actually in bed, tends to be equally immobile in an armchair. Probably the best prophylactic against pulmonary embolus is to get the patient home the day after operation.

Effect of the Knots Remaining under Skin

In the first 6 cases strong thread was used for the ligatures; most of these knots have since been discharged, some of them many months after operation, leaving a pigmented mark. In the next 4 cases fine thread was used; this has so far caused no trouble but was given up for nylon, which is very satisfactory. At first monofilamentous nylon was used, but since strong braided nylon has been available it has been preferred. Some of the monofilamentous nylon knots were palpable under the skin, and in 2 cases the patient complained of a knot, which was therefore removed.

Since braided nylon has been used, there has been no trouble. The patient is unaware of the knots which cannot be felt under the skin, and no knots have been spontaneously discharged.

Accidental Ligation of a Cutaneous Nerve

In view of the close relationship of the saphenous nerve to the vein in the leg, it might be expected that it would often be caught in a ligature. This has happened in 4 cases and has produced a small area of anæsthesia above the medial malleolus. Only 1 of these patients volunteered the information; the 3 others had not noticed it or did not think it worth mentioning.

Where large clusters of veins have been found they have been excised, and occasionally the internal saphenous vein is so large and tortuous that it is best excised. With these exceptions it can be said that, coupled with high ligation, multiple subcutaneous ligation has given good early results in 92% of 50 unselected cases, and that in only 14% of these were any subsequent injections needed.

The Question of Recurrence

Recurrences after operation for varicose veins are of two sorts, which might perhaps be termed true and false—the former due to recanalisation, and the latter due to dilatation of veins previously normal. As regards the former, if the knot remains tied tightly round the vein it will not permit blood to pass, even if recanalisation takes place on either side of it. If the veins are divided into short enough segments, this should prevent the points of obstruction from being bypassed by the opening up of collaterals. Perhaps, however, ligatures may partly ulcerate through the veins and, becoming embedded on one side, allow the circulation to be re-established. Recanalisation has been reported after the saphenous vein (Arthur 1944) and the femoral vein (Byrne and O'Neil 1952) have been ligated in continuity, but it is not stated what suture material was used. Recanalisation might be expected if catgut was used —Goldstone (1943) recommended catgut for his subcutaneous ligatures. It seems unlikely that recanalisation will take place when the ligatures are numerous and non-absorbable.

Where recurrence is due to dilatation of veins previously normal and is probably associated with incompetent deep and communicating veins, there can be no method of certain prevention. The best hope of keeping such recurrences at a minimum lies in careful marking and multiplicity of ligation to isolate as many communicators as possible.

Summary and Conclusions

According to McElwee and Maisel (1947) multiple ligature, coupled with high ligation, gives better end-results than do most other methods in common use for the treatment of varicose veins.

For the best results these ligatures need to be numerous.

A method is described by which a vein can be rapidly and (it is hoped) permanently ligated without making an incision. After a formal high ligation this method is used to tie the varicose veins at 2–4in. intervals down the leg.

The method appears to present the following advantages:

(1) It is thorough, in that enough ligatures to obliterate all the varicose veins can usually be made without inflicting a severe operation on the patient.

(2) Patients can walk about on the day after operation without much pain and can be sent home.

(3) The procedure is not complicated by the delayed healing and minor sepsis which may follow incisions in the leg.

(4) It leaves no visible scar.

(5) Further attendances by the patient for injections have been needed in less than a fifth of the cases.

(6) The operation takes much less time than ligation through incision.

The importance of careful marking is emphasised, and for this the assistance of infra-red photography is recommended.

I am grateful to Mr. D. G. C. Tasker and to Mr. R. V. Cooke for allowing me to operate on their cases and for their kindly and critical encouragement. I also want to thank Mr. F. A. Godman, of the department of photography, for the infra-red photographs and for his help.

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General Harsant observed that with the present static conditions, air superiority, and freely available helicopter evacuation, casualties could reach the surgeon within an hour or two With such rapid evacuation of casualties, the R M O could become responsible for initiating resuscitation and he could give transfusions of dextran, for example, before the case was evacuated by helicopter Dextran was used in preference to plasma, which carried a risk of hepatitis Blood was collected from local sources by a field-transfusion team for the Commonwealth hospital in Japan, but blood in Korea was freely available from American sources this was for the great part flown from the United States

The body armour that was in use gave efficient protection to the chest and abdomen Its main drawback was its weight Cases of traumatic anuria were sent to a special American research unit in Korea where there was an artificial kidney The Americans were very keen that research should be carried out as far forward as possible, and they had a research team at some of the M A S H s In total war they visualised having a forward research hospital The functions of these teams were to try to solve the problem of the last 1–2% mortality, to provide teaching facilities, and to act as a testing-ground for new ideas

Lieut -Colonel K P Brown described the hæmorrhagic fever first encountered by the U N Forces in the spring of 1951 It had previously appeared among Japanese and Russians There had been a further outbreak in the autumn of 1951, and in all about 1000 cases, mostly American A special M A S H was now dealing with all cases Only about 60 Commonwealth troops had been infected The Japanese view was that the disease was due to a virus, but it was now thought to be caused by a rickettsial-like body The disease was carried by mites and was commonest in scrub and marshy areas The incubation period was two to three weeks The disease was characterised by increased permeability and dilatation of the capillaries and by kidney damage The increased capillary permeability sometimes led to œdema, often in the retroperitoneal region The onset was acute, often with severe headache and chills, and a temperature of 103° There might be severe backache which was very difficult to relieve Considerable thirst was a feature of the early stages, and it had been found that giving too much fluid at this stage increased the tendency to vomit Petechial hæmorrhages began to appear about the third day After this injections and handling of the patients were liable in severe cases to cause echymoses Early diagnosis and treatment appeared to have reduced the liability to severe hæmorrhage later The fever lasted three to five days, ending with rapid lysis Some hypotension usually followed, and sometimes there was severe shock and hæmorrhage All patients had some kidney damage, and albuminuria appeared about the third day Oliguria, which could go on to anuria, followed the febrile stage, but it was not related to the hypotension About the sixth day there was a diuresis that could be so rapid as to require replacement therapy The specific gravity of the urine high in the early stages, fell to 1010 in the oliguric phase and to 1002–1004 during the diuresis After about three months the patient was usually able to concentrate urine to about 1025 The white cell count was low in the early stages but began to rise about the third day, with a slight shift to the left The platelet-count fell by the third or fourth day, and there was a definite increase in the capillary fragility Sometimes there was a characteristic dilatation of the capillaries of the face and sclera, giving a clue to the diagnosis, which was otherwise difficult The mortality-rate was about 5% There was no specific therapy and convalescent serum had been useless in treatment

Suspected cases of hæmorrhagic fever were evacuated Patients with this disease travelled badly and it was the custom to give strong sedatives before evacuation by helicopter Sedation was continued throughout the early stages of the disease Fluid intake was kept on the low side in the early stages, for too much fluid could produce œdema later The artificial kidney, which had been used in anuria and azotæmia, had not been successful in hæmorrhagic fever, but it had been a great help in traumatic anuria Commenting on the similarity between hæmorrhagic fever and scrub typhus, Lieut -Colonel Brown said that it was odd that hæmorrhagic fever should be prevalent in Korea when there had been only 2 cases of scrub typhus

Malaria had not been a great problem, and had been treated with quinine and pamaquin Infective hepatitis was the greatest waster of man-power and there were very large numbers of cases Nothing new had appeared in the treatment All U N troops were protected against Japanese-B encephalitis in 1951 but not thereafter There had been only 2 Commonwealth cases Seoul was the centre of an area where paragonimiasis occurred This was a lung-fluke infection the X-ray appearance of which was similar to that of tuberculosis , but there had been no cases in U N troops

Lieut -General Sir Frederick Harris, director-general, Army Medical Services, said that this campaign was unique in many respects—the absolutely static nature of the war, the complete air superiority of the U N Forces, and the wonderful way in which some twenty nations were working together in complete harmony This cooperation was, he thought, a remarkable achievement and one which would prove to be a great contribution to the peace of the world

Reviews of Books

The Nature of Virus Multiplication

The Second Symposium of the Society for General Microbiology Editors Sir Paul Fildes, F.R.S , and W E van Heyningen London Cambridge University Press 1953 Pp 320 35*s*

Opinion about recording the proceedings of congresses and symposia is evenly divided Some would like verbatim records of every word spoken or implied, while others would be content to let the hot air drift upwards to the stratosphere and the sound waves to fade gently into the distance The Society for General Microbiology has sensibly compromised in its account of the society s second symposium on the nature of virus multiplication Sir Paul Fildes and Dr van Heyningen are to be congratulated on having edited this " idealised " version of the proceedings in which the contributors to the discussion were given an opportunity to polish and paraphrase their questions and answers before these appeared in print Those who were present at the symposium may have some difficulty in recognising some of the contributions but they will still be able to follow with entertainment and interest the Lwoff-Boyd controversy on prophage, the Fulton-Hoyle dispute on influenza-virus growth, and a host of Bawden-Pirie-isms on every conceivable aspect of virus multiplication This symposium brought together workers with widely different interests and viewpoints, and the discussions covered protein synthesis in general as well as the growth of plant, animal, bacterial and insect viruses This book is therefore more than a record of the proceedings , it is a valuable textbook for those who require to know something of the general aspects of viruses and of their points of similarity and difference

The Pharynx

Abraham R Hollender, M.D , F.A.C.S , emeritus professor of otolaryngology, University of Illinois College of Medicine Chicago Year Book Publishers London Interscience Publishers 1953 Pp 550 110*s*

This new work " dealing with direct and related problems concerning the pharynx " seems to have been produced mainly because of the editor s " own special interest in the various aspects of this important organ,"

ASSESSMENT OF ADRENOCORTICAL ACTIVITY BY ASSAY OF 17-KETOGENIC STEROIDS IN URINE

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WITH the rapidly growing realisation of the physiological significance of adrenocortical hormones, and especially since the introduction of cortisone and A.C.T.H., the need for a reliable method of estimating steroids of adrenocortical origin in the urine has become evident. We hope that the method described here will, at least in part, meet this need.

Steroids isolated from the adrenal cortex have a structural feature that distinguishes them from all other natural steroids; this consists in a particular mode of substitution of the "side-chain" (carbon atoms 17, 20, and 21). The types of this characteristic substitution so far encountered are as follows: (I) 20:21-glycol; (II) 20:21-ketol; (III) 17:20:21-triol; (IV) 17:21-diol-20-one (dihydroxyacetone); (V) 17:20-glycol; (VI) 17:20-ketol. Urinary steroids containing one of these six side-chains can reasonably be assumed to be of adrenocortical origin. The terms (*a*) corticosteroids, (*b*) (adreno)cortical steroids, (*c*) (adreno)cortical hormones and (*d*) corticoids will be used to denote respectively (*a*) steroids of types I–VI, (*b*) corticosteroids known to occur in the adrenal cortex, (*c*) the physiologically active cortical steroids, and (*d*) all substances showing cortical activity by any biological tests.

A well-established method of chemical characterisation of corticosteroids, originally developed in the laboratories of Reichstein and of Mason, consists in the oxidative fission of the side-chain with periodic acid, followed by the identification of volatile products (formaldehyde for types I–IV, acetaldehyde for type V) and/or of the non-volatile products. Of the latter those derived from types III and V are 17-ketosteroids. On the basis of these observations analytical procedures have been developed for the estimation of formaldehydogenic steroids (Lowenstein et al. 1946, Daughaday et al. 1948, Corcoran et al. 1950), acetaldehydogenic steroids (Butler and Marrian 1937, 1938, Cox 1952), and 17-ketogenic steroids (Talbot and Eitingon 1944, Fieser et al. 1944). Within the group of steroids known to occur in urine and in the absence of extraneous interfering material the above methods are rigidly specific. By substituting sodium bismuthate for periodate as oxidising agent, the estimation of 17-ketogenic steroids can be extended to include corticosteroids bearing a dihydroxyacetone side-chain (type IV) (Brooks and Norymberski 1952). Analytical procedures such as the estimation of reducing steroids (types II and IV) (Talbot et al. 1945, Heard and Sobel 1946) and the colour reaction of Porter and Silber (1950) for dihydroxyacetone derivatives (type IV) are less specific. No established analytical procedure for estimating substances of type VI is known to us.

Biological methods for estimating cortical hormones have been reviewed by Dorfman (1950). Of the available tests those based on the deposition of liver glycogen (Venning et al. 1946, Dorfman et al. 1946, Eggleston et al. 1946) are well suited for the quantitative micro-assay of "glucocorticoids." A similarly efficacious bio-assay of "mineralocorticoids" has been described (Tait et al. 1952, Simpson and Tait 1952). The bio-assays are of great importance for the study of substances showing hormonal activity; their application to urine, however, is of limited value, since corticoids are excreted in small quantities and very likely represent only a random fraction of the total urinary corticosteroids.

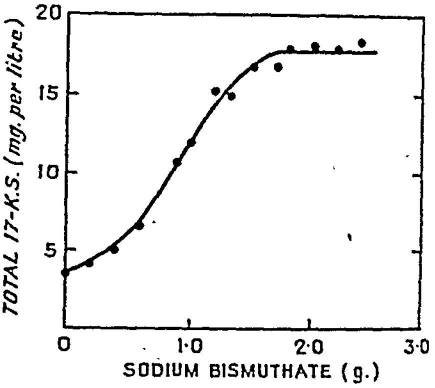

Fig. 1—Relation between quantity of sodium bismuthate and assayed "total 17-K.S."

Paper chromatography of corticosteroids has been described (Burton et al. 1951a, Bush 1952) and applied to urinary extracts (Burton et al. 1951b, Bush et al. 1952). In principle, paper chromatographic techniques offer an ideal means of separating small quantities of complex mixtures into their individual components, which can be further examined by physical or chemical methods. At present, and especially for routine purposes, chromatographic methods have not been sufficiently developed to permit a simple, comprehensive, and quantitative estimation of urinary corticosteroids.

The preparation of urinary extracts suitable for the application of any of the analytical procedures has proved most difficult, for the following reasons. Urinary corticosteroids are excreted mainly in conjugated form, demonstrably so as glucuronides and, by analogy with other urinary steroids, probably also as sulphates. Both types of conjugates are completely hydrolysed by heating with strong mineral acid: this procedure has been found reasonably satisfactory for the extraction and subsequent estimation of, for example, œstrogens, 17-ketosteroids, and pregnanediol, but unfortunately causes the destruction of many corticosteroids. Extraction of untreated urine yields only a small quantity of "free" corticosteroids; at pH1 the extracted amount is substantially increased, and a further increase is achieved by enzymatic hydrolysis with β-glucuronidase. Bayliss (1952) has compared the relative efficacy of the above extraction techniques as assayed by the formaldehydogenic method. It appears from the work of Bayliss and others (for references see Bayliss 1952) that none of the available methods will yield a urinary extract containing the total excreted corticosteroids or a constant fraction thereof which could be considered to reflect adrenocortical activity.

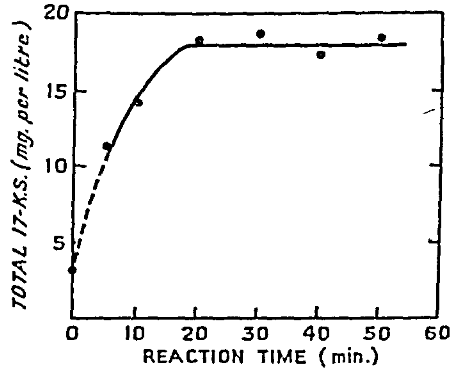

Fig. 2—Relation between reaction time and assayed "total 17-K.S."

Norymberski (1952) has shown that sodium bismuthate converts urinary 17-ketogenic steroids in situ to 17-ketosteroids; the latter can be hydrolysed, extracted, and assayed in the usual manner. Thus one group and it cannot be said to contain anything new Anatomy and physiology are well described, and there are some unusually good chapters—on the blood dyscrasias, on choanal atresia and on abscesses of the pharynx The problems of tonsillectomy and poliomyelitis focal sepsis and tonsillectomy in the allergic child are discussed wisely and at some length But, though carcinoma of the hypopharynx must surely be regarded as truly " pharyngeal "—in its site of origin, its natural history, its behaviour and its management—this highly important subject is dismissed in but a few words in a chapter on pathology Printing and production are excellent

Die körperlichen Behandlungsverfahren in der Psychiatrie

Ein Lehr-und Handbuch Vol I Die Insulinbehandlung Dr MAX MÜLLER, a o Professor für Psychiatrie an der Universität Bern Stuttgart Thieme 1952 Pp 295 DM 36

Prof Max Muller of Berne University, was one of the first to see the spark of genius and the novelty in Sakel's " insulin treatment " of psychoses, which shared the appearance of " foolishness " characteristic (in the words of A N Whitehead) of all really new ideas Müller applied the hypoglycæmic treatment in schizophrenia as early as 1935, and his well-equipped department at Munsingen Mental Hospital was to become a model of organisation and a centre of teaching for psychiatrists from all over the world Among his extensive writings on this and other treatments the present manual of nearly 300 pages deals with insulin treatment only

He attempts to cover the remarkable overgrowth of literature in this field in all languages, reviewing the varied publications critically, although in places not critically enough Of the 70 pages on physiology, pathology, and psychopathology, a good deal refers to work by clinicians without much insight into the physiological and pathological problems, and interests neither the expert nor the physician practising the treatment Similarly, some obsolete oddities could be usefully weeded out of the chapters on technique and its modifications and complications The section on indications, results, and theories is concise, and clearly shows the many debatable points in the mode of operation of the hypoglycæmic treatment and the difficulty in judging its efficacy

The great value of the book lies in its detached and objective attitude, based on an extensive practical experience and on a strong desire to help patients suffering from one of the most serious psychiatric diseases

African Highway

The Battle for Health in Central Africa Sir MALCOLM WATSON, M D, LL D, F R F P S, honorary consultant, Ross Institute of Tropical Hygiene London John Murray 1953 Pp 294 63*s*

IN 1929 the Rhodesian copper mines appointed Sir Malcolm Watson and other members of the staff of the Ross Institute as medical advisers This book sets out to explain how, in a quarter of a century, an unhygienic tropical rural area has been converted into a healthy and flourishing industrial mining district Sir Malcolm is clearly a great believer in the benefits which private enterprise, with sound medical advice, can confer on both European employers and native labour in the tropics, and he is highly suspicious of government schemes In the present uncertainty about the future political development of Central Africa, his great experience of health problems should be invaluable Unfortunately, however, his book is too largely composed of extracts from reports of malariologists, personnel managers, chief medical officers, and field engineers, of financial statements of copper mines and of detailed instructions for building for example, an African hospital and a smoking-pit latrine Much of the material is not recent, and though every reader, whether he has a wide knowledge of tropical life or has never left England, will find many bits and pieces of great interest, the work as a whole lacks continuity of presentation and style, and thus makes difficult reading The 79 excellent and well-chosen photographs are a more vivid testimony to the achieve

Cortisone et corticostimuline (A C T H) en rhumatologie

F COSTE, professeur de Clinique Rhumatologique, J CAYLA, chef de Clinique Rhumatologique, F DELBARRE chef de Laboratoire a la Faculté de Medecine de Paris Paris Masson 1953 Pp 414 Fr 2800

So much has been written about cortisone and corticotrophin that their relevance to the everyday needs of medical practice is perceived with increasing difficulty A comprehensive account of their use in rheumatic disease, where they were first applied, is timely, and Professor Coste and his associates in Paris have produced a useful account of hormone therapy in this field It is based on the study of 460 patients of their own, of whom a third had rheumatoid arthritis, and a fifth had rheumatic fever The indications, dosage, and prognosis are carefully assessed, and particular attention is given to the management of relapses In rheumatoid arthritis, and Still's disease, the use of concomitant gold therapy is described, but the authors are guarded about its value, gold therapy following hormone treatment is not favoured In rheumatic fever corticotrophin is represented as a great advance in treatment, arresting the progress of cardiac damage to a significant extent Professor Coste and his colleagues are aware that " quelques-uns en Angleterre surtout, restent sceptiques," and they make no final judgment, awaiting the results of later follow-up Indeed, in striving to honour impartiality, they have added considerably to the length of their book Methods and cases are described very fully, so that comparison may be made with the American and other European authorities quoted, and a bibliography of 28 pages is witness to diligence in this respect The practical value of the book perhaps suffers through this prolixity, but it is nevertheless a welcome account of this important subject

Advances in Cancer Research

Vol 1 Editors JESSE P GREENSTEIN, National Cancer Institute, U S Public Health Service, Bethesda, Maryland, ALEXANDER HADDOW, M D, D SC, Chester Beatty Research Institute, Royal Cancer Hospital, London New York and London Academic Books 1953 Pp 590 96*s*

THE present volume is the first of a series designed to reflect the " steady and inevitable march of the tides of our knowledge and increasing understanding " of cancer This tidal metaphor is based on the " mysterious and inexplicable ebb and flow of ideas and experimental approaches " to this widely ranging subject First acquaintance with the series shows that it is not intended for the general reader but rather for almost as many experts as there are individual chapters

Included are reviews of electronic configuration and carcinogenesis, epidermal carcinogenesis, the milk agent in the origin of mammary tumours in mice, hormonal aspects of experimental tumorigenesis, properties of the agent of the Rous no 1 sarcoma, applications of radio isotopes to studies of carcinogenesis and tumour metabolism, the carcinogenic aminoazo dyes, the chemistry of cytotoxic alkylating agents, nutrition in relation to cancer, and plasma proteins in cancer All are written by specialists in their own branch, 6 from the U S A and 4 from Britain Most of the contributions are comprehensive and objective, so much so that Reviews would be a more fitting title than Advances Subject and author references and indexes are extensive

The chapter on nutrition in relation to cancer is one that all workers, whatever their specialty, will need to consult One omission here may be regretted—that is the paper, a model of its kind, by J C Drummond in the *Biochemical Journal* (1917)

Those who are new to experimental mammary cancer would be greatly assisted if contributors would make clear whether the work they are referring to was done with or without the milk factor Frequently this was not yet known at the time, by the experimenters themselves Usually it is possible in the reviews in this volume to find out, but as the point is an essential one it might often be more clearly made

The series should be very useful to all who are trying to find their way about the subject r Law" (*British Medical Journal* 1909). This was view of doctors in private practice, and there were ications that at that time many of them would have n prepared to accept a salary for part-time public vice.

The full implementation of either of these proposals ght have prevented the division between the preventive l curative personal services. For the medical staff of ogressive public-health authorities were then extenely engaged in treatment as well as prevention of sease, and had both been sanctioned by Parliament it n hardly be doubted that a unified service would have own up—no doubt with serious effects upon private actice. Alternatively, had general practitioners been ermitted to undertake the work in schools, and later child-welfare clinics, it is also possible that the division ight have been avoided. In this case the attitude of octors to local-authority administration and payment by lary might later have been different from what it was. he Education Act, 1907, and the Maternity and Child Welfare Act, 1918, effected a compromise, by assigng the preventive personal services to public-health uthorities, while curtailing treatment in deference to he wishes of private doctors. This in effect made prevention a public responsibility, and left treatment a private one. The National Health Service Act removed his distinction, but left the machinery of administration of the personal health services essentially unchanged.

Against this background we turn to an examination of the work done at child-welfare clinics today, and to consideration of their future organisation.

Material of Study

We collected our data by investigation of work done at child-welfare clinics in Birmingham (population 1,112,340), and Coseley (an urban district in the adminisstrative county of Stafford, population 34,414).

In Coseley there is only one welfare centre, a well-equipped modern building designed for the purpose. School, antenatal, postnatal, and child-welfare clinics are held in this centre. There are no special sessions for toddlers, and the obstetrician responsible for the combined antenatal and postnatal clinics does not examine infants; consequently the child-welfare sessions, held twice a week, cater for preschool children of all ages. The medical officer who holds these clinics (J. T. A. G.) is also medical officer of health for Coseley. Two qualified health visitors attend each session.

In Birmingham, child-welfare clinics are held at 33 different centres. Of these, 2 (a church hall and a Friends' meeting-house) are in part-time use by the local authority; 31 are full-time child-welfare centres. Of the latter, 13 were designed and built as clinics; the remaining 18 originally served some other purpose (private residence, municipal house, public house) and were adapted by more or less extensive structural alterations for use as children's clinics. Some of these buildings are unsatisfactory, and but for building restrictions during and since the war would have been replaced.

In Coseley all child-welfare services, including immunisation against diphtheria, are provided at the same clinic session. In Birmingham, although all children under 5 years old may attend, the children's clinics are mainly concerned with the supervision of children between 3 and 18 months of age. Mothers with babies under 3 months are encouraged to attend special postnatal clinics, mothers with older children (18 months to 5 years) are given quarterly appointments for toddlers' clinics, and immunisation against diphtheria is offered at special immunisation sessions. The 33 welfare centres provide 64 children's clinics a week, and employ fifteen full-time and twenty-six part-time medical officers, of whom all but four are women. At each session two, occasionally three, health visitors are in attendance.

After a pilot survey conducted at Coseley two record cards were designed. The first was completed by a social worker, who interviewed mothers in reasonable privacy as they arrived at the clinic and recorded their reasons for attending on that particular day. The second card was completed in Coseley by the clinic medical officer (J. T. A. G.), and in Birmingham by one of two medical observers (J. T. A. G. or C. R. L.) who sat in with the clinic medical officer. Data recorded were: sex, age, and birth rank of each child; the reason for medical consultation; and the type of service or services given by the doctor. Direct questioning of the mother was usually unnecessary, since most of the information was available in clinic records or from the mother's conversation with the medical officer. The work of the health visitors at the clinics was not examined in detail.

In the pilot survey the health visitor recorded the reason for attendance at the clinic. This proved unsatisfactory, because health visitors were already fully occupied and because consultations were usually within earshot of those waiting. This part of the inquiry was therefore conducted by a social worker in Birmingham; it was omitted in Coseley.

The Coseley data were collected at 62 consecutive sessions at the child-welfare centre between the end of July, 1951, and the beginning of May, 1952; the Birmingham data were obtained by a single visit, between Feb. 11 and May 12, 1952, to a children's clinic at each of the city's 33 centres. At Coseley the same child was often seen at more than one attendance. In Birmingham, as the postnatal and toddler sessions were excluded, the material is weighted in favour of children between 3 and 18 months of age. Of children referred to medical officers, the proportions under 3 months were 48% and 17% in Coseley and Birmingham respectively. Neither of these features seriously affects the results of our analysis, which is concerned primarily with the work of the clinics and not with the children attending.

Results

REASONS FOR ATTENDING THE CLINIC

The reasons given for attending were to have the child weighed, to obtain advice from the health visitor or doctor on some specific problem, and to purchase proprietary foods (table I). On the recommendation of the medical officer proprietary foods are available at wholesale prices, and whatever the official view mothers evidently consider this function of the clinic important. Nearly half of them (44%) gave food purchase as a reason for attending, 19% gave it as the only reason, and 15% had not brought the child with them. (In principle mothers are not allowed to buy food unless the child has been seen within the preceding fortnight.) In addition, an average of 51 mothers per clinic session attended for the sole purpose of shopping at the branch food offices established at 26 of the 33 Birmingham centres. These mothers, who came without children, did not enter the clinic proper, and are excluded from all tables.

REASONS FOR REFERRING CHILDREN TO THE MEDICAL OFFICER

The proportions of children referred by health visitors to the medical officers were 39% and 27% in Birmingham and Coseley respectively (table II); the average numbers

TABLE I—REASONS GIVEN BY BIRMINGHAM MOTHERS FOR ATTENDING CLINIC

Mothers accompanied by children					Mothers not accompanied by children	
Routine weighing	Specific advice	Purchase of proprietary foods			Purchase of proprietary foods	Total
		Only	And routine weighing	And specific advice		
39·4% (*650*)	16·9% (*278*)	4·3% (*71*)	21·2% (*349*)	3·3% (*55*)	14·9% (*245*)	100% (*1648*)

TABLE II—PROPORTION OF CHILDREN REFERRED BY HEALTH VISITORS TO THE MEDICAL OFFICER

—	Children referred to M O	Children not referred to M O	Total
Birmingham	39 4% (*553*)	60 6% (*850*)	100% (*1403*)
Coseley	26 8% (*868*)*	73 2% (*2367*)	100% (*3235*)

*Of 868 children referred to the Coseley medical officer 325 immunised against diphtheria have been excluded from subsequent tables

of children attending per session were 43 and 52 and the average numbers seen by medical officers 17 and 14 Table III gives reasons for referring children to the doctors (Children referred for immunisation in Coseley have been excluded) About a third had been sent for routine examination In both local authorities a child paying its first visit to a clinic is automatically referred for medical inspection, but after the first visit practice differs in Coseley children see the doctor again only by special request, in Birmingham they are referred for medical supervision about once in three months There is a considerable difference in the proportions seen at the request of health visitors (Birmingham 19%, Coseley 1%), which suggests that part of the work done in Birmingham by medical officers was performed in Coseley by health visitors

More than 40% of the children medically examined had been sent to the medical officer at the request of the mother Since the National Health Service Act has removed the economic reason, we asked why these mothers chose to consult the clinic medical officer rather than their own general practitioner (table IV) More than 40% of the mothers had not considered the possibility of consulting their own doctor A further 10% had attended the clinic to collect food or to have the child weighed, and, having some minor problem, " thought they might as well see the doctor there about it " The remainder (almost half) gave reasons suggesting dissatisfaction with their general-practitioner service the surgery was too far away, a crowded surgery was no place for a child, afternoon consultation was more convenient, or the doctor was abrupt, rude, or too busy to make even a cursory examination

WORK OF THE CLINIC MEDICAL OFFICER

Table V gives details of the work done by clinic medical officers Some children (73 and 71 in Birmingham and Coseley respectively) had more than one service but we have considered only the more important service

Routine Examination —About 10% of the work done by the medical officers consisted in routine examination of children so healthy and well-cared for that no advice was considered necessary That is to say, 120 of the 338 children submitted for routine examination (table III) were thought to need no service of any kind

Reassurance —About 16% of children had minor ailments—sometimes real, sometimes imaginary—for which no treatment and little specific advice was needed (coryza, transient skin conditions, and minor general complaints)

Advice —About a third of the mothers (34 0% in Birmingham and 29 8% in Coseley) were advised about the feeding and general management of their Table VI gives details of the kind of feeding problem a which advice was sought—e g , weaning, breast fe or complementary feeding Under " general ment " (table V) are included instructions napkin hygiene, clothing, physical activity, and b bladder, and sleeping habits Also included " advice " in table V are cases in which the medical issued certificates or advised about priorities Birmingham and Coseley 1 8% and 7 7% respectiv were of this type In both local-authority areas chil were certified as fit to enter day or residential nurse and notes were written to expedite hospital admis In Coseley the doctor, as medical officer of health, also concerned with the rehousing of families for med reasons, and with the issue of free infant foods necessitous families

TABLE III—REASONS FOR REFERRING CHILDREN TO THE MEDICAL OFFICER

—	Routine examination		Specific request by				T
	First visit	Quarterly supervision	Clinic M O	Health visitor	Mother	Hospital or G P	
Birmingham	11 6% (*64*)	16 3% (*90*)	11 2% (*62*)	19 2% (*106*)	41 4% (*229*)	0 4% (*2*)	
Coseley	33 9% (*184*)		17 1% (*93*)	0 7% (*4*)	46 8% (*254*)	1 5% (*8*)	

Treatment at Clinic —In Birmingham about a (22 1%) and in Coseley a third (33 7%) of children treated at the clinic Table VII shows the conditions with—e g , umbilical hernia or polyp, phimosis, respiratory infections, and napkin and teething ras The official attitude towards treatment in child-wel clinics has always been that a child needing anyt more than the most trivial attention should be refe to his own doctor, and clinics in general stock onl few simple medicaments

Referral —Finally, 16 8% and 9 4% of Birmingh and Coseley children respectively were referred elsew for conditions similar to those met in the consulting r of the general practitioner—e g , p cough, diarrhœa and vomiting, media, and cellulitis (table VIII) Most of these pati (72% in Birmingham, and 92% in Coseley) were refe to their general practitioner, a few were sent direct hospital, or to local authority dental or remedial cli

Discussion

We may summarise the results of the foreg analysis of the work of child-welfare clinics as foll

In Birmingham, on the average 101 mothers atten each session, of whom 51 bought food at the branch f office, and 50 entered the clinic proper Of the 50 entered the clinic, 7 attended without the child obtain priority foods 43 attended with the child, whom 20 came to have it weighed, 8 to get specific adv and 15 to obtain priority foods Of the 15 who came foods, 11 wished also to have the child weighed, an to have advice about its management It is clear that whatever the official view of the clinic's function, the distribution of cheap food is still an important incentive for attendance

TABLE IV—REASONS GIVEN BY MOTHERS FOR NOT CONSULTING A GENERAL PRACTITIONER

—	Not considered by mother	Attending clinic for other reasons	Clinic hours or location more convenient	G P too busy	Advice wanted about need for consultation	No confidence in G P	Other and unspecified	Total
Birmingham	44 1% (*101*)	11 4% (*26*)	9·2% (*21*)	5 2% (*12*)	7 4% (*17*)	21 8% (*50*)*	0 9% (*2*)	100% ([illegible])
Coseley	40 6% (*103*)	10 6% (*27*)	7 9% (*20*)	5 9% (*15*)	11 8% (*30*)	21 7% (*55*)*	1 6% (*4*)	100% ([illegible])

* 9 Birmingham and 3 Coseley mothers had already consulted their general practitioners but were not satisfied with his advice

THE LANCET

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Cardiac Catheterisation

Some twelve years have passed since Cournand and Ranges[1] began to describe results of right atrial catheterisation; and it is nearly a decade since McMichael and Sharpey-Schafer[2] began to report on the application of the procedure in this country. Regarded at first with some suspicion and reserve, cardiac catheterisation quickly found a very important place in the selection of cases of cyanotic congenital heart-disease for operation. Every cardiac centre where surgery is undertaken now has a laboratory for catheterisation and allied procedures, such as angiocardiography,[3] and for related studies of pulmonary function. The old cardiologist with his quiet and mild stethoscopic and electrocardiographic studies has been replaced by a highly organised team surrounded by complex and expensive laboratory equipment. The cardiac laboratory is a hive of industry; here clinical investigation and research go hand in hand, and every obscure cardiac problem is illuminated—or sometimes made more difficult—by a mass of hæmodynamic data. Technical advances have been applied with alacrity. Instantaneous optical and other similar pressure-recording devices are now in routine use; and in cases of congenital heart-disease angiocardiography with special radiographic equipment is undertaken at the same time as catheterisation. Recently oximeters have been developed which, by transillumination of the ear on to a sensitive photocell, provide immediate information about the oxygen content of the blood, or even a continuous record of its changes. Moreover, the oximeter can be readily used to study the passage through the circulation of innocuous blue dyes after their rapid injection either into a peripheral vein or through a catheter into the heart itself. By this means intracardiac shunts may be recognised; and, where the heart is of normal configuration, the time of passage of the dye permits the estimation of intrathoracic blood-volume (mainly in the lungs).[4]

The place of cardiac catheterisation in congenital heart-disease and in other diagnostic cardiac problems is well reviewed in a Mayo Clinic symposium.[5] By intensive investigation of various types of pressure-recording systems a strain-gauge system has been found to give the most accurate reading of pressures and greatest freedom from artefacts. The report emphasises the value of catheterisation studies combined with intracardiac injection of dye. In the presence of a right-to-left intracardiac shunt, dye appears in the systemic vessels much more rapidly than dye passing through the lungs. Study of the curves of dye concentration may thus be of great value in locating the site of a shunt. Necropsy studies of hearts previously catheterised showed, however, that data from catheterisation could be confusing or even misleading. For example, slight patency of a foramen ovale may sometimes be important, and yet difficult or impossible to recognise by catheterisation.

Cardiac catheterisation has won an unassailable place in relation to these special problems of cardiac surgery, but knowledge of its risks has also increased. In the earlier years most investigators were satisfied with pressure measurements and blood samples from the right atrium, and little harm seems to have resulted.[6] Gentle passage of the catheter along ever-widening veins into the middle of a roomy right atrium need cause no trauma. But when the operator decides to probe beyond this, round the bend of the right ventricle and pulmonary artery and into as many accessible chambers as possible, in deformed and diseased hearts, it is not surprising that trouble may arise. The Mayo Clinic pathologists saw subendocardial hæmorrhage in 2 of 28 catheterised hearts in cases where the patient had died from other causes. Limited local thromboses in the arm veins and transient arrhythmias during catheterisation are common. The Mayo Clinic workers report 2 deaths and 4 cases of more persistent arrhythmia in 474 catheterisations. On the other hand, 3 patients died while awaiting the investigation, and other recorded deaths have usually been in seriously ill patients. McMichael and Mounsey[7] have recorded precordial pain and collapse, probably resulting from passage of the catheter into the coronary sinus. Hebert et al.[8] report a hæmatoma at the mouth of the coronary sinus in one case and hæmopericardium in another. Pyrogenic reactions are difficult to avoid completely, and in seriously ill patients these can be lethal; while occasionally thrombotic complications may lead to serious embolism. Lenégre puts the mortality from catheterisation at 0·7% (7 in 973), but resulting morbidity may be higher. The American Heart Association has appointed a committee to report on catheterisation and make recommendations, and its report will be awaited with interest. Meanwhile, all concerned with this type of investigation will no doubt apply it with full knowledge of both its advantages and its potentially harmful consequences. Technique must be rigorous, with careful precautions against the known complications; and correct indications should be accepted Discrimination is needed, because only a small proportion of cardiac patients require study by catheterisation. The reasons should be precise, agreed by responsible senior staff in consultation, and explained to the patient, who should give consent; and the cardiologist in charge of the patient should himself be responsible for the conduct of the catheter study. Where cardiac-output studies alone will suffice, catheterisation should not go beyond the right atrium, for the minor inaccuracies of mixed venous-blood samples from this

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1. Cournand, A., Ranges, H. A. *Proc. Soc. exp. Biol.*, N.Y. 1941, 46, 462.
2. McMichael, J., Sharpey-Schafer, E. P. *Quart. J. Med.* 1944, 13, 123.
3. See *Lancet*, May 30, 1953, p. 1082.
4. Kopelman, H., Lee, G. de J. *Clin. Sci.* 1951, 10, 383.
5. *Proc. Mayo Clin.* 1953, 28, 49, 89.
6. Zimdahl, W. T. *Amer. Heart J.* 1951, 41, 204.
7. McMichael, J., Mounsey, J. P. D. *Brit. Heart J.* 1951, 13, 397.
8. Hebert, J., Scébat, L., Lenègre, J. *Arch. Mal. Cœur*, 1953, 46, 325.

difficult in the past year to get a true picture of how this expenditure was going, but the drug bill had climbed from £31½ million in 1949–50 to an estimated figure of £46½ million in 1953–54. There had been a steady increase in the total number of prescriptions dispensed, and a rise in their average cost from 2s 9d in the first year to 4s 2d now. Much of the rise in cost was due to the introduction of new and valuable, though expensive drugs, and there had been a rise in ingredient prices until this year, although, again it was only fair to say that some of the most important drugs especially the antibiotics, had fallen substantially in price.

Under National Health Insurance in 1947–48, 7% of prescriptions dispensed were proprietary, in 1949–50 the figure rose to 15%, in 1950 to 18%, in 1951 to 23%, and in 1952 to 26%. There was no sign of a reversal of that tendency. The 1952 figure of 26% represented 52% of the ingredient cost and 44½% of the total cost. Everyone knew of examples in this particular field. The attention of the country—and of practitioners through *Prescribers' Notes*—had been drawn to a proprietary slimming preparation which if prescribed by its standard name would have produced a saving of £242,000 in 1951. The right way to look on that potential saving of nearly a quarter of a million pounds was to think what could have been done with the money.

"If that quarter of a million has gone—I don't suggest wholly—but partly unnecessarily, then it means that some hospitals have gone short and that I have not been able to authorise, as I would like to have done, certain improvements in many of the parts of the service that you all know need improving."

There were proprietary tablets which had as their main ingredients aspirin, phenacetin, and codeine which cost 6s 3½d for 50, whereas the same number of tablets of the comparable standard preparation cost 2s 11d. A review in the *British Medical Journal* showed that certain asthma inhalant preparations cost four or six times the standard equivalent, "and you have been told, not by the Ministry, but by your own organisation, that there is little or nothing to choose in merit between them." It was true that many preparations had no exact official equivalent—that many preparations, particularly the antibiotics, were in fact only made up in proprietary forms. It was also true that a most important contribution to our exports—not less than £30 million in a year—was made by the pharmaceutical industry. It was, true, too, that they devoted a good deal of money to research, from at least some of which all the people in this country might well benefit. But this was not true of all preparations and it was not true of all firms.

"It is here then that, quite frankly, I want your help. I cannot tackle this wholly by myself, and I do not pretend that I can. You know the way in which doctors can help. I know perfectly well it is easier to say these things than to do them, but we can make careful use of the *National Formulary* preparations. We can by referring to the two tables of proprietary preparations in the formulary—which shows those for which an equivalent standard preparation is available—decide whether they are of substantially the same therapeutic effect as perhaps another preparation which could be prescribed. I think it is important to stress here that while many formulary preparations are cheaper, there is no reason to regard them, as I am sure you do not on that account, as being inferior. They were recommended by medical and pharmaceutical experts quite independently of my Ministry; they conform, as you know, to the standards laid down in the *British Pharmacopœia* or the *B.P.C.* Again, I think you can help by satisfying yourselves, before prescribing a proprietary preparation that is not included in the two formulary lists that there are adequate grounds for believing that its therapeutic value is superior; and finally—and again this is easier no doubt to say than to do—by resisting pressure from patients to prescribe particular preparations which they have had recommended to them or about which they have read in technical or semi-technical or lay papers."

"You all receive copies of the *Prescribers' Notes* and I intend to issue to you a price list of preparations and proprietary preparations listed in the formulary which are frequently prescribed. We have had a clear lead from Sir Henry Cohen's committee, and when the official classification of proprietary preparations has been completed, which will be in a very short time, I propose to circulate this to you all. Finally, as I told the House of Commons, I must myself by cost investigations satisfy myself that the prices being charged are themselves not excessive. In my desire to help there I am setting on foot as many investigations as I can undertake into selected preparations in the categories which Sir Henry Cohen's committee advise me should be prescribable provided a satisfactory price agreement can be reached."

Nothing whatever in what he had said, or in what he intended infringed in any way on the doctor's right to prescribe.

HOSPITAL AND GENERAL PRACTITIONER

Among the things that we wanted to achieve, said the Minister, was that more patients were treated in their own homes and on the whole fewer in hospital.

"I do not put that forward on economic grounds, although that is certainly a factor, because hospital treatment works out at £700 a year, whereas domiciliary treatment is a quarter or less of that figure. But many patients would, in fact, benefit greatly if they could be treated in their own familiar surroundings without the disturbance and stress and anxiety of removal to a hospital. If the cost of the hospital service continues to grow, as it shows every sign of doing, it is inevitably going to absorb more and more of the money that can be set aside for the health service. So we must try, if we can, to lighten the load on the hospitals provided that can be done without any detriment to the patient."

The treatment of a greater variety of patients at home could add enormously to the value and interest of the work of the general practitioner. Mr Macleod regarded direct consultation between consultant and practitioner as of the first importance, and he would like to see here and there more advantage taken by the practitioner of the opportunity of meeting the consultant in domiciliary consultation in the patient's home. It was also of first importance that the practitioner should have direct access, not of charity but of right, to the X-ray and pathological services.

"He should be told, too, and he should be told at once, when his patient leaves hospital, and when he refers a patient for consultation he should receive the considered opinion always of a senior member of the staff. Then he should always be made welcome in the hospital no matter whether he is accompanying a consultant on his rounds or visiting a patient or just dropping in—he should be part, in the fullest sense, of the hospital service in his particular area. Now this is common practice in many places but there are many of you who know that this sort of welcome without jealousy is not always extended to the G.P. in every hospital."

As regards the liaison between the practitioner and the local health authority, particularly in preventive work, he had been struck by the differences apparent in different areas. In some places—usually where there was an able and energetic medical officer of health—there was the closest contact between health visitors and practitioners, but in others the partnership should be closer. Many people felt that too many cooks were concerned with the welfare of the patient, and feared that the practitioner might be crowded out; but there was no danger of that provided he was recognised to be the clinical head of the whole team—"the clinical leader of all the domiciliary health services, bewildering as they may be in their variety, which are provided for people in their homes."

SOLVING THE PROBLEMS

We were engaged in a magnificent experiment in social medicine, said Mr Macleod, and it must not be strangled by too much administration or central direction. Only situation are more than counterbalanced by considerations of the patient's safety and well-being. Where other methods of circulatory study, such as the dye techniques, will give sufficient information they should be used in preference to cardiac catheterisation. The presence of expensive equipment occupying valuable space should not determine the type of study pursued. Otherwise, man becomes the slave of his machines.

Nursing Problems in the Provinces

In our time the training of nurses, though still largely practical, has had a growing academic content; and many have suggested that this trend is becoming too pronounced. Hospitals which find it difficult to get enough recruits of a suitable type are especially apt to complain that the syllabus is too exacting; and indeed, from the administrator's point of view, the obstacles it can present are often serious. The hospital management committee of the Luton and Hitchin group no. 2 have lately approved a report[1] from Mr. R. E. LINGARD, their secretary, which speaks strongly on the subject.

Recruitment to nursing has improved very much in recent years. In 1947 there were 46,655 nurses in training; in 1951 there were 58,270. Since then the figures have levelled off, and it is probable that recruitment has reached its peak. Nevertheless, in Mr. LINGARD's opinion, expansion would still have been possible in "progressive schools and hospitals" but for three changes—one already in action and two still in prospect—in the regulations of the General Nursing Council. On Aug. 1 last year, the G.N.C. fixed the age of entry to nursing training at 18—a rule which we have long advocated and fully support, though there is no doubt that it has placed many hospitals in temporary staffing difficulties. The council have also drawn up a new syllabus, to come into force in January of next year, which increases the time spent by the student nurse in the classroom; and have announced their intention, at a date not yet specified, of raising the educational standard required of entrants. Mr. LINGARD believes that a year ago, before the new age of entry was enforced, the only reason why hospitals in his group could not enlarge their nursing staffs was lack of residential accommodation. For the past eight months, however, recruitment in this group has not kept pace with losses. This he attributes largely to the raising of the age of entry from $17^1/_2$ to 18. He argues that if girls of $17^1/_2$ formed 20% of the hospitals' intake in the past, this change of policy means a permanent reduction of 3000–4000 in the number of students working in hospitals. But a girl who is not accepted for training at $17^1/_2$ does not dissolve into air: she is usually still there six months later, and her wish to nurse may well have survived the interval, particularly if she is able to take a pre-nursing course and to complete part I of her preliminary examination before she enters hospital. It was inevitable that recruitment to hospitals formerly taking girls at $17^1/_2$ should drop seriously during the first six months after enforcement of the new rule; but we must wait for the figures for the second six months before we can say whether recruitment has been permanently injured.

Like the rest of us, Mr. LINGARD has been much impressed by the finding of the Nuffield Job-Analysis Team[2] that three-quarters of the time spent on nursing duties in the wards is contributed by student nurses. So long as this is the case, he argues, and so long as the greater part of the student nurse's time is spent in giving service to the hospital, as distinct from receiving tuition, her real status is something between that of an apprentice and one serving articles, and not that of a student. He therefore regards with misgiving any measures which lead "to an undue increase in the time spent in classrooms, with a consequential loss in the time spent in wards." It is easy to understand his anxiety—the anxiety of the administrator who has to see that beds are staffed and patients nursed. But it would be unfortunate if, at a time when all other countries are steadily advancing the standard of training and status of their nurses, we—the pioneers—reduced ours to the level of so many pairs of hands. A nurse fit to take responsibility in modern wards cannot be bred by the *practice* of ward work alone: she must have a theoretical training, and the time at present allowed to her for this purpose is small.

It is true, of course, that a nurse engaged in the routine tasks required to keep her patients comfortable does not necessarily need a high standard of academic ability or training. But that is why the grade of State-enrolled assistant nurses (S.E.A.N.) was set up—to keep within the nursing team the girl who has no academic gifts but has a natural bent for nursing. The nursing orderly, too, can be used in the team to supplement the nursing staff. Thus hospitals with recruitment difficulties are now in a position to consider a new staffing structure. If they cannot attract enough entrants of adequate educational standard they can either supplement their students with orderlies, or turn over to the training of S.E.A.N.S instead of S.R.N.S. Unfortunately, such a change in the type of training offered is felt to entail a loss of face. It also means, for the matron, a financial loss, for matrons of S.E.A.N. training-schools receive a slightly lower rate of pay than matrons of schools training S.R.N.S. This pointless distinction should surely be obliterated; and it is to be hoped that the nursing profession will themselves get that done. If the G.N.C. do raise the educational standard required of entrants it is probable that many hospitals will find it convenient to make this change. The proposed standard is still under consideration: it will probably be that reached by the ordinary girl leaving a secondary (grammar or modern) school at the age of 15.

We are looking towards a new structure in nursing, built on the notion of the nursing team. There will be room in it for women of high academic, technical, and administrative ability; for responsible women who combine gifts for ward management, clinical nursing, and the teaching of juniors; for comfortable competent bedside nurses with no academic pretensions; for intelligent orderlies attracted by an interesting job: and for students in training for either the register or the roll. It has always been a profession offering scope for many talents, but now the opportunities are expanding horizontally as well as vertically.

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[1] Some Current Problems of Nurse Training. Luton and Hitchin Group No. 2 Hospital Management Committee Report M.C.7/53.

[2] The Work of Nurses in Hospital Wards. London: The Nuffield Provincial Hospitals Trust, 1953. See *Lancet*, Feb. 21, 1953, p. 379.

because the necessities of the financial position at the moment forced him to do so did he keep the reins firmly in his hands All his instincts were towards giving greater and greater freedom to those who really worked the health service, and everything he did would be directed to that end however crabwise his movements appeared to be

"I don't assume, when proposals are put to me by the medical, dental, or nursing profession that they are necessarily biased or necessarily wrong On the other hand, I don't work on the assumption that you are necessarily right either But I would like to say this I want now, as I have always done since I became Minister, to seek your help and the help of all the other professions in the National Health Service This is not a job that the Minister can do alone, or the department alone, nor the doctors, or any of the other professions It is essentially a matter in which we must work together, it is essentially something in which I need your help, and I am very ready to come to you for advice Any help I can give is at your disposal, but it is only in partnership together that we are going to solve these problems and achieve the true potentiality of our National Health Service"

Dr **TALBOT ROGERS**, chairman of the General Medical Services Committee, in thanking the Minister for his address, referred to discussions with the Ministry during the past few years on the mounting cost of the drug bill The committee, he said, would do all it could to assist in stabilising the cost of the pharmaceutical service provided this was not incompatible with the essential needs of the patient

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Public Health

AN EXPLOSIVE OUTBREAK OF FOOD-POISONING CAUSED BY SALMONELLA DUBLIN

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ON Sept 25, 1952, an outbreak of food-poisoning caused by *Salmonella dublin* affected a large number of children in schools in Chard and the surrounding rural districts, and also a smaller number of adults mainly resident in the borough of Chard The outbreak was brought to my notice soon after the schools had assembled on Friday, Sept 26 As school children were involved, a rapid analysis of a large number of cases was possible, and evidence pointed strongly to milk as the most likely vehicle of infection The milk to the school originated on a farm supplying tuberculin tested (T T) milk, most of which was consumed at this and other schools, the remainder being delivered to the public On investigation of the herd concerned it was found that one cow had been taken ill and isolated on Sept 23 Within twenty-four hours of the start of investigation *S dublin* had been isolated from milk from the cow and from fæces of 2 of the victims

NOTIFICATION

On the morning of Sept 26 the acting head teacher of a large school in Chard found that about 100 children were absent and several in school were complaining of sickness and diarrhœa He immediately telephoned the health department

All the general practitioners working in the area were at once informed of the outbreak and asked to send any specimens of vomit and/or fæces to the Public Health Laboratory as soon as possible The director of the laboratory was also informed

Only 1 notification was received from a general practitioner Some practitioners, however, sent specimens to the Public Health Laboratory, and copies of the reports on these were sent to the health department

METHOD OF INVESTIGATION

The first information came from a secondary modern school Many of the children came from outlying villages and the head teacher was asked to make a list of absentees and their addresses, and to state whether they took school meals and/or school milk, or neither Other schools which could be approached on the telephone were asked to do likewise These lists were collected, and a rapid analysis pointed towards school milk, but it was found later that there were some cases of illness among children and teachers who had neither milk nor meals in school and some who had meals only

All the schools approached received their milk from the same source The supply was known to be T T non pasteurised milk, and the bottling and retail department of the suppliers was next visited The routine was for the bulk supply from the herd for the day—i e, morning and evening milk—to arrive in the bottling department in the late afternoon, when it was bottled and put in the refrigerator overnight The milk was sent out at 7 30 next morning The bottling machinery and refrigerator were all in good order, the methods of cleaning and sterilisation were satisfactory, and no member of the staff had been ill or had any symptoms of disease Of the 150 gallons of T T milk being handled daily 90 gallons went to schools

Fortunately all the milk came from one herd, and the farm was next visited The farm building and milking stalls were of modern type with a good water supply and concrete yards which were all in good condition Electrical milking apparatus was used The cows being milked were in good health, but it was discovered that one cow (Ladybird) had been isolated with mastitis on Sept 23 She was isolated about 11 A M, therefore it was possible that milk from her in the morning had got into the bulk supply distributed on Sept 24 A sample of her milk was taken and, together with a bottle thought to be left over from Sept 24, sent to the Public Health Laboratory The veterinary surgeon looking after Ladybird was informed of the outbreak He immediately examined her and expressed the opinion that she now presented a picture of a salmonella infection Immediate arrangements were made for all further milk from this farm to be heat-treated, and general practitioners were informed that a salmonella was a very likely cause of the outbreak This part of the investigation was completed by midday

By next morning the laboratory had isolated *S dublin* from the cow's milk and from the fæces of 2 patients The general practitioners were informed of this result and of the sensitivity of this strain of *S dublin* to chloramphenicol All the affected schools were informed of the cause of the outbreak and warned of the danger of secondarily infected cases The need for strict personal hygiene and extra cleaning of all cloakrooms was emphasised

SYMPTOMS

The order in which the symptoms presented varied All the patients had nausea, often but not always followed by vomiting The patients who did not vomit appeared to have severe abdominal pain, but so did many who also vomited A fairly common symptom in the early stages was severe headache, mainly frontal, with some giddiness This type of headache has been noted previously, and *S dublin* has been found to be the causal organism of meningitis (Guthrie and Montgomery 1939) Extreme pallor was a striking sign Temperatures varied from 99 5°F to as high as 105°F, but most were 100°–102°F The length of illness varied, but most of the patients recovered in three or four days There were no deaths

Treatment of Renal Tuberculosis

THE treatment of renal tuberculosis has been modified but not revolutionised by antibiotics. These new weapons, which are still being developed, are likely to play an increasingly effective part in the war against tuberculosis; but they have certainly not rendered obsolete the older weapons—constitutional treatment and surgery. They have indeed had the opposite effect by showing up the continuing need for constitutional treatment and the advantages of surgery. As COSBIE ROSS and his colleagues[1] remark, these three weapons are complementary, and surgery is only an incident in the course of treatment. The crude doctrine of Alberran, epitomised in the equation *tuberculose rénale=néphrectomie immédiate*, is based on a false conception of the disease by which the tuberculous process was regarded as starting as a solitary focus in one kidney and spreading from there to the rest of the renal tract, including the opposite kidney. It is far more probable that the disease starts in scattered hæmatogenous foci in both kidneys and that the macroscopic "solitary" focus is merely one of these lesions which has developed, the others having healed or become quiescent. In these circumstances nephrectomy for tuberculosis cannot be viewed as a radical operation, and the concept of *néphrectomie immédiate* gives place to that of *néphrectomie opportune*, in which the operation is delayed until constitutional measures and antibiotics have brought the infection as far as possible under control.

There is evidence that streptomycin can heal the small closed parenchymatous focus, but not the established caseocavernous lesion.[2] Fibrosis is a feature of the untreated tuberculous lesion, making an avascular wall around the lesion which hinders the access of blood-borne therapeutic agents. Streptomycin, by increasing this fibrosis, impedes its own action. In urinary tuberculosis the contraction of such fibrous tissue has other untoward effects, such as ureteric obstruction and vesical contracture. Altogether this action of streptomycin must be reckoned a serious defect, and it is encouraging to see the results of histological studies of the effects of isoniazid on tuberculous renal lesions, lately described in these columns by Dr. DICK.[3] One of the most striking findings was the absence of fibrosis in the more recent lesions in cases treated with isoniazid only. Even the old fibrotic lesions showed revascularisation, in striking contrast to cases treated with streptomycin and to untreated cases. Moreover isoniazid seemed to arrest caseation and even to promote absorption of caseated material. Thus isoniazid put the tuberculous process, so to speak, into reverse; but unfortunately this improvement was not maintained after three months' treatment in cavities and in open lesions of the calyces and pelvis; here there were signs of reactivation. These histological findings correspond with the clinical impression that the improvement brought about in the first three to six weeks of isoniazid treatment is not maintained. According to in-vitro bacteriological evidence tubercle bacilli resistant to isoniazid quickly appear; but this complication can be retarded by combining isoniazid with streptomycin. Moreover DICK found evidence that isoniazid reversed some of the fibrotic changes even in chronic lesions previously treated with streptomycin. Thus it seems that these two drugs are to some extent complementary.

Nephrectomy is still the standard surgical treatment of renal tuberculosis when the other kidney is free from infection or only slightly infected. This measure is based on the sound principle that a resistant tuberculous focus is best removed when this is anatomically and physiologically feasible. At a conservative estimate nephrectomy more than doubles the chance of cure; and the antibiotics have not much altered this, for although they have improved the results of non-surgical treatment they have also greatly improved the results of nephrectomy, particularly by promoting smooth healing after operation. Nevertheless the limitations and disadvantages of nephrectomy are obvious. The operation is at the same time too radical and not radical enough: it is too radical if the kidney contains healthy tissue, as is very commonly the case; and it is not radical enough because it leaves untouched the original extra-urinary focus, and possibly also small foci of disease in the other kidney. On these grounds there is a clear prima-facie case for partial nephrectomy; and SEMB,[4] in an account of 87 cases treated by this method, shows that this is both feasible and successful. SEMB compares renal with pulmonary tuberculosis in regard to pathological anatomy and surgical treatment. In both conditions small parenchymatous foci may heal, especially with the help of antibiotics; but cavities (the ulcerocavernous or caseocavernous lesions of renal disease) are much less likely to heal, especially in the kidney. Twenty years ago the surgical treatment of a solitary cavity in the lung which resisted lesser measures might have been total thoracoplasty; nowadays it would probably be segmental resection. A solitary caseocavernous lesion of a kidney is still usually treated by total nephrectomy; and SEMB considers this unjustifiable. The results of partial nephrectomy in his hands are, from the point of view of cure, at least as good as those of total nephrectomy. There is one reservation: none of his cases has yet been followed for more than five years, but even so the results are excellent. There have been no deaths, and the general condition of all the patients is satisfactory; in nearly 90% the urine remains free from evidence of tuberculous infection. In only 2 cases did the function of the partially resected kidney fail; and the series includes 13 cases in which part of the only remaining kidney was removed. These results at least justify a thorough trial of this method.

Partial nephrectomy is not a new operation. It was first performed as long ago as 1887 by CZERNY (for tumour), but until recently it was only rarely done. In 1937 GOLDSTEIN and ABESHOUSE[5] collected a series of 290 reported cases and described 6 of their own. Only 41 of these operations were for tuberculosis, and the results were poor; of the 41 patients, 5 died, 5 developed a urinary fistula, and 6 required a secondary nephrectomy. The operation was much more often and more successfully done for stone; and hitherto it has been practised mainly for this disorder. Of 155

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[1] Ross, J. C., Gow, J. G., St. Hill, C. A. *Brit. med. J.* April 25, 1953, p. 901.

[2] Jacobs, A., Borthwick, W. M. *Proc. R. Soc. Med.* 1950, 43, 453.

[3] Dick, J. C. *Lancet*, April 25, 1953, p. 808.

[4] Semb, C. *J. Oslo City Hosp.* 1953, 3, 45.

[5] Goldstein, A. E., Abeshouse, B. S. *J. Urol.* 1937, 38, 1.

INCUBATION

Incubation varied from four to forty eight hours, but most of the patients were affected from twenty four to thirty hours after taking the milk

DISTRIBUTION

The accompanying table shows the schools affected, 598 children were affected and 1276 school days lost

DISTRIBUTION OF CASES

School	No on roll	No of children taking milk	No of children ill	No of school days lost	No of adults affected
Buckland St Mary	43	42	28	90	—
Chaffcombe	32	32	11	11	—
Chard Infants	135	134	43	71½	—
Chard Junior	304	240	127	213	—
Chard Grammar (Boys)	116	118	34	53	2
Chard Secondary Modern	357	135	95	220	1
Combe St Nicholas	71	50	43	72	—
Otterford	26	26	11	14½	—
St. Gilda s Convent	210	192	82	195	3
Tatworth	99	91	64	188	1
Wambrook	17	14	14	29½	—
Whitestaunton	21	22	16	31½	—
School total	1436	1094	591	1266	9
Other notifications			7	10	3

Some children affected did not take school milk This is explained in two ways

(1) On Sept 24 the schools receiving midday meals from the central school kitchen had rice pudding Although this was made from satisfactory milk it was stodgy, and in some cases the school milk was used to make it more palatable

(2) Some children who did not drink the school milk came from homes supplied from the same source They were infected in common with other members of their family

The adults were affected in one of these two ways

No obvious difference in susceptibility was noticed, and there was no sex difference The fact that fewer older children were ill is explained by the fact that, whereas the percentage of milk drinkers is about 90 among young children, it is only about 50 in older children The small number of adults is explained by the fact that few went to the doctors for treatment, and therefore the exact number is unknown Less milk was distributed to the public than to the schools No doubt also most adults take their milk in some hot beverage, such as tea, and the bacterium is often destroyed in this heating

BACTERIOLOGY

All of the 7 specimens of fæces obtained from persons with symptoms of food-poisoning contained *S dublin* The Salmonella Reference Laboratory confirmed the identification

S dublin having been isolated from Ladybird's milk, it was important to discover how she had become infected She had calved four or five days before becoming ill, and her calf had been put on the herd nursing cow First, the farm hands were examined, and samples of their fæces were sent to the laboratory, all were negative It was discovered that one of the milkers (A B), who was on holiday during the week of the outbreak, had been infected in a smaller outbreak due to the same organism on an adjacent farm in 1947 He had assisted at Ladybird's calving, and this was regarded as highly suspicious However, repeated specimens of his fæces proved negative The report on his blood was as follows

S typhi	(O)	1/80 + 1/160 trace
S paratyphi B	(O)	Less than 1/40
S paratyphi B	(H)	
S enteritidis	(H)	1/40 " "

S dublin shares the (O) antigen of *S typhi* and the greater part of the (H) antigen of *S enteritidis* The paratyphoid antigens were used as controls The results suggested an old rather than a recent infection in agreement with his history His medical practitioner states from his records that A B had had pyrexia of unknown origin in September, 1950, and had been off work for thirteen days, he then had headache and abdominal pain and was treated with penicillin He did not respond, but his temperature subsided slowly, after being about 100°F for five days Infected persons have been known to carry *S dublin* for twenty one months (Harhoff 1941), but nobody for five years In spite of the rarity of carriers of salmonella and the negative findings, A B must remain under suspicion

As the milk from an adjacent farm had been the cause of a smaller outbreak due to the same organism in 1947, it was considered that there might be a link between the two farms, possibly a common contaminated water-supply Moore swabs (Moore 1948) were inserted in the water supplies to both farms, and in all streams and drains nearby None of the swabs were positive

As Ladybird's fæces were positive, it was suggested that the milk had been contaminated in handling She was slaughtered, and her udder was removed and opened aseptically, samples of milk were pipetted off from each quarter, and *S dublin* was recovered from the milk Her liver was enlarged and pale and showed signs of fatty degeneration, but it was not sent to the laboratory Clarenburg and Vink (1947) have found that, when other organs are affected the liver always contains *S dublin*

The remainder of the herd were examined by the regional veterinary investigation centre of the Ministry of Agriculture and Fisheries None of the samples of milk and fæces contained salmonella No samples of blood were taken Ladybird's calf, which had been on the mother for only two days before she became clinically ill was found to have *S dublin* in the fæces, it did not infect the nursing cow on whom it was put, and recovered after treament with sulphadimidine On Oct 2 a heifer developed symptoms of enteritis, it did not respond to treatment, and was slaughtered on Oct 9 A cow was similarly affected on Oct 11, and slaughtered on Oct 14 On Nov 5 a further cow was affected and was given treatment, she appeared to be healthy, but on Nov 24 still had *S dublin* in the fæces She has not been allowed to return to the herd It may be of significance that all the animals infected appeared to acquire the disease in a field which is used annually for the local agricultural show The possibility of infection persisting at the site of the latrines was considered, but a few bacteriological examinations of the soil were unproductive Another feature of this field may be of more importance alone of all those in use on this farm it depends for drinking water on a brook, the river Isle at Eleighwater, which rises some two miles away, near the farm which was the source of a small milkborne epidemic in 1947 Field (1948) has shown in West Wales that *S dublin* infection of cattle is not uncommonly waterborne

CARRIERS

In a boys' school, where 29 of the boarders were affected, samples of fæces were taken from them all on Sept 29 They were all negative

It was expected that secondary cases would follow due to healthy carriers In an effort to detect these carriers Moore swabs were inserted in the main drains of all the schools before they entered the sewers or soakaway four weeks after the outbreak Not one of these was positive

The only person known to be still unfit at the end of November was a kitchen hand Although specimens of her fæces were negative, she was still having abdominal discomfort and occasional severe diarrhœa She finally returned to work symptom-free on Dec 1, when her stools were still free from *S dublin* partial nephrectomies reviewed by Hanley[6] in 1950, 125 were for stone and only 8 for tuberculosis. Many patients in this series were operated on before the advent of streptomycin; this antibiotic has widely extended the field of partial nephrectomy, especially for tuberculosis because of its effectiveness against tuberculous infection of the wound. In total nephrectomy for tuberculosis the minimal requirements are that one kidney is tuberculous and that the other is free from infection and functioning adequately. For partial nephrectomy, more precise information is essential. The details of renal anatomy are of prime importance—particularly the arrangement of the calyces, with its variations, and the blood-supply. Semb adopts Fölgren's scheme, according to which the kidney has seven pairs of pyramids, dorsal and ventral. These pairs are grouped into three divisions; the uppermost three pairs constitute the upper division, and the remaining four pairs are divided equally between the intermediate and lower divisions. In addition to this, there are six different ways in which the pelvis may branch to make the calyces of the middle division. The ramification of the renal artery and vein varies considerably, especially outside the kidney. Semb's scheme of pathological anatomy divides tuberculous renal disease into three groups.

In the *first group* there are small tubercles or tuberculous infiltrations which may lead to the excretion of tubercle bacilli in the urine, but in which there is no macroscopic destruction and especially no open communication with pelvis or calyx. This he calls the "parenchymatous" group, and it is not a surgical problem. For one thing this type of lesion may now often be cured by medical treatment; and for another it does not lend itself to pyelographic study, so that a detailed anatomical diagnosis cannot be made.

The *third group* he terms the "total destructive," in that all three divisions of the kidney are macroscopically affected and often the ureter is also involved. Obviously partial nephrectomy has no place here.

The *second group*, termed "local-destructive," is the group for partial nephrectomy. Here the macroscopic destruction may involve as little as one part of one pyramid or as much as two complete divisions of the kidney.

This second group constitutes no less than 56% of all cases of renal tuberculosis in Semb's series—which shows how important a part may be played by partial nephrectomy.

By Semb's scheme, which he describes as selective medical-surgical treatment, the patient always undergoes preliminary sanatorium treatment, which may last as long as six months if there are other active foci or the general condition is poor. Antibiotics are used sparingly in this phase, streptomycin being restricted to a total amount of 15 g. In the postoperative phase a rather larger amount is allowed—up to 40 g. in uncomplicated cases. If operation on extra-urinary lesions is necessary, this is done before the operation on the kidney. The renal lesions are accurately charted by means of excretion and instrumental pyelography. Aortography is also much used; Weyde,[7] the radiologist associated with Semb, has described the technique and results. He emphasises the importance of the "nephrographic" effect, which maps out the areas of non-functioning parenchyma, in addition to the more obvious effect which delineates the individual vessels.

Ample exposure is necessary for partial nephrectomy, and Semb favours access through the bed of the eleventh or twelfth rib.

A bloodless field may be obtained either by clamping the pedicle or by compressing the renal substance; but Semb found when operating on cases with a sole remaining kidney that the renal function took a harder knock when the pedicle itself was clamped. In his series the extent of the resection varied greatly from case to case, and in 95% of cases the lesion or lesions were removed in one block of tissue; the upper division was involved more than twice as often as the lower. The pelvis or neck of the calyx is sutured (in contrast to Stewart's[8] advice when operating for stone); and the vessels are dealt with mainly by ligature in the cut surface of the kidney, and more rarely by securing individual vessels in the hilum. The cut surfaces are sutured with a double row of catgut, the outer row getting a hold on the capsule; no fat or muscle appears to be used as a further safeguard against hæmorrhage.

Postoperative complications have been remarkably few, consisting in wound infection (3 cases) and failure of function of the remaining tissue (2 cases); there has been no urinary fistula and no postoperative hæmorrhage.

These good results show that in the immediate postoperative phase partial nephrectomy can be no less safe and satisfactory than total nephrectomy. It is reasonable to expect that the late results will also be good, in view of the excellent showing at five years; for we know that after total nephrectomy 75% of the deaths occur within five years. The least that can be said is that here is a method of surgical treatment which is based on sound principles, conserves functioning tissue, and gives promise of improved results.

Annotations

COMFORTABLE CHILDBIRTH

The Government's campaign to ensure that every midwife shall know how to give gas-and-air analgesia for the relief of pain in childbirth has eventually been very successful. By the end of 1951, 94% of all midwives in England and Wales had been trained in the use of the method; and the National Birthday Trust Fund, as Mr. William Penman, the acting chairman, points out,[9] have done much to ensure that enough machines be available. He has analysed the official figures of domiciliary confinements attended by midwives in 1951, to show how many of the mothers received gas-and-air analgesia. The results show a wide variety of practice throughout the country.

There were 253,069 domiciliary confinements attended by midwives during the year; in 192,529 of them the midwife acted as midwife, and in 60,540 as maternity nurse. Analgesia was given in 60% of the first of these two groups and 51% of the second. Of the 146 administrative units in the country, 1 reported that confinements in which analgesia was given amounted to only 8% of the total, and in another 2 the figure was only 16%. At the other end of the scale, 15 units reported figures of 80–90%, and 5 others over 90%. The mean for the country as a whole was 58%.

Clearly it is one thing to train a midwife in the use of this method, and another to get her to use it. From the wide variation in the figures up and down the country it seems that she may be influenced by something more than the views of the mother—perhaps by the views of the medical officer of health. It would be convenient to know just how often relief in childbirth is really needed: medicine sorely lacks a handy little machine

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[6] Hanley, H. G. *Proc. R. Soc. Med.* 1950, 43, 1027.

[7] Weyde, R. *J. Oslo City Hosp.* 1951, 1, 269.

[8] Stewart, H. H. *Ann. R. Coll. Surg. Engl.* 1952, 11, 32.

[9] *Publ. Hlth*, 1953, 66, 79.

EFFECT ON SCHOOLS

The most serious effects of the outbreak were felt by the school population, the work of the smaller schools being completely disrupted The loss of 1256 school days in a term due to one outbreak is considerable If children work a five-day week for forty weeks a year, this is equivalent to more than six years In an epidemic of this size it would probably have been necessary to close the schools , but a weekend intervened, and by the following Monday the number of absentees was many fewer than when they had closed on the Friday

PASTEURISATION

The opponents of pasteurisation always use as one of their strongest arguments that children will never drink "cooked milk" Of course, if there is a cooked taste about pasteurised milk the technique is at fault, and usually it is impossible for a normal person to detect whether milk is raw or pasteurised

This outbreak occurred in a rural area and one of the most important milk-producing areas in the country Most of the children came from villages and probably have as sensitive a palate as any, so far as milk is concerned It is therefore interesting to see what effect the outbreak had on the school consumption of milk

Before the outbreak 1094 of 1436 children were taking milk in the affected schools Three months later 1030 of 1443 were taking milk The weather then was considerably colder, and there is a slight seasonal falling off in the consumption of milk every year Immediately after the outbreak there was a considerable drop in the numbers However, they have slowly increased, and now are 64 less than previously The fall in numbers has been greatest in the rural primary schools and the private girls' school There has not been one complaint by the children against the heat-treated milk The fall is entirely due to parents stating that they do not wish their children to take the milk It was noted in this part of the investigation that the number of children taking milk in schools depends a great deal on the head teacher, particularly in the smaller schools

DISCUSSION

In many previous outbreaks the milk has contained *S dublin* owing to fæcal contamination, yet efforts to isolate it from the milk failed (Conybeare and Thornton 1938) No record has been found of any outbreak in which so many persons have been affected Tulloch (1939) reported that, in 1926, 373 persons were affected by a milk-borne outbreak due to *S dublin* in Dundee The large number in the present outbreak may have been due to the fact that in this instance the cow was excreting *S dublin* in considerable numbers and the milk was more heavily contaminated than might otherwise have been the case The morning milk, which was the contaminated milk and was later bulked with the afternoon milking, was not refrigerated till evening, and in the meantime incubation could easily have taken place

The original source of infection is still undiscovered The fact that one milker was involved in two outbreaks in five years is interesting, but it must be remembered that *S dublin* is the commonest found in bovines (Ritchie and Clayton 1951) However, if he were the cause, which has not been proved, he might well have infected the cow during calving She was originally presented as a case of mastitis and only later developed bowel symptoms

CONCLUSIONS

Notification —This was a large outbreak which the health department was able to notify to the general practitioners It would therefore be reasonable to expect 100% notification of cases treated , but this was far from being achieved One is bound to assume that a large number of small outbreaks must occur which go unnotified or may be notified much too late for any useful investigation to be made The health department was fortunate in this instance that the acting head teacher of a school reported to it immediately by telephone The investigation could thus be brought to a satisfactory conclusion very much sooner than might otherwise have been possible

School Milk and Meals —In this area the medical officer of health is also the medical officer responsible for inspections in the schools The source of the school food and milk was therefore known to him without investigation, and this again was an important factor in avoiding waste of time

T T Milk —The source of infection in this outbreak was T T raw milk The fact that the milk supply is tuberculin tested leads to a false sense of security, as this outbreak has shown

RECOMMENDATIONS

General practitioners should be asked to inform the health department whenever two or more similar cases of food-poisoning occur simultaneously, because only a small percentage of patients seek medical advice The health department can then get in touch with other general practitioners, who may have like cases

Where the medical officer of health is not the school medical officer it is a great advantage for him to be informed of the sources of milk and meals at all schools in his area as a routine

Wherever possible, pasteurised milk should be supplied to schools, even if extra expense is incurred in so doing

SUMMARY

An explosive outbreak of food-poisoning due to *Salmonella dublin* affecting 610 known cases in Somerset in 1952 is described The food causing the outbreak was T T raw milk supplied to schools and the public

S dublin was isolated from the milk, udder, and fæces of the affected cow It was also recovered from all samples of fæces from patients showing signs of illness

When pasteurised milk was supplied the epidemic finished in a few days

My thanks are due to Dr J A Boycott, director of the Public Health Laboratory, Taunton, for laboratory work, for help and advice throughout the investigation, and for criticism of this report , to Mr W B Martin, M R C V S , for help in the investigation of the herd , to the sanitary inspectors of the Chard Rural District Council, especially Mr Eric Whisker, whose help was invaluable, particularly in the early stages of the inquiry , and to Mr J Handel, acting headmaster, whose prompt action in telephoning the health department had such an important bearing on the investigation

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Food-poisoning in Lancashire

The Minister of Health, answering a question in the House of Commons on June 18, said that 734 cases of food-poisoning had been notified in Preston and the surrounding district up to June 17 15 patients were still in hospital, and there had been 1 death The source of infection was meat pies, contaminated with a virulent form of salmonella The manufacture of these pies had been stopped, and investigations were continuing to determine the way in which they had become infected He was satisfied that all appropriate measures had been taken to control the outbreak, which now appeared to be at an end

Dr A Dodd, medical officer of no 3 division of the Lancashire county area, tells us that the food responsible was approximately 6000 meat pies manufactured in to measure and compare the interpretation of pain by different subjects. Childbirth presents peculiar difficulties. As Mr. Penman himself points out, we know that in a proportion of cases women either do not need, may not have, or refuse to accept analgesia; but he thinks this proportion is a small one. The average of 58% of administrations of analgesia is, he thinks, "much too low"; and it is very hard indeed to know whether he is right. Those experienced in training mothers to relax, in preparation for confinement, say that it is often possible to ensure a painless labour without analgesia. Many hospitals and antenatal clinics nowadays arrange classes in which mothers learn to exercise the voluntary muscles concerned in labour, as well as how to relax; and are also taught a little about their own physiology. We have lately mentioned the scheme of this kind run by Prof. W. C. W. Nixon's team at University College Hospital.[10] The Maternity Centre Association of New York holds an elaborate course, which includes not only exercises but also lectures, attended by both mothers and fathers, on the anatomy and physiology of reproduction. They have published a set of clear illustrations of the exercises, which are based on those of the late Helen Heardman.[11] The lecture course ends with a "labour rehearsal," in which the whole birth process is reviewed, and the parents are given the chance to ask plenty of questions. Thus prepared for the birth, mothers feel little fear, and avoid much of the pain associated with anxiety and tension.

It would be unfortunate if our concern over the pangs of labour diverted our attention from the mother as a whole. The Family Planning Association, in a sensible pamphlet,[12] put the picture in proportion. Anæsthesia or analgesia, they say, can render even the most difficult labour nearly painless, and the mother will wake to find her baby comfortably born. But, they add, it must not be forgotten that many women find childbirth an exhilarating experience, which, though hard work, is not attended by pain; and the question arises whether "this taking of the birth-process out of the mother's control produces in her the same feeling of accomplishment as when she has consciously coöperated in the birth of her child." The Birthday Trust Fund wish to see enough gas-and-air analgesia machines available, and enough midwives trained in their use, for every mother who asks for it to have relief in childbirth. It is not possible, without further research, to say what proportion do ask for it at present, still less how many need it, or whether fewer would need it if more were prepared for childbirth on the lines followed at University College Hospital. A rate of 8% of administrations is almost certainly unkindly low; but a rate of over 90% may be equally unkindly high. Training in relaxation takes time and trouble; analgesia is in some sense a short cut. If our aim is to do the best we can for the mother we must take all her needs into account, neither exposing her to wasteful needless pain, nor deposing her too officiously from control of her great occasion.

VEGETABLE JUICES

JUICES obtained by pressing vegetables in special apparatus have attracted little interest in Britain. They have been popular, however, in America as beverages or cocktails, and in German-speaking Continental countries as therapeutic agents. Dr. H. E. Magee,[13] of the Ministry of Health, has studied the evidence favouring the use of juices for either of these purposes. With the coöperation of Mr. Russell Allen, PH.D., he has also collected further information on the chemical composition and nutritional value of juices pressed from many common vegetables, including broccoli leaves, cabbage, carrots, celery, kale, melon, parsley, spinach, tomato, and watercress.

All the juices examined contained sugars, but in widely divergent amounts. Thus carrot juice contained 7·11%, estimated as glucose, in contrast to only 0·2% in the juice of watercress. Equally large variations were found for minerals. Thus iron averaged 2·12 mg. per 100 ml. in watercress and 0·08 mg. in tomato; calcium averaged 18·7 mg. in broccoli leaves and only 0·75 mg. in spinach. Vitamin B_1 was richest in cabbage juice, but this vitamin was completely absent from spinach juice. These divergencies may be traced partly to corresponding variations in the unpressed vegetables, for which Magee quotes official data, and partly to variations in the efficiency with which the nutrients are passed into the juice. Probably the low calcium contents of spinach juice may be related to the high concentration of oxalic acid in this vegetable, which may immobilise calcium in the form of its insoluble oxalate. On this idea it is difficult to explain, however, either why iron should be included fairly freely in the juice or why vitamin B_1 should be excluded. Too much faith, of course, cannot be placed in comparisons on sets of data which were obtained on the juice and unpressed vegetables on different occasions. Thus in order to reconcile the value of 3% found for sugar in broccoli juice with the value of 0·4% quoted for the unpressed vegetable we must suppose an efficiency of extraction which appears almost impossible. From 100 g. of leaves not more than 13 ml. of juice would have to be pressed, and this small volume of fluid would have to carry the entire sugar contents of the original material.

The antiscorbutic power of fresh vegetables is one of their most important nutritional virtues, and vitamin C might be expected to appear in the juice in company with other water-soluble substances. It is well known, however, that when plant cells are damaged they liberate enzymes which destroy the vitamin. High pressure would obviously rupture the cells and the juices would be expected to have antiscorbutic activity only if consumed very promptly, or if effective steps were taken to stabilise the vitamin. Since many of Allen's analyses for ascorbic acid were made several days after the expression of the juice it is not surprising that most specimens were quite inactive. A striking observation, however, was made on kale juice, which had retained no less than 46 mg. of ascorbic acid per 100 ml. By contrast, a specimen of cabbage juice, freshly prepared by Mr. V. L. S. Charley, contained only 8·5 mg. per 100 ml. Magee suggests that either kale does not contain ascorbic acid oxidase, or an anti-enzyme is present. Further attention to this interesting point seems highly desirable. Substantial amounts of carotene were found only in juices from carrots and watercress.

Reports that vegetable juices are effective in the treatment of obesity and allied conditions, such as hypertension, disease of the gall-bladder, and cardiovascular disturbances are explained by Magee on the assumption that dosing with juice is usually accompanied by a strict curtailment of the food intake. He attributes the benefits ascribed to vegetable-juice therapy in rheumatic conditions to their general nutritive value, although it is difficult to see what advantages they would have over the unpressed vegetables. He seems prepared to accept the strong claims of Cheyney[14] and others that large doses of juice, particularly from the cabbage, are effective in the treatment of gastro-intestinal disorders. Presumably the pectin present in raw juices absorbs toxic substances and bacteria from the bowel.

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[10] *Lancet*, April 25, 1953, p. 833.

[11] Reminder Sheets for Exercises in Preparation for Childbearing. Maternity Centre Association, 654, Madison Avenue, New York 21, N.Y., U.S.A. Pp. 32. $2·50.

[12] Pain Relief in Childbirth. Family Planning Association, 64, Sloane Street, London, S.W.1. Pp. 12. 6*d.*; 8½*d.*, postage paid.

[13] Magee, H. E. *Mon. Bull. Minist. Hlth Lab. Serv.* 1953, 12, 78.

[14] Cheyney, G. J. *California Med.* 1949, 70, 10; *J. Amer. diet. Ass.* 1950, 26, 668.

a large bakery on June 10 and 11 Possibly too some pies baked on June 9 and 12 were infected

A report on the morning of June 13 of 2 cases, and the information that meat pies, among other foods, had been eaten, resulted in a decision the same morning to stop production of meat pies Staff concerned were interviewed and excluded from work when this was justified, and fæcal specimens were submitted for investigation Steps were taken to get unsold meat pies destroyed or subjected to laboratory tests

Salmonella bovis-morbificans was isolated from fæces of patients affected and from the meat pies but not from the constituents (it has not been possible to obtain samples of meat from each source) Salmonella organisms were isolated from several persons employed at the bakery who were probably infected by eating meat pies, but the findings in one case may prove significant Investigations continue, particularly concerning meat-supplies

Clinically the incubation period has varied from 6 hours up to 30 hours—18 to 24 hours has been common Shivering and colic or vomiting (sometimes very prominent) has been followed by diarrhœa accompanied by headaches, pains in the limbs and general prostration The illness has lasted for from 8 hours to 5 days The severity of symptoms has been very variable Primary cases are still being reported, and also a few secondary cases

Up to last Monday the outbreak was thought to have involved over a thousand cases[1], and a death in Lancaster on June 20 may have been due to the infection[2]

Lining a Reservoir

A rubber bag holding 12 000 000 gallons of water is to be fitted into a reservoir at Easington near Sunderland, which was cracking because of coal workings After two years' experiments and tests Sunderland and South Shields Water Company have accepted the Dunlop Rubber Company's plan for fixing 16 000 square yards of rubber to the reservoir with a ton of adhesive The rubber bag will weigh 100 tons

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[1] *Manchester Guardian*, June 23, 1953
[2] *Ibid*, June 22 1953

Parliament

QUESTION TIME

Negligence in a Military Hospital

Wing Commander N J HULBERT asked the Secretary of State for War whether inquiries were now completed in regard to the death of Private Donald Harrison, of Stockport, who died in Moston Hall Military Hospital in April —Mr A H HEAD replied Private Harrison, a young man aged 18, was called up for military service in January, 1953, when he was passed as medically fit On March 13 at Wrexham he reported sick with a pain in his back which the medical officer in charge of his unit diagnosed as fibrositis He again reported sick on March 26 when the medical officer diagnosed "Query hysteria" and ordered his admission on March 26 to the military hospital at Chester

On admission he was given, by the admitting medical officer, a preliminary medical examination which included a detailed examination of the central nervous system for the purpose of allotting him to the appropriate medical division of the hospital The admitting officer made a firm but not final diagnosis of hysteria This preliminary examination was correct in so far as Harrison was undoubtedly suffering from hysteria The fact that it was not discovered that he was also suffering from a rare and malignant disease was not necessarily at this stage due to negligence since a more detailed subsequent examination should have taken place after admission to the ward

After admission Private Harrison was required by the medical staff of the hospital to fend for himself and other patients were forbidden to help him The treatment of hysterical patients does require that they should be encouraged to help themselves but in no circumstances should it entail harshness Although he complained that he could not use his legs he was left to get about as best he could by himself This treatment continued for five days during which time Harrison's condition deteriorated, and I am satisfied that the continuance of this type of treatment was due to negligence and undoubtedly resulted in harshness A full physical examination is always required before a diagnosis of hysteria can be justified and should have been made on the first day in the ward The medical specialist looking after Harrison should have satisfied himself that this had been done This he neglected to do Furthermore although during these five days Harrison frequently complained of pain in his legs thighs and back, and although this was recorded by the subordinate nursing staff, the day sister in charge of the ward never drew the attention of the medical specialist to Harrison's repeated complaints

This wrong and harsh treatment was continued despite the comments and protests of at least one other patient in the ward It was not until March 31 that Harrison was seen by a psychiatrist and thereafter received sympathetic handling but even at this stage a full examination had not been made On the night of April 1 the medical orderly became worried about Harrison's condition and called the orderly medical officer and then for the first time Harrison was given a full medical examination The orderly medical officer realised at once that Harrison was dangerously ill, and from this time he was treated for the malignant disease from which he was suffering Harrison died early on the morning of April 5 At the time of his admission to hospital Harrison's illness had undoubtedly reached a stage when death was inevitable since malignant disease of this type in youth, though rare, grows very rapidly I do not suggest that this in any way excuses the mistakes made in the handling of this case

After Harrison's death it should have been abundantly clear to the commanding officer of the hospital that serious irregularities and mistakes had occurred Yet as far as I can ascertain, no thorough inquiry was instituted by the commanding officer although on May 18 he stated that a full inquiry had already been made by himself and that he was satisfied that there was no truth in the allegations that there had been ill treatment of patients

I have been into the whole of this serious occurrence most carefully and I am convinced that it was caused not by any fault in the method of procedure laid down for Army hospitals but by the failure of certain individuals to carry out their duties Members of the Army Medical Services carry heavy responsibilities and those who fail to discharge them must be called to account The commanding officer will be called to account for his conduct in this matter and is to be tried by court martial The medical specialist concerned, who left the R A M C in May, will be reported to the General Medical Council The day sister concerned, who is a civilian, has had her contract terminated and will be reported to the General Nursing Council

I have written to the mother of Private Harrison expressing my extreme concern and disquiet about the way her son was treated, and I would like also to tell the House how much I regret this lamentable occurrence

N H S Specialists in Scotland

In answer to questions as to how many specialists were employed under the N H S in Scotland Commander T G D GALBRAITH gave the following figures

Date	Consultants			S H M O s			Total Consultants and S H M O s		
	Whole time	Part-time	Total	Whole time	Part time	Total	Whole time	Part time	Total
31 12 49	283 (43 8%)	363 (56 2%)	646	163 (59 5%)	111 (41 5%)	274	446 (48 5%)	474 (51 5%)	920
31 12 50	325 (45 9%)	383 (54 1%)	708	174 (59 8%)	117 (40 2%)	291	499 (49 9%)	500 (50 1%)	999
31 12 51	348 (47 6%)	383 (52 4%)	731	205 (63 9%)	116 (36 1%)	321	553 (52 6%)	499 (47 4%)	1052
31 12 52	372 (49 6%)	378 (50 4%)	750	219 (66 4%)	111 (33 6%)	330	591 (54 7%)	489 (45 3%)	1080
31 3 53	368 (49 2%)	380 (50 8%)	748	224 (67 3%)	109 (32 7%)	333	592 (54 8%)	489 (45 4%)	1081

In his own experiments he has proved the high buffering power of vegetable juices against acids. Spinach extracts are superior to milk in their buffering power, and would therefore be expected, for theoretical no less than for practical reasons, to be valuable in the treatment of gastric hyperacidity.

Despite these virtues Magee sees little future for the consumption of vegetable juices by healthy persons. Even the best pressed juices, unlike purées, contain only small fractions of the nutrients present in the original vegetable. The residue after pressing, moreover, contains not only assimilable nutrients but roughage which assists peristalsis. There seems to be no scope in this country for the more extensive use of vegetable juices, except as components of invalid diets and as occasional cocktails.

CHEMOTHERAPY OF ACTINOMYCOSIS

BEFORE the introduction of sulphonamide therapy actinomycosis caused by the anaerobic *Actinomyces israeli* was treated principally with potassium iodide; and even now, probably because of its effect on the granulomatous infiltration, this is sometimes a useful adjunct to the antibiotics.

Early results with the sulphonamides in the treatment of actinomycosis seemed very successful; but apparent cure was sometimes followed by relapse, and even long courses of carefully controlled treatment were often unsuccessful. The application of antibiotic therapy was attended by many dramatic cures, even in very severe cases; and soon penicillin eclipsed the sulphonamides. Continued use of penicillin, however, brought a crop of failures. Many of these were due to inadequate initial dosage with which the infecting micro-organism became resistant. This danger was largely averted by giving massive doses in the initial stages. Garrod[1] showed by in-vitro tests that each of the five antibiotics in common use—penicillin, streptomycin, aureomycin, chloramphenicol, and oxytetracycline (terramycin)—are bacteriostatic to strains of *A. israeli*. Streptomycin, aureomycin, and chloramphenicol have been administered chiefly in cases where penicillin had already failed; and often one of these three has effected a remarkable cure. This does not imply, however, that any of the three is always superior to penicillin: the antibiotic that is the most effective in one case may be the least effective in another. Kelly[2] described a case of abdominal actinomycosis in which, after unsuccessful treatment with penicillin in large doses, sulphadiazine, and streptomycin, clinical improvement was obtained with chloramphenicol; but relapse ensued, and eventually cure was rapidly effected by administration of aureomycin. In another case, reported by Torrens and Wood,[3] streptomycin arrested the disease after penicillin, the sulphonamides, iodides, and surgical measures had failed.

It seems possible that the infecting strains of *A. israeli* may differ in their sensitivity to particular antibiotics; but a preliminary sensitivity test of the culture against the individual antibiotics should enable the most suitable to be chosen. So far the newer antibiotics have had only a very limited trial in the initial treatment of actinomycosis; so a fair comparison with penicillin is not feasible. The first important therapeutic trial of oxytetracycline in actinomycosis is reported by Lane et al.[4] who successfully treated with it 7 cases of the oro-cervico-facial type of the disease. The disease, which was of dental origin and in some cases followed extraction of teeth, was in the lower jaw and was related to the molars and bicuspids; it was localised and acute; its average duration before the start of treatment with oxytetracycline was only five and a half weeks. Suppuration occurred in all cases, and *A. israeli* was isolated in culture from the pus. In 6 of the patients the disease was rapidly cured by oxytetracycline in doses of 500 mg. by mouth every six hours for adults, with proportionately smaller doses for children; treatment was continued for from two to six weeks. Of these 6 cases, 3 had previously been treated unsuccessfully with penicillin, and 1 had become penicillin-resistant. The 7th case was treated at first with penicillin and chloramphenicol and responded well to the latter; but an urticarial rash appeared and the treatment was stopped. Six weeks later, oxytetracycline was given in doses of 250 mg. every six hours for eight days, and this short course of treatment brought about apparent clinical cure. The disease recurred eight weeks later, but it responded well to a further course of oxytetracycline in doses of 500 mg. every six hours, supplemented by small doses of potassium iodide.

Another group of drugs has proved useful in treating actinomycosis. Schoenbach et al.[5] reported encouraging results from the treatment of 3 cases of blastomycosis (*Blastomyces dermatitidis*) with stilbamidine intravenously and propamidine applied locally to the lesions. A diet low in protein and purin is advisable during this treatment. Miller et al.[6] treated a case of actinomycosis of the jaw with stilbamidine injected intravenously at rather longer than daily intervals, starting with 0·05 g., which was increased rapidly to 0·15 g., in 200 ml. of 5% glucose solution. The first course lasted three weeks; and, after an interval of sixteen days, a second course was given over a period of two weeks, which resulted in apparently complete clinical recovery. This patient had previously been treated unsuccessfully with procaine penicillin and sulphonamides. Another agent, pregnenolone acetate, was used with success by Lamb et al.[7] in treating a local infection by an acid-fast actinomycete (*Nocardia* sp.) in a girl aged 6. No indication of toxicity or metabolic disturbance was found after a total dosage of 60 g. given over a period of eight months.

COLONIAL HEALTH SERVICES

IN the Colonial territories increasing population, urban concentration, improved transport, and ever more lively awareness of the benefits of Western medicine are straining the medical services, especially in the main centres. Thus in Singapore the annual hospital outpatient attendance, which averaged 90,000 immediately before the late war, is now approaching 600,000; and in some maternity wards deliveries number about 90 per bed per annum. As regards medical staff, a high rate of recruitment from the United Kingdom and other Commonwealth countries was achieved in 1951; and the latest Colonial Office report[8] records that this rate was maintained in 1952, when 147 doctors were appointed (18 for West Africa, 42 for East and Central Africa, 47 for South-east Asia, 24 for the West Indies, 9 for the Pacific area, and 7 for other territories). In addition medical officers of local origin are steadily increasing, particularly in the Far East, West Africa, the West Indies, Cyprus, and Mauritius; and at the end of January this year 638 Colonial students were studying medicine in the United Kingdom or Eire. The number of specialist posts has been increased; it has proved impossible to fill all such posts from within the service, and, notably in the fields of radiology, anæsthetics,

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[1] Garrod, L. P. *Brit. med. J.* 1952, i, 1263.
[2] Kelly, H. H. D. *Ibid*, 1951, ii, 779.
[3] Torrens, J. A., Wood, M. W. W. *Lancet*, 1949, i, 1091.
[4] Lane, S. L., Kutscher, A. H., Chaves, R. *J. Amer. med. Ass.* 1953, 151, 986.
[5] Schoenbach, E. B., Miller, J. M., Long, P. H. *Ann. intern. Med.* 1952, 42, 31.
[6] Miller, J. M., Long, P. H., Schoenbach, E. B. *J. Amer. med. Ass.* 1952, 150, 35.
[7] Lamb, J. H., Kelly, F. C., Shackleford, P. O., Robell, G., Koons, R. C. *Arch. Derm. Syph., N.Y.* 1953, 67, 141.
[8] Colonial Office: The Colonial Territories, 1952–53. Cmd. 8856. H.M. Stationery Office. Pp. 157. 5*s*.

Tuberculosis in Glasgow

Mr **John Rankin** asked the Minister the number of new cases of pulmonary tuberculosis notified in Glasgow in the first quarter of 1953, and how this compared with each quarter of 1952 and 1951 —Commander **Galbraith** replied There were 622 notifications of pulmonary tuberculosis in the first quarter of 1953, a higher figure than in any of the quarters in 1951 or 1952 except the 644 in the second quarter of 1951

Mr **Rankin** asked the Minister how many beds were available, per 100 new notifications, for the treatment of pulmonary tuberculosis in the whole of Scotland and in the area under the Western Regional Hospital Board —Commander **Galbraith** replied At the end of 1952, the ratio was about 82 beds per 100 notifications for Scotland as a whole, and about 77 beds per 100 notifications for the Western Region alone

Nurses and Pencillin Sensitivity

Mr **Alfred Hargreaves** asked the Minister of Health the number of district nurses who had developed a sensitivity to penicillin and could not undertake further nursing duties, and what special precautions were available to protect nurses exposed to this risk —Mr **Iain Macleod** replied The total number of district nurses affected is not known, but a special inquiry has shown that in 70 local health authority areas 73 nurses had become sensitive to penicillin, and had to give up nursing for varying periods There is evidence that the incidence can be reduced by strict observance of technical precautions and I have at once obtained advice on this from my Standing Medical Advisory Committee I am circulating this advice urgently to local health authorities and others concerned Nurses who have to give up work by reason of sensitivity to antibiotics are entitled to the normal sick leave allowances and may, in appropriate cases, qualify for incapacity benefit under the National Health Service (Superannuation) Regulations They may also, when the circumstances warrant it, qualify for industrial injuries benefit The numbers, if any, who may have to give up nursing permanently are not yet known

Mr **Hargreaves** Would the Minister consider approaching the employing authorities so that they may gain the requisite information from their nursing superintendents? Would he compare the means whereby penicillin is administered in hospitals where the incidence of this sensitivity is less, and possibly learn of a method by which this risk can be reduced for nurses who have to undertake the administering of a great deal of penicillin? Mr **Macleod** I will look carefully into what the hon Member says I know there is a great deal of truth in it Perhaps I might send him a copy of the advice I have been given by the Medical Advisory Committee, which covers many of the points he raises

Chalk Content of Flour

Dr **Barnett Stross** asked the Minister of Food the total amount of chalk added to flour in any given year, and from what source the chalk was obtained —Major **Gwilym Lloyd George** replied In the twelve months ended May 23, 1953, 11,369 tons of calcium carbonate were added to National flour The whole of the supplies conformed to the specifications of the *British Pharmacopœia* and were obtained from home sources

Dr **Stross** Is the Minister aware that a great deal of discussion is going on whether there is any need to add chalk to our flour today, and that the original views are suspect? Are the Ministry of Food doing anything to check up on this problem and see whether the use of this substance can be discontinued?—Major **Lloyd George** The hon member knows that unanimity very seldom exists on these points This was the result of the Committee of 1941 The reason that it is still being maintained is because there is a proved deficiency of calcium intake in our diet Dr **Stross** Does not the Minister agree that recent experiments in South Africa have shown that the work in 1941 may well be not as accurate as we should like and may not justify the use of 11,000 tons of chalk in our flour every year? Will the Ministry of Food look at this question again? Major **Lloyd George** I am always prepared to look at important matters of this sort, but it is admitted that there is a very serious shortage of calcium intake

In England Now

A Running Commentary by Peripatetic Correspondents

One of my most cherished possessions, purchased regardless of cost—five shillings, to be exact including frame—from a cottager patient of mine is a later version of the German picture *The Broad and Narrow Way* originally designed by Mrs Charlotte Reihlen of Stuttgart in 1862 and painted for her by young Herr Schacher of that city

Not much happens along the narrow way, which may be why it is attracting all too little custom There is a chapel, a Sunday School, a deaconess institute you may have a drink of water if you like and there is a loose lion to be negotiated, but after that it is all plain sailing or, rather, a short and gentle uphill stroll to a heaven of golden towers and minarets How different is the broad way Once through the inviting gate surmounted by "Welcome!" in large letters there is never a dull moment Small wonder that most people go this way, some of them by car and one of them on a bicycle Hardly are you inside before you are beckoned into a cottage by an attractive young woman If you prefer alcohol there is to your left a pleasant outdoor café, and within a stone's throw not only a theatre, but also a ballroom flying a union jack and open on Sundays

Beyond, with a loan office conveniently situated under the same roof is a gambling house, from an upstairs window of which is suspended the corpse of a (presumably unsuccessful) gambler On coming out of the loan office you may spend an amusing half-hour at the lottery table before going on past a couple of convicts to witness a pitched battle with a cavalry charge in progress backed by artillery and infantry (in that order) All the troops taking part are in full dress Just this side of hell there is a Sunday train, and dominating all is what is apparently an optician's sign Between heaven and hell there is a pretty solid looking rainbow

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One of the many responsibilities of the present day householder is the execution of minor day-to day repairs A few weeks ago a disorder of function developed in an important piece of hydraulic machinery, and my own efforts at repair having resulted in the loss of what little remaining function there was, I was constrained to seek consultant advice from the local plumber He and his assistant soon restored the contraption to working order and in due course their bill was dropped through my letter-box

"Dr to Wm Bloggs & Bro
To taking down waste water preventor cistern, removing syphon box, making and fixing new copper clack, re assembling and refixing £1 1s

Reading this elegant document, my thoughts went back to those spacious days in the '30s when our paying patients provided us with both our bread-and butter and our motor-cars and when everything from the removal of a wen to an abdomino perineal resection was discreetly cloaked under the all-embracing term "For professional services" How much more satisfying for our patients, I thought, had they received bills after the style of my friend, Bill Bloggs

"Dr to Sir Probyng Lancet
To making 2 ft incision in abdominal wall, removing 5 ft of colon, joining lower end of small intestine to upper end of rectum and testing same for leaks, supplying, fixing and removing 24 mattress sutures 100 guineas

The only drawback would have been that our waiting-rooms would no longer have re-echoed to the tales of our past triumphs Instead our patients would have sat silently reading each other's bills

* * *

As part of our Coronation celebrations members of the staff planted trees in the hospital grounds It was a pretty expression of loyalty but I cannot help feeling that in their unanimous choice of ornamental cherries they missed a big opportunity for self-expression Would it not have been more appropriate, for instance, pathology, and psychiatry, it has even been difficult to recruit from the United Kingdom.

In most territories the full approved establishment has been reached or nearly reached; but this does not mean that needs are being fully met. As the report remarks, industrialisation, with its corollaries of migration of labour and the creation of new urban centres, has especially serious health implications in countries where tropical diseases are endemic and where local customs have not yet been fully adapted to the change from a predominantly rural economy. While the peoples of the various territories are turning with growing eagerness to the curative services, the trained personnel are growingly aware that in the long run their time might be more fruitfully spent on preventive action—and the report describes some striking instances of such action. A somewhat similar situation prevails in every country; but it is especially clear in the Colonies, where doctors are too few and there is great scope for prevention of endemic disorders. These two conflicting calls cannot be satisfactorily met without further expansion of the medical and allied services; and such expansion will depend chiefly on the recruitment and training of personnel from the territories concerned.

THE LISTER INSTITUTE

GOOD wine, it is said, needs no bush; and the governors of the Lister Institute do nothing to vaunt the distinguished work that proceeds under their ægis. Their latest report,[1] no less sober than its forerunners, records that during the past year Dr. A. A. Miles has taken up the directorship of the institute, and that Prof. W. T. J. Morgan, F.R.S., who heads the biochemistry department, has taken over the duties of deputy director.

Professor Morgan and Miss W. M. Watkins, PH.D., have been examining the reactivity of saline extract of certain plant seeds against human red cells of known phenotype, and have studied the inhibition of these reactions by preparation of the human blood-group substances and simple sugars of known constitution. It appears that L-fucose is of greater importance for H specificity than for A and B specificity, and that the N-acetylchondrosamine configuration may play an important part in A specificity. In another department Miss J. M. Horton, PH.D., has continued her work on the chemical fractionation of *Hæmophilus pertussis*, to extract the protective immunising antigen.

Polysaccharides extracted for formamide, alone or in conjunction with globulin, proved to be inactive although preliminary experiments had indicated some activity. The protective antigen, previously shown by F. L. G. Masry to be distinct from the hæmagglutinin and the toxin of *H. pertussis*, now appears to be distinct from the agglutinogen also. The protective action of rabbit antisera to the whole bacillus is unaffected by absorption with purified agglutinogen; and purified agglutinogen will not immunise mice actively. Alkaline extracts of *H. pertussis* yield a polypeptide antigen that appears to be antigenically pure agglutinogen. Variation in the potency of protective antisera with the route of administration of antiserum and infecting dose indicate that more than one type of antibody is concerned.

Dr. L. H. Collier, continuing his investigation of methods of preserving vaccinia virus, has found that purified virus freeze-dried in 5% peptone yields 100% succesful primary vaccinations after storage for four months at 37°C. Such a vaccine can be manufactured economically, and is shortly to be tested on a large scale. Should the trial prove successful, it is hoped to issue to tropical countries dried vaccine instead of the lanolinated lymph used at present. The dried vaccine would also be useful for epidemic reserves.

These and many other investigations are mentioned in a report that sets a standard in meiosis.

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[1] The Lister Institute of Preventive Medicine: Report of the Governing Body, 1953. Issued by the institute, Chelsea Bridge Road, London, S.W.1.

MÉNIÈRE'S DISEASE

IN 1861 Prosper Ménière,[1] a French physician, reported the case of "a girl who, journeying on the box seat of a stage-coach, became as a result of the cold suddenly and completely deaf." Her main symptom was vertigo, and she died on the fifth day. Necropsy showed a "red, plastic matter, a sort of bloody exudate" in the inner ear. Many years later Hallpike and Cairns[2] found in 2 cases of Ménière's disease dilatation of the whole of the membranous portion of the inner ear—so-called hydrops of the labyrinth. This change has since been repeatedly confirmed; but its cause is still undecided. The suggested causes include disturbances of water and salt metabolism, vitamin deficiencies, allergy, and toxic labyrinthitis from a septic focus. According to the belief, the patient is deprived largely of fluid and wholly of salt, fed on vitamins or filled with anti-histamine drugs, or asked to submit to operation for the drainage of infected sinuses or the removal of teeth or tonsils. With these various régimes relief is common, but cure rare; and simple sedation is the chief medical standby. Should the crippling attacks of vertigo continue, resort is had to operation, which in this country usually consists in destroying the labyrinth—and thus also the hearing on the affected side.

To the late E. R. Garnett Passe the paroxysmal nature of the attacks suggested a temporary disorder, which he thought might be a neurovascular disturbance, possibly arising from "underlying autonomic imbalance." Portmann and Despons[3] had reported hyperexcitability of the labyrinth after administration of drugs stimulating the sympathetic nervous system. Passe himself had observed gross dilatation of the vessels of the membranous semicircular canal during the fenestration operation, as a result of procaine block of the stellate ganglion. So, he reasoned, the labyrinthine vessels may go into spasm, and this may cause hyperexcitability; and the spasm might be relieved by interrupting the sympathetic pathways to the head and neck.[4] In a paper published posthumously Passe[5] reported that if stellate-ganglion block with 1% procaine subdued the tinnitus and improved hearing by air conduction, the patient was regarded as suitable for operation. In a first group of 45 patients the postganglionic fibres were interrupted by resecting the stellate ganglion; while a second group of 46 patients underwent preganglionic section. In the five years after operation over 60% of the patients in each group were completely relieved of their vertigo; and the condition of 33% was improved. These results have not been reproduced by other workers; and one wonders whether the Horner's syndrome which inevitably develops in patients who have had the stellate ganglion resected is not an even greater price to pay than the destruction of what little hearing may remain by the time that destruction of the labyrinth is undertaken. On the other hand, in the difficult cases of bilateral Ménière's disease, destruction of both labyrinths is to be avoided at almost any cost.

Rosen,[6] of New York, claims to have shown "for the first time since Ménière that the internal ear is not the exclusive seat of Ménière's disease." He had earlier reported that electrical stimulation of the chorda tympani nerve under local anæsthesia produced auditory impressions of hissing, buzzing, roaring, or ringing, and that such stimulation sometimes gave rise to severe rotatory vertigo. He had also described the effects of sectioning the chorda tympani, alone or together with the tympanic branch of the glossopharyngeal nerve, if the psychiatrist had planted nuts? The geriatrician should obviously have provided an elder, the obstetricians a plot of gooseberry bushes, and the venereologist a hawthorn because of its fruit and the number of pricks (intramuscular) which his calling demands. A bed of sweet peas outside the diabetic department might be rather old-fashioned, but what about a few sugar canes? The anæsthetists might well protest if offered a sycamore and ask for an olive, as they bring peace into the midst of turmoil. The surgeons could have any sort of tree that provides barber's poles, possibly an ash though as stools are made from this the pædiatrician has prior claim. The orthopods could have roses on account of the fruit. Dermatology might be represented by an eczemous tree (useful on Dec. 25) well covered with lichen. The hæmatologist could look up from his rhesus grouping to see a monkey puzzle of another sort, and the pathologists would find something with a lot of dead wood outside the mortuary. Aspens might be shared by the neurologists, who deal with the shaking palsy, and the general physician and his thyrotoxic patients. Any G.P. who needed a quiet life could plant an apple, and night sister might provide a cocoa plant. The urologists should try ground-nuts, bladder campion or possibly some of the stone fruit. The administrative officer from headquarters could be invited down to put in a large box bush as rulers are made of its wood. Those who say that box is a euphemism for coffin would be asked to keep their mouths shut. We would welcome a contribution from the Editor of *The Lancet*, and he no doubt would choose a blue cedar, as we understand that that is what pencils are made from.

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[1] Ménière, P. *Gaz. méd. Paris*, 1861, 16, 597.
[2] Hallpike, C. S., Cairns, H. *J. Laryng.* 1938, 53, 625.
[3] Portmann, G., Despons, J. *Rev. Laryng., Paris*, 1928, 49, 1.
[4] See *Lancet*, 1951, i, 783. Mitchell, G. A. G. *Ibid*, p. 909. Passe, E. R. G. *Ibid*, p. 1280.
[5] Passe, E. R. G. *Arch. Otolaryngol., Chicago*, 1953, 3, 257.
[6] Rosen, S. *N.Y. St. J. Med.* 1953, 53, 1095.

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The frequent clotting of London traffic during these last few weeks has given rise in pathological circles to the fear that it may stop altogether through coronationary thrombosis.

* * *

A *perambulation* of pædiatricians seems an apt collective noun, though we were by no means pushed around when members of the local pædiatric club inspected a veterinary research unit last Saturday afternoon. Indeed, we were so interested that we abandoned the toddler's gait customary on these occasions, and fairly gambolled round the laboratories and grounds.

The magnificent bulls for artificial insemination attracted most attention. Lest we should imagine, however, that there are no problems in the bovine Welfare State, we were told of difficulties which do arise. For instance, spermatozoa whose ardour has been cooled during months of frustration in the ice-chest sometimes take it on themselves to go backward *au moment critique*.

Vets vie with even the most recently fledged pædiatricians in "cubicilisation," and they are far in advance of obstetricians in their devotion to the antenatal care of fathers, a prospect which produced envious comment from the males in our party—and some wholly male pædiatricians do, somewhat anachronistically, persist.

What would an older generation have thought of the fact that we saw not a single horse during our visit? We did, however, see three dogs, though they were visitors and not inmates. We were also informed that when Dartmoor ponies are turned loose in lush grass they tend to develop dermatitis, owing to the unaccustomed high level of chlorophyll in their diet. Clearly, we shall have to watch those children who use the modern, widely advertised toothpastes.

In the museum two exhibits astonished us. One was an example of osteopetrosis, which was casually attributed to virus infection; the other, a specimen of muscular dystrophy, which is regularly cured with methylene-blue. On Monday morning I expect to see a crowd of would-be therapeutists in the records department of the children's hospital, anxiously looking up names and addresses in the diagnostic index of patients.

* * *

He is wise who knows that he
Dust has been and dust must be
But a fool is he who must
Fill the interim with dust

Letters to the Editor

ONE-STAGE PROTHROMBIN-TIME TEST

SIR,—It is being gradually recognised that the simple one-stage prothrombin-time test was largely responsible for bringing blood clotting out of the doldrums and confusion into which it had been plunged by reckless theories promulgated during the first third of the present century. So great was the bewilderment that the very existence of prothrombin was at times denied. It is beginning to appear as if the cycle of confusion is about to be repeated. The clear concept of prothrombin as a constituent of the blood which becomes diminished by depletion of vitamin K or after the administration of dicoumarol is gradually being dimmed by the introduction of a multitude of new factors such as proconvertin, factor VII, and *co-thromboplastin*. As a result of this trend, the one-stage prothrombin-time has again become the target for condemnation. To be sure, its clinical value and reliability is no longer denied or questioned, but now the accusation is that it does not measure prothrombin. The statement in your editorial of April 25 that "The use of the Quick one-stage clotting test (the doubts about the 'prothrombin' it measures have, we suppose, made 'prothrombin-time' out of order) . . ." epitomises the views that at present seem to be in the ascendancy.

Before dismissing summarily this test as a quantitative measure of prothrombin, it may be judicious to reconsider it in the light of some recent findings, particularly those on the prothrombin in the blood of the newborn infant. As is well known, when the prothrombin is determined by the two-stage method, it is found to be 30% or less in spite of a normal prothrombin-time. It was in a vain attempt to explain the paradoxical results of the two-stage method that hypothetical prothrombin converting factors were first introduced. Yet one is still waiting for concrete proof that such agents exist as primary factors in circulating blood. Attempts to show their presence in blood in the newborn have failed.[1] The findings in infants' blood can be satisfactorily explained without introducing accelerator factors. The blood of both newborn and adults contains the same concentration of active prothrombin, which accounts for the normal prothrombin-time in both bloods.[2] In adults, however, the blood contains in addition a high concentration of prothrombinogen (inactive prothrombin), which is absent in newborn blood; consequently, the total prothrombin which is measured by the two-stage method is much lower in newborn than in adult blood. No agent such as factor VII need be postulated to explain the normal prothrombin-time of infant blood.

It seems reasonably certain that failure to recognise the existence of prothrombinogen in human blood has been largely responsible for the present array of hypothetical accelerator factors. In a recent publication[3] we have shown that the prothrombin-time remains a reliable measure of prothrombin, provided the procedure is carried out as originally outlined. The findings which are now attributed to converting factors can probably all be more simply re-interpreted by the conversion of prothrombinogen to active prothrombin.

If the reliability of the one-stage method is unjustifiably undermined, the interpretation of the prothrombin-consumption test would likewise become a hopeless jumble, despite the fact that this test furnished the first practical explanation for the coagulation defect of both hæmophilia and thrombocytopenia. It would be most unfortunate if progress in the thromboplastin-deficiency states were arrested by a deluge of new theories and in 14 cases of Ménière's disease; in 11 the attacks of vertigo ceased. These results, he claimed, led to the "inescapable inference that the internal ear is not the *sole . . . portion of the nervous system from which the* symptoms of Ménière's disease derive [and] that these symptoms may be mediated by way of sonic and equilibratory afferent fibres in the chorda tympani." Rosen now describes 2 cases of what he believes to be Ménière's disease, both unilateral and both with dead labyrinths on the affected side. The persistence of "Ménière attacks" despite a dead labyrinth he takes to be further evidence of some extralabyrinthine pathway by which symptoms are produced. In both cases the vertigo ceased after section of the chorda tympani. Of these 2 patients, 1 had had a fractured skull, after which "there was total absence of caloric response and total loss of hearing" on the affected side; in the other case the symptoms developed after mumps. Both fracture of the skull and mumps are recognised causes of unilateral perceptive deafness.

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[1] Quick, A. J., Hussey, C. V. *Proc. Soc. exp. Biol., N.Y.* 1953, 82, 449.

[2] Quick, A. J., Murat, L. G., Hussey, C. V., Burgess, C. F. *Surg. Gynec. Obstet.* 1952, 95, 671.

[3] Quick, A. J., Hussey, C. V. *New Engl. J. Med.* 1953, 248, 624.

Fowler and Zeckel [7] pursue the search at a higher level. They declare that "certain personality types tend to develop tinnitus and perhaps vertigo under stress." The attacks, they find, are associated with certain types of life-stress, including personal antagonism, sexual abstinence in the male, sexual conflicts in the female, and death of a near relative. Fowler and Zeckel do not, however, give convincing evidence of Ménière's disease in the 23 cases on which their report is based. In those cases where the deafness is described in detail, it is said to have been for low tones; whereas in Ménière's disease the loss is for high tones.

It cannot be said that great strides have been made in the attack on this troublesome disorder.

HALLUX VALGUS

CORRESPONDENTS, commenting on a leading article,[8] have expressed the view that the badly shaped shoe is the main cause of hallux valgus. This is not the only cause—even in some peoples habitually going barefoot hallux valgus is not uncommon [9]—but the evidence that shoes force the toes out of line is difficult to refute, and their deforming action is almost certainly the major ætiological factor in most cases of hallux valgus.

If we accept this, what are we going to do about it? There has long been a tendency to reverse the Victorian custom by which the foot had to fit the shoe rather than the shoe the foot. Knowles [10] describes an instance of an adult with mild hallux valgus who for three and a half years wore shoes, made on a special last, which were basically triangular and had a perfectly straight inner border. Foot symptoms were immediately relieved, and the degree of hallux valgus was materially lessened. In this country Mr. Pratt [11] has been pressing for the introduction of shoes with a straight inner border.

Shoes with a truly straight inner border are difficult to obtain; but some makers [12] specialise in shoes with fairly stringent inner borders. There would be, of course, no difficulty in producing such shoes if the necessary lasts existed. The trade, through the knowledge gained by the British Boot, Shoe, and Allied Trades Research Association, is well aware of the physiological need for these shoes. But two things militate against such a change. First, it would be very expensive to change every last; secondly, few people—and hardly any women—would buy the new shoes. The pioneer manufacturer of this type of shoe will meet a small demand from the highly foot-conscious; but unless the change is introduced simultaneously throughout the civilised world, with the support of massive publicity, we see no prospect of the demand increasing. It is not that the new shape of shoe would be intrinsically ugly; in such matters it is simply a matter of what one is used to (vide men's hats). The change could, we suppose, be introduced step by step if the trade and their designers agreed that they would gradually make shoes with straighter and straighter inner sides. But what stimulus is there for them to follow this costly course, so much against their immediate interests? There is only one rapid solution. At the command of a Schiaparelli or a Christian Dior waist-lines rise or fall. Cannot a shoe designer be groomed to similar stardom? Of course the trade for its part may be waiting for a lead from the medical profession: but what form should this lead take?

SPONTANEOUS PNEUMOTHORAX

IN the early 19th century when Itard [1] first used the word "pneumothorax" and Laennec published his excellent description of the condition,[2] the qualification "spontaneous" was not used. Subsequently—for instance, in Powell's textbook of 1893 [3]—this qualification was applied to pneumothoraces where no cause could be found, as opposed to those associated with pulmonary tuberculosis or other disease. But when the production of a pneumothorax became a therapeutic procedure, all other varieties, except traumatic, were grouped as "spontaneous," since they arise through natural processes. Unfortunately, the group name is now commonly used for a single subgroup. Thus, a recent report by DuBose and others,[4] although entitled "Spontaneous pneumothorax: medical and surgical management," deals only with pneumothoraces unassociated with active pulmonary inflammation or neoplasm.

Laennec knew that air could be present in the pleural cavity without any perceptible change of structure of the pleura; and it was later recognised that a pneumothorax could occur in apparently healthy people.[5] In 1932 Kjaergaard [6] defined the condition as one in which there is a pneumothorax "without demonstrable cause in healthy individuals . . . in whom the lesion is not accompanied by fever or by [a clinically recognisable] pleural effusion." He called this "pneumothorax simplex"; others have named it "benign" or "idiopathic." Kjaergaard's definition is no longer adhered to, and the term is now applied even to cases where a cause for the air leak has been found. For instance, Brock [7] described "recurrent and chronic spontaneous pneumothorax" in 71 patients where a probable cause was discovered in all but 6; there were 25 with generalised or bullous emphysema, 11 with solitary or multiple cysts, 15 with small apical bullæ, and others with apical scars, pleural tears, or minute subpleural air-bubbles. DuBose and others found radiographic evidence of bullous emphysema in 57 of their 73 patients. This is a surprisingly high proportion, even in a series of patients ill enough to be admitted to hospital; the frequency of radiographically detectable pulmonary abnormalities in all cases of simple pneumothorax is probably very much less. As the majority have only one mild attack, which does not warrant extensive radiographic or thoracoscopic investigation, a cause will be found in only a few; and thus most cases will still fall within Kjaergaard's definition. But if a lesion seems with reasonable probability to have caused the pneumothorax, it would seem worth while removing the case from the category of simple spontaneous pneumothorax and classifying it according to the cause.

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7. Fowler, E. P. jun., Zeckel, A. *Psychosom. Med.* 1953, 15, 127.
8. *Lancet*, Feb. 14, 1953, p. 331.
9. Kalcev, B. *Ibid*, 1952, ii, 937.
10. Knowles, F. W. *Med. J. Aust.* April 25, 1953, p. 579.
11. Pratt, C. A. *Lancet*, April 11, 1953, p. 746.
12. For example, Messrs. Hardy and Son, 6, Baker Street, London, W.1. See *Lancet*, May 9, 1953, p. 956.

1. Itard, J. M. G. Dissertation. Paris, 1803.
2. Laennec, R. T. H. De l'Auscultation médiate. Paris, 1819.
3. Powell, R. D. On Diseases of the Lungs and Pleurae. London, 1893.
4. DuBose, H. M., Price, H. J., Guilfoil, P. H. *New Engl. J. Med.* 1953, 248, 752.
5. West, S. *Brit. med. J.* 1887, ii, 393.
6. Kjaergaard, H. *Acta. med. scand.* 1932, 77, suppl. 43.
7. Brock, R. C. *Thorax*, 1948, 3, 88.

hypothetical factors that not infrequently owe their existence to laboratory tests which often seem to be more impressive in their name than in the validity of their control

Milwaukee, Wisconsin. **ARMAND J QUICK**

TREATMENT OF HYPERTENSION

SIR,—Your annotation of April 25 reviewed with admirable brevity one side of this topic It left other aspects barely mentioned These can be approached through the viewpoint of 1933 We had then virtually no good hypotensive drugs We assumed that in perhaps 95% of cases the hypertensive needed his high arterial tension to provide adequate circulation to his vital organs (to what extent we were emulating the fox contemplating the desirables beyond his reach I cannot say) The past twenty years are noteworthy for the accumulation of data which warrant the abandonment of that concept, but many practitioners, in my country at least, are not aware of this

Perhaps the early work with thiocyanates was responsible for the beginning of the collapse of the concept In those few cases where irregularities of excretion, skin rashes, &c, were long enough delayed (by blood-level control or by good luck) real reductions in blood-pressure were shown to be well tolerated.[1] Soon the results of sympathectomy in favourable cases showed that many patients could function normally at much reduced arterial pressures The revival of *Veratrum viride* which followed the preparation of dependable, purified, and standardised extracts contributed similarly, since it quickly became clear that parenteral administration would strikingly lower the blood pressure of virtually 100% of hypertensive patients[2–6] At the resulting lower levels of blood pressure, which were often within the normotensive range, these patients could walk about and experienced no postural hypotension, and no embarrassment of cerebral, renal, or hepatic function The presence of a slow heart rate emphasised that normal function in the hypertensive at lower pressure was not gained at the expense of increased cardiac activity Despite their unphysiologic mechanism, hexamethonium salts have likewise contributed evidence of the capacity of the hypertensive to get along with reduced pressure

A direct result of this alteration of concept has been the enhancement of value attached to agents reducing pressure in individual cases Much improvement can be gained for certain patients from particular drugs[6, 7] It becomes important now to stop rejecting drugs which on oral administration effectively lower hypertensive blood pressures in only a limited percentage of cases We need to screen the active hypotensive agents in each patient in an orderly way, to find out which drug acts best for him We need to weigh the improvement the patient obtains from therapy against the dangers of toxic actions and against the discomforts of side actions produced by each drug Recently it has become clear that combinations of these drugs increase the percentage of patients who will respond and make possible reduction in discomfort due to side actions[8, 9]

The past ten years have focused attention on four agents worth screening in this orderly manner. Of these, three are drugs of great potency The fourth, *Rauwolfia serpentina*, is a basal agent[10, 11] Rauwolfia's mild action, its vagotonic effects, its freedom from side-actions, its ease of management consequent on low increment of response with dose (increasing dosage beyond the minimal effective produces neither fall in blood-pressure nor severe side effects), and very low toxicity combine to make it a basal hypote analogous to the ideal basal anæsthetic (nitrous o Rauwolfia, like veratrum, requires careful identifica extraction, and standardisation if its advantages to be obtained fully 'Rauwiloid' is a prop compound that may fulfil these criteria

The three full-potency hypotensives, while im are far ahead of classical substances Your anno made no mention of standardised *Veratrum* extract ('Veriloid' is an example) *Oral* tion of this agent deserves mention because it is safest of the three (no risk of organ toxicity, w margin against lethality), and because it will pro excellent results in 20–40% of patients[12] Its outsta disadvantage is the narrowness of the range be good hypotensive effect and emetic side action, makes management difficult The spread be hypotensive and emetic doses appears to be wi by combination with rauwolfia[8] Thus the percen of patients controlled by veratrum may be improved

From hexamethonium salts one can obtain the gre hypotensive action Acknowledging the side act and dangers mentioned in your annotation, recent w has revived hope that these compounds can be by mouth, since rauwolfia apparently can reduce required dosage and the incidence of side actions[9]

Hydralazine is a useful agent despite tolerance and unpleasant side actions of headache and tach but the risk of toxic effects (drug rash, drug possibly agranulocytosis[13]) must be weighed C tion with rauwolfia and even with hexamethonium from recent reports, to offer much advantage

In summary, I do not agree that the immediate pr pects for helping the individual hypertensive are poor If we use the tools now available against disease, our patients will benefit in proportion to skill

Los Angeles,
California U S A **GEORGE L MAISON**

POLIOMYELITIS

SIR,—The case described by Mr Hyman (April 2 exemplifies the danger of over-exertion during recovery from poliomyelitis I do not agree with Dr Ritch Russell (May 2) when he brushes aside *too vigoro* exercise as the cause of the deterioration of muscle power in this case

Between the antiquated method of rigid splintin and exercises to the point of fatigue there is such range of possible variations that it is difficult for the le experienced to decide which to adopt In the subacut phase it is difficult to estimate from the, sometimes scanty, symptoms the stage of the lesion

With regard to the handling of affected limbs I try to avoid the muscles of, for example, a painful calf being pressed by the "dead weight" of the tibia In a few cases of very painful calves I have used what might be termed an "air cushion *gutter* splint," consisting of two inflated lengths of bicycle inner tubes These tubes are glued with latex to a length of 'Sorbo' in such a way as to form a gutter with varying width according to the shape of the calf Thus the lower leg is gently supported at both sides of the midline from the heel to the back of the knee, the midline itself remaining free from any pressure A layer of gauze cotton wool is placed on the rubber to prevent condensation Any device can be added as a foot support I have found very tender lower limbs surprisingly comfortable with such an arrangement

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[1] Barker M H *J Amer med Ass* 1936 106 762
[2] Mellman, E Krayer, O *J clin Invest* 1949 28 798
[3] Stearns, N S Ellis L B *New Engl J Med* 1952 246 397
[4] Goldman R W Frierson, H R *Amer J Med* 1953 14 168
[5] Kauntze R., Trounce J *Lancet* 1951, i 549
[6] Wilkins R W Stanton J R Freis, E D *Proc Soc exp Biol, N Y* 1949 72 302
[7] Mills L C, Moyer J H *Arch intern Med* 1962 90 587
[8] Wilkins R W Judson, W E *New Engl J Med* 1953, 248, 48
[9] Ford R V Moyer J H Unpublished data
[10] Vakil R J *Brit Heart J* 1949 11, 350
[11] Ford R V Livesay W R, Miller S I, Moyer J H *Med Rec Ann* (in the press)
[12] Kauntze R Trounce J *Lancet* 1951 ii, 1002
[13] Kaufman M *J Amer med Ass* 1953–151, 1488

Special Articles

RESULTS OF A QUESTIONNAIRE CONCERNING CONTROLLED HYPOTENSION IN ANÆSTHESIA

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DURING the past few years the problem of excessive bleeding during surgical operations has been the subject of numerous investigations. The problem is scarcely new, and for many years surgeons and anæsthetists have found a solution in the use of chloroform anæsthesia, high spinal analgesia, or the meticulous posturing of the patient so that the operation site might remain superior. Gardner (1946) introduced arteriotomy by which blood was withdrawn from the patient preoperatively and later was partly or completely replaced in the same manner at the end of the operation, or even during the operation if necessary. Such preoperative reduction of the amount of circulating blood lowers the blood-pressure and causes peripheral vasoconstriction; and, when it is combined with the proper positioning of the patient, the net result is the reduction of bleeding at the site of operation. A more physiological approach was total sympathetic block (Griffiths and Gillies 1948). In this method the blood-pressure is reduced by spinal anæsthesia to achieve paralysis of the entire efferent sympathetic outflow. Gillies (1952) has stated that this technique is without doubt "physiological trespass" but has assumed that the arteriolar dilatation guarantees normal oxygenation of the tissue cells, and that the decreased cardiac output inherent in the technique is compensated for by the decreased peripheral resistance and therefore the decreased work of the heart. Proper posturing of the patient is again an essential feature of the control of bleeding, as it is in all methods of "controlled hypotension." The introduction of the methonium compounds (Barlow and Ing 1948, Paton and Zaimis 1948) provided a simple method of ganglionic blockade merely by injection, and led to the widespread use of induced hypotension for the control of excessive vascular bleeding in the field of operation, again in combination with proper positioning of the patient (Davison 1950, Enderby 1950).

AIMS AND EXTENT OF QUESTIONNAIRE

These techniques of induced hypotension for the control of excessive bleeding and the production of a relatively bloodless operation site have become increasingly popular among both surgeons and anæsthetists in the British Isles. Only within the last year or so has the method been used to any great extent on the American continent. Within this same period alarming warnings have been sounded, for it appears that certain complications of the technique have been much more common than were previously supposed (*Anæsthesia* 1952, Davison 1952, *Lancet* 1952). Knowledge both of these disasters and of the beneficial effects possible for a given patient are essential to the proper assessment of the technique and a true estimate of its position in anæsthesia and surgery.

Since the experiences of the anæsthetists in the British Isles with the technique of "controlled hypotension" greatly exceeds that of the anæsthetists on the American continent, questionnaires were sent to 602 members of the Association of Anæsthetists of Great Britain and Ireland in an attempt to obtain utterly anonymous, but unbiased, reports of the results of the technique, most particularly those fatal and non-fatal complications that might have been observed in its use. In the belief that the results of this questionnaire might be of some interest to those from whom the results originated, and with a feeling of deep gratitude toward those physicians of integrity who took part in this investigation, we submit this report.

Of the 602 questionnaires sent, 289 have been completed and returned up to now. This constitutes a return of 48%. The questionnaire was poorly worded, in certain instances; hence many of the figures are only approximate, and some editorial corrections became mandatory. For these reasons no statistical significance can be attributed to the results. These results do, however, indicate that "controlled hypotension" has been widely used, that complications have followed its use, and that deaths have been associated with, if indeed not due to, the technique.

RESULTS OF QUESTIONNAIRE

Each question from the questionnaire is printed below in its original wording, together with the results derived from an analysis of the 289 returned questionnaires:

(1) *Have you employed "controlled hypotension" to secure a bloodless operating field during surgical interventions?*

Yes	170
No	111
Yes, but have abandoned technique	8

(2) *What technique have you employed to obtain "controlled hypotension"?*

Arteriotomy	5
Spinal	51
Methonium compounds	166
Others (please state):	
Posture, plus deep ether or Pentothal	11
Veratrum viride	1
Chloroform	5
Amyl nitrite	1
Extradural block	7
Intercostal and sympathetic blocks	1
Local injection with adrenaline	2
Pronestyl with methonium compounds	1
Venesection	1
Various vasodilator agents	1
Barbiturates and Pentothal	1
Pethidine	1

Some anæsthetists used more than one technique.

(3) *In approximately how many cases have you used the technique?*

Arteriotomy	206
Spinal	6922
Methonium compounds	11,979
Others	2018
Total cases	21,125

(4) *What level of blood-pressure do you strive to attain?*

	Anæsthetists	*No. of cases*
60 mm. Hg or less	44	4571
60–80 mm. Hg	54	6847
70–80 mm. Hg	50	5727
80–90 mm. Hg	17	1392
90 mm. Hg	4	666
100 mm. Hg	3	232
Not stated	6	1690

(5) *Do you employ posture as a factor in obtaining a bloodless field?*

Yes	152
No	9
Sometimes	17

(6) *Do you employ vasopressor agents to return the blood-pressure toward normal?*

Yes	38
No	50
Sometimes	90

I add one word about the transfer of poliomyelitis its from fever hospitals to other units for further nent Transfer after 3 weeks as now practised l be regarded as an expedient to ease the burden e fever wards—not as justified from every point w Opinion on the danger of spread of infection this period is not yet unanimous, and, even after first 3 weeks, treatment is still—except in very cases—restricted by pain and the general afters of the illness The later the patient is exposed ercises to the point of fatigue, the better

efield **OSKAR TURGEL**

ANTICOAGULANT DRUGS

,—Mr Rowden Foote (May 16) is concerned about icting opinions regarding deep-vein thrombo- ntis

the United States the split is between advocates nticoagulant therapy and advocates of ligating or resecting veins—even including the inferior cava!

to dicoumarol causing the skin eruptions—or for matter any toxic manifestations except hæmorrhage solutely No, Professor Boyd and Mr Foote No, r!—with hardly a *Pinafore* qualification

e make a distinction between "thrombophlebitis" milk leg) and "phlebothrombosis" The former elf explanatory, implying an inflamed vein with ing of blood within the vein This condition rarely es embolism Apparently this is what Professor d refers to as "deep vein thrombophlebitis"

lebothrombosis refers to the almost silently developing vascular clotting developing, for example, in calf and deep veins Pulmonary embolism is fairly common his type—in fact it often occurs before evidence of lebothrombosis" is noted We in the New York (and I think through most of the country outside Boston) rely almost entirely on anticoagulants in e cases—beginning with heparin plus dicoumarol, dropping the heparin in two days or so when daily hrombin tests have shown that dicoumarol is becoming tive

arsdale, N Y, U S A **BERTON LATTIN**

THE NURSE'S RESPONSIBILITY

IR,—Your leading article of June 6 and the subsequent ers from Dr R E Smith (June 13) and two members the nursing profession (June 20) cover very rough und and anyone who joins in the discussion may well nble!

urely this new problem of how much a nurse should expected to do in the management of the sick patient et another expression of the increasing fear of litiga- which is dominating hospital policy and regulation fessional bodies in medicine and nursing, no less n the many hospital authorities, are seeking to tect themselves from persecution by their patients welter of circular letters issued by regional boards l by the Ministry itself is an endeavour to manage whole of medicine by regulation If the nursing ff—that is the trained staff—are to be restricted to t some would call the "maternal" aspects of sing, who then is prepared to undertake the scientific rk involved in modern treatment?

There is a gross shortage of house officers, consultant ncs are overloaded, waiting-lists are large, and many hospitals lack of operating-theatre accom dation restricts the turnover Medical treatment is m-work, and any member of the team, no matter at his or her official training has been, must surely be pared to undertake such tasks as are delegated by leaders of the team We are repeatedly hearing rnings that the nurse must not be turned into a on-registered doctor," but modern surgery in particular demands that skilled nursing must be based on scientific understanding Much of the nurse's interest in her work in the past has been lost by "parrot-wise" teaching in which the nurse has learnt the answers to questions she may be asked in examinations, but has had no real understanding of the meaning and purpose of her actions

Those who accept any part of the treatment of the sick must also accept responsibility which cannot be defined by rules and regulations Herein lies the difference between the clinical staffs of our hospitals and the lay administration, which, though it may fail to provide the personnel and facilities for adequate treatment, is always itself protected by the fact that it (the impersonal administration) has had no contact with, or personal responsibility for, the patient If the restrictive ideals which have now been suggested were put into practice, many of our hospital beds would be put out of action We are much dependent upon the work which our nurses undertake beyond their training syllabus, and indeed beyond the number of hours officially allotted for their duties Any suggestion of "working to rule" must never be allowed to come into our hospital service on the professional side, no matter how much we are *all* provoked by the many impositions placed on both medical and nursing staffs as the public and its legislators continue in their struggle to squeeze a quart into a pint pot

London S E 19 **D F ELLISON NASH**

IMMEDIATE RESULTS OF SANATORIUM TREATMENT

SIR,—In 1951[1] I described the results of treatment, judged by "sputum conversion," of male adult patients discharged from Colindale Hospital in the years 1938–50 These totalled 3332, but after deducting sputum-negative patients, and those whose stay was too short for conversion to be attained for three consecutive months before discharge, 2472 entered the survey

Up to 1947 the conversion-rate was below 29%, but it rose in 1948 to 36%, in 1949 to 55%, and in 1950 to 63% I attributed this improvement partly to the admission of less advanced cases, but mainly to the effect of streptomycin and *p* aminosalicylic acid

I can now bring the investigation up to date, by giving results for 1951 and 1952, during which 731 male patients have been investigated, of these 385 were sputum-positive and stayed long enough to satisfy the criteria for sputum-conversion The following is a summary of the results

Year	Sputum-negative	Sputum positive on admission		Converted	Total	% conversion
		Not converted	2/12-converted			
1951	170	64	10	111	185	60
1952	176	70	10	120	200	60

The conversion-rates of 60% attained for both years are slightly lower than for 1950 (63%), and, although I previously expressed the view that, as chemotherapy was now fully exploited, the curve was likely to flatten out, this actual fall, though slight, deserves some explanation especially in view of the introduction of isoniazid in 1952

The above summary shows that in 1951 and 1952 no fewer than 346 patients (47%) were sputum-negative In 1950 the corresponding proportion was 37% and in previous years it was 22% or less Of the 176 sputum-negative cases in 1951, 121 (68%) had been sputum-positive at some previous date, commonly shortly before admission, and of 100 consecutive admissions

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1 Snell, W E *Lancet*, 1951, ii 415

(7) *What contra-indications do you consider exist to the use of the technique of "controlled hypotension"? Please state:*

Cardiovascular disease in general, or any thrombosis	48
Cerebrovascular disease	32
Coronary disease	62
Arteriosclerosis	51
Cardiac disease, valvular disease, angina pectoris, myocardial infarction, decompensation	46
Hypertension	43
Renal disease	48
Hepatic disease	8
Too old: more than 40–50 years	51
Too young: less than 16–20 years	30
Anæmia	18
Hæmorrhage, preoperative	10
Shock	18
Hypotension	22
Poor physical condition, dehydration, low blood volume, chloride loss, &c.	30
Type of surgery: "luxury," minor, &c.	55
Difficult posture required: non-Trendelenburg, steep Trendelenburg, lithotomy	9
Dangerous, inexperienced, slow, or old-fashioned surgeon	4
Inexperienced anæsthetists or difficulties in anæsthesia	14
Poor operating-room or postoperative facilities	6
Pulmonary disease	4
Neurological disease	2
Diabetes mellitus	4
Miscellaneous—obesity, pregnancy, acute toxic disease, &c.	15

(8) *Have you encountered any of the following complications? If so, please check opposite the complication, and state the number of times that each complication has arisen:*

Anuria	54
Oliguria	30
Cerebral thrombosis	20
Retinal thrombosis	2
Coronary thrombosis	15
Mesenteric thrombosis	0
Reactionary hæmorrhage	164
Delayed postoperative recovery	190
Difficulty with vision	126
Others (please state):	
Cardiovascular collapse	6
Cardiac arrest	6
Auricular fibrillation	1
Ventricular fibrillation	1
Sudden blood-pressure drop	5
Pulmonary embolism	1
Air embolism	1
Hypoglycæmia in diabetes	2
Persistent hypotension	3
Ileus	1
Paralysis of bladder	1
Casts in urine	3
Spinal arachnoiditis	1
Vague cerebral anoxic states	3
Postoperative mental confusion	3
Postoperative lassitude	4
Prolonged drowsiness	3
Painful back and legs due to position	7
Total (1 in 38 cases)	553

(9) *Have you encountered mortalities with the use of the technique of "controlled hypotension"?*

Yes	37
No	130
No, but have knowledge of deaths	11

If "Yes," please state the number of cases and the presumptive causes of death:

Renal failure	8
Cerebral thrombosis or cerebral anoxia	11
Coronary thrombosis	7
Cardiac arrest or failure	6
Reactionary hæmorrhage	2
Mismanagement (high spinal)	2
Over-heparinisation (arteriotomy)	1
Sudden death, cause unspecified	1
Death, cause not stated	1
Miscellaneous (4 probably unrelated)	7
Total (1 in 459 cases)	46

SUMMARY

Questionnaires were sent to 602 members of the Association of Anæsthetists of Great Britain and Ireland concerning the use of "controlled hypotension" in anæsthesia. Of these questionnaires 289 (48%) were completed and returned, 178 anæsthetists reporting the use of the technique in more than 21,000 cases.

The results of this questionnaire should by no means be construed as an indictment of "controlled hypotension." When wisely used, in the carefully selected case, for an urgent and rational indication, the technique may prove most beneficial for a given patient.

However, a mortality-rate of more than 1 in 500 indicates that this technique is potentially dangerous, and it should therefore never be used in the absence of a specific and urgent indication or for the convenience of surgery. Obviously, it must never be used by the unwary, the unknowing, or the unskilled. Further, it is specifically contra-indicated in certain conditions; these contra-indications must be respected.

"Controlled hypotension" is indeed "physiological trespass"—the anæsthetist can never afford to forget this fact.

We are indebted to Dr. Georgina Y. Goodwin, resident in anesthesiology, for invaluable assistance in the tabulation of the figures.

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THE PRACTITIONER IN THE N.H.S.

The Minister's Appeal

ADDRESSING the Annual Conference of Local Medical Committees, held in London on June 17, Mr. IAIN MACLEOD, the Minister of Health, said that when Sir Stafford Cripps in 1950 found it necessary to impose a ceiling on expenditure on the National Health Service, it became obvious that, with costs of all kinds tending to rise, we should sooner or later be forced into the position of selecting priorities. This was a problem that went wider than the health service.

"I made a rough calculation a week or two ago which told me that I could justify to the House of Commons and to the country, if medical need alone were the criterion, a capital programme of something like £1000 million, taking no account of the many hundreds of millions of pounds on maintenance expenditure that would involve in other years. But so, of course, could the Minister of Education in her field; so could the Home Secretary with all our needs for new prisons and institutions to replace some of our outmoded buildings; so could the Minister of Housing and Local Government and the Minister of Transport for the roads and so on."

If too much was spent in any particular field there would be all the less available for the more essential services.

THE DRUG BILL

Were we getting full value for the £40 million spent on prescriptions by general practitioners? (Taking into account the whole range of drugs, medicines, and appliances the figure was more like £60 million.) Partly because of fog, flood, and influenza, it had been very taken at random at least 60 had received "chemotherapy" either at home or in other hospitals before admission In other words, those cases which were amenable to conversion by bed rest and chemotherapy had been converted before admission, leaving a more resistant group to enter this survey

A factor hindering improvement in conversion-rates is the number of middle aged (over 45) patients who, because of delayed diagnosis with resulting irreversible changes in the lungs and chronic respiratory disability characteristic to their years, and consequent unsuitability for surgery, often constitute insoluble problems in treatment My 1951 paper showed that the chances of conversion regularly receded with advancing years, and the new figures, though small, support the previous findings

CONVERSION BY AGE GROUPS 1951 AND 1952

Age (years)	Not converted	2/12 converted	Converted	Total	% conversion
Under 20	5	1	11	17	
20–29	30	6	94	130	72
30–39	37	5	67	109	61
40–44	16	2	22	40	55
45 and over	46	6	37	89	42
Totals	134	20	231	385	60

In view of changing fashions in treatment, it may be again of interest to note the methods by which conversion was attained, but the increasing complexity of treatment makes classification ever more difficult The accompanying table indicates the broad lines by which success was achieved Comparing the two years, the second shows fewer conversions by artificial pneumothorax and thoracoplasty, a static number by plombage, and more conversions by resection and especially (perhaps surprisingly), by pneumoperitoneum, which was of course associated in most cases with chemotherapy. Over the previous twelve years the main treatments producing conversion were artificial pneumothorax 35%, routine treatment 21%, and thoracoplasty 17% Owing to the widespread use of chemotherapy and the greater variety of surgical treatment, conversions by routine treatment alone are now very few, but the sanatorium régime nevertheless remains, for all patients, the fundamental basis of treatment

Summary —In this investigation sputum conversion is held to have taken place when the sputum has been found free from tubercle bacilli on direct examination and culture, for the three consecutive months preceding discharge (Patients converted for the final two months only are also recorded but are considered as unconverted) Of 385 sputum-positive patients treated at Colindale in 1951 and 1952 231 (60%) underwent conver Of the 346 sputum-negative patients admitted du this period, approximately 68% had been sput positive shortly before admission they had under conversion mainly by "chemotherapy," leaving a tively resistant group who were still sputum posi when admitted Of the sputum-positive patients 2 were aged 45 or over—the group least susceptible conversion Comparing the last two years at Coln more conversions have been obtained by resection pneumoperitoneum, and fewer by artificial pneu thorax or thoracoplasty

Colindale Hospital,
London, N W 9

W E SNELL

TREATMENT USED IN CASES SHOWING CONVERSION

Treatment	1951		1952		1951 and 1952
Artificial pneumothorax (right)	8	28 (2 had P P)	8	17	45
" " (left)	11		5		
" " (bilateral)	9		4		
Thoracoplasty (right)	25	36 (1 had contralateral A P, 1 had P P)	13	28 (2 had contralateral A P 1 had contralateral plombage)	64
" (left)	11		15		
Resection (partial)	8	10	11	18 (2 had contralateral A P, 1 had phrenic crush)	28
Pneumonectomy	2		7		
Plombage (right)	7	11 (2 had contralateral A P, 1 had phrenic crush)	6	15 (1 had contralateral thoracoplasty 2 had contralateral A P 1 had P P)	29
" (left)	6		7		
" (bilateral)	1		2		
Extrapleural A P	1	1	0		1
Pneumoperitoneum	12	12 (4 had phrenic crush)	29	29 (1 had phrenic crush)	41
Chemotherapy alone	9	9	11	11	20
Routine	1	1	2	2	3
Total	111*		120†		231

* 73 had "chemotherapy" in addition † 99 had chemotherapy including 20 treated with isoniazid
A P = artificial pneumothorax P P = pneumoperitoneum

MEDICAL HISTORY OF THE SECOND WORL WAR

SIR,—In your review (June 13) of the *Medical Hist of the Second World War* you remark that the book unlikely to raise the pulse rate of many of those served under the motto *Per arduis fidelis*

I think it possible that the blood pressure of m of those who served in the R A M C (at any rate of th who have had the advantage of a classical educati may be raised, when they see their noble motto so vi misquoted

Wakefield

G E MACALEVLY.

*** We apologise for our inadvertence The mo is, of course, *In arduis fidelis* —ED L

OBSERVATIONS ON PEPTIC ULCER

SIR,—It is not for me to discuss the physiologi aspects of Dr Csato's original and stimulating let (May 16) But may I draw attention to the cruc change of attitude towards a certain interesting group diseases implied in his approach ?

The emphasis he places on periodicity as opposed t the static evidence of the X ray plate has a relevan far wider than merely to the treatment of peptic ulce It adds, in fact, the fourth dimensional quality o time/motion to the consideration of those diseases i which periodicity plays a major part As he rightl claims, periodicity is a factor which has often been noted, but in treatment consistently ignored

Among philosophers Heraclitus, echoed centuries late by Bergson, has compelled recognition of time and motion as prime factors in the structure of the Universe, and it is now some time since physicists discovered, to their temporary confusion, that the weights of certain things were different when in motion than when at rest But medicine, as far as treatment is concerned, doggedly persists in its static, three dimensional approach

TABLE V—WORK DONE BY THE MEDICAL OFFICER

—	Children not needing treatment					Children needing treatment		Total
	Routine examination only	Mother reassured	Mother advised about:			Treated at clinic	Referred	
			Feeding	General management	Priorities and certificates			
ningham ..	10·5 % (*58*)	16·6 % (*92*)	25·7 % (*142*)	6·5 % (*36*)	1·8 % (*10*)	22·1 % (*122*)	16·8 % (*93*)	100 % (*553*)
cley	11·4 % (*62*)	15·7 % (*85*)	17·5 % (*95*)	4·6 % (*25*)	7·7 % (*42*)	33·7 % (*183*)	9·4 % (*51*)	100 % (*543*)

Of the 43 children who attended in Birmingham, 17 re referred by health visitors to the doctor, whose rk consisted of routine examination of the child and, here necessary, reassurance of the mother (4), advice out feeding, management, or priorities (6), treatment), and referral (3). In Coseley, on the average 52 mothers tended with children, of whom 14 were referred to the octor. The work of the doctor consisted of immunisaon (5), examination and reassurance (2), advice (3), eatment (3), and referral (1). The work of health isitors was not examined in detail; it comprised advisory ervice, routine weighing, simple treatment, and selection f cases for referral to the medical officer.

VALUE OF THE SERVICES

The work of the clinics evidently still consists essentially f the four traditional services: food distribution; advisory ervice; routine examination; and medical attention. t is difficult to assess their value, which has recently been uestioned (Banks 1952), since no objective data exist by hich their work may be measured. Their development as coincided with a reduction in mortality-rates; but n the same period there have been other changes likely o improve the health of children—for example, a decrease n mean family size, improvement in the standard of living, nd, more recently, the introduction of effective therapy. We must therefore rely on a common-sense appraisal of ach type of service. Probably no-one would question the importance of the food distribution and medical attention, but the advisory service and routine examination require further discussion.

TABLE VI—ADVICE GIVEN TO MOTHERS ABOUT FEEDING

—	Birmingham	Coseley
Veaning	17·6 % (*25*)	16·8 % (*16*)
laintenance of breast-feeding ..	13·4 % (*19*)	23·2 % (*22*)
upplementary, complementary, and test-feeds	20·4 % (*29*)	15·8 % (*15*)
egurgitation, wind, looseness, and constipation	12·7 % (*18*)	7·4 % (*7*)
ther and unspecified problems ..	35·9 % (*51*)	36·8 % (*35*)
Total	100 % (*142*)	100 % (*95*)

Whatever reservations one may have about the usefulness of some of the activities currently promoted as health education, there can be little doubt that the instruction of an uninformed mother by an experienced health visitor or doctor is valuable. Breast-feeding, bowel-training, preparation of artificial foods, and weaning are not matters in which it is possible to rely either on a mother's instinctive good sense, or on the advice given by friends or relatives. A few women in favourable circumstances have received suitable instruction elsewhere—mainly from private doctors—but most women have obtained it from clinic medical officers and health visitors, or not at all.

TABLE VIII—CONDITIONS REFERRED ELSEWHERE

Conditions	Birmingham	Coseley
Bronchitis, pertussis, early pneumonia, &c.	10·8 % (*10*)	41·2 % (*21*)
Diarrhœa and vomiting, threadworms, pyloric stenosis, &c.	8·6 % (*8*)	11·8 % (*6*)
Eye deviation, conjunctivitis, blepharitis, &c.	11·8 % (*11*)	19·6 % (*10*)
Dental caries	15·1 % (*14*)	2·0 % (*1*)
Otitis media	16·1 % (*15*)	7·8 % (*4*)
Hernia or phimosis	4·3 % (*4*)	3·9 % (*2*)
Other conditions (orthopædic and skin conditions, cellulitis, injuries, P.U.O., &c.)	33·3 % (*31*)	13·7 % (*7*)
Total	100 % (*93*)	100 % (*51*)

On the value of routine examination opinion will inevitably be divided. Regular medical inspection has always been a feature of the child-welfare movement, and is generally believed to serve two purposes—early detection of remediable disabilities, and collection of anthropometric data. Our own view is that the data collected have hitherto been of little scientific value, but

TABLE VII—CONDITIONS TREATED AT CLINIC

Condition	Treatment	Birmingham	Coseley
Umbilical hernia	Strapped	11·5 % (*14*)	29·5 % (*54*)
Umbilical polyp	Copper sulphate, silver nitrate	3·3 % (*4*)	2·7 % (*5*)
Phimosis	Prepuce separated	15·6 % (*19*)	28·4 % (*52*)
oryza and bronchitis	Narist. ephed., or menthol	16·4 % (*20*)	3·8 % (*7*)
kin conditions (napkin and teething rashes, seborrhœa, impetigo, scabies, &c.)	Lot. calamin., ung. H.A.D., crem. zinc. et ol. ric., applic. benzyl benzoate	23·0 % (*28*)	10·4 % (*19*)
Gastro-intestinal conditions (diarrhœa, vomiting, constipation, flatulence, threadworms)	Tab. sod. cit., tab. hyd. c. cret., tab. gent. violet, milk of magnesia	13·1 % (*16*)	9·8 % (*18*)
Debility (post-operative, -portussis, -pneumonic, &c.)	Syr. ferri. phos. co., syr. ferri et ammon. cit., maltoline	7·4 % (*9*)	5·5 % (*10*)
Other (eyes, teething, maternal anæmia, &c.) ..	Ung. hyd. ox. flav., tab. ferrous sulph.	9·8 % (*12*)	9·8 % (*18*)
Total		100 % (*122*)	100 % (*183*)

TABLE II—PROPORTION OF CHILDREN REFERRED BY HEALTH VISITORS TO THE MEDICAL OFFICER

—	Children referred to M O	Children not referred to M O	Total
Birmingham	39 4 % (*553*)	60 6 % (*850*)	100 % (*1403*)
Coseley	26 8 % (*868*)*	73 2 % (*2367*)	100 % (*3235*)

**Of 868 children referred to the Coseley medical officer 325 immunised against diphtheria have been excluded from subsequent tables*

of children attending per session were 43 and 52 and the average numbers seen by medical officers 17 and 14 Table III gives reasons for referring children to the doctors (Children referred for immunisation in Coseley have been excluded) About a third had been sent for routine examination In both local authorities a child paying its first visit to a clinic is automatically referred for medical inspection, but after the first visit practice differs in Coseley children see the doctor again only by special request , in Birmingham they are referred for medical supervision about once in three months There is a considerable difference in the proportions seen at the request of health visitors (Birmingham 19%, Coseley 1%), which suggests that part of the work done in Birmingham by medical officers was performed in Coseley by health visitors

More than 40% of the children medically examined had been sent *to the medical officer at the request of the* mother Since the National Health Service Act has removed the economic reason, we asked why these mothers chose to consult the clinic medical officer rather than their own general practitioner (table IV) More than 40% of the mothers had not considered the possibility of consulting their own doctor A further 10% had attended the clinic to collect food or to have the child weighed, and, having some minor problem, " thought they might as well see the doctor there about it " The remainder (almost half) gave reasons suggesting dissatisfaction with their general practitioner service the surgery was too far away , a crowded surgery was no place for a child , afternoon consultation was more convenient , or the doctor was abrupt, rude, or too busy to make even a cursory examination

WORK OF THE CLINIC MEDICAL OFFICER

Table V gives details of the work done by clinic medical officers Some children (73 and 71 in Birmingham and Coseley respectively) had more than one service but we have considered only the more important service

Routine Examination —About 10 % of the work done by the medical officers consisted in routine examination of children so healthy and well-cared for that no advice was considered necessary That is to say, 120 of the 338 children submitted for routine examination (table III) were thought to need no service of any kind

Reassurance —About 16 % of children had minor ailments—sometimes real, sometimes imaginary—for which no treatment and little specific advice was needed (coryza, transient skin conditions, and minor general complaints)

Advice —About a third of the mothers (34 0 % in Birmingham and 29 8 % in Coseley) were advised about the feeding and general management of their Table VI gives details of the kind of feeding problem which advice was sought—e g , weaning, breast fee or complementary feeding Under " general ma ment " (table V) are included instructions conc napkin hygiene, clothing, physical activity, and bladder, and sleeping habits Also included " advice " in table V are cases in which the medical issued certificates or advised about priorities Birmingham and Coseley 1 8 % and 7 7 % were of this type In both local-authority areas chil were certified as fit to enter day or residential nur and notes were written to expedite hospital In Coseley the doctor, as medical officer of health, also concerned with the rehousing of families for med reasons, and with the issue of free infant food necessitous families

TABLE III—REASONS FOR REFERRING CHILDREN TO THE MEDICAL OFFICER

—	Routine examination		Specific request by				T
	First visit	Quarterly supervision	Clinic M O	Health visitor	Mother	Hospital or G P	
Birmingham	11 6 % (*64*)	16 3 % (*90*)	11 2 % (*62*)	19 2 % (*106*)	41 4 % (*229*)	0 4 % (*2*)	[illegible]
Coseley	33 9 % (*184*)		17 1 % (*93*)	0 7 % (*4*)	46 8 % (*254*)	1 5 % (*8*)	[illegible]

Treatment at Clinic —In Birmingham about a fift (22 1 %) and in Coseley a third (33 7 %) of children we treated at the clinic Table VII shows the conditions dea with—e g , umbilical hernia or polyp, phimosis, mil respiratory infections, and napkin and teething rash The official attitude towards treatment *in child* welfa clinics has always been that a child needing anythi more than the most trivial attention should be refer to his own doctor, and clinics in general stock only few simple medicaments

Referral —Finally, 16 8 % and 9 4 % of Birmingha and Coseley children respectively were referred elsewher for conditions similar to those met in the consulting roo of the general practitioner—e g , pneumonia, whoopin cough, diarrhœa and vomiting, conjunctivitis, otit media, and cellulitis (table VIII) Most of these patient (72 % in Birmingham, and 92 % in Coseley) were referre to their general practitioner ; a few were sent directly to hospital, or to local authority dental or remedial clinic

Discussion

We may summarise the results of the foregoin analysis of the work of child-welfare clinics as follows

In Birmingham, on the average 101 mothers attended each session, of whom 51 bought food at the branch food office, and 50 entered the clinic proper Of the 50 who entered the clinic, 7 attended without the child to obtain priority foods 43 attended with the child, of whom 20 came to have it weighed, 8 to get specific advice, and 15 to obtain priority foods Of the 15 who came for foods, 11 wished also to have the child weighed, and 2 to have advice about its management It is clear that whatever the official view of the clinic's function, the distribution *of cheap food* is still an important incentive for attendance

TABLE IV—REASONS GIVEN BY MOTHERS FOR NOT CONSULTING A GENERAL PRACTITIONER

—	Not considered by mother	Attending clinic for other reasons	Clinic hours or location more convenient	G P too busy	Advice wanted about need for consultation	No confidence in G P	Other and unspecified	Total
Birmingham	44 1 % (*101*)	11 1 % (*26*)	9 2 % (*21*)	5 2 % (*12*)	7 4 % (*17*)	21 8 % (*50*)*	0 9 % (*2*)	100 % [illegible]
Coseley	40 6 % (*103*)	10 6 % (*27*)	7 9 % (*20*)	5 9 % (*15*)	11 8 % (*30*)	21 7 % (*55*)*	1 6 % (*4*)	100 % [illegible]

* 9 Birmingham and 3 Coseley mothers had already consulted their general practitioners but were not satisfied with his advice

that most temporal and motionable of entities—the human organism. The real originality of Dr. Csato's contribution will not, I hope, be sidetracked as just one more therapeutic suggestion for a single ailment.

London, W.1. ALAN McGLASHAN.

HOSPITAL COSTING

SIR,—The letter from "Administrator" (June 20) calls for a response from me. I read with interest that he assumes that I am "unaware not only of the lessons of practical accounting but also of the important psychological advantages that can flow from purposeful accounting in terms of individual responsibility."

I had some ten years' experience of practical accounting, both in the profession of accountancy and in industry. During this period I became a chartered accountant, and subsequently engaged in reorganisational work in large-scale industry—particularly in connection with clerical routines. All this was years ago, but the essential problems are still much the same; punched-card routines, the problems of the unreliability of primary data in costing schemes (time-sheets, &c.), the difficulties of seeing the wood for the trees—these are still features of the accounting landscape.

"Administrator" appears to be defending the principles of cost-accounting against the ill-informed doctor; I sympathise with his imagined predicament, but I am sorry that he should thus misunderstand my article (May 16), for I am primarily interested in achieving real coöperation between doctors and administrators. His anxiety to defend himself against imaginary attack leads him to make criticisms which are I think unjust. I devoted some space to emphasising the need for extracting items of expense which were controllable by the individuals concerned, so that individual responsibility should be fostered; yet "Administrator" accuses me of being unaware of this necessity!

He considers that my object of "providing a corrective to any too-enthusiastic adoption of detailed schemes" is at variance with the title of my article; I cannot see this. This criticism would be valid only if my object had been the exclusion of anything to do with costing from hospital accounting.

The terms "subjective" and "objective" in costing parlance are quite clear in their meaning to accountants and administrators—but my article was addressed primarily to doctors, and they might be forgiven if they expected these words to have the meanings assigned to them in ordinary speech. Hence my brief explanation that, in costing practice, each operated as an extension of the other. My simple little diagram to illustrate this process was introduced solely for this purpose; your correspondent's attempt to read into this diagram a detailed scheme, as if a costing system were a huge grid of rows and columns in a literal sense, is surely unjustified; I cannot believe that he really thought I meant just that.

It is true that "to accent the objective classification of expenditure does amount to a fresh outlook"—but the *freshness* of this change is felt mainly by those trained in the subjectively orientated accounting systems. The idea was fresh to me, twenty years ago—but lay people do not suffer from the disadvantages of such a training, so there was no need for me to labour the point in an article addressed to doctors.

Your correspondent's grumble that (in my suggestion that statistical statements should be adapted to the various tiers of administration) I omitted to mention the individual hospital, is unfounded: I referred to the obvious fact that hospital management committees review the costs of running "the various separate clinics and hospitals within their group."

Possibly my warning against the misuse of costing systems was "platitudinous"—but maybe I shall be forgiven, for it was also "no doubt much needed." Just how much this warning may be needed in the future is problematical, but I may refer "Administrator" to one of the three reports on hospital costing now available, in which he will find that the detailed time-study of surgical operations is envisaged as part of an interesting research project. Is it impossible that this might lead some readers to suggest that, for example, a subtotal thyroidectomy should take x minutes? Can your correspondent not see that some enthusiastic technicians in time-and-motion study might write down as "unproductive time" that interval in which the surgeon is not visibly acting, but thinking?

It is precisely *because* I have seen the enthusiast in action that I warn my colleagues against this kind of "too-enthusiastic adoption of detailed schemes."

I assure "Administrator" that I normally use the right end of my microscope; but, if some costing enthusiasts had their way, I might find myself having to take a bus journey to another laboratory to visit the microscope installation, there centralised so that a shift system could be operated—"thus raising to a more satisfactory level the percentage usage of the instruments" (I quote from a possible future Costing Report to the Minister).

To be serious, I repeat my plea that doctors and administrators should discuss the whole problem. No-one likes being administered, and no-one likes being ill; but administrators and doctors are often quite pleasant people. Both have problems—and opportunities—of avoiding the most irritating features of costing systems in the context of hospital work.

Let it be recognised that there is a likelihood that doctors may be a little on the defensive (or just not interested) in relation to costing schemes; and that administrators also may be a little sensitive when alterations in accounting procedures are contemplated. If this is the situation, then surely informed discussion will clear the air?

London, N.W.3. A. F. MOHUN.

SIR,—Mr. R. S. Murley (June 6) takes me to task for suggesting that low bed-occupancy rates imply inadequate use of hospital beds. I can best reply by quoting the experience of our hospital in recent years. Pressure on our beds had greatly increased, as the number of new outpatients referred to us had gone up by 20% a year. Nevertheless, without an increase in beds, we have done much towards dealing with the resulting increased demand for admissions. This has been done by raising the bed-occupancy rate and by reducing the average length of stay, *without any apparent loss of medical efficiency.* The following figures are quoted from the last available annual report (1951):

—	1949	1950	1951
Beds			
Complement at end of year ..	853	862	862
Daily average number of beds occupied	769	806	807
Percentage of available beds occupied	90·15	93·5	93·6
Discharges and deaths during the year	13,684	14,431	15,639
Average length of stay (excluding confinements, pulmonary tuberculosis, mental observation, and chronic sick) in days	18	17·05	15·85
Outpatients			
New patients (excluding casualty)	24,355	30,254	34,089

The changes in the indices may not appear impressive until it is appreciated that, with virtually the same number of beds, we have admitted a further 2000 patients a year—an increase of 15%, and equivalent to building a 100-bed extension. This achievement has been made possible by having a whole-time admission officer and a geriatric physician, by the careful planning of elective that the discovery of disability has possibly justified the cost of the examinations Whether these examinations could equally well be conducted by health visitors is another question

FUTURE ORGANISATION

In spite of some reservations about *routine examinations*, we do not share the doubts which have recently been expressed about the present usefulness of the clinic services What seems to us to be in question is not their value, but the efficiency of their organisation under the National Health Service Act

Before considering their future organisation it may be helpful to state three principles which would probably be generally acceptable.

(1) It is unnecessarily expensive for doctors to undertake duties which can equally well be performed by health visitors

(2) It is undesirable to divide between more than one doctor personal services which are well within the competence of a single doctor, or could be made so with slight modifications in his training or experience

(3) The supervision and treatment of children can be conducted more satisfactorily from a local-authority clinic or health centre than from a general practitioner's surgery

There is little in the advisory work of the clinic doctor which could not equally well be done by the health visitor Indeed the conditions for which medical advice was given (weaning, maintenance of breast-feeding, complementary feeding, &c) are those with which the health visitor has been trained to deal, and undoubtedly would deal if no doctor were present During the late war many clinics were run by health visitors without medical assistance It therefore seems reasonable to suggest that if alternative arrangements were made for the strictly medical functions of the clinic (treatment, referral and possibly routine examination), the other services (food distribution, regular weighing, and advice) could be conducted by health visitors without a doctor More emphasis could profitably be placed on the domiciliary work of health visitors, since there is still force in the criticism that the clinic is most regularly attended by mothers least in need of advice

The fact that the preventive and curative personal services are still divided between local authority medical officers and general practitioners is well known What is not generally appreciated is that clinic doctors give a substantial amount of treatment of 1096 children seen in Birmingham and Coseley 279 (25%) were treated at the clinics and 130 (12%) were referred elsewhere

The *principle that all general medical services* for children should be undertaken by the same doctor seems unexceptionable Moncrieff (1950) has written of the infant-welfare service "Its medical officers should logically be the family doctors who will be carrying out the work in the homes as well as at the infant welfare centres" Moreover it is easy to see that such a proposal could be realised at health centres Parsons (1947) looked forward to the time when "among a group of medical practitioners working at a health centre, there will be *some who are keen on work* amongst children, whereas there will be others who will be glad to hand over their care of the children, both in health and disease, to their colleagues The former in time will come to be regarded as the pædiatricians of the centre, and specialize more and more in this work" The question is whether all progress in this direction must wait upon the appearance of health centres

It seems to us that it need not Some general practitioners already do their antenatal and postnatal work at local authority clinics, and there is no obvious reason why at the same sessions they should not provide a comprehensive service for children on their lists These services might include medical consultation, treatment, immunisation, vaccination, such routine inspection as is considered necessary the extent that the services go beyond those he has hitherto provided, the general practitioner should receive additional payment Probably the most satisfactory means of arranging this within the present administrative framework would be to pay an increased capitation fee for children to practitioners prepared work at the clinics and to provide a full child health service It has been objected that few of them are at present equipped to give such a service, and certainly the present inquiry suggests that many mothers are dissatisfied with the service offered by general practitioners to their children But we must begin somewhere, and unless circumstances are created which provide general practitioners with the incentive and opportunity to do this work, it seems unlikely that their training and experience will progress very rapidly

It would be wrong to end this discussion without some reference to the future of the clinic medical officers For many years they have provided a service for a substantial section of the child population when it was available from no other quarter Some of them have thus acquired from experience, if not from formal postgraduate training, a considerable knowledge of children's diseases If their responsibilities are eventually to be taken over by general practitioners, it seems reasonable to propose that the more experienced clinic medical officers should be given the opportunity to find a place within the new class of general practitioner pædiatrician which will in time emerge Such an arrangement would help to ensure a continuity of service, and the unification of the preventive and curative personal services would finally remove an anomaly which owes its origin to circumstances which no longer exist

Summary

An examination of the work done at child welfare *clinics in Birmingham* shows that on the average 101 mothers attended each session, of whom 51 bought food at the branch food office, and 50 entered the clinic proper Of the 50 who entered the clinic, 7 attended without the child to obtain priority foods, 43 attended with the child, of whom 20 came to have it weighed, 8 to get specific advice, and 15 to obtain priority foods Of the 15 who came *for foods, 11 wished also to have* the child weighed, and 2 *to have advice about its* management

Of the 43 children, 17 were referred by health visitors to the clinic doctor, whose work consisted of routine examination of the child, followed, when necessary, by reassurance of the mother (4), advice about feeding management, or priorities (6), treatment (4), and referral (3) Similar results were obtained in Coseley, an urban district with a population of 34,414

It is suggested that the advisory work of the clinic medical officer might now be taken over by the health visitor, and his medical duties (treatment, referral, and *routine examinations) by general practitioners* This could be done, in the absence of health centres, by paying an increased capitation fee for children on the lists of general practitioners prepared to provide a full child health service from local authority clinics The more experienced clinic medical officers might then be given the opportunity to find a place within the new class of general practitioner pædiatrician which would *in time emerge*

For permission to conduct this inquiry we are indebted to Dr Matthew Burn and the Public Health Committee in Birmingham and to Dr G Ramage in Staffordshire The work in the Birmingham child welfare clinics was greatly assisted by the generous coöperation of Dr Jean Mackintosh

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British Medical Journal (1909) Editorial i 1446
Moncrieff A (1950) *Brit med J* ii 795
Parsons I G (1947) Child Health London p 14

admissions by all members of the senior staff, by the excellent coöperation of the pathological and X-ray departments in the rapid introduction of new methods of diagnosis and in the control of treatment, and because the level of medical and nursing staffing was adequate.

The bed-occupancy rates reported in the Ministry's Annual Costing Returns, to which I referred in my previous letter, reveal extraordinary discrepancies between hospitals of a similar type doing the same class *of work. Even more striking* are the variations in the average length of stay (as yet unpublished). Taking five large general hospitals, in Greater London, chosen only for their similarity of function, the average length of stay *per patient* is recorded as 27, 25, 19, 19, 16 days, with bed-occupancy rates of 77·0, 89·6, 90·8, 82·0, 83·2 respectively.

I am fully prepared to admit that there may be important fallacies in relation to many of these mass hospital statistics. There may be a difference between the working total number of beds and the figures recorded by the hospital administrators; beds long since taken down may still appear in the administrative total from which the bed-occupancy rate may be calculated. The association of chronic or convalescent units must be taken into account. The lowest average length of stay for a large general hospital in this country is only 12 days, but this particular hospital has a big convalescent unit closely associated with it. It is important to distinguish between optimum and bare minimum length of stay; a shorter length of stay for a particular disease does not necessarily imply better treatment. While appreciating these fallacies, from my own personal observations I suspect that the wide variations in these indices mainly correlate with the numerical adequacy of the medical and nursing staff, and if this is so, it is important that it should be clearly and officially recognised.

My point, which I maintain is a reasonable one, is that in spite of possible *fallacies*, the wide *variations* in these indices, together with our own experience, suggest that some hospitals are using their available beds inadequately and that this is an extravagance which *the nation cannot afford. Hospitals are a particularly* expensive social service, and it is reasonable that every effort should be made to ensure that the maximum use is made of their facilities—particularly of beds related to the expensive ancillary departments.

Lay members of medical committees are perfectly right in raising queries about bed-occupancy and similar indices of hospital efficiency and in seeking assurance that the problem is being studied. However, they should realise that the subject is a complex one which can be dealt with adequately only by senior medical and nursing staff and the administrators—who must be prepared to recognise the existence of a problem and study its solution. Once any problem is defined, one is already half-way towards a solution. Simple measures may help enormously. In one large Midland hospital it was customary to discharge patients in the afternoon, and by a local nursing tradition the beds were not filled until the following day. By discharging patients in the morning and filling the beds the same day (except those for duty admissions), the hospital made some 6000 extra bed-days available each year—sufficient for the admission of another 300 patients.

Mr. Murley is quite wrong, I believe, in suggesting that an increased turnover almost inevitably means a fall in the percentage bed-occupancy. Indeed the reverse is the truth.

I wish to underline my previous statement that a general community hospital should have at least a 90% bed-occupancy and that 93% is perfectly feasible. My private opinion is that even this figure could be increased by further reorganisation; and indeed last month we recorded a 96% bed-occupancy. The wide application of our experience should result in an appreciable fall in waiting-lists. Mr. Murley says tha "unoccupied hospital beds are surely less of a extravagance than an unnecessarily occupied one." My point is that if there are these unoccupied beds, a suggested by the Hospital Returns and confirmed b Mr. Murley himself, they should be mobilised to dea with the national waiting-list, which stands at approximately 500,000. There is a strong case for every hospita medical advisory committee to review carefully its ow experience. I anticipate that the King's Fund repo will make many practical suggestions which could b implemented.

Central Middlesex Hospital,
Park Royal,
London, N.W.10.

F. AVERY JONES.

INJURIES OF SPINAL CORD

SIR,—In your annotation last week you refer experimental injuries produced in rats and dogs. Th you go on to state that "the direct trauma used these animal experiments is not really comparable wi the indirect trauma which commonly causes spi injuries in man." Of course it is not, nor is it like that early incision of the pia and posterior myelecto in cases of human spinal injuries will produce go results. I maintain that such experiments, apart fro causing needless suffering especially to dogs, is a she waste of time. My confirmed belief is that on the wh animal experimentation has become an obsession and not furthering our knowledge of practical medicine surgery.

Edinburgh.

JAMES BURNET.

PREVENTION OF POSTOPERATIVE CHEST COMPLICATIONS

SIR,—We would like to draw attention to a m quotation in Dr. Davidson's article last week.

According to this article, a description of the use benzocaine and urethane for the treatment of pain stumps was given by Ritchie Russell and Spalding 1950. There is, however, no reference to benzocai urethane in the article referred to,[1] which deals wi percussion therapy for painful stumps. The descripti of the use. and the principle underlying the mode action, of benzocaine urethane was published by Ko and Vitali in August, 1950,[2] following the article Ritchie Russell and Spalding.

As to the rationale of Dr. Davidson's method, it not clear why benzocaine should be first made up in o and injected separately before the urethane is introduc *Injected oil is not always well tolerated*; and there do not seem to be a necessity for introducing it, sinc benzocaine in a proportion of 2% is well soluble in a aqueous urethane solution and it can therefore b injected as such a solution. The effect is the same—i.e the formation of microcrystalline deposits of benzocai in the tissues. Benzocaine, being insoluble in water, almost immediately precipitated by the watery tiss fluids, and the urethane is absorbed.

In connection with the increasing interest in th problem of local anæsthetics of long action it migh be worth mentioning a few data. *Benzocaine* in urethar was first introduced, and its mode of action described, b *Rappaport*[3] *in 1946, and its clinical application* reporte by Spiro.[4] Following their publication a 2% solutio of benzocaine in urethane was manufactured by Messr Zori, of Tel Aviv, under the trade name of 'Prolonga Benzocaine.' Further reports were published by Drosel Rachet et al.,[5] Hirsch in Scandinavia, and others.

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1. *Brit. med. J.* 1950, ii, 68.
2. *Ibid*, p. 415.
3. *Acta med. orient.* 1946, 5, 115.
4. *Ibid*, p. 119.
5. *Ibid*, 1949, 8, 43.
6. *Arch. Mal. Appar. dig.* 1950, 39, 242.

tioners has already been mentioned in this column[1] Of course no one would expect acknowledgment in all cases The man who sends a patient straight to hospital with a scrawl "Buzzing in the pants ? piles" cannot expect to be immortalised when his colleagues Professor Katz and Mr Kittenz later publish An Unusual Case of a Mechanical Mouse in the Rectum But the good general practitioner who refers his patient to a hospital consultant as an act of consultation after doing his best, supplies an adequate history, and is responsible for the patient's pre- and post- hospital care, is surely entitled to some credit Moreover, such an acknowledgment might help to impress on hospital staffs that they deal with people, not cases, whose visit to hospital may be but an interlude in the family doctor's continuing and life-long effort to maintain their health

No doubt a dignified rebuke on college notepaper will do the trick

* * *

12TH NIGHT

The tumult and the shouting dies,
The devilled bones have been consumed,
All pudding spent, the cold mince pies,
With cakes and ale and sugar plums,
Have been engulfed and rest entombed
Uneasy in distended tums
Nothing remains of nuts but shells,
Nothing of tangerines but pips
For supper there is nothing else
But cœlacanth and chips

* * *

Crump! That was the door of the doctor's car I stopped smoking, switched off the wireless, and assumed the air of one fighting for life Relaxing afterwards, I recalled an earlier illness The purple warning then was the brisk plink-plonk of a pony, and the red was a round brass bell dangling from its neck The trap and its accoutrements were spotless Doctor and coachman were alike as two peas—silk hat, frock coat, moustaches and all I remember the tonsilloscopy by teaspoon and the rattle of starched cuffs when the thermometer was shaken

The bedroom wallpaper was an endless replication of roses, and a glass globe encased a fish-tail burner A jug stood in its bowl in front of heavy lace curtains By night I watched the flickering firelight on the ceiling By day I was visited by ladies in huge hats transfixed by pins and further secured by veils discreetly lifted to admit fancy cakes They sang *Sunshine and Butterflies* and *Little Grey Home in the West* But what are the wild waves saying today? They are saying *Moon over Madagascar*, a fantasia for electric organ We are back in England now!

* * *

A friend of ours who dabbles in psychiatry recently purchased a young horse, partly in order that his waistline could be held to the limits of his present wardrobe, and partly so that his children could add equitation to their other numerous accomplishments The animal has taken charge of the household very satisfactorily, and apart from a tendency to request admission to the warmth of the kitchen fire at inopportune moments, has settled in well For some time now our friend has been superintending the erection of a covered shelter of concrete blocks to protect the horse from the inclemencies of the English winter, and in this charitable work he has been assisted by a youth who has an aptitude for the compounding of concrete but little talent for conversation On several occasions our friend has observed the youth and the horse eyeing each other with undisguised apprehension, and finally he taxed his helper with an un-English lack of sympathy with the great family of *Equidæ* The unnatural boy readily agreed "You see," he explained, "my mother was frightened by a horse before I was born"

* * *

Overheard after lecture on rhesus factors—"Clear as blud"

Letters to the Editor

FROM TEACHING TO LEARNING

SIR,—Your leading article of Dec 27, d of the activities of the Commonwealth Fund in th of university medical education in the United prompts me to record some impressions I received recent visit The Fund invited me, as a former f of the foundation, to visit some centres where in medical education were under way Perhaps the enterprising is that taking place at Western Re University School of Medicine in Cleveland, Ohio I was fortunately able to attend the opening exer of the first year of the new curriculum

Eighty new students were enrolled The first days ("orientation period") were devoted to intro the students to the school and faculty, to the curriculum and modern medicine On the first day were the usual University Convocation, registrat physical examination, and photographing, and int ductory remarks by the dean of the faculty of medic On the morning of the second day, in the college amp theatre, the associate dean, a physician, described t *historical background of medicine*, the evolution of med education, the history of the Western Reserve Univers Medical School and its administrative organisati relation to hospitals, and finances This was informati explanatory, and put over in an able and pleas manner It was the first step As one doctor said to afterwards "Hell, it took me years to see that" In t afternoon the *new programme of medical education* described in more detail by a physician, a biochemi pathologist, and a surgeon Reasons, difficulties, an plans, and procedures were discussed Then an anatom talked of *the examination system* as a part of educati and the session finished with a discussion by a profe of preventive medicine on the *evaluation of medi education*

On the second morning there was first a discus by the professors of anatomy, pathology, and mic biology on the *importance of the basic sciences* (anato physiology, biochemistry, microbiology) in relation research, medical progress, and education The story diabetes was described The growth of our knowledge respiration, vitamin K, and immunology were used *illustrate the theme* Then followed a description, by t associate dean, of the *modern organisation of medi care* community agencies, hospital team work, a the rôle of the family physician (The term "gene practitioner" was not used)

In the afternoon the meeting-place was the univer hospital amphitheatre Here the associate dean, t professor of preventive medicine, and other member the staff cooperated in the *presentation of three patie*

The first patient told his story with the encouragement a assistance of one of the staff He had recently had an opera for mitral stenosis He described the vague symptoms rheumatism in childhood, the apparent cure, his surpris being rejected by an army board in 1941, his efforts at tr to find out what was wrong, the indifferent attitude of doctors and employers, the sympathy from a factory doc the endeavour of one firm to fit him in, the effect of worry a lack of money on the happiness of his home and sudde the tragedy of a cerebral embolism He recovered difficulties in earning his living, then symptoms of he failure, and finally unemployment and debt His state arrival in hospital, his attitude, physical capacity, sympto and signs were described and illustrated, and finally the g result achieved by dilatation of his mitral orifice was il trated He was back at work, paying his way, and ab care for his family All this was brought out in a simple a telling manner There were poignant moments and co ones too

The second case was of a young lady intern who contracted poliomyelitis while on hospital duty From

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[1] *Lancet*, 1951 i 853

In this hospital a benzocaine urethane solution, prepared in our own dispensary, has been used for a variety of orthopædic and surgical conditions since 1949.[2] The application of benzocaine urethane in upper abdominal surgery was reported by Winkler in 1951,[7] and in this country by Rutter in 1952.[8] It might also be interesting to note that first reports on another local anæsthetic of long action—namely, 'Efocaine'—were not published in the U.S.A. until 1952 (without, by the way, any references to the previous work on benzocaine urethane, the use and mode of action of which are based on exactly the same principle as efocaine).

Queen Mary's Hospital,
Rochampton.

J. KOHN
M. VITALI.

JUNIOR HOSPITAL STAFFING

SIR,—The article by Dr. Forrester in your issue of June 13 is very interesting and stimulating: but it is, I think, misleading in its comparison of the incomes obtainable by the whole-time specialist and the general practitioner. Out of his £3000 the latter has to find a considerable sum for expenses, while the former does not need to supply even a stethoscope or a sheet of notepaper.

The glittering prizes of the specialist are admittedly now very rare, but on the other hand the early years are surely much better than in the old days even allowing for the changed value of money. But was it the financial side of the glittering prize which induced a young man to take up a specialist career?

Wirral.

K. COBBAN.

LOCALISED MUSCULAR ATROPHY IN DIABETES

SIR,—I was interested in the comments of Dr. Harris-Jones (May 30) and Dr. Robertson (June 13) on the tentative view expressed in my note on isolated muscular atrophy in diabetes. On photographic rather than bedside evidence we are unlikely to agree as to whether a muscular component was or was not present in the lesions described. It is noteworthy that relatively non-fatty regions—the jaw and thumb—were involved in one case. In the absence of surgical exploration (a hole cannot be subjected to biopsy) doubt must exist.

However, the existence of "space-vacating" lesions in diabetes unrelated, at least in site, to insulin injections is not in doubt, although apparently it is not commonly recognised. To accept such lesions, again in the absence of histological investigation, as ectopic insulin atrophy is not entirely helpful. An explanation becomes necessary for an insulin effect which is simultaneously both localised and yet quite remote from the site of injection.

Royal Northern Hospital,
London, N.7.

CEDRIC HIRSON.

TROUBLESOME TAPEWORMS

SIR,—The course of treatment for tapeworm recommended by Dr. Asher (May 23) lasts 4–5 days and has to be carried out in hospital. Whilst serving with the R.A.M.C. at the 43rd General Hospital, I introduced the following simple treatment:

> The patient is admitted to hospital at lunch-time and is given a light meal. At 3 P.M. 2 teaspoons of magnesium sulphate are given as a purge. At 7 P.M. the patient gets for supper chopped herring with onions, 1 piece of toast, and a cup of tea without milk. At 6 A.M. *next morning* the patient is given 0·25 mg. of atropine, and at 7 A.M. a duodenal tube is introduced into the stomach. Every 10 minutes the tube should be advanced about 2 cm. until by aspiration with a syringe it is confirmed that it has passed into the duodenum. Now, 8–10 ml. of extract. filicis in 20 ml. liquid paraffin as an emulsion is passed through the tube into the duodenum. Usually at about 10 A.M. the complete worm is passed. If it is not passed by then a dose of magnesium sulphate should be given, followed 2–3 hours later by a high enema with fol. sennæ.

This treatment is completed in less than 24 hours and can be carried out in hospital or at home. I do not remember the number of cases we treated in this way, but it was quite considerable. There was never a failure.

Petah-Tiqvah, Israel.

E. FRANKL.

BREAD

SIR,—May I congratulate you on your leader last week, as well as on your able review of the controversy over flour improvers (March 21)?

Bread is the staple food of the population of Great Britain, and no economic change is likely to alter that. The quality of the national diet, based on this staple, itself contributes largely to the health, or morbidity, of our population. Experience shows that a diet based on whole wheat flour has kept other peoples relatively free from disease, and experiment has shown that diets of the same specification have also kept rats in health (R. McCarrison). Again, at the Rowett Institute near Aberdeen it has been demonstrated that not only deficiencies in the B group of vitamins but also inbalance of that group affects growth. The case for first-quality bread rests therefore not only on intuitive understanding but also on such experimental biological evidence as is available.

In his Sanderson-Wells lecture the arguments which Professor Dodds brings to the "brown versus white bread controversy" rest not on biological or medical experiment but on history, economics, and politics. What you call "economic and commercial convenience" stems no doubt from the vast capital investments in the milling and baking trades. It is in the interest of these investments that the present customs of their trades be maintained. Enlightened professional and public opinion is uneasy that the bread policy of the nation should be so largely governed by the investment policy of the past. Does this policy contribute to the high national morbidity? Let us say that we do not know, and then the best opinion will demand that we use every resource to find out.

It was disturbing to find Professor Dodds, with the secretary of the Medical Research Council in the chair, asking "who is going to do this work?" and opining that "the charge, surely, should not fall on public funds." If a question which touches the health of the whole population should not be a charge on public funds, and if other research endowment cannot finance such inquiries, the public must question the whole structure and administration of the moneys on which research depends. If those who have a virtual monopoly of the means cannot "do the work," then reform—which many of us believe is overdue—is surely called for.

With great respect, it seems to me a pity that Professor Dodds's review of the problem of chemicals and food should contain so little evidence of a scientific kind.

East Suffolk and Ipswich Hospital,
Ipswich.

K. E. BARLOW.

SIR,—May I congratulate you on your fiery and courageous leader last week, taking up the cudgels laid down by your illustrious predecessor Thomas Wakley a hundred years ago. It ought to be brought home to the public that the addition of the arbitrarily chosen "token" nutrients (aneurine, nicotinic acid, and iron) to white flour still leaves it with a lower (probably much lower) nutritional value than the 80%-extraction National flour.

While I agree with Professor Dodds about the importance of modern food technology, as a doctor I find it disturbing to see the chemical manipulation of food considered on the same level as technical advances in heating, housing, or transport. Have we to put up with agene and other "improvers" on a national scale only because the small baker in this country has been replaced by big-scale "plant bakeries"?

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[7] *Wien. med. Wschr.* 1951, 101, 692.
[8] *Brit. med. J.* 1952, ii, 1418.

reacted indifferently to cortisone, but 1 reacted extremely well The 4 patients who temporarily improved with butazolidine also improved rapidly with cortisone

G D **Kersley**
D **Watson**
J **Bremner**
J B **Millard**

Royal National Hospital for
Rheumatic Diseases,
Bath

PERFORATION OF COLON AFTER BARIUM ENEMA

Sir,—The two interesting case reports of accidental injection of barium sulphate into the peritoneal cavity [1] [2] stimulate me to offer a further case-report

A man, aged 62, was admitted to the West London Hospital on Oct 25, 1952, with complete intestinal obstruction The pattern of the distension suggested colonic obstruction with a possibility of volvulus of the sigmoid colon I therefore did a sigmoidoscopic examination, using the standard Yeoman instrument with the patient in the knee chest position No resistance was encountered, nor did he complain of more than mild discomfort No lesion was seen up to 8 in, and the instrument was removed

In order to locate the site of obstruction, radiography with a barium enema was arranged No sooner had a few ounces of the fluid been run into the rectum than the patient became pale, and sweated and complained of abdominal pain The examination was therefore stopped, no radiographs having been taken

Laparotomy was performed the same evening On opening the peritoneum it was found that it contained a considerable quantity of milky fluid, and that all the intestines, mesentery, and omentum were sugared with barium A ring carcinoma of the splenic flexure was found to be the cause of the obstruction, and the site of the perforation was a linear tear 1 in long on the antimesenteric border of the sigmoid colon, far below the growth, and about opposite the promontory of the sacrum

The perforation was sutured and a Senn Kader cæcostomy performed The patient's recovery was complicated by peritonitis and a very irregular pulse, but he stood very well a resection and end to end anastomosis of the splenic flexure three weeks later, and has made a good recovery

This case closely resembles one reported by Isaacs [3]

General Infirmary,
Leeds

A V **Pollock**

LIGATION OF THE POPLITEAL VEIN FOR THE GRAVITATIONAL SYNDROME

Sir,—Despite the somewhat guarded wording of the conclusions and summary to his paper last week, Mr Moore has none the less conveyed the impression that ligation of the popliteal vein is a procedure of some value in the treatment of gravitational leg ulcers

I would suggest that the facts recorded in his paper warrant no such conclusion He admits that in his experience popliteal vein interruption alone has generally not caused leg ulcers to heal He has therefore combined ligation with a period of bed rest and skin grafting and thereby completely confused the therapeutic issue It is of course well known that leg ulcers, whatever their cause, can almost invariably be induced to heal by strict bed rest and grafting alone without any interference with the veins The only way, therefore, in which the benefits of popliteal vein ligation might be revealed in Mr Moore's cases submitted to this combined treatment would be by a significantly lower incidence of recurrence of ulceration after discharge from hospital We are told that 7 of his 11 patients showed no signs of recurrence for periods from 9 months to 3 years I do not consider that these results are very different from what might be obtained after bed rest and grafting alone especially if the patients were careful to support the leg by an elastic stocking or bandage as apparently did most of Mr Moore's cases

My own experience of interruption of the deep venous system for leg ulceration due to old thrombosis or apparent valvular incompetence of the deep le has been confined to superficial femoral vein li but the principle of this operation and that of l of the popliteal vein is the same, and the results presumably also be similar I have now done 26 of operations, and, so that these patients might b up and about, the ligation was done in the outpa department, or was followed by at most 36–48 of hospitalisation Subsequently the patients att the varicose vein clinic for local treatment with U paste or elastic adhesive bandage It was thus pos compare their progress with that of other similar c treated only by bandaging There were variati usually quite unpredictable—in the rate of heal individual ulcers in both groups, but it could not claimed that in general the surgically treated g healed any more rapidly than the other, the time taken for complete healing was 9–10 month cases were particularly instructive, because they h ulcers on both legs and superficial femoral vein ligat was practised on one side only in each case, the oppo side serving as a control There was no obvious dif ence in the rate of healing in the two legs in ea case

These experiences have led me to abandon interrupti of the deep venous system in the treatment of leg ulcers

St Mary's Hospital,
London, W 2

J C **Goligher**

REPRESENTATION OF WHOLE-TIME SPECIALISTS

Sir,—On Dec 19 a deputation of representatives of t Association of Whole time Salaried Specialists met t staff side of Committee B of the Medical Whitley Counc and at that meeting matters affecting whole time offic in the National Health Service, including the questi of their representation on the staff side of Committee B were discussed [1]

In view of the well-known dissatisfaction in the min of whole time officers regarding the disparities whi have existed and still exist in their terms and conditio of service, as has been emphasised recently by mu correspondence in your columns, I should like to gi a brief résumé of the points which were put forward b our deputation to the staff side of Whitley Committee on behalf of whole-time consultants The following ar the particular matters to which we referred

1 The difference in remuneration between the two clas of consultants (whole time and part time) is $1^1/_2$ sessions or, expressed in cash on the basis of the top grade of salar £375 per annum

2 To offset this difference of £375 per annum, the part ti consultant has the following

(a) Private practice
(b) Payment for domiciliary visiting up to £840 per annum
(c) The right to claim mileage allowance from his home t consulting room
(d) The ability to claim, without difficulty, income ta relief for many items for which the whole time consultant cannot claim, such as subscriptions to learned societies, purchase of medical books and periodicals expenses of attendance at congresses and clinica meetings, and car and telephone expenses

3 The importance of car allowances for whole time consultants was stressed It was pointed out that a car i essential as all whole time consultants must be quickly available for emergency calls and domiciliary visits if agreed to be undertaken The same applies to telephone rentals At the request of the staff side, concrete instances were giv of the unsatisfactory mileage arrangements and the anomalies that arise out of them

4 It was pointed out that the Spens Report on Consultants (para 17, 6) in our view recommended that all specialists should be on an equal basis in regard to payment for domiciliary visits, and we asked for reconsideration of th interpretation of this paragraph

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[1] Serjeant J C B Raymond J A *Lancet* 1952 ii 1215
[2] de Loncka C P *Ibid* p 1246
[3] Isaacs I J *Amer med Ass* 1952 150 615 case 2

[1] *Brit med J* 1952 ii suppl p 231

It has occasionally been argued that the digestibility of bread prepared from high-extraction flour is inferior to that of white bread. I may have been particularly fortunate with my dyspeptic patients, but I hardly remember anyone suffering from peptic ulcer who could not enjoy whole-meal bread after proper instruction how to take it.

London, W.1. Z. A. LEITNER.

RELIEF OF MENTAL HOSPITALS

SIR,—May I suggest that, to relieve our overcrowded mental hospitals, every suitable general hospital should set aside two small wards each of, say, 10 beds for male and female patients with affective disorders whose condition does not necessitate treatment in a mental hospital. Patients with nervous disorders have as much right to be treated in general hospitals as maternity, surgical, or medical cases. A trained registrar could be put in charge of these psychiatric units and the work supervised by a visiting consultant. Minor psychotherapy could be carried out there, and refractory cases could be referred to a mental hospital.

The advantages of such a measure would not be limited to the relief of overcrowding. Patients with affective disorders are likelier to respond to treatment in a general hospital than in a mental hospital, where for the time being neurotic patients have to be mixed with chronic incurable cases. Moreover neurotic patients would escape possible stigma in the public's view for having been treated as "mental patients." Lastly, the general hospitals themselves would benefit; for house-officers would be able to familiarise themselves with the managemental of mental patients. The arrangement would bridge the artificial gap dividing those who treat physical disorders from those who treat mental disorders.

Powick Hospital,
Worcester. J. W. MULLNER.

THE ILLEGIBLE CANDIDATE

SIR,—Everyone will agree with Mr. E. W. Playfair (June 13) that bad handwriting is to be condemned. Everyone will also congratulate him on having learnt, at the age of 22, to write well after a few hours' lessons, spread over a few days, and will also admire his signature. My experience is, unfortunately, very different. When I was 21, I was told by Dr. Walter Morley Fletcher that, although he could read *my* writing, I *must try* to improve it. I spent the Christmas vacation going to Clark's College, Chancery Lane, three or four days each week, and was taught to write in the way the girls who were sitting for the Post Office examination wrote. I also practised hard for the next two years, and the legibility of my handwriting was greatly improved: but it was very difficult to maintain it in the stress of examinations and in writing notes at hospital on my knee. Now that I am old, I have writer's cramp if I do much writing. I can still write legibly if it is necessary, but it is a slow and painful process. My usual writing is bad.

The ability to write well varies as much as the ability to play games. Everyone seems to expect a boy or girl to be able to write well without any difficulty, though no-one expects people to be equally good at games. For instance, some people, having great ability, learn to play golf very easily, and soon reach a "handicap" of scratch; some after a few lessons likewise improve easily and reach a low "handicap"; others, like myself, after many lessons and much hard practice attain a moderate "handicap." Others, no matter how many lessons they have, or how much they practise, never attain a "handicap," and give up golf in disgust, and find some other means of taking exercise or spending their time. Unfortunately, people who cannot improve their handwriting still have to go on writing, and so distress the recipients of their letters especially when they
do not type their names under their signature
possible that if I had been taught by another
I might have written better; but I am afraid I
never have been a good writer. Similarly I
think any teaching would have made me a scratch

I have never consciously marked down a ca
either for his handwriting or his bad English, s
may make a very good doctor in spite of these dra
I once failed to read an examination paper for
degree because the candidate wrote his words a
above as below the lines, and his paper looked
series of small waves. I managed to decipher en
realise that he was talking sense, and my co-ex
and those who read his other paper agreed to gi
half marks, and let his fate be decided by the
and vivas. He passed very easily, and we request
he be told that his handwriting was very bad, a
he ought to try to improve it.

I hope *these* confessions of a notoriously bad
will support Sir John Conybeare's plea that bad
should not be penalised, though they should be
in the interests of the pharmacists and of their fri
write more legibly.

London, W.1.

GEORGE GR

SIR,—As an examiner, I have never been
worried by the bad manners of the illegible candida
I have often been surprised by his stupidity. *Ha*
by an illegible script, I feel that I ought to deduct
but I never do—consciously, at least. Bad handw
stamps a candidate as lacking in ordinary n
serious failing in any student who hopes to qualif
doctor. However, until examiners as a whole ag
this, and warn candidates in advance that illeg
will be to their disadvantage, it is not fair for indi
examiners here and there to exact penalties for bad
writing (let alone crude spelling, or the *inability* to
a clear English sentence).

The illegible candidate is a fool to treat his
examiner so. Let him envisage what happens t
scripts.

They arrive in two or three large parcels at the home
examiner—who is almost without exception a kindly,
pathetic human being. They make a rather bulky-l
pile, to be marked in time, and (if there are many whi
difficult to read) maybe against time. They probably r
on his desk until he gets home at the end of a day's
has his dinner, and settles into an armchair in front
fire. He starts with a sense of interested and, indeed, h
anticipation. Most candidates will not misunderstan
however, when I add, with great respect, that exami
scripts, in bulk, are not unduly inspiring reading.
examiner makes full allowance for this; but if by cha
comes upon a set of answers well and soundly set out in
handwriting and readable English, he warms to the cand
perhaps even a little excessively because of the contr
the "general form."

Sooner or later comes the inevitable unreadable
writing. The examiner stumbles *on for a sentence or tw*
then comes across a word which he cannot recognise
turns the page through various angles in the effort to de
it; he re-reads the previous sentences to see if they wil
him to the sense of the word; or he *may* even ask his
opinion (if, indeed, she has not already gone to bed). E
time it has been deciphered, he has probably forgotten
the candidate has said earlier. "Blast this chap," he m
good-humouredly, "why wasn't he taught to write pr
at school?" But he stumbles again, and again, an
again, loses the thread of the argument, re-reads, and
even have to make notes on paper, to ensure that he will
the candidate's meaning, and to assess whether he has co
the essentials of any proper answer to the question.
examiner, poor chap, has taken three or four times as lo
go through this paper as through a normal *one*, wit
altogether needless expenditure of energy. If he is as adm
as some of my friends who *have contributed to* this discu

MORE DOCTORS OR MORE ANCILLARIES?

SIR,—Your excellent leading article last week raises one of the most important problems for the future of medical practice under the N H S in this country

Since, as you rightly assume, it is all-important that we shall maintain the standards of medical training, it seems to be inevitable that more and more of the techniques of medicine and surgery must gradually be decentralised on to the ancillary medical professions This is probably a legitimate form of "dilution"

The central problem at present inherent in this tendency is, as you suggest, to determine at this stage whether these professions shall be regarded for this purpose as "daughter" or "sister" professions of medicine It was presumably in recognition of the need to face this problem that the Ministry of Health in 1950 set up the eight Cope Committees Important majority and minority reports were published embodying their findings and recommendations about eighteen months ago Since then little or nothing further has been heard of the matter

This is a very unsettling situation both for us and also for the members of the ancillary professions It has led to some members of the latter being encouraged by this interregnum to plan for autonomous status within the N H S

In view of your statement that "the proper use of ancillaries is a major issue on which doctors ought to be forming a considered opinion," it would seem desirable that the authorities should proceed to the next step, which is presumably to draft a Bill based upon the findings of the Cope report and submit it for further discussion in Parliament

London W 1 W S C COPEMAN

CLINICAL STUDY OF ADRENOCHROME

SIR,—The interesting letter by Dr Srinivasan (Oct 4) prompts us to make a few comments

Our experiments in the same field led us to consider the action of the products of oxidation of adrenaline upon the adrenal cortex of rats and men

We found that intraperitoneal injection of adrenochrome, trihydroxy N methylindol (T H N I), and *semicarbazone* of adrenochrome (adrenoxyl), in doses of 100 µg per 100 g body-weight to intact male rats, produced biochemical and hæmatological signs of adrenal hyperactivity [1]—i e, adrenal ascorbic acid depletion, decrease of adrenal cholesterol, and a fall in the level of circulating eosinophils The action of 100 µg of each of these substances is, however, less than that of *l*-adrenaline in doses of 20 µg per 100 g body-weight The semicarbazide chlorhydrate and the semicarbazone of glucose are inactive in the same doses Thus, adrenal stimulation by adrenoxyl does not seem to depend on the semicarbazone radical, as was suggested by Gabe and Parrot [2]

As adrenoxyl does not enhance the effects of adrenaline, then the stimulation of the adrenal cortex by the doses used in our experiments is not due to this sympathicommimetic hormone Moreover, the action of adrenaline does not depend on the oxidation products because adrenaline is active in a smaller dose

The urinary excretion of reducing steroids and 17-ketosteroids was estimated in patients who had had an intravenous injection of 1 mg of adrenochrome twice daily for five to ten days, and in other patients who had had 9 mg of adrenoxyl (in 3 doses) every twenty-four hours for three successive days No significant change was found in the urinary excretion of the steroids, though there was a significant and regular decrease in the circulating eosinophils This discrepancy between animal and clinical experiments may be due to too small a dose in man, and further investigation may decide this point

But there is no disagreement between animal clinical experiments with salicylates in large do our results with salicylates [3, 4] suggest that it is s which is in fact the "poor man's cortisone"

H VAN CAU
J LECOMTE

Department of Internal
Laboratory of Pathology
University of Li

CHRONIC OTITIS MEDIA

SIR,—I must have expressed myself badly at Royal Society of Medicine for your reporter to h misinterpreted me (Dec 20, p 1208) I do not beli "failure of pneumatisation" of the mastoid bone, b radiography shows the presence of diploitic cells a apophysis develops Somehow some of these com communicate with the antrum, forming the pneu cells Then a non-suppurative otitis media from the respiratory tract results in a cond periostitis under the mucosa which is also the inter periosteum of these cavities According to the nat and severity of such inflammations the mastoid pro may be modified from the normal cellular type into t so called diploitic type or the sclerosed mastoid T must, I think, be the process that causes these anom

Evidence is hard to produce, but various bits may b pieced together First, there is the occasional unilat sclerosed mastoid Anatomical variations such as th cannot be called normal Nature does not build sy metrical bilateral structures in that way Then again otologist whose work was concerned almost entirely w the acute inflammations, as mine was, did not come acr any other than cellular mastoids under adult or l adolescent life Nor does he see them by radiograph It was in the '20s that this first taught us that t normal mastoid is a cellular structure, and that t patterns of the cells in the two sides, though not identic are similar one to another I have often confirm this by using the radiogram of the normal mastoid to t me how far I must go when operating on the disea side, finding, more than once, cells in the squama of t temporal bone of which there was no sign in the blurr photography of disease, or going downwards and bac wards or up into the area where posterior and midd fossæ of the base of the skull meet on their later aspects

Sometimes, but very rarely, one picks up eviden from isolated cases

About twenty four years ago the first mastoid X picture was taken at the North eastern Hospital, not decide whether a mastoid operation should be done bu study otitis media And there was the bad side "all blurre in distinction with the clearly outlined cells on the other and this within forty eight hours of the first symptom exploded the old hypothetical pathology of successive jump and in course of time the modern concept of inflammat of the middle ear cleft took its place

Twenty years later the boy became one of my last dre The old plate had been destroyed, but a new one showed th cells on the two sides with patterns similar—but not identic because the cells in the side that had been inflamed we smaller than those on the other, with thicker walls betw them

One other case I had A young lady of the W R N had been sent back from Algiers for operation, with t diagnosis of mastoiditis The depth of the meatus was acutely tender that I wondered whether she had ever had inflammation of the middle ear cleft at all or whether the co dition might not be an otitis externa kept up by the irrita drops that had been used And so a radiogram was tak and there was a cellular mastoid as clear as the stippling t one sometimes sees on the background of an engraving said to her "Have you ever had anything wrong with t other ear?" and she answered "Oh yes! I had it bad

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[1] Van Cauwenbergh H Lecomte, J Fischer P Vliers M Goblet, J *Arch int Pharmacodyn* (in the press)

[2] Gabe M, Parrot, J L *C R Acad Sci, Paris* 1951 232 2355

[3] Roskam J Vivario R, Van Cauwenberge H Heusghem Betz H *Bull Acad Méd, Belg* 1951 16 501

[4] Van Cauwenberge, H, Betz H *Lancet*, 1952, i, 1063

FRANK STOREY CLIFF

M D Lond, M R C P

Dr Frank Cliff, who died at Blackpool on Dec 3 at the age of 46, was for many years physician to the Queen Victoria Hospital, Morecambe, and to the Royal Lancaster Infirmary where latterly he also had a clinic in dermatology

He was a native of the city of Lancaster and proud of his connection with the red rose He got his early education at the Lancaster Royal Grammar School where he proved himself a keen scholar, a sturdy rugby forward, and an imperturbable cricketer In 1924 he entered University College Hospital, London where he maintained his reputation for scholarship and sportsmanship He played rugby and cricket for his hospital, and he qualified in 1929 Within the next three years he also acquired the M B, M R C P, and M D

While Cliff was holding a house-appointment at U C H he was closely associated with Sir Archibald Gray, who gave him his first and lasting ambition to become a dermatologist His last house-appointment was in his native Lancaster where he was senior house-surgeon at the Royal Infirmary Later he joined a general practice as the physician in a large firm in Morecambe where for many years he did much of the specialised medicine, and in a short time he was universally recognised as giving a sound opinion on medical and dermatological cases

"With Frank Cliff's experience and qualifications" J McF writes, 'one would have expected him to specialise early, but he wanted to learn medicine the sure way During those years of achievement, he served a community which will always be grateful for his work Under the National Health Service he achieved his ambition to become a consultant dermatologist, but, while this was what he himself desired most of all, many of his colleagues thought that the gain of dermatology had been the loss of medicine He served a large and scattered area stretching from Barrow to Blackpool and including Kendal Lancaster, and Morecambe, and throughout this wide area he made many friends He will be sorely missed in Lonsdale, both north and south of the sands and with his wide experience and encyclopædic knowledge of two specialties he will be a hard man to follow and one whom it will be almost impossible to replace"

FRANCIS CARLTON OLIPHANT

M.B Melb, D C H

Dr F C Oliphant, assistant pathologist to the Dudley Road group of hospitals, Birmingham, died on Dec 27 at the age of 17

He qualified at Melbourne in 1933, and he had practised in Australia both in city hospitals and up country when he came to England before the late war After holding house-appointments at the Woolwich and District Hospital, and at Great Ormond Street, he took the D C H in 1941 During the war he served with the Royal Navy as a surgeon lieutenant in several theatres After the war he held pathological appointments at Cheltenham and Birmingham, and at the time of his death besides his appointment to the Dudley Road group of hospitals he was visiting pathologist to the Yardley Green Sanatorium and a member of the coroner's panel of pathologists

F E D G writes 'Oliphant had had almost 20 years of varied medical practice It was as a pathologist that I knew him, and it was abundantly clear that his work in pathology was greatly influenced by his wide clinical experience His appreciation of the basic values in medicine, his innate common sense, and his intuitive mistrust of charlatans made him an invaluable colleague As a person his approach was shy yet direct His sense of humour was highly developed—dry, and full-bodied like a fine sherry His knowledge of the classics was extensive, though he would rarely give evidence of its existence He had a wide knowledge and appreciation of good music, and considerable ability as a pianist He was an excellent raconteur and his stories spiced with shrewd reflections on men and their failings and occasionally embellished with those adjectives for which Australia is famed made him a delightful companion Modesty and a kind heart were his greatest virtues, and I never knew him to display a trace of malice He was admired greatly both by his clinical colleagues and by the technicians who worked under him His death will leave a gap in the lives of all who were happy to work with him"

Appointments

ALCOCK WILLIAM M B Sheff B HY Durh D I H M O H and divisional M O S W Hertfordshire

ARDLEY, JOHN, M B Durh, D P H deputy M O H an school M O, Southport

BEGG, T L M B Aberd D I H asst M O H (menta Liverpool

CHANCE, T H O M R C S D M R T asst radiotherapist L shire radiotherapy centre, Scunthorpe and district war hospitals

CONN HERBERT, M D I H D Berlin asst psychiatrist, M Hospital, Derby

DAVIDSON LAMB WILLIAM M C, M B Aberd, D P H M O Gloucestershire united districts

East Anglian Regional Hospital Board

EDWARDS J C M A, B M Oxfd anaesthetic registrar Suffolk Hospital

LINN J C M B Lond D M R D registrar in radiology, N and Norwich Hospital

PRESTON, K S, M B Edin D M R T asst radiotherap Suffolk and Ipswich Hospital

Manchester Regional Hospital Board

BOLAND, J W D S C M B Dubl F R C S I D M R T radiotherapist, Christie Hospital and Holt Radium In Manchester

GARRUS, H N L R C P asst physician in geriatrics Wit Hospital

MALLOX, F R M D Belf D P M consultant child psych Booth Hall Hospital, Manchester senior child psych Manchester child guidance clinic and lecturer in c psychiatry Manchester University

OLEESKY, SAMUEL, M B Manc, M D Washington St L M R C P consultant physician Crumpsall Hospital M chester

RAINES, KATHLEEN, M R C S D A consultant group anaest Lancaster and Kendall hospitals

WILLIAMS E L M D Wales M B Lond tuberculosis phys Oldham and Ashton areas

South Western Regional Hospital Board

GORDON-RUSSELL J B M B Aberd, M R C P D P M con psychiatrist, South Somerset clinical area

HART, R J M A, M B Lond orthopaedic registrar, N Gloucestershire clinical area

SAUP Z L M B Witwatersrand, D M R, D M R D asst r therapist Exeter clinical area

The Hospital for Sick Children, Great Ormond Street, London

GEORGE PHYLLIS, M B Lond house surgeon

HALL, J I M B L'pool research asst in anaesthesia

JACO N T B M Oxfd M R C P D C H house physician

RAJASURIYA K, M R C P, D C H house physician

RAULIN COLETTE, M B Lond, D A senior resident anaesth

SCOTT J E S M B Camb house surgeon

WILKINSON, R H M D Camb asst chemical pathologist

Births, Marriages, and Deaths

BIRTHS

BELSHAM —On Dec 26, at Woolwich Daphne Frances (*Sedgwick) and Captain W Frank Belsham, R A M C*—a daughter

BRYAN BROWN —On Dec 25 at the Belvedere Nursing Ho Scarborough, to Evelyn (née Smith) wife of Dr P Bryan Br —a son

ELLIS —On Dec 28 at Newcastle upon Tyne General Hospital Alysoun (née Benson) wife of Dr Errington Ellis—a daugh

FERGUSSON —On Jan 1 at Queen Charlotte's Hospital Lon to Rosemary (née Howard) wife of Dr Ian Fergusson—a daughter

GRAY —On Jan 1 at St David's Hospital, Cardiff, to Mar (née Muir) and Dr Peter Gray—a daughter

SEARS —On Dec 30, at Hammersmith Hospital London to Janet Sears (née Conn) wife of Dr H T N Sears—a (Charles Alistair Newton)

SHARPEY SCHAFER —On Dec 30 at Lambeth Hospital, Lond to Dr Sheila Howarth wife of Prof E P Sharpey Sch —a daughter

TITMAS —On Dec 27, at Middlesex Hospital London to Ma (née McGowan) wife of Dr J M Titmas—a daughter

MARRIAGES

MURRAY—BUCKLER —On Dec 29 at Woking, Surrey, James Hi Murray M D *to Edith Daphne Buckler, of Bath*

PEARCE—RANSOME —On Dec 27 in Tripoli, Libya Jack H Pearce M R C S major R A M C to G Brenda Hawth Ransome

DEATHS

BUCHANAN —On Dec 21 in Glasgow Donald Campbell Buchanan M A M B Glasg of Albany Drive Rutherglen

HICKS On Dec , at Friargate Derby Henry Thomas Hi L R C S aged 81

OUTRED —On Dec 30, at Weybridge, Charles Deane Outr M R C S L D S D P H aged 76 of Tunbridge Wells a formerly of Gloucester and Gravesend

RICHARDS On Jan 1, at Brynhyfryd Aberavon Port Ta William Jones-Richards L R C S aged 79

SHIELS —On Jan 1 in London Thomas Drummond Shiel K M C M B Edin

WILLIS —On Jan , at Hampstead General Hospital Fr Edward Saxby Willis M C M D Lond aged 67 of Holne London

The Health of London in 1951

he decline in the *number* of children who are being unised against diphtheria each year continues: in county of London, for example, 40,656 children were unised for the first time in 1951, compared with 389 in 1950, and 22,908 had boosting doses—over 0 less than in 1950. The county medical officer. J. A. Scott, in his report for 1951,[1] says that one son for the decline is the publicity given to exaggerated orts of cases of paralysis following inoculation in 49 and 1950. Moreover, the success of the immunisan campaign has taken away much of the parents' ead of diphtheria and led them into apathy. Dr. ott's department is seeking further means of convincing em of the seriousness of their omission. On the other nd, the total number of people vaccinated rose from ,583 in 1950 to 35,470 in 1951, and there were more an three times as many revaccinations. The smallpox idemic at Brighton in January, 1951, was reflected in substantial increase in the number of vaccinations in ondon at that time.

The general death-rate in London went up from 1·3 per 1000 population in 1950 to 12·6 in 1951. The rise attributed to more deaths from cancer, heart-disease, nd respiratory disease in a gradually ageing population. nd to the influenza epidemic. The increase in cancer of he lung shows no sign of stopping: during the last wenty years the mortality among London men has ultiplied three and a half times, and the rate for vomen is now two and a half times its 1931–33 level. Deaths due to diabetes declined steadily between 1939 nd 1947, but the rate has been going up again since hen, supporting "the impression that the previous lecline had been connected with the dietary stringency of the war and post-war years." There were 282 deaths rom motor-vehicle accidents in 1951—37 more than in 1950—and the report points out that each year there are more deaths from this cause than from poliomyelitis. The infant-mortality rate, at 25·4 per 1000 live births, was lower than ever before; and the neonatal rate of 17·3 was well below the average of 20·4 for the past ten years.

The report mentions some figures from the 1951 census. The population of the administrative county of London has fallen by just over 1,000,000 (24%) since 1931. The decrease has been greatest in the East London boroughs; and only Hampstead, Woolwich, and Lewisham have shown an increase. The main reasons for the change are "slum clearance, migration into outer London, change in the class of user of residential accommodation, and bomb damage."

Dr. Scott has also published some preliminary figures for London in 1952. The infant-mortality rate is provisionally given as 23 per 1000 live births, which would again be lower than ever before; and the suggested neonatal rate of 15·6 per 1000 live births would also be a record. The birth-rate continues to fall, as it has done since 1947, and the estimated figure for 1952 is 15·4 per 1000 population, compared with 20·9 in 1947 and 15·6 in 1951.

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[1] London County Council: Report of the County Medical Officer of Health and School Medical Officer, 1951. Pp. 161. 2s. 6d.

Infectious Diseases in England and Wales

Disease	Week ended Dec.			
	6	13	20	27*
Diphtheria	29	23	23	26
Dysentery	260	329	332	184
Encephalitis:				
Infective	2	5	3	1
Postinfectious	3	5	4	5
Food-poisoning	55	74	58	42
Measles, excluding rubella	16,207	17,800	19,653	14,189
Meningococcal infection	33	39	38	31
Ophthalmia neonatorum	36	32	29	9
Paratyphoid fever	4	4	1	3
Pneumonia, primary or influenzal	720	1135	1156	826
Poliomyelitis:				
Paralytic	48	41	36	30
Non-paralytic	10	17	12	3
Puerperal pyrexia	215	234	160	145
Scarlet fever	2260	2233	1891	1358
Smallpox	—	—	—	—
Typhoid fever	3	1	5	2
Whooping-cough	2069	1870	1555	1117

* Not including late returns.

In England Now

A Running Commentary by Peripatetic Correspondents

OUR lecture room exemplifies the British ideal of the maximum of inaudibility with the minimum of ventilation. The seating is carefully designed so that the knees of the student become painfully and inextricably wedged against the sharp edge of the bench in front, while the spines of his scapulæ are assailed by the sharp edge of the bench behind. The occupants of the back benches, out of earshot and almost out of sight of authority, spend their time happily playing pontoon. In contrast, the seekers after truth in the first two rows either gaze soulfully at the lecturer's face, their lips moving silently to the rhythm of his discourse, or feverishly attempt to record in their notebooks every word and every significant cough or pause in the hope that it will come up in the exam.

In the middle rows between these two extremes is the great student body, vast, inchoate, and drowsy. When one of its legs goes to sleep it painfully shifts round on to the other, and when darkness falls it gratefully closes its eyes to the slides and scratches its itchy places. It is not learning, it is not even listening, it is merely indulging the herd instinct and a sense of cosy companionship in the dark. It is this middle section we have long desired to reach. We are paid to communicate our experience to these young minds, to lay our burden of knowledge at their feet, to pass on the torch. Till now our oratory, our sarcasm, our highly polished witticisms, and our depth of erudition have alike failed to project our personality beyond the front row. At last, however, we have found the answer.

In the January number of *Family Doctor* some exhilarating experiments are reported in which university students were given words to memorise. Without warning the light went out, the backs of their chairs fell off and the arms became electrified. In addition a revolver was fired and a sheet of iron fell to the floor. This is the technique for us. "Mark my words!," we shall roar. "You, sir, at the end of the fourteenth row, what have I just been saying?" And as we press the appropriate button the floor of his seat will give way, a bucket of water will fall on his head, and he will automatically be precipitated down the gangway to our feet. "Let this be a lesson to you, sir" we shall say sternly, as we speed him back to his place with a well-aimed revolver bullet. It beats us why we didn't think of it before.

* * *

Strange as it may seem, one often finds that even the queerest remarks of the psychiatrists have a grain of truth in them. I remember some years ago how a psychiatrist friend was trying to explain how he had got over his dislike of the phone ringing at night. He was a rather incoherent Irishman and at the end of his monologue all I could discover was that he had solved his problem by stuffing an old sock into the bell. I hadn't an old sock handy and anyhow I treated his idea with contempt. But three years later I found there was something in it. It isn't the call itself which is so disturbing. It is the sudden loud ring of the bell. Now I leave the bell switched through to the surgery at night instead of to my bedroom. I still hear the bell perfectly, waking perhaps at the second ring instead of the first. It disturbs the family no more than before, but to my mind the slightly more gradual awakening takes away the initial alarm and sense of urgency which a sudden awakening brings. Others may not be affected in the same way, but I commend my idea to fellow sufferers. Incidentally, why didn't the psychiatrist explain more fully in the first place? I suppose he wanted to make me think it out for myself. It worked in the end, but it seemed to be doing things the hard way.

* * *

One small but psychologically important job which the new College of General Practioners might tackle is the retention of the family doctor's "copyright" in his more interesting patients when the latter are written up as published cases by hospital staffs. The decline to vanishing point in acknowledgments to general practi-

University of Oxford

Prof T Pomfret Kilner has been appointed Nuffield professor of surgery in succession to the late Sir Hugh Cairns

Mr Pomfret Kilner is a graduate of Manchester and London Universities At Manchester he was Dauntesey scholar and Sidney Renshaw exhibitioner and he won medals in anatomy and physiology before graduating M B with distinction in surgery and pathology in 1912 He took the London degree in the following year After serving with the R A M C in the 1914–18 war he was appointed plastic surgeon to Queen Mary's Hospital for Face and Jaw Injuries Sidcup, in 1919, and he became F R C S in 1921 In the years following he was appointed plastic surgeon to many hospitals including St Thomas's Hospital London, Manchester Royal Infirmary and Birmingham United Hospitals and he took charge of the plastic surgery division of the Ministry of Pensions In 1935 he was a Hunterian professor of the Royal College of Surgeons He took up his present appointment as first Nuffield professor of plastic surgery at Oxford in 1944 when he became head of the new department of plastic surgery

The appointment of Dr Alice Stewart as reader in social medicine has been approved for the years 1953 to 1959

Order of St John of Jerusalem

The Queen has sanctioned the following promotions in, and appointments to, this order

As Knights—Arthur Wai Tak Woo F R C S , Sir Horace Evans K C V O , F R C P , Brigadier R M Gorssline, D S O , M B , G B Peat M D , Major General F A Maguire C M G D S O , F R C S , Lieut Colonel E A H Russell O B E M B C A Verco M B

As [illegible] , M B

As [illegible] M B E H Lodge, M B , Colonel [illegible] C McGibbon, M D H R Mustard M D , W P Warner, C B E , D S C , M B

As Officers—J K Thomas, M B John Brown M B , D P McIntyre, F R C S , T P Eddy, M R C S Louis Gerard Blaze, L R C P F , C H Drake, M R C S G W J Bousfield, M D , P P Lynch, M D , H H Barnett F R C S , Arnold Perry, O B E , F R C S , W G Rich, M B , Colonel W A Jones, O B E , F R C P (C) R J Brown M D G D W Cameron, M D , Emmet Dwyer M D , H J Ferrier, M D , J L R Gendron, M D , C D Gossage O B E , F R C S , H D Hebb, M D Major A S Lewis F R C S , J H A Paquette, M D W S Stanbury, M B E , M D John Prentice, M B , H H C Fuller, M D , L M Comissiong M R C P E Surgeon Rear Admiral Frank Hutton Nimmo, E R B Murray M B , G K Thornton M B R M Paterson, L R C P E N L Birkett M B , W H C Romanis M CH F R C S , Lieut Colonel S H Heard, M B E M R C S Colonel J E Snow R A M C , J J du Pré Le Roux, L R C P E , R S Steel, M R C P H H Hurst M B T C James, M B ; Brigadier C W Nye, O B E M B

British Association of Plastic Surgeons

At the annual meeting of this association in December the following officers were elected for 1953

President Mr J N Barron hon treasurer Mr R P Osborne, hon secretary Mr J P Reidy council Prof T P Kilner Sir Archibald McIndoe Mr Rainsford Mowlem, Mr G M FitzGibbon, Mr J S Tough Mr D N Matthews (vice president), Mr A B Wallace (editor)

Renal Association

This association is to hold a meeting at the Ciba Foundation, 41, Portland Place, London, W 1, on Jan 28, at 4 P M , when Mr A W Wilkinson will speak on Biochemical Changes after Transplantation of the Ureters, and Mr D Innes Williams on Long term Results of Transplantation of the Ureters for Ectopia Vesicæ

Patient Selection

Speaking at Cardiff on Jan 5 at the beginning of his four-day tour of Wales, Mr Iain Macleod, the Minister of Health, said that too many people were in hospital who ought not to be there and too many people were not in hospital who should be (*Times,* Jan 6) He believed this could only be put right by closer integration between the local authority and the hospital authority "I am not satisfied" he added, "that we have found the right relationship between local authorities and those rather arbitrarily appointed regional boards"

CORRIGENDA *Persistent Hiccups*—In our annotation on this subject (Dec 27, p 1262) we erroneously referred to the phrenic nerve as arising from thoracic roots This nerve originates in cervical roots

University of Sheffield—Dr T M Abbas has been appointed lecturer in obstetrics and gynæcology, and not senior lecturer as we reported last week

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EMERGENCY BED SERVICE—In the week ended last Monday applications for general acute cases numbered 1836 The proportion admitted was 84 41%

CORRIGENDUM *Steribac*—On Dec. 13 (*Lancet* General Advertiser p 2) we printed an advertisement of Messrs Clay & Abraham's Steribac solution for the storage and sterilisation of surgical instruments and needles By an oversight we gave the price wrongly The correct price is 3s 9d for 20 oz and 12s 9d for 80 oz

[illegible]

[illegible]

Diary of the Week

JAN 11 TO 17

Monday, 12th

ROYAL EYE HOSPITAL St George's Circus Southwark, S E 1
5 P M Dr T H Whittington Non paralytic Strab Care and Treatment of Squinting Child
MEDICAL SOCIETY OF LONDON 11, Chandos Street W 1
8 30 P M Dr R W Cockshut, Dr Wilfrid Sheldon M Maladies of Children

Tuesday, 13th

ROYAL COLLEGE OF PHYSICIANS Pall Mall East S W 1
5 P M Dr D A K Black Body-fluid Depletion (Fi two Goulstonian lectures)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Med Keppel Street, W C 1) Prof A Huggett Physiolo Parturition
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
8 P M *Section of Psychiatry* Prof J Elkes Pharmaco Approach to Psychiatry
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle St W C 2
5 30 P M Dr P D Samman Reticuloses
CHELSEA CLINICAL SOCIETY
8 30 P M (South Kensington Hotel, 41, Queen's Gate Ter S W 7) Sir William MacArthur The Small Pocks a the Great Pocks

Wednesday, 14th

ROYAL SOCIETY OF MEDICINE
4 30 P M *Section of Physical Medicine* Lord Amulree Dr Cosin Dr A Talbot Rogers Rôle of Physical Med in Geriatric Practice
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Parapsoriasis, Poikiloderma a Mycosis Fungoides.
INSTITUTE OF UROLOGY St Paul's Hospital Endell Street, W
4 30 P M Mr Harland Rees Differential Diagnosis of Frequ of Micturition
HARVEIAN SOCIETY OF LONDON
8 15 P M (11, Chandos Street, W 1) Dr James Barn Links (Presidential address)
MANCHESTER MEDICAL SOCIETY
4 30 P M (University of Manchester) *Sections of Pathology a Medicine* Prof L J Witts Ulcerative Colitis.

Thursday, 15th

ROYAL COLLEGE OF PHYSICIANS
5 P M Dr Black Body fluid Depletion (Second of t Goulstonian lectures)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicin Prof G F Marrian F R S Metabolism of Adrenocort Hormones
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Childr Great Ormond Street W C 1
5 P M Dr J M Tanner Growth and Development
BRITISH [illegible] 32 Welbeck Street, W 1
8 P M [illegible] Dr T H Hills Dr C J Hod Mr A J Minns, Mr Problems Affecting Radiology
ROYAL [illegible] Millbank S W 1
5 P M [illegible] R S Rôle of Trauma and St in Organic Nervous Affections
ST GEORGE'S [illegible] Hyde Park Corner S W
5 P M Dr [illegible] lecture demonstrati
ROYAL SOCIETY [illegible] AND HYGIENE, Man House
7 30 P M Dr D S Bertram Laboratory Studies on Fila in the Cotton Rat
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpo
8 P M Dr David Johnston Dr Thomas Seager Gen Practice—Present and Future
UNIVERSITY OF ST ANDREWS
5 P M (Medical School, Small's Wynd Dundee) Prof G Brown, F R S Sympathetic Nervous System

Friday, 16th

ROYAL EYE HOSPITAL
5 30 P M Mr Howard Reed Visual Fields
ROYAL SOCIETY OF MEDICINE
8 15 P M *Section of Radiology* Dr C P Moxon Radiol of Cervical Disc Lesions Dr H W Holland Tab Spinal Arthropathy Dr F H Howarth Interl Sequestration in the Lungs
INSTITUTE OF DERMATOLOGY
5 30 P M Dr P J Hare Xanthoma Necrobiosis Lipoidica a Granuloma Annulare
FACULTY OF RADIOLOGISTS
2 15 P M *Diagnostic section* (Royal College of Surgeons Linco Inn Fields W C 2) Dr I Macpherson Dr R E Ste Mr J A Slwin Mr P R Allison Mitral Di ease
OSLER CLUB OF LONDON
7 45 P M (11 Chandos Street, W 1) Mr Leslie T Mort Dr William Brockbank Dr R Scott Stevens R C Brock History of British Medical Journalism

Saturday, 17th

BIOCHEMICAL SOCIETY
10 30 A M (King's College, Strand, W C 2) Scientific pap

l-chair she described her own initial inexperience of the se, which was epidemic in Cleveland this year, what she ially learned, what plans should be made for the future, the different ways in which the disease started and its different results. She recounted her own initial symptoms e fears they aroused, her reactions to those fears, and the going to bed. When paralysis set in she believed all was ith her. She was sure she felt short of breath at times she had nightmares about artificial respirators. Her ors varied. Then, when paralysis receded her hopes rned, and although left with some disability she described t she could do, what sort of careers were still open to her, what long-term care was going to mean.

he third case was of a young working man, married, fit, had never been ill before. He described an attack of te lobar pneumonia which had brought him to hospital an emergency a few weeks previously. The results of mination and treatment were described and illustrated and parison made with the disease and its effects as between '30s and '40s of this century. The development of motherapy and the antibiotics was sketched in.

The whole afternoon went with a swing and three rs passed without notice. I talked with students erwards and it was obvious that their enthusiasm had en roused. Terminology had been simple and that re were many aspects of illness was clearly appreciated. e student said to me "I'll never forget it." Another d apologetically "I feel dedicated already." I myself s deeply impressed. Here we had young people ginning their medical career who were introduced to k people on their third day in college. They were own that illness is an intricate affair which could be oked at in many different ways. The implications of ness and the doctor-patient relationship were portrayed, and the prime importance of the basic sciences as there for all to see. The whole afternoon was refully planned and the contributions of the staff re thoughtful, clear, and sympathetic. To me it was great improvement on the traditional address with a gh-sounding title delivered by some distinguished sitor. The hoary old themes of art and science, medical manism, hippocratic tradition, changing patterns, tegration and disintegration, specialism, the *profession*, ospect and retrospect, theory and practice, which orn the columns of our journals at the opening of each ademic year, seem unsuitable and unhelpful to the new udent.

There is much more that could be said about the estern Reserve experiment. No-one there is dogmatic. taff coöperation has been remarkable, and authoririanism, that stumbling-block of the curriculum atin: "race chariot!") is laid flat. And how!

Cardiff.

JOHN D. SPILLANE.

PITUITARY EXTRACT IN OBSTETRICS

SIR,—Professor Nixon and Dr. Schild (Jan. 3) call ttention to the very real danger of giving whole posterior ituitary extract in obstetric practice. The toxic vasoressor factor, in addition to its toxic action on the oronary vessels, invokes a rise in blood-pressure which ay be unfavourable or fatal. Unfortunately the loose se of the word "pituitrin" may cause it to be given hen these vasopressor actions have serious ill-effects.

Some years ago a new house-surgeon delivered a rimigravida who had hypertension and albuminuria hich had appeared just before labour. He ordered a c.c. of pituitrin," and within a short time the patient tarted having eclamptic fits. There was no doubt that he vasopressor part of the posterior pituitary extract ad raised the patient's blood-pressure and precipitated he eclampsia.

In my hospitals we use pituitary extracts very little ecause ergometrine has such a reliable action and ecause the oxytocic effect of injectio oxytocini, *B.P.*, r 'Pitocin' is so variable. But we have had to make rrangements to prevent the pituitrin accident recurring. The hospital pharmacist no longer supplies the extract of posterior pituitary to the maternity department, but he does provide injectio oxytocini, *B.P.* ($^1/_2$–1 ml. or 5–10 units), or the similar preparation, pitocin. Furthermore, if anyone uses the term pituitary extract or pituitrin, whether he be a member of the staff or an examination candidate, I take up the word and ask him whether there is any doubt of his using the word correctly.

London, W.1.

ALISTAIR GUNN.

ORAL ANTIBIOTICS AND SPONTANEOUS HÆMORRHAGE

SIR,—Dr. Payling Wright's letter[1] prompts me to report a case of spontaneous hæmorrhage due to hypoprothrombinæmia occurring within 48 hours of the administration of aureomycin.

The patient was a primigravida at term, who developed a concealed accidental hæmorrhage with complete suppression of urine from the moment of onset. When she was first seen five hours later, the fœtus was dead; there was no urine in the bladder, and none had been voided since before the onset of the catastrophe. The blood-pressure was 160/110 mm. Hg. A lower-segment cæsarean section was performed, and a typical large retroplacental clot was discovered; there was no evidence of retroperitoneal hæmorrhage.

The anuria was treated by the method recommended by Bull et al.[2] Diuresis commenced on the sixth day. On the twelfth day the patient developed basal pneumonia, which was treated by aureomycin. By this time she was having a moderate diet by mouth, and had had 6 pints of packed red cells by three separate transfusions. Forty-eight hours later the patient developed a large spontaneous hæmorrhage into the abdominal wall, which burst the healed abdominal wound, and multiple purpuric spots over the body. The blood-prothrombin time by the Quick method was over 100 seconds. The condition was treated by injections of vitamin K continued for some days. Thereafter the patient made an uneventful recovery.

Galway, Eire.

D. T. O'DRISCOLL.

BUTAZOLIDINE AND SALT EXCRETION

SIR,—In view of the widespread use of butazolidine, a preliminary report on one aspect of its toxicity —i.e., œdema—and on the comparison of its clinical effect with that of cortisone does not appear out of place.

14 patients with rheumatoid arthritis were put on a salt-free diet, and then 7·5 g. sodium chloride per day was issued as a ration. The total daily urine was collected for a preliminary week, for one to two weeks during which the patients had 600–1200 mg. butazolidine per day, and for a subsequent week; and in 7 cases the results were compared with a period during which 75–150 mg. cortisone was administered.

In 11 of the 14 cases there was slight retention of sodium on the first two days of administration, and in the remainder there was a similar period of retention about four days after treatment was started. After this initial decrease in excretion the levels fluctuated; but in 6 cases there was a distinct increase in salt excretion directly butazolidine was discontinued, and in 5 others this peak excretion occurred on the eighth to tenth day of treatment—as not uncommonly happens during cortisone treatment. At no time during this experiment was any change in excretion of uric acid observed, although the usual increase was found when 2 of the cases were checked with administration of salicylate. The clinical response did not correlate with the excretory pattern in this group of patients. In this series of cases no gross œdema occurred; and neither in these cases nor in others where œdema developed has any albuminuria or hæmaturia been produced.

7 patients subsequently received cortisone. Of 3 who gave a poor clinical response to butazolidine 2 also

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1. Payling Wright, H. *Lancet*, 1952, ii, 1180.
2. Bull, G. M., Joekes, A. M., Lowe, K. G. *Ibid*, 1949, ii, 229.

Orthopædic and manipulative surgery, including such things as the repair of hernias, the treatment of hæmorrhoids, and the various ways in which a gynæcologist can rescue a middle-aged woman from chronic invalidism—all these have been of incalculable benefit In much the same category are the developments in traumatic and plastic surgery which made it possible to say in 1945 that any wounded soldier reaching hospital alive had an 80% chance of survival and almost as good a chance of being capable eventually of earning his own living

On the medical side the change is not so striking, but our maintenance therapies—insulin for diabetes, liver or B_{12} for pernicious anæmia—are in a sense analogous to the surgical or prosthetic triumphs I have mentioned

In the whole application of surgery to human disease and disability there have been four great discoveries anæsthesia, aseptic technique, blood-transfusion, and antibiotic control of infection from within The art of the surgeon is to use his knowledge, his ingenuity, and his craftsman's skill to apply these discoveries to each individual problem There is infinite scope for improvement in methods of cutting and manipulating body tissues with the safety made possible by the four great discoveries, but for the most part what is needed is men to make the best use of what is available rather than to find new approaches In regard to surgery I believe that there is perhaps one important field still to be fully explored—namely, means of dealing with the complex functional conditions which cause death from shock Otherwise the whole field is one for clinical rather than fundamental research

The Gaps in the Present-day Picture

The great advances in the hundred years, then, are the virtual elimination of infectious disease and malnutrition as major causes of death, the provision of prosthetic or surgical help for bodily defects, effective surgical treatment of traumatic, mechanical, or infective emergencies, and a wide variety of symptomatic remedies, particularly means of diminishing pain Two important types of maintenance therapy to make good a gradually developing genetic weakness have been successful in diabetes and pernicious anæmia, while a third type is or may be emerging in the treatment of rheumatoid arthritis with cortisone

What are the major medical problems which have not been effectively dealt with? The first and most important is of course insanity and feeble-mindedness, probably the next *is functional disease of the nervous system*, with its manifestations in the psychoneuroses and psychosomatic disorders It would be in line with modern thought to add that crime, delinquency, and general bad manners are hardly distinguishable from the medical manifestations

We may look at the matter from two points of view (1) the major remaining causes of untimely death (i e, of persons dying under 60 years of age), and (2) the main reasons for individuals being incapable of normal economic activity

In the first group we have

(a) *Death of infants* in the first month of life from various forms of congenital malformation or disability

(b) *Death from cardiovascular inefficiency* of one sort or another, with coronary disease taking an increasingly important part

(c) *Cancer*, the incidence of which increases steadily with age but is still of great importance under 60 years

(d) *Death from violence*, especially automobile accidents

Many of these will also be responsible for a more or less prolonged period of social dependence before death ensues, especially cancer and a variety of cardiovascular conditions In civilised countries of Western European origin the major causes of disability for which there are no clearly defined preventive or curative procedures are

(1) Manifestations of *genetic anomaly*, of which p anæmia and diabetes almost certainly are example shall point out later, this group may include in part s almost every human disability

(2) *Psychogenic disorders*—i e, disease caused or p tated by emotional factors On the one hand we hav orders of behaviour and personality, on the other the so psychosomatic diseases—conditions in which by one m nism or another the emotional difficulty leads to ph lesions that may range from backache and skin comp to essential hypertension, exophthalmic goitre, and p ulcer

(3) *Allergic disturbances, representing essentially a dis* of the immunity mechanism Rheumatic fever and prob rheumatoid arthritis, nephritis, and some forms of asth may be related to bacteria as the sensitising antigen multiform assemblage of troubles—hay fever, asthma a many types of skin lesion—may be associated with n bacterial sensitisers

(4) There remain many conditions where it is impo to say that any single cause is responsible—gall stones a kidney stones, obesity, chronic bronchitis, varicose veins, a many others

In general, therefore, methods are well developed f dealing appropriately with the impact of tangi environmental agencies on the body—micro organis infection, trauma, poisonings These are things wh are easy to understand, which can be reproduced animals, and which have provoked the combination laboratory work and clinical ingenuity that has b responsible for most of our successes in medicine

Where we are at a loss is to assess and compensate f the influence of factors intrinsic to the patient Eve human being who is not one of a pair of identical tw is uniquely *different from every other* human bei Probably every single one of us has genetic charact which he would be healthier without And every doc will agree that in *one way or another* the patient's "co stitution" is concerned in his every illness Also intrin to the individual in the sense I am using the word is emotional attitude toward his environment A ma temperament is probably very largely inborn, but at a given point in his life it is what his life's experience h made of his inherited make up There is no doubt th many diseases are psychogenic in origin—i e, they wou not have occurred if the patient had not been exposed *worry, frustration, and other* non-material impacts the environment Equally we can feel certain th there are people whose inheritance is such that no co ceivable amount of frustration or fear would ind peptic ulcer or chronic colitis Finally we have recognise that death *is a* necessary end—a unive evolutionary necessity—and to die is as much part our inheritance as to cease growing at 18 or 20 T healthiest of men finds his tissues hardening and fail as he passes 70, and in one place or another the fin breakdown will come eventually The rate of sen degeneration in different tissues will vary from pers to person, presumably mainly for genetic reasons

From this point of view, once we get away from th extrinsic causes of disease and disability we face a vast more difficult problem The patient presents us with disease condition whose nature is determined (1) b certain aspects *of his genetic constitution*, (2) by h past experience, which may well include a sequence o low-grade impacts from the environment, and (3) t psychosomatic components, which in one form or anoth will always be there

In contrast to the "extrinsic" *disabilities*, these a complex and difficult to understand—they can b reproduced in animals only in rather crudely and d tantly analogous forms—and at the present time the is virtually nothing we can do to prevent their occurre There is no short cut to their understanding via th laboratory bench, they can be tackled only by the dire study of the human material *But these are the* problem

The question of representation of whole-time con- its on the staff side was also discussed at some length. s pointed out by our deputation that there was not a whole-time consultant employed by a regional hospital l on the staff side, and that therefore there had never available to the staff side of Whitley Committee B the e of anyone competent to speak for the whole-time nal board consultants.

e would like to state that we received an extremely pathetic hearing from the staff side of Whitley mittee B, and it is realised that one of the greatest ; to progress has been the predominating influence he Ministry of Health and the absence of an arbitra- agreement either within or without Whitley Council.[2]

Association of
hole-time Salaried Specialists,
45, Lincoln's Inn Fields,
London, W.C.2.

RUFUS C. THOMAS
President.

DANGER OF PHENOL WITH PENICILLIN

SIR,—The hazard demonstrated by Dr. Aronson, Leys, and Dr. Swift (Dec. 20) can be avoided by eful supervision of all injectable solutions. It is, or ould be, normal practice for the pharmacist who epares the solution to indicate on the label the nature d concentration of any added bacteriostatic. Injections ould not be prepared by a nurse, for this and other asons. The *British Pharmacopœia* directs that solutions medicaments intended for intrathecal, intracisternal, peridural injection shall not be sterilised by heating ith a bactericide, nor issued in multi-dose containers, hich may be taken to mean any containers closed with a ncturable rubber cap. The force of the latter pro- sion is that solutions in multi-dose containers are variably required to contain bacteriostatic substances.

The golden rule for safety is that intrathecal solutions, hatever their nature, shall be drawn from sealed glass mpoules, and from no other type of container. Normally e pharmacist will prepare such solutions with rigid sepsis, transfer them to sterilised ampoules, and seal em by fusion of the glass. When stored, preferably r periods not exceeding 48 hours, they are refrigerated. mpoules, warmed to blood heat, should be scratched ith an *efficient* file or diamond point before opening, avoid contamination with glass spicules.

There is one serious objection to intrathecal injections repared directly in a rubber-capped vial of antibiotic. e have satisfied ourselves in this hospital that fine articulate matter is by no means rare in solutions so repared. Furthermore, rubber fragments may be resent, or may be introduced by the needle used for ithdrawal; they constitute a serious hazard. Ampouled olutions, examined in a powerful indirect light before eing passed for issue, have given no such trouble.

Pharmaceutical Department,
Southmead Hospital, Bristol.

PETER COOPER.

SPLENOMEGALY IN SCARLET FEVER

SIR,—Dr. O'Reilly's letter in your issue of Dec. 20 as very interesting.

A few years ago while stationed at an R.A.F. hospital saw about 80 cases of scarlet fever, all in young men ged 18–20 years. Of these, 7 were found to have alpable spleens.

In each case the spleen was firm and not tender; and it was ever enlarged beyond three finger-breadths below the left ostal margin. In most cases the enlargement was noticed on dmission to the wards and subsided slowly during the ollowing fortnight, although in 1 case the spleen was palpable s long as four weeks after the onset.

All the cases of scarlet fever were mild, and there was no ifference between the symptoms of those with palpable pleens and those without. Total and differential white lood-cell counts and Paul-Bunnell reactions were performed n all the cases of splenomegaly, and in none was there any hæmatological evidence of infectious mononucleosis.

Some 300 cases of tonsillitis and upper respiratory infections were seen during the same period. In none of these was splenomegaly recorded. Throat-swabs from all the cases of scarlet fever and a large number of the cases of tonsillitis were cultured; and almost invariably these yielded hæmolytic streptococci, which were, however, not typed. As might be expected perhaps, a rather high incidence of rheumatic fever was found on this station, which was a recruit centre; but no obvious correlation was found between this and the incidence of splenomegaly.

In general practice I have since seen two or three children with tonsillitis who have had palpable spleens.

Wolverhampton.

D. P. FITZGERALD.

HEPATITIS

SIR,—Your encouragement of clinical and epidemiological observations of hepatitis [1] prompts me to comment on the American studies [2 3] to which you referred in the light of work done in England.[4]

The American observations of anicteric cases in young children and of symptomless infections revealed by liver-function tests are an extension of Pollock's [5] demonstration of a positive Hunter's test for bilirubin in the urine of apparently healthy young children during an outbreak in a residential nursery.

The lack of effect of isolation of "suspected children" on the spread of infection in the American epidemic may have been due to the occurrence of infectivity during the early part of the incubation period (25–35 days [4 6]). Infectivity at this time was thought to account for an explosive outbreak in some wards of an institution for mental defectives.[4] Infectivity is usually greatest shortly before and after symptoms appear, as is shown by the few cases where transmission by a short and single exposure has allowed the identification of the time at which a case was infectious, and by the general experience that successive cases in close contacts in the family [7] or in Army units [8] commonly occur at intervals of approximately one month.

The disease in young children is rarely as severe as in the cases reported by Wylie and Edmunds.[9] In England in several outbreaks in day and residential nurseries there were no severe cases, and in epidemics in villages deaths from acute yellow atrophy were very few and occurred in children of school age and in adults. In families where a case occurred, young children were usually not ill at all, though parents and grandparents quite frequently became jaundiced.

The suggestion [3] that infective hepatitis virus may be a cause of "infantile diarrhœa" is not in agreement with my experience in England, where (1) in a hospital with hepatitis endemic in nurses there was no undue incidence of diarrhœa in infants in maternity and children's wards, and (2) in several outbreaks of "infantile diarrhœa" there were no cases of hepatitis in nurses in the hospital at the relevant time. From the data available, it is more likely that the diarrhœa in the American children was due to some other virus and a precursor of the hepatitis cases in the same way that epidemics of typhoid,[10] intestinal infections,[11] and upper respiratory infections,[12] have preceded some epidemics of poliomyelitis.

Cambridge.

A. M. McFARLAN.

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[2] *Ibid*, p. 233.

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1. *Lancet*, 1952, ii, 1212.
2. Capps, R. B., Bennett, A. M., Stokes, J. *Arch. intern. Med.* 1952, 89, 6.
3. Bennett, A. M., Capps, R. B., Drake, M. E., Ettinger, R. A., Mills, E. H., Stokes, J. *Ibid*, 90, 37.
4. Infective Hepatitis. *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 273. H.M. Stationery Office, 1951.
5. Pollock, M. R. *Brit. med. J.* 1945, ii, 598.
6. Pickles, W. N. Epidemiology in Country Practice. Bristol, 1939.
7. McFarlan, A. M. *Lancet*, 1945, i, 592.
8. McFarlan, A. M. *Quart. J. Med.* 1945, 55, 125.
9. Wylie, W. G., Edmunds, M. E. *Lancet*, 1949, ii, 553.
10. Seddon, H. J., Agins, T., Bernstein, H. G. G., Tunbridge, R. E. *Quart. J. Med.* 1945, 14, 1.
11. McFarlan, A. M., Dick, G. W. A., Seddon, H. J. *Ibid*, 1946, 15, 183.
12. McFarlan, A. M. *J. R. Army med. Cps*, 1946, 87, 37.

At the medical level most bacteriology today is almost confined to the great commercial drug houses, which alone have the resources to undertake the systematic and effective study of the thousands of possible compounds that might be used therapeutically Microbiology is a flourishing science in the universities and research institutes, but except to a limited extent it has almost wholly deserted the medical field The most flourishing aspect of bacteriology is what is called microbial genetics, and though this is throwing much light on the basic processes of life its bearing on the treatment and prevention of disease is almost nil Those of us in the virus field have rather more responsibility from two points of view First viruses are rather liable to flare up into sudden unexpected epidemics large or small Our Australian encephalitis epidemic in early 1951 was an example on a small scale, and the 1918-19 pandemic of influenza on a world-wide one The second justification is that a study of the interaction of virus and cell may throw light on the cancer process Cancer is certainly not a virus disease in any reasonable sense, but there *are* virus like agents associated with some types of cancer I have often said that a virus is the most subtle probe we have with which to explore the interior of the cell When we know a lot more about the interior of the cell we may find an effective clue to the processes which turn a normal into a cancerous cell—or we may not

That leads me to cancer research On the one hand we have every variety of study into cell processes of a wide range of organisms—any one of them *may* add a contribution of value to cancer work, but 99% or more will certainly not do so On another angle we see the attempt to find agents which will selectively damage or kill cancer cells but leave normal cells unaffected Radiations (X ray, radium, and artificial radioactive isotopes), a variety of poisons like nitrogen-mustard gas and chemically distorted nutrients, and viruses "trained" to attack cancer cells only—these are the three main lines of research today I am not in very close touch with cancer work, but I am much impressed by the difficulty of the problem and I feel rather pessimistic about the prospects of gaining any significant influence over the mortality of cancer for many years to come I might guess that the most useful way to diminish cancer incidence would be to close the cigarette factories

There is not likely to be any great change from the present rule that the best hope in cancer is early diagnosis and appropriate treatment by surgery and/or radiation therapy

In the field of what we may call metabolic diseases—i e, such maladies as diabetes, pernicious anæmia, and rheumatoid arthritis—there is great activity in the application of known methods to the clinical problems that arise But there is little likelihood of major changes of approach, and even smaller likelihood that there are other major diseases in which hormonal deficiencies of this general type are concerned Though we deal, or attempt to deal, with these diseases on physiological and biochemical principles their origin is almost certainly genetic Future developments in their understanding, though not necessarily in their control, will come when the genetic approach is properly exploited

I wish that I could say something hopeful about research into disease of the nervous system, whether its manifestations are physical or mental With some minor reservations the position today is much the same as it was in my student days when every patient with a physical disorder of the nervous system was given antisyphilitic treatment The basis was simply that if the disorder was due to syphilis it might be cured, if not, it was certainly incurable There is admittedly much being done at an empirical level in treating mental disease by the very crude procedures of leucotomy or the electrical or toxic shock treatment Both procedures have their uses but they are obviously onl transitional approaches to problems of almost insup- difficulty

In the laboratories there is great activity in the of the nervous system, and most physiologists now are electrophysiologists The immense comm development of electronic equipment in recent years provided gadgets of infinite adaptability for the m ment of electrical changes in nervous tissues ingenious experimenter can find an infinity of prob to study He can also take pride in the way his is joining hands with that of the makers of "elect brains," and introducing "cybernetics" to the phi sophers It is magnificent, but it has no bearing what on the pressing problems of insanity, behaviour d orders, and feeblemindedness Probably every sci has felt at times that most other scientists are guil the sin of infinite and futile elaboration I am al feel that way about electrophysiology, but I must admit that from the president of the Royal Soc downwards electrophysiologists have the highest sta today in the scientific world

I am not competent to discuss psychological psychiatric research Like most scientists outside th special field, I find it impossible to digest what of th psychological literature there is time to read As biologist I fancy that the effective generalisations th are needed may eventually be found more readily fr the study of animal behaviour than from too undu an attention on the

We can be sure tha persists, resear on all these aspects of medicine, from infectious dis to psychiatry, will go on They will change their chara mainly in response to the discovery and utilisation of t techniques

But all the work that I have discussed is from a point of view at a superficial level It has been concer only with the body and mind as we find them It is the essence of all the problems that body and mi have arisen by a process of evolution In the broad sense genetics can be defined as the science concer with the transfer of pattern from one generation another, pattern of bodily structure, pattern of behavi and in humans and domesticated animals pattern disease I turn therefore to what I feel will be th important topic of medical research for the futu human genetics

The Central Place of Genetics in Modern Biolog

There has been a general attitude of defeatism in regard to medical genetics Every doctor will ad that inheritance plays a part in every illness, but there is nothing that can be done to alter it he usually feel that there is no sense in attempting to st the genetic aspects of the illness more closely This i perfectly justifiable attitude to the clinical problems today—but not, I think, a correct one

Let us begin by considering the main types of gene study now going on

We all know that the inheritance of all human char teristics is determined by the sorting out of chromosom that takes place when germ cells mature and then fu in the process of fertilisation There is great activit in the study of problems of this sort in plants a animals For historical and accidental reasons a lar amount of the theoretical research has been done on tw organisms—one a little fruit fly, drosophila, the other a important food plant, maize Most of the agricultural important plants and animals have been and are be studied genetically with both theoretical and practi aspects in mind The most important commerc application has been the development of hybrid corn the United States In most types of stockbreedi theoretical genetics has been helpful in rational

I was quite a little girl"; and she described a typical of acute otitis media. On that side the radiogram ed the cells with patterns similar to the other—but again dentical, because all the cells were smaller, with thicker between them.

each practising otologist finds one such case in the se of his career we may, in a century or so. have a ectable body of evidence in favour of this hypothesis.

ngfield, Surrey. T. B. LAYTON.

BOVINE TUBERCULOSIS AND HUMAN TUBERCULOSIS

IR,—Mr. Pitcher's thesis (Dec. 6) is, to a first approximation, perfectly logical. The argument runs thus:

1) Pulmonary tuberculosis is due almost exclusively to ction by the human type of tubercle bacillus.

2) There is a high degree of cross-immunity between man and bovine tuberculosis. Therefore, a diminution in ections due to the bovine tubercle bacillus will increase number of people susceptible to both types, and, other ngs being equal, will lead to an increased incidence of lmonary tuberculosis. Mr. Pitcher's figures purport to show at this theoretical possibility has been realised in Scotland.

Before considering Mr. Pitcher's data, let us remember at bovine tuberculosis is not to be regarded merely as beneficent immuniser against infection by the human acillus: bovine tuberculosis was estimated to have used some 2600 deaths in 1931.

Mr. Pitcher's tables compare notifications for 11 ounties in two quinquennia. In his first table the second uinquennium is virtually the same for all counties, but r the first quinquennium he chooses five different eriods. I do not wish to suggest that Mr. Pitcher has isled us by *choosing the periods to support the thesis.* o doubt his choice was governed by availability of data, ut he should certainly try to show that his results have ot been sophisticated thereby.

It seems to me that at least the first table contains rrors of simple arithmetic. The last column, "increase r decrease," seems to have been calculated as a simple ifference, and this would be legitimate if, as is probable, he populations of the counties did not alter greatly etween the two quinquennia. If my assumption be orrect, then the last column figures for West Lothian nd Dumbarton should read +119 and +12 respectively. t may be that Mr. Pitcher has made his calculation by ome other method, in which case the figure which he ives for Dumbarton may be correct, but that for West othian is certainly wrong on any basis of computation.

Finding the rates for Glasgow incredible, I have taken he liberty (which I hope Dr. Laidlaw will forgive) of xtracting the real figures from the annual reports of the lasgow medical officer of health. They are as follows:

Year	*Population*	*New registrations of pulmonary tuberculosis*
1930	1,088,810	1687
1931	1,088,461	1702
1932	1,095,263	1722
1933	1,103,357	1616
1934	1,115,590	1523
1946	1,075,000	2809
1947	1,100,000	2765
1948	1,110,000	2775
1949	1,110,000	2829
1950	1,100,000	2446

It follows from these figures that the notifications per 100,000 population were 152 and 247 respectively, and not 2 and 3 as Mr. Pitcher states. It is possible that the terms "new registrations of pulmonary tuberculosis" and "notifications" are not quite synonymous; for example, the first term might include "transfers in," but this could not account for the gross discrepancy.

Apart from the unreliability of the data there is a fundamental defect in the logic of Mr. Pitcher's argument. The immunological consideration which underlies his argument is whether or not *living* tubercle bacilli are ingested. The extent to which a milk-supply is pasteurised or sterilised is, therefore, of the first importance. It means very little to say that 50% of the milk consumed by a community is from non-attested herds if in fact the bulk of this 50% is adequately heat-treated before consumption; unless of course, Mr. Pitcher intends to argue that the ingestion of killed tubercle bacilli can produce immunity. For this there is, so far as I know, not a scrap of evidence.

D. B. BRADSHAW
Leeds. Deputy Medical Officer of Health.

Obituary

THOMAS DRUMMOND SHIELS

Kt., M.C., M.B., Edin.

Sir Drummond Shiels, who died in London on Jan. 1, had made a career for himself in politics as well as medicine: and he had used his experience in each calling to enrich his work for the other.

He was born in Edinburgh in 1881 and when he left school began work as a photographer. During the 1914–18 war, while in command of a trench-mortar battery, he was mentioned in despatches and was awarded the M.C. and the Belgian croix-de-guerre. After the war he returned to Edinburgh and began to study medicine, taking his M.B. in 1924. Meanwhile he had been elected to the Edinburgh town council, and in the year he graduated he also became a Labour member of Parliament for East Edinburgh.

[Walter Stoneman

His political advancement was rapid. In 1927 he was appointed a member of the Royal Commission on constitutional reform in Ceylon. Two years later he became Parliamentary under-secretary for India, and later to the Colonial Office. After he lost his seat in Parliament in the 1931 election he became secretary to the British Social Hygiene Council, a post for which his judgment and turn for lucid exposition well fitted him. But the decision not to seek re-election to Parliament had been a hard one, and he eagerly seized the opportunity, when it arose, to join the staff of the Empire Parliamentary Association. As deputy secretary of that body he was brought back to the atmosphere of Westminster in which he thrived, and which gave scope for his genial personality. In 1946 he was appointed public relations officer to the Post Office, and in the same year he also became a member of the Colonial Economic and Development Council. He was vice-president of the Royal Empire Society, on whose council he had served for many years, he was also a member of the governing body of the British Postgraduate Medical Federation. He was knighted in 1939.

R. F. writes: "The Clydesiders considered Drummond Shiels's views to be pale pink, but they never questioned the honesty and sincerity of purpose of their Edinburgh colleague. The inevitable ins-and-outs of the politician's life meant for him hardship and financial stringency, but he never complained, and he always showed those qualities of toleration, loyalty, and humour for which he was held in general esteem. In speech he was slow, deliberate, and almost ponderous, but he never took himself too seriously. If his demeanour was grave, his smile at once removed all trace of the funereal. His manner was tactful and persuasive, but that jowl of his denoted dour persistence: his humour was pawky rather than sly, for there was nothing but good nature behind it. At home in any company, he never forgot that he was a Scot: and when he presided over his fellow-exiles at the dinner of the London Burns Club in 1951, we little guessed that his life of public service and private kindliness was so near its end."

Sir Drummond Shiels's first wife died in 1948. In 1950 he married Miss Gladys Buhler, M.B.E., who survives him with the daughter of his first marriage.

become recognisable There are two important practical implications here The first is that by early recognition of such premonitory signs we may be able to institute a régime that will delay the full or fatal expression of the disease, the second is that it may allow a more accurate prognosis of the life expectation of individuals for any sort of actuarial purpose

4 It would provide a magnificent and varied clinical training for a succession of young doctors passing through the unit giving an approach to patients as full human beings that tends to be lost when men are trained in clinical research too closely at the physiological level

5 With the extension of such work over the whole medical world there would slowly develop a consciousness of the importance of inheritance, an accurate knowledge of the mode of inheritance of the common as well as the rare and striking human genetic anomalies, and an understanding of what can and cannot be accomplished by conceivable forms of control of human reproduction

6 As in every type of effective research, there would arise new ideas and approaches which until the work is done are quite literally unthinkable It is even possible that ways of preventing genetic deterioration may be found that could be tolerated by a free human community

This brings me to my final point—that sooner or later ways *must* be found to reverse that process of genetic deterioration of our species that is demonstrably in process at the moment

As a biologist I regard it as certain that man has evolved by the same process as other living organisms, as a doctor and for my present purpose I am concerned only with the health of the body The evolution of tradition and civilisation is outside our province and uniquely human The evolution of the body and of the defects of the body falls within the realm of genetics Mendel's laws hold for man, there are biochemical mutants in man as well as in the moulds and bacteria that the microbial geneticist studies Equally we can be certain that the line of mammalian evolution that led up to man was directed by the same process of gene mutation, recombination of gene patterns, and natural selection that can be seen at work in organisms susceptible to direct genetic investigation Mutation by its very nature must normally be harmful—the mutation or combination of mutations leading to improvement of the type must inevitably be rare Progressive evolution, in Fisher's words, is a miracle wrought by selective survival in the teeth of a storm of deleterious mutations

If man is outside the workings of Nature, if his continuing progress toward his own bodily and spiritual ideal is predestined and determined by supernatural means, then what I am saying is meaningless and unnecessary But if we accept the working hypothesis of scientific medicine that man is wholly a part of Nature and that his diseases can only be understood and remedied in the light of comparative biology, then I think we have got to face the situation realistically

It has been estimated that the harmful mutation to hæmophilia occurs once in 50,000 births Most hæmophiliacs have little chance of passing on the altered gene, and the symptomless female carriers would gradually diminish in number unless fresh mutations occurred But as Muller has pointed out, if a maintenance therapy like insulin for diabetes was discovered which allowed hæmophiliacs to lead a normal reproductive life, nothing but deliberate human action could prevent a slow but inexorable increase in the proportion of hæmophiliacs until they became a majority of the human species Every deleterious mutation which in one way or another does not prevent or diminish the fertility of those carrying it must eventually spread through the race like a slow-moving infectious disease Somehow some means must be found to counteract the present trend by which the unhealthiest elements in the population of Western countries reproduce more rapidly than the healthy I have already mentioned the evidence that in England the one measurable aspect of human value—intelligence—is falling at the rate of 1 6 points per generation. democratic welfare State may have its virtues transitional compromise, but unless it finds an to the problem of genetic deterioration it will be doo In my gloomier moments I feel that a case might be for the thesis that it will be the descendants of the race to receive the blessings of civilisation who eventually rule the world In the old days of birth-rate and very high infant mortality many hea babies died, but almost certainly more of the genet unsound than the sound and thus there was some au matic control of quality Today the combination of two child family and preventive medicine has prod a situation highly desirable on the short term view b on the long-term biological view leading straight catastrophe

There is no *politically possible* way of remedy this at present, but at the back of everything I h been saying is my conviction that here is *the* great t of future medical research—to plan the ways by w the bodily health and intelligence of human b may last from generation to generation It is a t for centuries rather than decades but the sooner it started the better I hold no brief whatever for a present interference with the traditional but sp taneously changing pattern of human mating a reproduction We know far too little, and wh knowledge there is is far too little known to peo generally The task of the next hundred or even fi *hundred years is to gain the knowledge and* educa the people till effective action at length becom possible.

THE LATE RESULTS OF REPAIR OF LARG HERNIAS WITH TANTALUM MESH

D M Douglas
M B E, Ch.M St And, F R C S F R C S E
PROFESSOR OF SURGERY IN THE UNIVERSITY OF ST ANDRE

An experimental study of the reaction of living tis to tantalum mesh, together with a preliminary repo *on its clinical use, was published in this journal four yea ago (Douglas 1948)* The late results of the repair of *cases of large or recurrent hernias are now presented*

DETAILS OF OPERATIONS

The details of the operations for incisional an umbilical hernias are seen in figs 1 and 2, which are s explanatory It is most important to achieve a go overlap of fascia over the implanted mesh In the cas of inguinal hernias in males the testis was transpo through the conjoined tendon in the manner of Schnede (1934) to avoid pressure of the edge of the mesh on th spermatic cord

MATERIAL

13 inguinal, 8 para umbilical, and 15 incisional hernias have been operated on (see table) Most were larg hernias considered by colleagues unsuitable for repa by other methods The remainder were recurrent hernias, no primary small hernias were treated wit tantalum mesh

CASES OF HERNIA REPAIRED WITH TANTALUM GAUZE

—	Type of hernia			Total
	Inguinal	Para umbilical	Incisional	
No of cases	13	8	15	36
Postoperative deaths	0	0	1	1
Death from other diseases since operation	2	0	2	4
Untraced	2	0	0	2
Recurrence	1	0	0	

Notes and News

THE WORK OF THE N.A.P.T.

HE better success we are having at present in preserving uberculous from early death must not blind us to the fact for every one who dies of the disease in any year. 5 or 10 ll. The National Association for the Prevention of Tuber- sis is thus in no danger of losing its occupation for some to come. The annual report [1] for 1951–52 notes how much k the voluntary tuberculosis care committees still do for ients—even though the tuberculous now have a legal right such things as extra milk, new bedding, or (if need be) a poration house and a sheltered job. Yet "one's legal nts in this world are seldom quite sufficient," and, as the A.P.T. points out, the voluntary committees can help ients in ways which are not legally open to local health horities—by subsidising them financially, for instance, or in a case quoted in the report) by providing for the training an unsuspected talent. The N.A.P.T. acts as a consultant ntre for these voluntary bodies, giving them advice about y, administration and procedure. A piece of social research anced by the association is being carried out in Scotland Mrs. J. F. Wilson. She will assess the social effects which diagnosis of tuberculosis and the subsequent treatment has the patient, his family, and his relations with the com- unity; and it is hoped that the study will give information out the use made of the health services, the gaps in it, the gree of disruption of family life produced by the disease nd the social handicap it imposes. The N.A.P.T. is also oviding bursaries of £100 yearly for men and women who tend, or propose to attend, the university, and whose reer has been interrupted by tuberculosis; the first award as made this year. Other scholarships have been awarded nurses, to enable them to visit Denmark, Norway, and weden to study tuberculosis control there.

A semi-documentary film *Personal Episode* has been made or showing to the general public, with the intention of putting ne subject of tuberculosis in a sympathetic light, and emoving some of the apprehension felt about sanatorium ursing. The setting is Scottish, and the story is of a girl tudying to be a teacher, at Edinburgh University, who reaks down with tuberculosis, goes to a sanatorium, recovers, nd decides to become a nurse. The N.A.P.T. has renewed n arrangement, in action before the war, by which district nurses and Queen's nurses from rural areas are able to take a course of 4–8 weeks in postgraduate training at one of the arger tuberculosis hospitals, and has also arranged for ectures to medical audiences: last year, for instance, lectures were given in Inverness and Lewis by Dr. Marc Daniels (on treptomycin and B.C.G.), and in Lewis by Mr. F. J. Sambrook Gowar (on lung resection for pulmonary tuberculosis).

The membership of the N.A.P.T. is divided into sections, which are more or less autonomous, some active groups being he medicolegal section, the sanatorium matrons' section, and he nurse teachers' section. These arrange their own meetings and lectures for themselves. Art therapy continues to be very popular, and art competitions are held four times a year. There are some 500 entries on each occasion and it takes the selection committee a week to judge the entries and dictate their criticisms. Besides being good for the patients, this should in time contribute to a revival of painting in England as stirring as the revival of music achieved by the B.B.C.

Besides these and many similar undertakings fostered by the association, a great annual stream of books, pamphlets, leaflets, and journals proceeds from the N.A.P.T., nourishing the growth of sound ideas about tuberculosis, and fertilising the minds of doctors as well as of laymen.

HELPING THE LONG-STAY PATIENT

THE preparatory training department of the British Council for Rehabilitation helps long-stay patients in hospital and long-term convalescents in their own homes to prepare themselves to earn their living when they are once more fit. The department arranges for them correspondence courses, supplemented so far as possible by supervisory visits, and where possible tuition by a visiting instructor. Every course is arranged subject to the approval of the patient's doctor. The department works in coöperation with local education authorities who refund tuition fees and help in other ways. Patients are also encouraged to contribute to the cost as their means permit. Courses in 250 subjects, ranging from secretarial work to radio engineering, and from commercial art to criminal psychology, have been provided by the department or through one of the local affiliated committees which are being formed throughout the country.

Further particulars may be had from the registrar, Preparatory Training Bureau, British Council for Rehabilitation, Tavistock House South, Tavistock Square, London, W.C.1.

PROPOSED AMENDMENT TO ABORTION LAW

ON Feb. 27 Mr. Joseph Reeves's Abortion Bill is due for second reading in the House of Commons. But, as it is preceded by two other Bills, it is doubtful whether it will be reached.

The Bill adds the following proviso to section 58 of the Offences against the Person Act 1861, which makes it a felony to administer drugs or use instruments to procure abortion:

> Provided that—(*a*) no person shall be found guilty of an offence under this section unless it is proved that the act charged was not done in good faith for the purpose of preserving the life of the mother; (*b*) no registered medical practitioner who acts with the concurring opinion of a second registered medical practitioner shall be found guilty of an offence under this section unless it is proved that the act charged was not done in good faith for the purpose of preventing injury to the mother in body or health.

HOSPITAL STATISTICS

THREE weeks ago, in a critical review [1] of *Statistics of the Hospital and Specialist Services for England and Wales* for 1950, a correspondent mentioned that the next volume in the series was to appear very shortly. It has now been published,[2] and the Ministry of Health hopes in future to present the *Statistics* "by the middle of the year following the one to which they relate."

The 1951 volume gives figures for over 3000 hospitals and clinics which are either part of the N.H.S. or linked with it under contractual arrangements. It is possible, for example, to find out how many staff in any of over 40 categories—from consultants to laundry staff—were employed in any particular hospital at the end of 1951. Other information given in respect of every hospital is: bed complement; number of beds available; average daily bed occupation; total of inpatients who died or were discharged during 1951; total of new outpatients; and total attendance of outpatients and at casualty departments.

PRODUCTION OF A.C.T.H.

MANUFACTURE of A.C.T.H. in Britain has been started by Crookes Laboratories Ltd. Supplies of this substance, which is being made from the pituitary of home-reared oxen, are expected to satisfy home demand; and it is also to be exported.

POISONS LIST AND RULES

REVISED versions of the Poisons List and the Poisons Rules came into force on Jan. 1. The changes in the list are set out in schedules to the Poisons List Order, 1952,[3] which also includes the current list in full. The Poisons Rules, 1952,[4] consolidate with amendments the rules issued in 1949, 1950, and 1951.

University of London

The following have been successful in examinations for the degree of M.S. (branch 1, surgery):

Claude Brun, W. D. Corfield, D. H. Jenkins, P. F. Philip, M. C. T. Reilly, H. H. Renyard, J. J. Shipman, K. W. Wilkinson.

University of Manchester

Dr. T. R. Malloy has been appointed lecturer in child psychiatry.

National Association for Mental Health

At a meeting of this society to be held at the Royal College of Nursing, Cavendish Square, London, W.1, on Friday, Jan. 16, at 2.30 P.M., Mr. Claud Mullins, the former Metropolitan court magistrate will speak on Crime and Mental Health.

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[1] Progress and Hope in Tuberculosis, 1951–1952. N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.

[1] *Lancet*, 1952, ii, 1219.

[2] National Health Service: Hospital and Specialist Services, England and Wales. Statistics for the Year Ended Dec. 31, 1951. London: H.M. Stationery Office. 1952. Pp. 268 £1.

[3] Poisons List Order 1952 (S.I. 1952 no. 2085). H.M. Stationery Office. 4*d*.

[4] Poisons Rules 1952 (S.I. 1952 no. 2086). H.M. Stationery Office. 1*s*. 3*d*.

Recurrence 1—A man, aged 56, had a large right scrotal hernia with a widely dilated deep inguinal ring The Schmieden manœuvre was used, *the testis and cord being transposed* through the conjoined tendon Within eleven months of this operation *a small bulge appeared at this site, and this has* become a little larger over the last four years The patient does not wear a truss

Recurrence 2—A woman, aged 35, had a recurrent right inguinal hernia It was difficult at operation to *find in the* region of the inguinal ligament sufficient tissue under which to countersink the *mesh The recurrence is in the form of* a diffuse bulge over the operation site and causes some discomfort

In the remaining 27 cases there has been no recurrence, and it is of particular interest that in none of the incisional or para-umbilical hernias has a recurrence been noted. There have been no discharging wound sinuses after the use of this technique, though in a series of cases which we are now studying in which nylon mesh was used there have been 2 cases of discharging sinuses

DISCUSSION

Inguinal Hernia

The method is clearly *not good for inguinal hernia,* the reason, I think, being that it is difficult in recurrent cases to find enough tissue inferiorly to anchor the mesh securely. Further, in males there does not appear to be any satisfactory method of fitting the gauze snugly round the issuing spermatic cord The Schmieden manœuvre obviously carries its own special risk of recurrence through the new deep inguinal ring

Incisional and Para umbilical Hernia

In view of the size of the hernias dealt with and the absence of recurrence in this group the method is clearly of value In the past I have found it difficult to close any defect in the abdominal wall greater than 7 cm in diameter by any technique If the edges are pulled together with silk, fascia, or nylon, the sutures simply cut through the living tissue as they would through cheese With mesh there is no such problem Flaps are turned in from the edges of the defect, allowing the first layer to be closed easily without tension, the resulting defect is next filled with tantalum mesh

Fracture of Mesh

As the result of repeated bending the mesh ultimately fractures This does not seem to influence the result of *the repair, probably* because the strong fibrous tissue layer has grown through the framework of the mesh *But the ends of the wire gave rise* to an uncomfortable pricking sensation in the woman in whom a recurrence was noted She was very thin, and perhaps there was insufficient subcutaneous tissue to cover the fractured edge of the mesh *She was the only* patient who complained of this sensation I had thought that the late results of these herniotomies would be less satisfactory than the immediate results, but this follow up study has shown this to be untrue Both recurrences were seen within a year of operation

SUMMARY

36 large or recurrent hernias have been repaired with tantalum mesh, the shortest period since operation being 4 years, the average 5 years

There have been two recurrences, both in inguinal hernias

There have been no recurrences in para-umbilical or incisional hernias

No wound sinuses have developed

The method is of little value in inguinal hernia but may be used with confidence in large incisional and para umbilical hernias

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CLINICAL ASPECTS OF THE TOXICIT POLYMYXINS A, B, AND E

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THE polymyxins are polypeptide antibiotics d from different strains of *Bacillus polymyxa* Five h been described and are designated by the alphab suffixes A to E They are *bactericidal and at le* hundred times more active against most gram neg *bacilli than against the gram-positive organisms* (Br lee et al 1952) Although there were early repor their clinical use (Swift 1948, Schoenbach et al 19 polymyxins A and D have not become popular, ow probably to the introduction of antibiotics with w antibacterial spectra and to the attention focused on t proteinuria associated with the parenteral injectio polymyxins A and D, but recent reports (Yow 19 Jawetz 1952, Swift and Bushby 1951, Jackson et a 1951, Tomlin 1951, Kagan *et al* 1951) on the effic of the polymyxins in certain types of meningitis, uri *infections, and burns, especially when the infect* organism is *Pseudomonas pyocyanea,* have reawak interest in these antibiotics

As a class, polypeptide antibiotics have undesir side-effects which often render them unsuitable f parenteral use, and our early experiences with p myxins A and B suggested that they were not exceptio Proteinuria, ranging from a trace to 0 2 g per lit developed in 26 of 27 children given polymyxin A *doses of 4000 to 10,000 units per kg of body* wei four-hourly for five days Relatively impure polymyx B* in similar doses given to 24 children, and in doses 250,000 units given to 8 adults caused no proteinur but caused severe reactions at the sites *of injecti* pyrexia up to 102°F, malaise, and in 3 *of the* adu paræsthesia In contrast, our more recent experienc with polymyxin E and with purer preparations polymyxin B have shown that these polymyxins a suitable and safe for parenteral use, and, since there now little doubt that the polymyxins are potent chem therapeutic drugs, we are prompted to record observations on the side effects produced in 61 pati treated with these two polymyxins

RESULTS

Polymyxin E—Forty-seven patients, including adults, were given intramuscular polymyxin E four hour for five days Seven of these had longer courses of fou teen days or more for *Hæmophilus influenzæ* meningi along with intrathecal injections of doses ranging fr 25,000 to 100,000 units once or twice daily for from fi to fifteen days For children individual doses were bas on the scale of 10,000 to 12,500 units per kg of bod weight The dosage for adults was 250,000 units exce in 2, when it was increased to 500,000 and 1,000,0 units (see below)

In contrast to our earlier experiences with polymyxin and polymyxin B the toxic effects from polymyxin were few and trivial and caused little discomfort to t patient Protein, red cells, and casts appeared in t urine of 1 child only This child, under treatment f *H influenzæ* meningitis, died from an intercurre infection, and the case has been described elsewh (Swift and Bushby 1951) *Microscopy of the kidne* revealed that the secretory epithelium of the kidne

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* This early sample of polymyxin B and the polymyxins A and were prepared by the Wellcome Research Laboratories more recent polymyxin B was prepared by Chas Pfizer & C for Burroughs Wellcome & Co U S A

THE FUTURE OF MEDICAL RESEARCH*

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MEDICAL research is a very human activity carried out men of diverse types who have entered and stayed the field for a variety of reasons. It has a history and continually changing approach to its material. Like e broader field of scientific research of which it is a rt, it has developed its own sense of values and a nviction of its own intrinsic importance. These do t always coincide with the ideas of the community nerally. It has grown out of human need, but its ajor contributions to human welfare have mostly come by-products of its own intrinsic activity—an intrinsic tivity which nowadays has almost lost contact with cial need.

My object here is to consider in what directions edical research must develop if it is to be of maximal se to the community—having due regard to the fact at there is a well-defined cultural pattern of research hich like any other established pattern of tradition and ctivity cannot be changed suddenly without dire onsequences.

This puts the problem neatly into two halves. What oes the community need from medical research ? And ow can the present pattern of research activity be more ffectively directed toward those socially valuable ends ?

The Aims of Medical Science

The aim of medicine in the broadest sense is *to provide or every human being, from conception to death, the greatest ullness of health and length of life* that is allowed by his enetic constitution and by the accidents of life.

We are all aware of the importance of preventive as ell as curative medicine, and we are equally aware of ow indefinite is the boundary between social amelioration and preventive medicine. A rising standard of iving, and the spread of "upper class" demands for omfort and of "upper class" habits of cleanliness hrough the community, have been the most important actors in the vast increase in health and length of life hat has taken place since the middle of last century. lorence Nightingale is perhaps the key figure of that hange. Aristocratic, religious, neurotic, and with a errifying capacity for work, she realised that the physical omforts of food, space, cleanliness, and good manners hat were available to her own class were the important hings lacking in the handling of the sick and wounded oldier or the sick pauper. Since then public health has lways included an interest in housing and working onditions and all that complex of social philanthropy nd regulation which in our day has flowered into the "Welfare State."

Medical research in any ordinary sense has had little r nothing to do with this social revolution, which, I hould guess, has been responsible for at least half the mprovement in the expectation of life that has taken lace in the last hundred years. Florence Nightingale never believed in bacteriology, and, though in due course he bacteriologists found good reasons for the benefit btained by improving drains and supplying pure water, he whole process was well under way before the scientists had any influence whatever in administrative circles.

I have perhaps unduly stressed this point because I eel that when we are considering the social aspects of medicine we have to recognise that health depends on more than a regard for the bodily well-being of the individual as such. To give a current example—if in India or China the rapid application of known techniques produced an immediate reduction of infantile and general mortality to a Western level, within ten years there would be an intolerable strain on the food resources of the world and famine in the countries concerned.

I suggest that we need to add an even broader concept of the rôle of medicine in the modern world. Out of the idea of public health there is growing the concept of human biology with its own central objective. Perhaps this can be stated as simply to find means *to ensure the indefinite continuance of the human species at a level of physical and mental health not inferior to that of the present.* It is perhaps characteristic of the present time that we have reduced our aspirations for the future to such a negative statement. But I think we are realising every year the complexity and the difficulty of accomplishing the task that I have stated. Its implications go into every phase of human life—politics and economics even more than medicine. But here I shall try to confine myself to aspects bearing directly on the bodily health of human beings, including mental and social factors only in so far as they affect the body.

Our modified definition of the aim of medical science, then, is to provide for all human beings the greatest possible health and length of life and to ensure that the possibility of providing those benefits shall not diminish from generation to generation.

The Changing Problems of Medicine

A hundred years ago the major causes of premature death resulted from infectious disease and malnutrition, especially in infancy and childhood. Infantile mortality in London then was near 300 per 1000 live births. Improper food and infectious disease of one sort or another were mainly responsible.

Infectious disease will always be with us, and there will always be room for further refinement in prevention and treatment; but as a major cause of death in the years of youth and maturity it is becoming relatively unimportant. Similarly the knowledge we have of the fundamentals of nutrition is such that the problems in that field are wholly educational and economic. Scurvy and rickets are virtually unknown in Australia where our only important nutritional disease, tooth decay, is due not to a food deficiency but to excess of a luxury.

Though it may seem an inappropriate remark for one whose whole professional life has been concerned with infectious disease, I believe that, provided the established mechanism of preventive medicine, medical care, and drug production continued to function, fundamental work on the nature of micro-organisms and on the diseases they produce could stop today without influencing the current process by which all the main infectious diseases except poliomyelitis are disappearing. This is of course an over-statement: as long as the human race exists there will be long-term changes and sudden new episodes of infectious disease that will need intelligent investigation and appropriate action to counter them. My point is only that it is extremely unlikely that any new principles will be needed to maintain our present very effective control of infectious disease; in that sense fundamental research is not called for by an expressed human need. I can leave you to make precisely the same sort of qualification about nutritional disease.

Apart from the disappearance of infectious disease and gross malnutrition, the main changes in the medical scene in the last hundred years have been the provision of means for minimising physical or functional defects of the body, whether congenital or acquired.

Spectacles, false teeth, and hearing-aids may be slightly comic, but they have probably done more for human happiness than any other application of medical science.

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* From a lecture given before the Actuarial Society of Australasia at Melbourne on Sept. 11, 1952.

restricted to the tubules, and only when there is proteinuria are high concentrations of the antibiotic excreted in the urine (Brownlee et al 1952) This evidence suggests that the nephrotoxic polymyxins A, C, and D pass through the normal glomerulus and damage the tubule during resorption Polymyxins B and E, on the other hand, do not usually cause renal damage and are present in the urine in low concentrations It is therefore a reasonable conclusion that it is the molecular configuration which permits or prevents passage through the normal glomerulus

Some of the subjective side effects of the polymyxins may be due to histamine, for the intradermal injection of polymyxin in man produces a typical histamine triple response, and Kagan et al (1951) found that the subjective side-effects of the polymyxins were relieved by anti-histamine drugs Experimentally, however, no significant quantity of free histamine can be detected in polymyxin Nevertheless polymyxin may cause the release of endogenous histamine, since the intravenous injection of 20,000 units per kg of body-weight into dogs often produces a pronounced and sustained fall of blood-pressure closely resembling that produced by the powerful histamine-release drugs—e g , 48-80 (Paton 1951)—and an increase of histamine can be demonstrated in the blood (Bushby and Green 1953)

All these side-effects have been reported before, but their frequency has varied according to different reports Kagan et al (1951) comment especially on the variability in the reports of the toxic reactions of polymyxin B Referring to the pyrexial reactions they draw attention to the fact that of five separate workers only one noted pyrexial reactions and these in 62 of 66 patients Most reports, however, agree that the polymyxins B and E seldom damage the kidneys

It is unfortunate that the first polymyxins in man should have been the polymyxins A and D, which attracted publicity by their effect on the kidneys The use of the group name, polymyxin, has also led to confusion, thus Hayes and Yow (1950), who successfully used polymyxin B in the treatment of infection with *Ps pyocyanea*, state that Schoenbach et al (1949) noted the commonest complication of polymyxin therapy to be renal damage, whereas the workers cited were referring only to polymyxin D

After oral administration all the polymyxins are poorly absorbed (Brownlee et al 1952), and in 12 children with gastro-enteritis treated by us with polymyxin A 40,000 units per kg of body-weight four-hourly for 5-8 days no toxic side effects were observed Although polymyxin is effective in the local treatment of infected burns, absorption from such surfaces is poor, for no polymyxin is detectable in the blood, and no toxic symptoms are produced, when 1% polymyxin E ointment is used (Jackson et al 1951) The side effects observed by us after intramuscular administration occur only when the antibiotics are given by this route Our experience shows that although polymyxin B and E cause some side-effects, these are not serious, causing at the most only temporary discomfort to the patient The most troublesome of these subjective effects is the pain that persists for some hours at the injection site, this is less with polymyxin E than with polymyxin B, but is so mild that the use of these antibiotics can be confidently recommended

SUMMARY

Polymyxin E given parenterally to 53 patients, and polymyxin B given parenterally to 32 patients, caused no proteinuria, this contrasts strongly with the high incidence of proteinuria produced by polymyxins A and D

Early experiences with polymyxin B showed that it caused troublesome reactions, especially pain at the injection sites, and in some patients pyrexia, malaise, and mild paræsthesia The incidence of pyrex malaise seems to be smaller with purer material

Polymyxin E caused less pain at the injectio than did polymyxin B, but the incidence of paræs was about the same

It is suggested that the different side effects o polymyxins are due to differences in molecular stru and that some of the subjective effects are due to release of endogenous histamine

Although the side-effects from parenteral polymyx and polymyxin E may be annoying to some pat they are not, especially with polymyxin E, sufficie contra-indicate their use

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ANALYSIS OF THE NORMAL ELECTRO-ENCEPHALOGRAM

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For some years electro-encephalographers have bee occupied with the problem of differentiating quantit tively between normal and abnormal electro encephal grams (E E G) Because of the complexity of the materi the characteristics of the E E G have mostly been asses by direct inspection of the primary trace and measur ment of trace height wherever a single frequen appeared in the record, description of the component par being based largely on qualitative assessment Metho have been evolved to quantify the material (Davis a Davis 1936, Hoagland et al 1937, Golla et al 1943, Lo et al 1944), but none of these has been widely adopte Several methods of wave form analysis have be developed for this application (Grass and Gibbs 193 Knott and Gibbs 1939, Gibbs 1940, 1942, Barbour 194 Hoefer et al 1949, Prast 1951, Krakau 1951).

Here we report on the results obtained in a norm population with the automatic wave analyser devis by Grey Walter (Walter 1943a and b, Baldock a Walter 1946) Our material consisted of fifty men ag 20-58 and fifty women aged 17-61, who were eith members or relations of the staff of the hospital

METHOD

Electrodes were so placed that on either side o similar areas were bridged , of these the fronto occip frontal, occipital, and precentral transverse posit have been used for this study Bipolar recordings ma medical research must face in the future—and we have to make a considerable reorientation of our of medical research to do so.

The Pattern of Medical Research Today

would hold that science springs from the same root raftsmanship and art, and I should define science simply as the systematisation of methods for the t effective satisfaction of human desires. But with development of research and scholarship as a profes al occupation, science has become a pattern of llectual techniques and judgments of values, with a archy of prestige and a subtly graded system of ards. In many ways the modern community of ntists has as definite a social structure as the medical fession or the Protestant clergy. It is a structure that well adapted to the functioning of those who compose I doubt if there is any other human activity in which wards are so closely related to the value of the work ne, or in which the typical and most sought after ward is the opportunity to do more and better work.

All scientific activity springs from the drive to satisfy uman needs and desires, but in finding the most effective eans of doing so scientists have become on the whole ore interested in the means than in the end. To do a ing properly demands an understanding and control many relevant factors, each of which in turn depends others. Any experimental scientist of imagination nd intelligence can start with any problem whatsoever, nd by following where it leads spend a lifetime in eritorious scientific work. There is a tradition well unded in experience that important advance in practical s well as in theoretical science comes not from the direct ttempt to cater for some practical need but by working t the advancing edge of knowledge. Very often nowa ays the procedure is to apply to the advancing edge of ne field, ideas or techniques that have been developed a different field.

Being an academically minded scientist myself, I know hat the typical research man is happiest when he has all he materials for his experiments or observations immedi tely under control. It is much more gratifying to study pidemics in mice, where everything from the strain f virus to the diet of the mice is known, than to try to nake sense of a human epidemic, where all the factors re intrinsically complex and are made worse by health lepartments taking all sorts of action to stop it.

There are of course many people engaged in applied esearch in industry, agriculture, medicine, and sociology; ut it is inescapable that in the cultural pattern of cientific activity this ranks lower than "pure" science. am making no personal value-judgment here: I am nerely reporting the fact that in scientific circles generally t is the development of ideas and generalisations on a asis of sound experimental work that gives status, not he production of life-saving drugs or money-spinning nventions. Take the recent presidents of the Royal ociety—Rutherford, Bragg, Robinson, Sherrington, Dale, Adrian, a wonderful sequence of names—men who ave influenced enormously the development of know edge and in many indirect ways the practical life of the ommunity. But none of them have produced by their wn work discoveries or techniques that were immediately aluable to industry or medicine.

The academic point of view might be expressed in its xtreme form by saying that scientific research is an ctivity of value for its own sake, and that, provided the project is attacked by the accepted methods of experimentation and logic, the actual material investigated is quite unimportant—so long as it is of such a nature as to uncover ideas and generalisations applicable to more than the situation actually studied. A good example is Sonneborn's studies of the genetics of the protozoon paramoecium. Paramoecium has no conceivable "useful" interest to human beings. It has a faint resemblance to some pathogenic forms, but that is all. Nevertheless we academic biologists all agree that this work of Sonneborn's is of first-rate theoretical importance. This is the type of value-judgment that runs through scientific work today, and which has become an integral part of the pattern of science.

In practice most fields of scientific study are chosen with some regard to the possible human implications of the work. For fundamental studies of how viruses multiply in cells I feel happier in using the virus of human influenza than I would in using a virus acting on some common bacterium. But the general approach to the problems, and the satisfaction of discovery when it came, would be precisely similar in the two cases.

What I want to stress is that one cannot present a scientist or group of scientists with an important human problem—let us say the cause of breast cancer—and expect a straightforward advance to an acceptable answer. What is allowable is to ask that an investigation be undertaken in some field which in the light of current knowledge seems relevant to the human problem. There is, for instance, much current interest in Bittner's ideas about a virus-like agent being responsible for breast cancer in mice. It would be reasonable to apply the mouse techniques to a series of cases of human cancer, or to study the interaction in mice of the "virus" factor with such things as age of infection or influence of hormones. For progress to occur we are almost compelled to have a number of individuals or groups working on the problem in different parts of the world and cross-stimulating one another with their different approaches.

Even a very young scientist knows nowadays that the chances of his discovering something equivalent to penicillin, nuclear fission, or the cause of cancer are vanishingly small; but he also knows that if his intelligence, curiosity, pertinacity, and imagination are up to the necessary standard there is a well-defined path by which he can make a continuing series of contributions to knowledge and in the process gain prestige and reasonable economic security. He will be disinclined at any stage to step off that moving staircase and adopt an attitude to science out of line with the current tradition.

I am not saying that this is a good thing: I think in fact that in many ways it draws some of our best brains away from the fields where they could make their best contribution to human welfare. There must be many first-rate academic scientists who if their interests lay that way could make a far more effective contribution in industry or practical medicine. But it does represent the pattern of today's high-grade scientific activity. And it must be remembered in any attempt to mould research activity toward what the community or any influential section of it feels is needed. Every major applied research organisation finds that if it is to keep its best men these must have opportunity for the fundamental work that brings them satisfaction and prestige of the sort they cherish. Experience suggests that a first-rate man is more useful if he is contented, even if he is in fact not primarily interested in the job that he is paid for.

All that this adds up to is that it would be quite foolish to lay down even the most enlightened programme for medical (or any other type of scientific) research and expect it to be carried out in that form. Sometimes under stress of urgent need a man will find the drive to go straight ahead for a definite and limited objective, but that is by no means the usual approach.

Current Activity in Medical Research

Once medical research was almost synonymous in the lay mind with bacteriology; and certainly it is in the field of infectious disease that laboratory research has had its main practical triumphs.

CORRELATIONS BETWEEN AMPLITUDES AT DIFFERENT FREQUENCIES IN CYCLES PER SEC, COMBINED DATA F[illegible] FIFTY MEN AND FIFTY WOMEN, LEFT AND RIGHT HEMISPHERES, FRONTO-OCCIPITAL DERIVATION

4	5	6	7	8	9	10	11	12	13	14	15	16	18	20	22	24	2[illegible]
1	−0 783	+0 681	−0 555	+0 132	−0 060	−0 160	+0 036	+0 210	+0 312	+0 527	+0 361	−0 169	+0 408	+0 240	+0 213	+0 135	−0 [illegible]
	1	+0 797	−0 676	+0 307	+0 047	−0 063	+0 037	+0 260	+0 276	+0 564	+0 352	+0 231	+0 390	+0 242	+0 231	+0 198	+0 [illegible]
		1	−0 838	+0 551	+0 195	+0 004	[illegible]	[illegible]	[illegible]	567	+0 501	+0 343	+0 417	+0 264	+0 280	+0 205	+0 [illegible]
			1	+0 706	+0 357	+0 158	[illegible]	[illegible]	[illegible]	539	+0 437	+0 292	+0 375	+0 246	+0 156	+0 107	+0 10[illegible]
				1	+0 726	+0 446	[illegible]	[illegible]	[illegible]	193	+0 317	+0 223	+0 182	+0 104	−0 002	−0 016	−0 [illegible]
					1	+0 614	+0 388	+0 218	+0 146	+0 002	+0 285	+0 135	+0 166	+0 212	−0 017	−0 019	−0 113
						1	+0 625	+0 424	+0 260	−0 025	−0 020	+0 106	+0 156	+0 291	+0 047	−0 001	−0 13[illegible]
							1	+0 842	+0 503	+0 214	+0 196	+0 312	+0 296	+0 311	+0 300	+0 196	+0 10[illegible]
								1	+0 725	+0 500	+0 355	+0 433	+0 432	+0 393	+0 413	+0 288	+0 20[illegible]
									1	+0 640	+0 338	+0 441	+0 526	+0 471	+0 437	+0 328	+0 [illegible]
										1	+0 507	+0 550	+0 613	+0 427	+0 434	+0 311	+0 31[illegible]
											1	+0 638	+0 5[illegible]	[illegible]	[illegible]	358	+0 391
												1	+0 7[illegible]	[illegible]	[illegible]	596	+0 59[illegible]
													1	[illegible]	[illegible]	671	−0 64[illegible]
														1	+0 810	+0 766	+0 645
															1	+0 851	+0 781
																1	+0 84[illegible]
																	1

women shows an almost symmetrical distribution about the peak frequency of 10 cycles per sec

Side —The curves for the right and left occipital areas are shown in fig 3 Side differences have been described (Brazier and Finesinger 1944, Cornil and Gastaut 1947), but, because of differences of technique, comparison with our results is not profitable In our findings it is noteworthy that the differences between the right and left sides are similar to those existing between men and women This side/sex correspondence has been found in other fields (Holt 1949)

Areas —The considerable difference between areas is illustrated in fig 4 The dominance of the alpha activity occipitally is in accordance with generally accepted findings The activity in the precentral area is maximal in the higher frequency range with a peak at 20 cycles per sec, the secondary peak at 9 cycles per sec is evidence that, even this far forward, the alpha rhythm is not inconsiderable Theta activity reaches its maximum in the frontal lobes, though the fast group of frequencies is still the dominant component, as in the precentral area

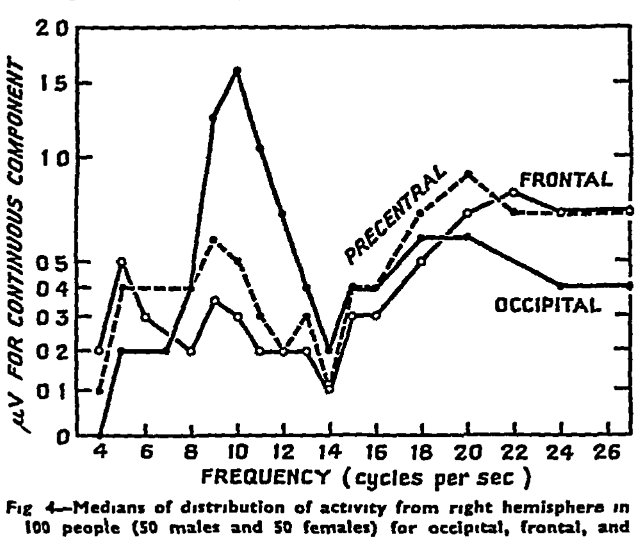

Fig 4—Medians of distribution of activity from right hemisphere in 100 people (50 males and 50 females) for occipital, frontal, and precentral transverse derivations

Frequency Intercorrelations

The method of treatment of the material so far presented has masked completely individual patterns and effects An attempt was therefore made in this study to assess the relationships between frequencies and groups of frequencies within individuals to see whether specific patterns or associations emerged Calculations were made to obtain correlation and intercorrelation products between amplitudes at all frequencies measured The accompanying table, which shows the combined results for both hemispheres of our 100 cases, illustrat[illegible] the value of this sort of study The following are th[illegible] main features of this mixed grouping •

(1) The correlations within the band of theta frequenc[illegible] (4–7 cycles per sec) are high and positive, showing that it [illegible] usual for these components to rise and fall together

(2) There is a positive correlation between the band [illegible] theta frequencies and 14 cycles per sec and, to a lesser degre[illegible] 15 cycles per sec This association, if unexpected, is [illegible] particular interest

(3) The individual frequencies in the alpha range [illegible] remarkably independent of other influences and show li[illegible] correlation with anything except their immediate neighbour[illegible] Activity at 8–10 cycles per sec is, in fact, marked by a hi[illegible] proportion of negative values

(4) Frequencies of 16 or more cycles per sec show a w[illegible] and progressively increasing spread of association with [illegible] frequency

These findings will want further analysis with separa[illegible] tion of areas, sides, and sexes, but they show how [illegible] normal pattern of correlation can be established

SUMMARY

The electro encephalogram of 100 normal adul[illegible] divided equally for sex have been investigated with [illegible] automatic low-frequency wave analyser

The several techniques used for treating the result[illegible] are described

Distribution diagrams and curves of activity in th[illegible] range of frequencies from 4 to 27 cycles per sec are show[illegible]

Comparisons and intercorrelations between sex[illegible] cortical areas, and hemispheres are illustrated

The value of a study of relationships betwe[illegible] frequencies and groups of frequencies is suggested

This work was made possible by a grant from the Medic[illegible] Research Council *We have much pleasure in thanking* Dr [illegible] Strom Olsen for his encouragement, and Prof L S Penr[illegible] for the advice and the considerable amount of help he and [illegible] colleagues have given us

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No-one will get tuberculosis unless he is infected with the tubercle bacillus, but if, as in New York State, a 90% level of infection is reached by the time of early adult life, other factors are obviously of great importance. If they were environmental (nutrition, housing, parental care, for example) they should be similar within each family. We should therefore expect siblings, whether they were twins or not, to show approximately similar incidence of tuberculosis. On the other hand, if inheritance is of high importance, we should expect a correspondingly high proportion of identical co-twins of people with known tuberculosis also to have the disease while non-identical co-twins and non-twin siblings should have a much lower incidence.

Now Kallmann *and* Reisner *obtained the following figures* for relations of the index twins with tuberculosis:

Identical co-twins	87 %
Non-identical co-twins	25·6 %
Other siblings	25·5 %
Marriage partners	7·1 %

In addition it was found that identical twins very frequently showed marked resemblances in the type and intensity of the disease.

This work leaves us in no doubt as to the importance of genetic factors in tuberculosis. It is so important, in fact, that we could say that in a modern civilised environment it is possible to eliminate tuberculosis in two ways. We may (and I think we shall) get rid of the tubercle bacillus, or we could eliminate genes for susceptibility to tuberculosis by selective breeding.

In tuberculosis we have three alternatives for control —prevention by public-health measures, cure of established disease, and genetic elimination of susceptibles. We are all rightly convinced that the first of these is the most important; but, if neither the first nor the second was possible, should we be justified in neglecting the genetic approach? The question takes on very much the same form when we think of the great variety of human disease and disability not due to microbes, poisons, or trauma, and susceptible only to symptomatic treatment. To what extent are these conditions genetic in origin, and should we begin to think about their control by genetic means?

The twin-study method is capable of supplying the answer to the first of these questions in regard to any reasonably common condition. I have often suggested that this particular method of clinical research could readily be developed in any major teaching hospital. The requirements are (1) a mechanism for finding whether each patient entering the hospital had a twin, (2) funds and facilities for finding each co-twin and persuading him or her to submit to medical study on those aspects relevant to the condition for which the index twins had sought treatment. About 1 in every 80 births is a twin birth, and, allowing for the higher mortality among twins, about 1 patient in 50 coming to hospital will have a living twin. Of these about 30% will be identical twins, 70% non-identical. At the Royal Melbourne Hospital there are about 65,000 patients per annum. This means that 4 or 5 index twins are admitted each day and that about 300 pairs of identical twins would potentially be available for study in the year. Assuming that half the available material *could be investigated* the task would be about appropriate to keep a small full-time unit fully occupied.

Let me try to make clear what such a type of investigation could accomplish:

1. It would gradually build up knowledge about the relative importance of environment and inheritance in regard *to an increasing number of clinical conditions.*
2. With that background, the possibility of preventive action (i.e., modification of the environment) could be properly assessed even in conditions where the influence of inheritance is very strong.
3. The premonitory signs of inherited disease that precede its full expression should in many instances

only other keto-acid detected by paper chromatography in the blood samples from these patients was aceto-acetic acid, however, owing tò the partial decarboxylation which the hydrazone of this acid undergoes during the extraction and chromatographic procedures, we cannot yet estimate it quantitatively

Chromatographic separation therefore confirms our findings with the Friedemann and Haugen technique of raised blood-pyruvate levels in these three cases of subacute combined degeneration Our observation that treatment, limited to the parenteral administration of vitamin B_{12}, led to a rapid return to normal of these levels is in agreement with the earlier finding of normal pyruvate levels in six treated cases of this condition (Joiner et al 1950) We have found normal blood-pyruvate levels in one untreated case of pernicious anæmia with no neurological signs or symptoms

These findings clearly need confirmation, but our tentative conclusion that in subacute combined degeneration of the cord there is a defect of pyruvate metabolism which can be rectified by treatment with vitamin B_{12} is to some extent supported by the demonstration by Scheinberg (1951) of a diminution in the oxygen consumption of the brain in pernicious anæmia and subacute combined degeneration, the degree of which appeared to be related to the severity of the neurological involvement

SUMMARY

Raised blood-pyruvate levels were found in three untreated cases of subacute combined degeneration of the cord

Treatment with crystalline vitamin B_{12} led to a rapid return to normal of these levels

We wish to thank Dr J W Aldren Turner, Dr A C Hampson and Dr M J McArdle for permission to study and report on their cases Dr R L Waterfield for hæmatological reports, Mr D H Burchett for technical assistance, and the Medical Research Council for a grant to one of us (G R W)

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CONGENITAL ADRENOCORTICAL HYPERPLASIA

A METABOLIC STUDY

A Stuart Mason
M D Camb, M R C P

C J O R Morris
Ph D, F R I C

From the Medical and Endocrine Units, London Hospital

The syndrome of bilateral adrenocortical hyperplasia, associated with pseudohermaphroditism in the female infant and with sexual precocity in the male, has been well recognised for many years It is now accepted that the sexual abnormalities of these patients are due to excessive secretion of androgen by the hyperplastic adrenal glands No metabolic disturbances were recorded in these patients until Wilkins et al (1940) reported a case of sexual precocity in a young boy who had an electrolyte disturbance similar to that of Addison's disease He died with the symptoms and signs of an addisonian crisis At necropsy both adrenal cortices were found to be hyperplastic Wilkins et al concluded that in this case the adrenals had secreted excessive androgenic hormones but insufficient salt retaining hormone

There are now several records of similar cases, both in boys and in female pseudohermaphrodites, where death from adrenal insufficiency has taken place despite gross hypertrophy of the adrenal cortices We describe here a patient with female pseudohermaphroditism, char terised by excessive adrenal production of androgen, w died in addisonian crisis Studies with adrenocortic tropic hormone (A C T H) and cortisone were carried in an attempt to elucidate the underlying physiolog disturbance in such cases

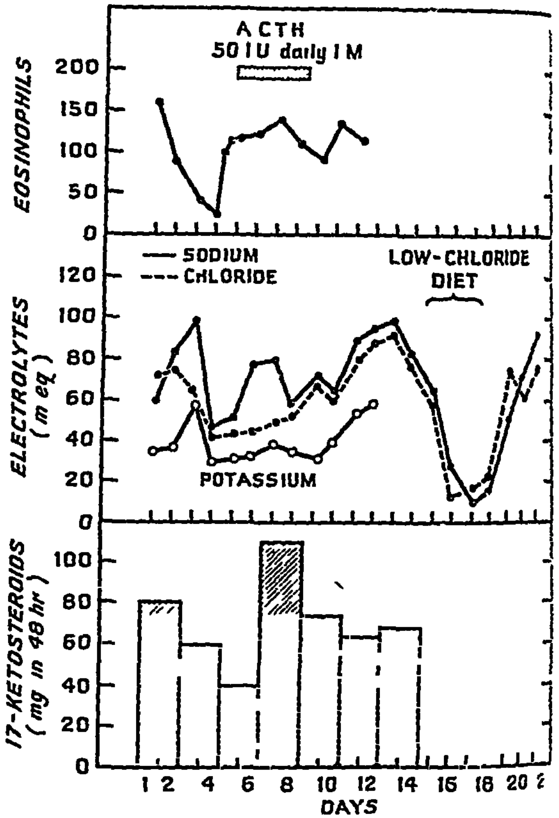

Fig 1—Response to A C T H and to restriction of dietary chlor

CASE RECORD

A girl, aged 6 years 9 months, was admitted to the Lond Hospital in September, 1950 The third of five children in normal family, she was born at full term, by normal labo and weighing 7 lb Her clitoris was noticed at birth to b larger than normal and had since slowly increased As a baby she was breast-fed and healthy, and did not vom At the age of 18 months she had a mild attack of whoop cough without any undue constitutional upset At the age of 2 years she started to have attacks of frontal headache wi nausea and vomiting, lasting two or three days and occurr every two or three months Pubic hair began to grow at th age of 3 years, and at the same age she had chickenpox an measles without complications The attacks of vomitin became more frequent and caused some prostration, b ceased altogether soon after her fourth birthday From th time she remained very well and seemed to be stronger an slightly taller than most girls of her age At the age of 5 years her 17 ketosteroid excretion was 11 mg in twenty fo hours

On examination she was 47½ in tall and weighed 60 l She was a feminine looking little girl of normal body p portions and considerable muscular strength Her skin wa normal, and she had no acne Her scalp hair was norm and she had no excess hair on limbs or face There was slight growth of axillary hair and a moderate growth of pu hair No breast tissue was palpable Her clitoris was 1 i long, her labia majora were hypertrophied, and her ureth orifice was separate from her vagina Otherwise n abnormality was found

Investigations —Radiography show a normal skull and s turcica and bones of wrist, elbow, shoulders, and kn resembling those of a girl aged about 12 years An intrave pyelogram was normal The excretion of 17 ketosteroids wa 30 mg in twenty four hours (average of four estimations by th polarographic method of Barnett et al 1946) The B fract was 4 5% (average of four estimations) rical procedures, but in general has not greatly ified breeding techniques.

recent years, however, genetics has become con- ed with wider fields than those of normal inheritance nimals and plants. There are three new subsciences opulation genetics, biochemical genetics, and micro- genetics—all likely to have very great influence *on* future as well as in the future. Population genetics oncerned essentially with the mechanism of evolution ow selective survival acts on populations of known etic structure to produce the sort of changes seen in olutionary series. When we discuss such matters as y the intelligence quotient of children is negatively related with the number of other children in the nily and why as a result the average intelligence otient in the British Isles is probably falling by 1·6 ints per generation we are dealing with a problem in pulation genetics. When we go to the mental hospitals d find a group of congenital aments who are such nply because of the genetic absence of an enzyme henylpyruvic oxidase) in their cells we are in the realm biochemical genetics. This may well emerge as the aster biological science of the future. In the last nalysis all the changes produced by genes are expressed rough a series of chemical reactions, and there is a rowing belief that in some way each gene controls no ore and no less than a single type of enzymic action. f the generalisation " one gene—one enzyme " is finally stablished, it will represent one of those great simplifying oncepts like the idea of evolution by natural selection r the quantum theory. How far it will have practical earing on medical or social aspects of human life may be roblematical, but it will I think bear importantly on the rowing industrial fields of microbiological chemistry. Most of the activity in the third offshoot from classical genetics—microbial genetics—is at a biochemical level. The microbe is the most versatile of synthetic chemists and by genetic study we can often learn much about the steps by which a given synthesis is made. Few people are aware that the commercial production of penicillin only became really practicable when the microbial geneticists sorted out a high-producing variant of the mould. There are infinite practical possibilities for the organic chemist in this field of study. Microbial genetics is not all chemical. At the present time there is a group of workers in my laboratory who have shown that influenza viruses can be in a sense hybridised—a phenomenon which is going to throw much light on how the virus multiplies in the cell it infects.

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Let me try to make clear what such a type of investigation could accomplish:

1. It would gradually build up knowledge about the relative importance of environment and inheritance in regard to an increasing number of clinical conditions.
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without any disturbance of electrolyte balance Nevertheless injection of A C T H in a dose known to cause electrolyte and eosinophil changes in a normal adult did not produce either retention of salt or loss of potassium and did not lower the eosinophil count By contrast the already excessive output of 17-ketosteroids was significantly increased These results confirm the findings of Bartter et al (1951) in 3 similar cases, and show that the physiological abnormality of the syndrome lies in the adrenal, which responds to A C T H by an increased production of androgens without significant increase in the secretion of the other adrenocortical hormones

The administration of cortisone to the patient was followed by slight retention of salt and a considerable decrease in the number of circulating eosinophils The most striking effect was the depression of the output of 17-ketosteroids to normal levels Further treatment led to a continued diminution of the output of 17-ketosteroids, and virilisation did not appear to progress The growth of axillary hair noted before cortisone was given had disappeared at death In other reported cases more intensive and prolonged cortisone therapy has led to a definite regression of virilisation and emergence of feminine characteristics (Wilkins et al 1951) If cortisone suppresses adrenal function by inhibiting secretion of A C T H rather than by direct action on the adrenal, the excessive androgen production in these cases is brought about by A C T H The presence of bilateral adrenocortical hyperplasia favours the concept of increased secretion of A C T H In an attempt to obtain direct evidence of this the urine of our patient was tested for A C T H -like activity Considerable quantities of some substance which caused severe depletion of adrenal ascorbic acid in hypophysectomised rats were found This substance was not present in the urine of normal adults

The failure of increased production of A C T H to elicit a comparable increase in adrenal secretion of metabolically active hormones must be due to some abnormality in the synthesis of hormones within the adrenal The probable nature of this abnormality is revealed by studies of the synthesis of hormones in perfused adrenals (Hechter et al 1951) The action of A C T H seems to be limited to the initial stage in which cholesterol is converted to C_{19} and C_{21} compounds The subsequent conversion of these compounds, as yet unidentified, into adrenocortical hormones is under the control of various enzyme systems of the adrenal gland These subsequent enzymic reactions are not controlled by A C T H The C_{19} precursors formed under the influence of A C T H are finally metabolised to 17-ketosteroids, and their biological activity is androgenic The C_{21} precursors are converted into glucocorticoids and possibly mineralocorticoids by the action of adrenal enzymes Therefore a deficiency of one or more of these enzymes would lead to deficient production of corticosteroids despite an adequate stimulation of the adrenal by A C T H Sayers (1950) has shown that the amount of A C T H secreted by the pituitary is regulated by the level of circulating adrenal corticosteroids on the basis of a feed-back mechanism A deficient production of these steroids will therefore lead to increased secretion of A C T H Adrenal androgens, on the other hand, do not have a significant effect in controlling the output of A C T H

The facts outlined above can explain the adrenal abnormality seen in the female pseudohermaphrodite and the male infant with sexual precocity associated with adrenal hyperplasia We suggest that the primary defect in these cases is an absence of one of the enzyme systems essential to the normal production of metabolically active adrenocortical hormones The familial incidence of the condition, its occurrence in both sexes and its onset in fœtal life make it probable that the enzyme deficiency has a genetic origin The low level of circulating corticosteroids leads to an excessive secretion of A C T H The adrenal responds to th cellular hyperplasia and the excessive product androgens Directly after birth either the baby dies f failure to elaborate corticosteroids or the secret A C T H is so great that enough vital hormone i formed through some type of synthesis to enable the to live Gross virilisation of the female and sexual prec in the male are inevitable side-effects of the att to produce sufficient corticosteroids to maintain l

Thus the condition is not considered as a prim disorder of sex hormones but as an inborn error metabolism, in which the pituitary-adrenal mechan is over-stimulated to compensate for adrenal insuffic

SUMMARY

A case of adrenal pseudohermaphrodism is report

The patient's response to A C T H was abnormal

Cortisone diminished the excessive output of 17 k steroids

Death was due to adrenal insufficiency

It is suggested that the essential lesion in these ca is the absence of an adrenal enzyme system leading t defective production of corticosterones

ADDENDUM

Since this paper was submitted Kelley et al hav reported a metabolic study of female pseudohermap rodites, and their conclusions are very similar to o (*J clin Endocrinol* 1952, 12, 1140)

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PARONYCHIA

T G LOWDEN

B M Oxfd, F R C S

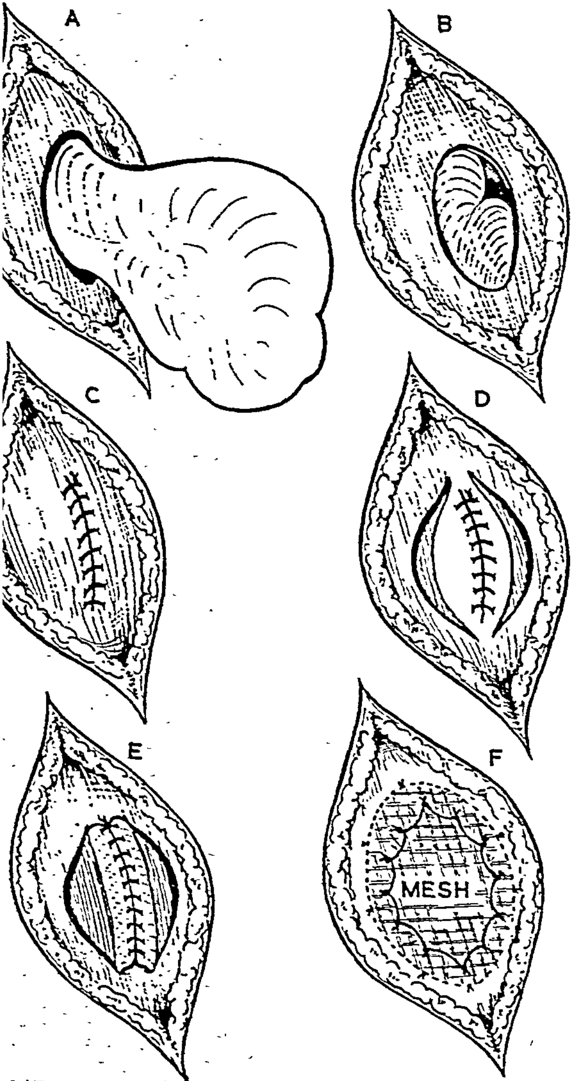
SURGEON, SUNDERLAND ROYAL INFIRMARY

IN subcutaneous infections, including those of the digital pulp space, it may be assumed that in most cases (1) the infection is due to a staphylococcus, associated occasionally with a streptococcus, (2) the longer th infection has been established, the more likely it is to have destroyed tissue with or without the development of fibro fatty slough and (3) the longer the infection has been established, the more extensive is the anatomical involvement, the larger the abscess if there is one, th more likely it is to cause skin necrosis or ulceration (Ellis 1952), and the more likely it is to produce complica tions involving bone, joint, or tendon sheath Allowance, however, must be made for the natural resistance of th patient, the virulence of the invading organism, and other variable factors—e g, the horniness of the hand, and how much it has been kept at rest The principl of treatment are based on these assumptions and sup ported by the results Penicillin reduces the length of incapacity (Pilcher et al 1948, and many others), early treatment with penicillin allows a high percentage of cases to resolve without operation, and cases coming up late for treatment show a higher incidence of bone and amples of the types of hernia dealt with are seen . 3. The average interval from operation to follow-up 5·05 years, the shortest 4, and the longest 5 years onths.

RESULTS

ere was one postoperative death in the series. A an of 50 had a very large recurrent incisional hernia e right hypochondrium. So great was the amount owel in the exteriorised sac that it was difficult to space in the abdominal cavity for it. Perhaps for reason the patient vomited a large amount of gastric ents while recovering from the anæsthetic and inhaled od deal of the material. She was bronchoscoped in an hour of the mishap, but there was gross soiling he distal bronchi. She died from bronchopneumonia the third postoperative day. This is a real hazard he repair of very large hernias. A Ryle's tube should assed before operation and aspiration of the stomach e frequently during and after operation until the ent is fully conscious.

n the remaining 35 cases there have been four late ths from intercurrent disease: one from carcinoma of rectum, two from coronary occlusion, and one from a brovascular accident. We were unable to trace 2 he patients: a vagrant of 58 who had an inguinal nia, and a woman of 53 with an incisional hernia who changed her address and left no trace. The total e-rate was therefore 34 out of 36 cases (94%).



1—Technique of repair of incisional hernia with tantalum mesh.

Among the 29 patients alive at the time of follow-up there have been two recurrences—both in inguinal hernias.

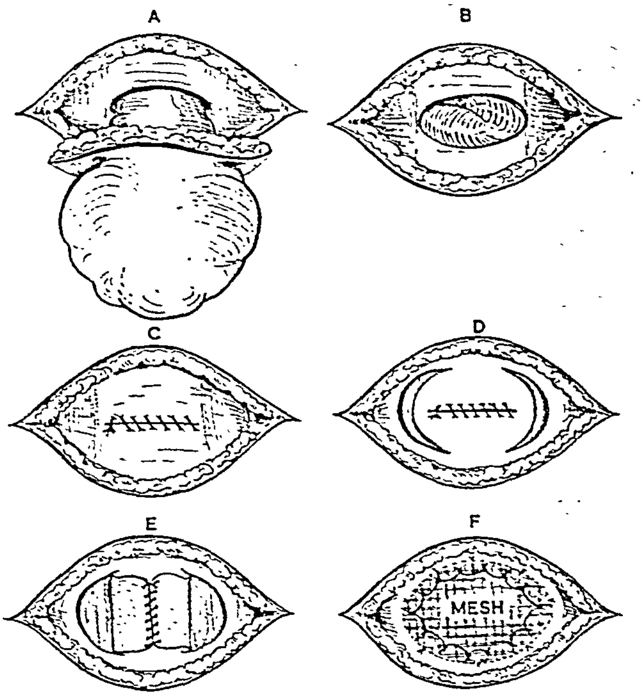


Fig. 2—Technique of repair of para-umbilical hernia with tantalum mesh.

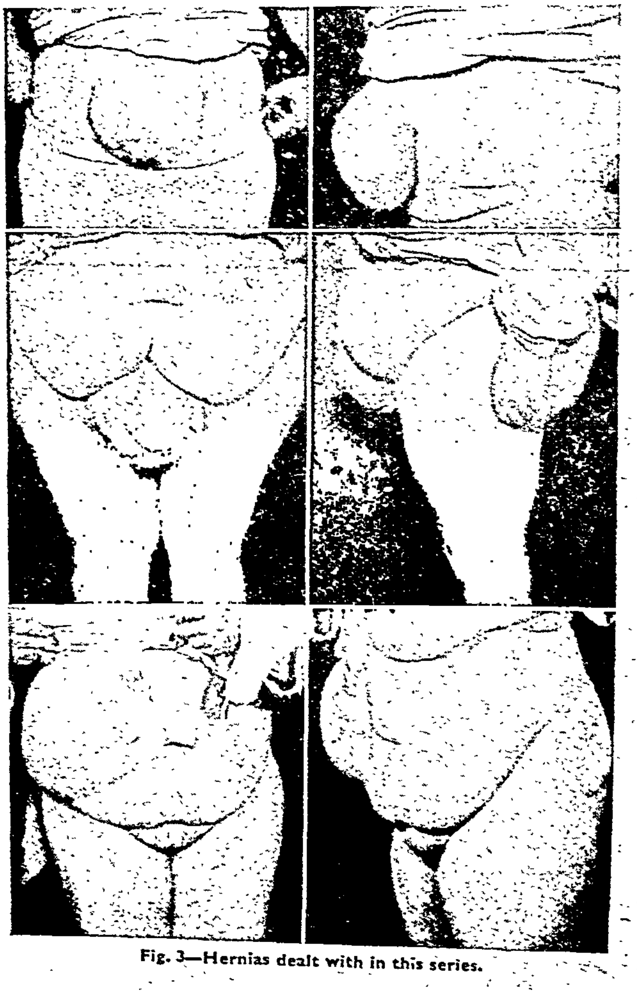


Fig. 3—Hernias dealt with in this series.

FURTHER DEFINITIONS

Certain other cases should be carefully distinguished from paronychia The *terminal pulp-space infection with distal subonychial localisation is probably a clinical entity (Bailey 1952)* It is usually included in analyses of pulp-space infections and seldom spreads as far as the nail fold or sulcus

It is sometimes a little difficult to decide whether foreign bodies under the nail should be included, because they often suppurate, and sometimes a typical paronychial infection is said to have begun when a sliver of wood was run under the nail and removed at home On the other hand, practically every case of foreign body under the nail that is seen and treated promptly heals without any spreading sepsis—even those with pus round the foreign body—and these cases present none of the problems referred to above I have therefore omitted them

COMPLICATIONS

Circulatory inadequacy is not a complication of *paronychia, but is an important predisposing condition* and a condition operating against satisfactory results The *refractory cases of paronychia occur mainly in the* winter months, and it therefore appears probable that *inadequate circulation in the fingers may operate to* some extent in many cases In the aged, in those with Raynaud's phenomenon, and in small children (who have insufficient wit to keep their fingers warm) it may be of considerable importance I have seen 2 cases of gangrene of the finger, and 3 of the great toe, provoked by operations for paronychia It is perhaps insufficiently realised that many cases will recover in due time without any operation, and that in any case a chronic paronychia is better than a gangrenous digit Unless, therefore the first two of these three classes respond to 'Priscol,' it may be wiser to leave them alone If they are operated on they benefit by admission to the warmth of a ward *for two or three days*

Suppurative Arthritis—Bailey (1952) reports 1 case *in a series of subcutaneous infections In 1947 this* clinic had 2 cases from paronychia caused, I believe, *by too extensive reflections of the nail fold* Since then there have been no cases attributable to paronychia The usual cause of this (fortunately rare) complication is a dorsal subcutaneous infection, which, if distal, may closely simulate a paronychia and may later discharge into a nail fold while it is infecting the joint Joints already afflicted with chronic arthritis are particularly susceptible to secondary suppuration from adjacent inflammation, they require special care and an especially conservative approach

Osteitis of Phalanx—There has been no case of bony disease secondary to paronychia in the last five years Paronychia and bony disease may coexist as twin *complications of pulp-space infection* in very rare cases

Stiffness of Joint—Some digital infections produce a sympathetic effusion into the adjacent interphalangeal joint If the suppuration heals rapidly, the effusion may prolong incapacity If the lesion is slow to heal, the *effusion has usually disappeared before the patient* returns to work This condition must obviously be *related to the complication of suppurative arthritis,* but both are more commonly associated with dorsal *subcutaneous and hair-follicle infections*

Strictly speaking, therefore, there should be no complications of paronychia, *though it is important* to discuss the foregoing conditions, if only to dismiss them

CAUSES OF DELAYED HEALING

In a clinic where unsupervised house surgeons, as well as a junior casualty officer, are responsible for many of the operations, some of those cases which fail to h promptly must be attributed to faulty surgery Th particularly so in the surgery of paronychia, bec if it is decided to remove a nail, failure to remove t *amount of nail decided on* prolongs the healing ti Bailey (1952) remarked that the original advice gi in 1948 (to remove only that portion of the nail i by infection) had been superseded by a decision to rem the whole width of the base at least, and there i doubt that, if no incision is made, this change of pol is sound Small pieces of nail inadvertently left behi or cut edges covered by the nail fold, are a comm cause of persistent discharge and further spread o infection

Where incision into the nail flap is indicated, faul siting gives bad results If it is intended to drain a sulcus, the incision should lead down to it unerrin Meticulous precision in operating brings its ow rewards

Pilcher et al (1948) have already emphasised th error of wholesale removal of adherent and unaffecte nail, and their influence has spread so widely that o can say theirs has become the accepted method of treatment *Nevertheless one occasionally still sees* cas where a whole nail has been unnecessarily removed an *a granulating ulcer of the nail bed results* The avul of a normal, or mainly normal, nail almost inevitabl means at least eight days' incapacity

ASSESSMENT OF RESULTS

Bailey's (1952) review assesses the cases in his clin from the day of onset to the day of discharge, and h maintains that this is the most reliable method of estimating the length of industrial incapacity At a teachin centre it is regarded as part of their own responsibility to get the cases in early Nevertheless all clinics have to acknowledge that some of their cases attend much later than is good for them, and all clinics should endeavour to keep the *proportion* as low as possible This clinic often finds that delay in attendance is associated with delay in giving up work, and that many a patient regards *being operated on* for a septic hand (rather than contracting a septic hand) as the cause of his incapacity It seems, too, from Bailey's figures, that the average period of delay is considerably less in London than in this area, though it must be repeated that he discards all cases with delay of over a fortnight In the series about to be cited the average delay was 7 6 days, including 6 cases in which it was *two* or three week In this area patients are astonishingly vague in their ideas about *how long their trouble has been going on* Further, in paronychia the period of delay is no measure of the anatomical situation, and *only in the broadest sense* a measure of the bacteriological situation Under present conditions patients who *attend one day may be referred* for operation to the next, a few patients benefit by twenty four hours' delay, and one or *two may be under treatment* for two or three days before it is decided (usually by someone else) *that operation is indicated* For all these reasons it has been considered profitable to report results in *two ways* by assessing the *period of incapacity* from the day of first attendance, and by assessing the postoperative period of incapacity in addition Othe principles adopted in calculating results have already been set out in a report on pulp space infection (Lowden 195

Conditions of work, both for patients and for doctors vary so much from one part of the country to anoth that I place very little store on comparisons between one clinic and another The *only reliable evidence* that one's routine of treatment is successful is a comparison with *one's own results in previous years* Seasonal variations in incidence and response to treatment make it advisable that *these results should be assessed again* a corresponding season in previous years, or against othe glomerular tufts was slightly swollen, but the elium lining the proximal convoluted tubules was ore affected than the rest. The cells showed cloudy ling, and in some there was nuclear degeneration. David Trevan, of the Wellcome Research Laboras, reported that there was nothing to suggest damage olymyxin E.

3 children there were rises of temperature up to F, considered to have been caused by the antibiotic, 6 other children had pyrexia reaching 99·8°F which ided while polymyxin E was still being administered, was probably not attributable to the antibiotic. Mild l reactions at the sites of injection occurred in 7 dren. In 6 of them the dosage had been relatively e—i.e., 150,000–250,000 units—but the reactions ed little discomfort, never being so severe or so istent as those due to the earlier polymyxin B. Of 7 adults 2 developed slight pyrexia, and only 1 had ht local reactions, although all felt some pain at the ction site lasting a few hours. Such reactions seem lepend chiefly on the size of the dose injected.

ive adults complained of irritation and flushing of the or trunk, and some dizziness when walking. Rashes eloped in 2 children on long courses; in 1 of these a nsient urticaria of the face and trunk appeared on the h day and disappeared while treatment was still being en, and in another, who had previously had papular icaria, transient lesions typical of this condition eloped on the eighth day.

he side-effects after intrathecal injection have been y discussed elsewhere (Swift and Bushby 1951). art from pleocytosis and mild signs of meningeal tation with the higher doses there were no reactions.

COMPARISON OF POLYMYXINS B AND E

ntil recently we had treated only 1 patient, an infant, h the purer polymyxin B (Pfizer), and in this patient side-effects were very like those seen in the children eiving the less pure British product. Now we have n able to compare the side-effects of polymyxin B izer) with those of polymyxin E by treating 6 adults h a three-day course of the American product, and a ek later giving them a similar course of polymyxin E. ree patients were given the polymyxin B as received m America, and 3 were given it after further purificaon by a crystallisation method (Wilkinson 1949). The age was 250,000 units four-hourly intramuscularly. 2 men of the second group the dose of polymyxin E s raised to 500,000 units and further increased to 00,000 units for the last three doses of their courses.

n every patient pain at the injection site was less with ymyxin E than with polymyxin B, even when the e of polymyxin E was twice that of polymyxin B, t not when it was four times as great. Similarly, uration at the site of injection was considerably less d of shorter duration with polymyxin E, except haps when compared with the more highly purified ymyxin B. Pyrexia and malaise occurred with polyxin B, whether purified or unpurified, but with lymyxin E only when the fourfold dosage was given. her subjective sensations occurred with similar quency with either drug.

ince all the patients in this group had infections of urinary tract, there was some proteinuria before atment but it was not obviously increased during or mediately after treatment, and no cellular casts were ssed.

A child was also treated with both polymyxins, the lymyxin B (Pfizer) being given during a course of atment with polymyxin E. The polymyxin E proced only very slight induration at the injection site, ereas definite induration and erythema occurred th polymyxin B.

INCIDENCE OF TOXIC REACTIONS

Polymyxin	No. of patients treated	No. of patients showing renal damage	No. of patients with local reactions	No. of patients with pyrexia	No. of patients with rashes
A	27	26	0	7	0
B (W.R.L.)	24	0	19	18	0
B (Pfizer)	8	0	6	3	0
E	53	0	8	4	2

DISCUSSION

The incidence of side-effects following intramuscular injection are summarised in the accompanying table, the subjective effects being omitted because so many of the patients were infants. There are striking differences between the side-effects of these antibiotics: polymyxin A produces renal damage but little or no reaction at the site of injection, whereas polymyxins B and E cause variable reactions at the injection site but no proteinuria. Polymyxins B and E produced paræsthesiæ in some patients; but, since only children were treated with polymyxin A, it is not known whether this antibiotic also produces these side-effects. The early samples of polymyxin B almost invariably caused malaise with pyrexia, but this has been much less with the more recent and purer polymyxin B.

Polymyxin A is apparently closely related to polymyxin D, for this antibiotic also produced proteinuria (Schoenbach et al. 1948), and polymyxin C, which has never been given to man, causes renal damage in animals. The polymyxins may therefore be divided into two groups according to their toxic effects: (1) polymyxins A, C, and D; and (2) polymyxins B and E.

Their toxic differences are interesting in view of their indistinguishable antibacterial activities, and may be explained by the differences in their molecular size and structure. Other polypeptides cause inflammation, and Spector (1951) found that peptides of about five amino-acid chain-length were not precipitated by ammonium sulphate, and caused only a mild reaction when injected, whereas peptides of 8–14 amino-acid chain-length were salted out by 75% saturation with ammonium sulphate, and caused more severe reactions. Polymyxin A appears to be closely related to the shorter chain-length peptides not only in producing insignificant local reactions but also in not being precipitated by ammonium sulphate. Polymyxin B resembles the longer peptides in causing a more intense inflammation, and being precipitated by 70% saturation with ammonium sulphate. Polymyxin E lies between polymyxins A and B, requiring 80% saturation to precipitate it.

Spector's observations offer an explanation for the differences in the local reactions of the polymyxins, and accordingly polymyxin A should have the smallest and polymyxin B the largest molecule. Bell et al. (1949) from osmometrical measurements calculated the molecular weights of polymyxins A and B to be 1293 and 1150 respectively, and Short (1948), calculating from the phenyl-alanine and threonine content, found the molecular weight of polymyxin B to be 2500.

Spector considers that peptides play a major part in the inflammation caused by burns and bacterial infections, and the similarity between the properties of these peptides and those of the polymyxins offers an explanation for the anomalous fact that the polymyxins are non-toxic to leucocytes yet cause inflammation when injected (Brownlee et al. 1952). The inflammation is not due to direct damage of the tissues but to the fact that the antibiotics behave as peptides derived from damaged tissue.

Differences in molecular weight and shape may also explain the differences in renal toxicity. Experiments on animals show that the damage to the kidneys is

A HÆMORRHAGIC STATE RESEMBLING HÆMOPHILIA

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THE diagnosis of hæmophilia *depends on a family* history showing a sex-linked recessive inheritance, on clinical evidence, and on certain laboratory findings But, because of the high mutation-rate and the high death-rate among young hæmophilics, the family history is often absent or inconclusive Moreover, the clinical features are merely those associated with defective blood coagulation, and are not specific for hæmophilia Consequently, the diagnosis often rests entirely on the laboratory findings

Merskey (1950) studied the laboratory diagnosis of hæmophilia in some detail, and he has shown that the most satisfactory laboratory test is the demonstration that the patient's plasma does not correct the clotting defect of the plasma of a " known hæmophilic "—that is a patient in whom the required genetic, clinical, and laboratory criteria are fulfilled Small amounts of normal plasma and of the patient's plasma are added to citrated plasma from the known hæmophilic, and the clotting-times after recalcification are recorded Very small proportions of normal plasma will shorten the calcium clotting-time of hæmophilic plasma almost to normal *If similar proportions of the patient's plasma* fail to do so, he presumably has hæmophilia This test has the advantage of being independent of the nature of the defect in hæmophilia, it simply shows that two patients have the same deficiency The purpose of this article is to describe a case in which the usual laboratory findings supported a diagnosis of hæmophilia, but in which the patient's plasma corrected, and was corrected by, the plasma of other known hæmophilics

CASE-REPORT

N J is a five year old boy in whom a tendency to excessive bleeding has been observed since the age of 3 months He bruises very easily, and his ankles and knees have been swollen ever since he started to walk There is no convincing family history, but his mother was one of the possible hæmophilic carriers who were found by Merskey and Macfarlane (1951) to have an unusually high prothrombin consumption index (37%)

His admission to hospital with severe epistaxis and hæmorrhage into the muscles of the thigh provided an opportunity to study his condition more fully than had been done before His bleeding time, and the tourniquet test, platelet count, and one stage prothrombin time were normal The whole blood clotting time was 52 minutes (Lee and White) and 10½ minutes (Dale and Laidlaw) The prothrombin consumption index was 150% His plasma did not progressively lengthen the clotting time of normal plasma, so it was presumed *that no anticoagulant was present* The results of mixing his plasma in different proportions with the plasma of 3 undoubted hæmophilics is shown in the accompanying table

CLOTTING TIMES OF RECALCIFIED MIXTURES OF THE CITRATED PLASMA OF THE PATIENT N J AND 3 UNDOUBTED HÆMOPHILICS J D, A N, AND F N

0 1 ml of	Clotting time (min) after adding 0 1 ml of plasma from			
	N J	J D	A N	F N
Normal saline	40	20	17	22
1 100 normal plasma	6½	4½	4	3¼
1 100 N J 's plasma	—	4½	8	4¾
1 100 J D 's plasma	6¾	—	16¾	21
1 100 A N 's plasma	4½	16	—	19
1 100 F N 's plasma	5½	16	14½	—

DISCUSSION

The discovery of this case raises a serious difficult the definition of hæmophilia By the usual criter the boy would be confidently classified as a hæmoph But if we accept him as having hæmophilia, then we postulate mutually correcting subgroups of hæmoph and abandon the idea of excluding hæmophilia demonstrating correction of a known hæmophil plasma However, among the considerable numb patients studied by Merskey no instance was found two supposedly hæmophilic plasma samples correct one another Merskey's series included J D and A 2 of the 3 patients whose plasma is shown here to corr and be corrected by N J 's plasma, clearly, therefo it is N J who is anomalous

The clotting defect in N J was subsequently inves gated more fully by Biggs et al (1952), and other pati with a similar defect have been found Cases of th type have been shown to be deficient in a factor pre both in normal plasma and in the plasma of patie belonging to the group which includes J D, A N, a F N Furthermore, N J and the other patients resembl him are not deficient in antihæmophilic globulin Th these two hæmorrhagic disorders, similar in their clinic features and in most laboratory findings, are in realit distinct from the point of view of their coagulati defects Patients like N J seem to be comparativ rare, and it is therefore suggested that the term hæm philia should be restricted to the larger group in wh plasma samples fail to correct each other, and wh *evidently includes the large majority of cases* hither classified as hæmophilia N J and other patients wit his defect should be regarded as having a different dise for which Biggs et al (1952) suggest the name " Christma disease " after the name of the first patient they examin in detail

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RETURN OF LIVER FUNCTION TESTS TO NORMAL AFTER RELIEF OF OBSTRUCTION IN CHRONIC BILIARY CIRRHOSIS

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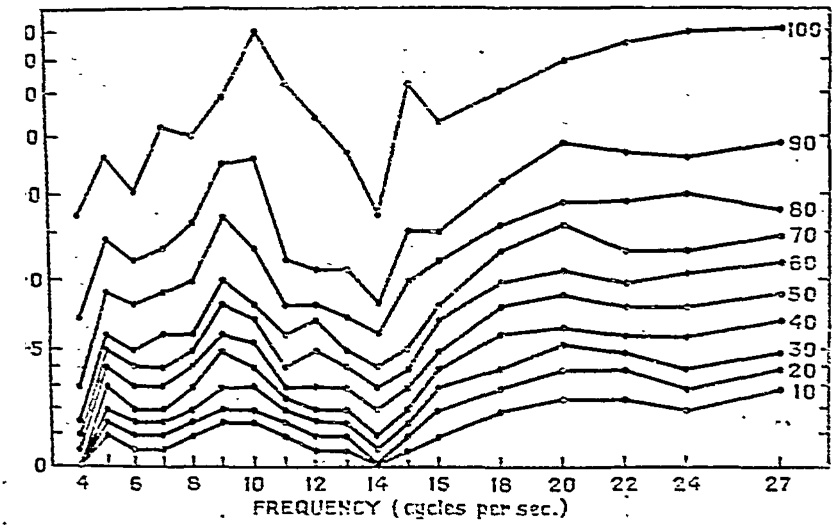
THE opportunity of following a patient with bilia obstruction for a reasonable length of time before a after operation seldom arises The interest of the pre *case lies in the serial liver function tests* (see table) I view of the severity of the liver damage the restorati of function following the relief of obstruction was s prising, especially since the patient was aged at least

The patient (record no 3647/48) is well known at the Lond Hospital She was born in Russia about 1893 Her exact a is uncertain because all her papers were lost when she cam England in 1900 She was married in 1927 and has two child who are now grown up and married Her husband die cancer in 1936, and since then she has lived with a niece

Her first visit to the London Hospital was in 1920, wh she underwent hysterectomy for fibroids and a leiomyosarc was found In 1937 she was admitted with an appen abscess In 1945 she attended the gynæcological depart with a pelvic tumour which was thought to be possibly metastasis from her leiomyosarcoma Since she refus operation she was given intensive deep X ray therapy (34

In December, 1945, six months after the conclusion of X ray therapy, the first symptom developed which co possibly be ascribed to the biliary tract She had a seve attack of vomiting, which was diagnosed by her doctor gastritis In June and October, 1946, there were furt attacks of nausea and vomiting During the second att



. 1—Distribution curves of activity from 4 to 27 cycles per sec. for left precentral transverse ·area in 100 cases, independent of sex. Numerals attached to curves denote centiles.

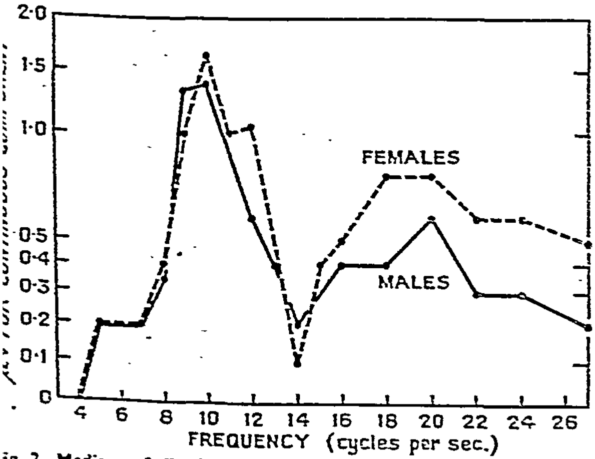
om these areas in each person were taken by standard chniques and fed simultaneously into the wave-analyser. ie instrument was set to write out the average of five ccessive 10-sec. epochs of analysis.

This period of 50 sec. has been used throughout this ries; choice of this period was based on the consideration of the ratio of variability within the individual to constancy from one individual to another. This epoch n be shown to be a reasonable compromise between, the one hand, extreme fluctuation in the individual ie to short period and transient changes and, on the her, masking of broad individual characteristics.

The over-all sensitivity of the instrument was such iat, at the standard setting, a continuous signal of 2μV any of the frequencies in the range led to a write-out ight of 1 cm., and this condition was repeatable to ithin ±10% of any setting at any level.

Voltage/time discontinuity presented without non-nearity or the introduction of spurious harmonics up 100 times this level, though it was usual to use creased or decreased sensitivity settings of the apparatus here necessary. This setting was determined by choosing satisfactory visual level of record in the primary trace, in-to-gain cross-check accuracy being included in the er-all figure of ±10%. Part of the instrumentation has en described (Ellis 1950).

The examination took place in a quietened half-dark om. The patient's eyes were open for 10 sec. during ch 50-sec. period. Analysed frequencies below 4 cycles per sec. were excluded from this study because, in this range, artefacts could not be differentiated from the cortical rhythms with any degree of certainty. The upper end of the spectrum used was fixed at 27 cycles per sec. after an investigation into the frequency distribution of the electromyogram had shown that muscle potentials influenced the analysed result above that frequency.



ig. 2—Medians of distribution of activity from right occipital area for men and for women.

The write-out height of each frequency for each area for these one hundred cases was measured in centimetres; measurement error at all levels was not greater than ±0·05 cm. This measurement was next corrected so that a standard gain setting applied for any one area; this correction was necessary for purposes of comparison and did not introduce any error into the result. The amplitude scale on the ordinate was further corrected by a factor in the form log $(x+0{\cdot}2)$, which is a near approximation to the integral of the summed error of ±10% ±0·05 cm. together with normalisation of the distribution; the same factor has been applied to the statistical procedures used. The corrected measurements in centimetres were plotted, frequency by frequency, against amplitude in the form of dot distribution diagrams. These diagrams were used to check the adequacy or inadequacy of the recording level for the particular area investigated.

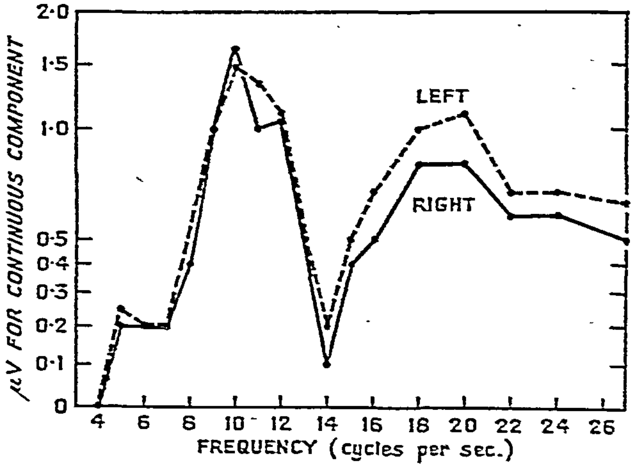


Fig. 3—Medians of distribution of activity from right and left occipital areas for women.

Distribution curves derived from the basic plot show the centile levels from 10 to 100 (fig. 1). The values below the 5th and above the 95th centile are controlled by a small number of people. These values show such a high degree of scatter that their exclusion is justified, particularly since the remaining 90% of the population can be adequately represented by the median; for this reason the median has been used in the illustrations that follow.

RESULTS

Sex.—Fig. 2 shows the results obtained for men and women in the right occipital areas. In the range of frequencies from 15 to 27 cycles per sec. the activity is of a significantly higher amplitude for women than for men. The curves also differ in symmetry over the alpha range, in that the curve for men is skewed, whereas that for

The Mechanisms of Disease

A Study of the Autonomic Nervous System, the Endocrine System and the Electrolytes in their Relation to Clinical Medicine JOSEPH STAMBUL, M D chief cardiovascular dept, Albert Einstein Medical Center (Eastern Division), cardiologist, Deborah Sanatorium New York Froben Press 1952 Pp 746 $15

IN Augustine Birrell's *Obiter Dicta* we read that Borrow's *The Bible in Spain* gained admission to the narrowly selected reading-matter of the Victorian Sabbath by virtue of its 'dear deluding title' This is partly relevant to the volume under review, in that the title is deluding, and the book is dear The practitioner or teacher of medicine to whom the book is commended in the foreword would we believe expect an attempt to explain disease processes in terms of generally accepted physiology and pathology, but Dr Stambul offers something very different

His central theme is that our preoccupation with the physiology and pathology of organs has blinded us to the importance of cell biology disease processes he thinks, can be best understood in terms of alterations in cell permeability, brought about by autonomic nervous impulses by hormones or by changes in electrolyte concentration in the surrounding fluids With this hypothesis in mind, he embarked on a long search of the literature whose results are presented in this massive volume Many of his conclusions are surprising for instance 'bacterial toxins affect tissue cells by way of the autonomic nerve fibres that supply these cells" 'the degree of effectiveness of a diuretic depends upon the ease which which it ionises calcium , "the hormone of the pancreas insulin influences the deposition of glucose in the muscle cells by counteracting the membrane semipermeability and permitting the glucose from the surroundings to enter the cells." These are matters of theory but they are less astonishing than his assertion that adrenal cortical hormone therapy "should be instituted early in acute infections in order to prevent irreparable damage to the tissues caused by pathogenic micro organisms"

The clarity of the writing makes apparent the highly speculative nature of the contents

Saving Children from Delinquency

D H STOTT, PH D research fellow Institute of Education University of Bristol London University of London Press 1952 Pp 266 12s 6d

IT is an unfortunate feature of human psychosymbolism that rational proposals for the prevention of crime are less effective in exciting our public, our press and our judges than sadistic methods of punishing it Dr Stott's Carnegie study on *Delinquency and Human Nature* was a humane and hard-headed study of child criminals praiseworthy for both its good sense and its psychological eclecticism His new book is of wider scope in suggesting remedies The commonest cause of delinquency in his view, is desperation. child crime is essentially an explosive disorder. The Bench or some of its members at least are likely to welcome the book for it provides a background to every decision which has to be made in a case of childhood delinquency and gives a remarkably accurate idea of the sort of help in elucidation and treatment which can be expected from sensible psychiatry The roots of the desperation which Dr Stott cites lie deeper in our culture pattern than his non-anthropological approach seems to suggest, but the programme of prevention and treatment he outlines is practicable if our society is culturally able to accept it

There have been other good books of this kind, but few better Dr Stott writes persuasively out of a very wide personal experience

Physical Diagnosis

HARRY WALKER M D, F A C P, professor of clinical medicine, Medical College of Virginia London Henry Kimpton 1952 Pp 461 60s

TEXTBOOK instruction on methods of physical examination is never an easy task, for these are essentially practical arts to be taught at the bedside. In this volume one of the main aids to a clear understanding of clinical methods—namely, the use of illustrations and diagrams—is disappointing Of the 126 illustrations, som be of little importance and inferior quality The tions of physical signs are also often brief and unin tive Some 30 chapters cover all the principal d and there are introductory chapters dealing wi things as habitus body-temperature, speech, gai inspection and palpation There is an exceedin short account of methods of psychiatric examin

Scoliosis

Pathology, Etiology, and Treatment SAMUEL KL M D, assistant orthopædic surgeon, Hospital fo Diseases, New York City London Baillière T & Cox 1951 Pp 286 37s 6d

AN orthodox review of the anatomy of the sp the different types of lateral curvature leads th to conclude that the ætiology of idiopathic s remains an unilluminated page but he is imp with the evidence implicating asymmetrical distur of vertebral epiphyseal growth in some cases a foresees future treatment of established curv surgical inhibition of growth on the convex side, by stapling or by other means He does not m how greatly the prognosis differs in the different of curvature and attaches little importance to the ex measurement of curve angles preferring the s visual comparison of serial radiographs Neither he share current pessimism on the value of non-op management in structural scoliosis, exercises in ticular are described in detail, though he does not s dogmatically that these can undo rotation, and does refer to the specific derotating exercises used by experienced physiotherapists There is a full acc of methods of forcible correction plaster technique apparatus, and, though Dr Kleinberg is conserv in advising operation his success in obtaining f with preserved beef bone makes one wonder whe "bone bank" of refrigerated homogenous bone is necessary

Surgical Papers

WILLIAM STEWART HALSTED, late professor of sur Johns Hopkins University Editor WALTER C BURK *Baltimore Johns Hopkins Press London Ox University Press* 1952 Two vols Pp 586 and £10

A PART of the centenary celebrations, held last at Johns Hopkins Medical School of W S Halsted's birth is the re-issue of his collected writings Vo of these contains his papers on surgical techni conduction anæsthesia, intestinal surgery with spe regard to methods of anastomosis, the surgery of t blood-vessels, and some shorter contributions on cellaneous subjects Vol II contains his work on c of the breast, the surgery of the thyroid, parathy and thymus glands, the surgery of the bile ducts pancreas some miscellaneous papers, and a bibliograph

Halsted's papers are models of what scientific pap should be—lucid, well documented, and bearing evide of the most intensive work and study in their preparati Apart from their presentation they contain a mas original observations which are still pertinent, many these are still not widely known The general princip enunciated are continually illustrated in his writings they are the same now as they were in his day cannot be reminded too often of the importance of g handling of the tissues, exact hæmostasis, and t sacrifice of theatrical operating to care and thorough His insistence on the importance of applying the resour of the laboratory and the teachings of surgical patholo to clinical problems is an object-lesson The pape vol I are perhaps of less interest than those in vol except for the remarks on surgical technique and ligat of the large arteries Much of the elaborate work intestinal suture is of historical interest only, and wrote very little on his classical contribution to anæsthesia Vol II contains his wonderful pap cancer of the breast which could be read with p by any surgeon who operates on this condition nowaday The paper on the operative story of goitre finishing details of the Halsted technique, beautifully illustrate is absorbingly interesting His remarks on the train of the surgeon are as apposite as they were in 1904

OOD-PYRUVATE LEVELS IN SUBACUTE COMBINED DEGENERATION OF CORD

EFFECT OF VITAMIN B_{12} THERAPY

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IN the course of a study of pyruvate metabolism in eripheral neuritis and myelitis we have had the pportunity of investigating three untreated cases of bacute combined degeneration of the cord, and of bserving the effect of treatment with vitamin B_{12} n the blood-pyruvate levels in these cases. In view f the difficulty of obtaining cases of this condition at have received no treatment with either liver con-entrates or vitamin B_{12} we describe here the results btained.

METHOD

On admission to hospital blood-pyruvate levels were easured by the method of Friedemann and Haugen 1943) in the fasting state and at 60 and 90 min. after loading dose of glucose (Williams et al. 1943). The ean levels which we have obtained in healthy people nder these conditions are 0·76 ± 0·18 mg. of pyruvic cid per 100 ml. of blood in the fasting state, and ·92 ± 0·17 and 0·94 ± 0·20 mg. per 100 ml. at 60 and 0 min. respectively (Joiner et al. 1950). The test was epeated after a course of parenteral therapy with itamin B_{12}.

CASE-RECORDS

Case 1.—A married woman, aged 28, admitted to hospital December, 1950, with two years' history suggesting ernicious anæmia, had had no effective treatment. Two eeks before admission there had been a sudden onset and apid progression of paræsthesiæ and loss of feeling and ower in both feet and legs. Just before admission the aræsthesiæ spread to the hands.

On examination the patient was pale, had a smooth tongue. nd could not walk. Muscular tone in the legs was increased, oördination was grossly impaired, and there was some weak-ess of hip flexion. Light touch and position sense were npaired in both legs. Deep reflexes were increased, and oth plantar responses were extensor.

Investigations showed histamine-fast achlorhydria. Hb 9%, red cells 2,300,000 per c.mm., mean cell diameter (M.C.D.) ·6 µ, conspicuous anisocytosis and poikilocytosis, and ternal marrow typical of pernicious anæmia.

Treatment with vitamin B_{12} 50 µg. three times a week was tarted on Jan. 9, 1951. No other vitamin therapy was given. his produced a reticulocyte response and by March 1, 1951, he blood picture was normal. Improvement in the neurological ondition was slower, but by March 16 the patient could alk unaided, although the plantar responses remained eakly extensor.

Pyruvate metabolism was as follows:

Date	Blood-pyruvic acid (mg. per 100 ml.)		
	Fasting	*90 min. after glucose*	
an. 8 1951	0·55	1·70	before vitamin B_{12} therapy
,, 22 ,,	0·78	1·46	14 days after start of vitamin therapy
larch 15 ,,	0·41	1·02	2 months ,, ,, ,, ,, ,,
une 29 ,,	0·83	1·10	6 ,, ,, ,, ,, ,, ,,

Case 2.—A man, aged 60, was admitted to hospital in larch, 1952, with six months' history of numbness of the ands and feet.

On examination his skin was pale yellow, his tongue smooth, and his gait grossly ataxic. There was weakness of the hand muscles and of hip flexion, with impairment of sense of position and of vibration in the arms and legs, and of superficial sensation below the knees. The calves were tender, and the knee and ankle jerks were absent.

Investigations showed Hb 76%, red cells 3,400,000 per c.mm., M.C.D. 7·9 µ, with anisocytosis and poikilocytosis. There was a histamine-fast achlorhydria.

Treatment with vitamin B_{12} 100 µg. twice weekly was started on May 31. No other vitamin therapy was given. The blood picture was normal on July 15, and there was a fairly rapid improvement in walking and physical signs.

Pyruvate metabolism was as follows:

Date	Blood-pyruvic acid (mg. per 100 ml.)		
	Fasting	*90 min. after glucose*	
May 30 1952	0·75	2·60	before vitamin B_{12} therapy
June 12 ,,	0·87	1·26	13 days after start of vitamin therapy

Case 3.—A married woman, aged 57, admitted to St. Bartholomew's Hospital under Dr. J. W. Aldren Turner in June, 1952, had noticed numbness of the finger-tips and of the feet for eight months, and had had difficulty in picking up small objects. For six months before admission her gait had been unsteady.

On examination power was normal, but muscle tone in the legs was slightly increased, and coördination was slightly impaired. Knee-jerks were feeble, ankle-jerks absent, and plantar responses doubtfully extensor. Superficial sensation was impaired below the knees, vibration sense absent in the lower limbs, and position sense impaired in the toes.

Investigations showed Hb 92%, red cells 4,350,000 per c.mm., colour-index 1·07, mean corpuscular volume 92 c.µ, histamine-fast achlorhydria, and sternal marrow like that of subacute combined degeneration.

Treatment with vitamin B_{12} 40 µg. on alternate days was started on July 18. No other vitamin therapy was given. No change in physical signs occurred within fourteen days, but the patient thought that the numbness was less. Two months later there had been a progressive slow improvement in her condition.

Pyruvate metabolism was as follows:

Date	Blood-pyruvic acid (mg. per 100 ml.)		
	Fasting	*90 min. after glucose*	
June 27 1952	0·83	1·77	before vitamin B_{12} therapy
July 15 ,,	0·81	0·91	17 days after start of vitamin therapy

COMMENTS

Since, so far as we are aware, no evidence of any clear-cut relationship between pyruvate metabolism and vitamin B_{12} has been described, and since the method of Friedemann and Haugen (1943) is not completely specific for pyruvic acid but also estimates other keto-acids to some extent, we thought it advisable in cases 2 and 3 to separate the blood keto-acids by paper chromatography and so to obtain individual estimates for the pyruvic and α-ketoglutaric acids normally found in human blood (El Hawary and Thompson 1953). The results obtained are shown in the accompanying table. The values of 1·29 and 1·15 mg. of pyruvic acid per 100 ml. of blood for the 90 min. specimens obtained before treatment are significantly higher than the corresponding levels of the separated pyruvic acid found in normal people by this technique. It will be seen also that the 90 min. samples after vitamin B_{12} therapy are only 0·37 and 0·39 mg. per 100 ml. respectively in these two cases—i.e., within the normal range.

The values for α-ketoglutaric acid are not raised and are unaffected by treatment with vitamin B_{12}. The

LEVELS OF SEPARATED BLOOD KETO-ACIDS BEFORE AND AFTER TREATMENT WITH VITAMIN B_{12}

Case no.	Pyruvic acid (mg. per 100 ml.)		α-Ketoglutaric acid (mg. per 100 ml.)	
	Fasting	90 min.	Fasting	90 min.
2:				
Before treatment ..	0·33	1·29	0·20	0·19
After treatment ..	0·24	0·37	0·20	0·19
3:				
Before treatment ..	0·37	1·15	0·17	0·31
After treatment ..	0·31	0·39	0·23	0·31

Epidemiology in Reverse

When KOCH announced his famous postulates the ætiological agents of most infectious diseases were unknown Now that these have been satisfactorily established for nearly all infectious diseases, a new situation has arisen viruses are being discovered without diseases to match To the pure bacteriologist this *may seem natural enough, for the great majority* of bacteria are harmless or even beneficial saprophytes and the pathogen is very much the exception But those who work with viruses have learnt to recognise them by their ability to produce disease, and a scientist who isolates a new virus without knowing the disease it causes is looked at askance by his colleagues Let him beware, however, of the temptation to short-circuit KOCH's postulates, either in letter or in spirit, in his anxiety to find a parent disease for his foundling

A good example of this epidemiology in reverse comes from the Coxsackie viruses During investigations on poliomyelitis, DALLDORF and SICKLES[1] isolated from the stools of two children with paralysis a virus which in suckling mice caused fatal disease with widespread muscular necrosis They proposed the name Coxsackie virus for this new agent, but it was not immediately obvious what disease it caused Some 15–20 serological varieties of Coxsackie virus have now been recognised and they have been accused of causing many diseases It seems likely that they are responsible for epidemic pleurodynia[2] (Bornholm disease), herpangina,[3] and certain non-specific summer febrile disorders[4] Their distribution is very similar to that of poliomyelitis viruses *and their relation to* this disease is intriguing There is still no evidence that they cause poliomyelitis-like diseases alone, but some varieties may convert a subclinical attack of poliomyelitis into a paralytic one Coxsackie viruses seem to be extraordinarily widespread, they have been recovered in large numbers from the four corners of the earth, and their association with human disease may be the exception rather than the rule

Epidemiology in reverse has also been encountered in East Africa A group of workers in Entebbe, Uganda, while looking for reservoirs of yellow fever, inoculated various materials into mice and recovered a number of curious viruses This led to a search for the corresponding diseases Dr G W A DICK, who for some years was a prominent member of the team, described some of the results in a lecture to the Royal Society of Tropical Medicine and Hygiene on Dec 11 Two of the agents discovered by these workers in East Africa—Bwamba fever[5] and West Nile[6] viruses—were isolated from the sera of patients with febrile disease, although the exact relation of these viruses to human disease is still not clear Most of the other viruses—for example, Uganda S[7]—were isolated by inoculating suspensions of mosquitoes into mice, but the possibility that some of these injections activated latent mouse viruses has not b excluded with certainty Attempts were mad estimate the importance of these viruses to di in man by antibody surveys of human sera,[8] bu interpretation of such tests is not always si The presence of virus neutralising substances i small proportion of human sera is of itself evidence (as KOCH would have agreed) of pre infection with that virus Even the demonstrat of a rise of antibody to a virus during a prim illness must be interpreted with caution T although a herpetic may show a rise in antibody herpes-simplex virus during an ordinary bact pneumonia, no one would infer from this that herpes-simplex virus is the cause of lobar pneum Nevertheless, inferences of this sort are all common

Dr DICK is aware of these difficulties, he arg that these new viruses deserve study since they m at any time break loose and cause serious dis such as occurred in the recent Australian epidemic Murray Valley encephalitis[9] His remarks should *taken seriously, although, of course, the same* warn applies in greater or lesser degree to all bacteria a viruses Even the harmless staphylococcus on th bacteriologist's bench may conceivably turn vic and bite the hand that feeds it, and the scient has a duty to the community to estimate these r in the case of any newly discovered potential pathog *He cannot do this, however, until he has* a sou knowledge of its distribution in nature, its path genicity, and its general behaviour in the laborator These fearsome-sounding new viruses are of gr biological interest, but it would be no surprise t learn that many of them are harmless, seek nothing but food, warmth, and comfort from th hosts, anxious not to disturb or to be disturbed living the most luxurious of what LAIDLAW call "borrowed" lives

Topical Application of Histamine Antagonists

THE intrinsic value of remedies designed to relieve subjective symptoms is never easily gauged and uncontrolled trials, however large, may be deceptive Anti-histamine drugs incorporated in various ba are widely used as local applications for the relief of pruritus and itching dermatoses, and they have be reported to bring relief in 60–90% of cases

WALDRIFF et al[10] describe the effect of anti*histamine creams in 277 cases of neurodermatoses* a generally superior to that obtained by the intern administration of these drugs (78% of all patient relieved by topical use, compared to 56% by or administration) About a third of the patient with neurodermatitis were "semipermanently c permanently cured" In this trial eczemato reactions ensued in 4 5% of the cases, and we commonest in patients with denuded, excoriated c weeping dermatoses—for example, some forms c anogenital pruritus and of disseminated neuroderm titis Local application of anti-histamine drugs to ar of mild, dry, circumscribed contact dermatitis ga

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esponse to Injection of Adrenaline.—No eosinopenia was ːrved at four or six hours after the injection of 0·4 ml. of)00 adrenaline.

esponse to Restriction of Salt.—On restriction of dietary ium chloride to less than 0·5 g. daily there was prompt mal diminution in output of sodium chloride (fig. 1).

esponse to A.C.T.H.—The patient was kept on a diet of stant sodium, potassium, chloride, and fluid intake. .T.H. prepared in our own laboratory (Cortis-Jones et al. 9) was injected six-hourly in a dose (daily total 50 I.U.) own to stimulate the adrenal glands in a normal adult. e results are shown in fig. 1. There was no evidence of inopenia, retention of salt, or loss of potassium in response A.C.T.H. On the other hand, the output of 17-ketosteroids s significantly increased.

esponse to Cortisone.—The effect of cortisone on circulating inophils and urinary excretion of sodium. potassium, oride, and 17-ketosteroids was studied during the second mission in January, 1951. Cortisone acetate 50 mg. was ected twice daily for ten days. A progressive decrease in inophils followed; there was slight retention of salt; and output of 17-ketosteroids was strikingly diminished . 2).

Effect of Continued Cortisone Therapy.—It was impossible keep the child in hospital and in view of these results it s decided to treat her at home with oral cortisone daily. r progress over the subsequent seven months is shown in . 3. Two weeks after the ten-day course described above, ·5 mg. of cortisone was given daily for ten days. A mild tack of vomiting developed, and cortisone was withheld by e mother. At this time the output of 17-ketosteroids had en to an abnormal level. The dose of cortisone was raised 25 mg. daily for seven weeks. At the end of this course the tput of 17-ketosteroids had fallen to less than 1 mg. in enty-four hours. Clinical examination showed no change the child's appearance since the first admission. Cortisone erapy was discontinued, and her condition remained satis- tory for a month. A severe attack of headache and miting then came on, followed by much weakness for five ys. The output of 17-ketosteroids after the attack was ain abnormally high. Two months after the attack cortisone erapy (50 mg. twice weekly) was resumed. During the rth week of this course a further attack of vomiting came and was followed by extreme prostration and death. fortunately it was difficult to maintain close contact with e patient, and it was impossible to make any observations ring the attacks.

Necropsy revealed a grossly dehydrated child. Pubic hair s present, but no axillary hair. The clitoris was enlarged, t the vagina, uterus, fallopian tubes, and ovaries appeared rmal. The urethra was separated from the vagina. Both adrenals showed considerable cortical hyperplasia (left 13·3 g., right 11·6 g.).

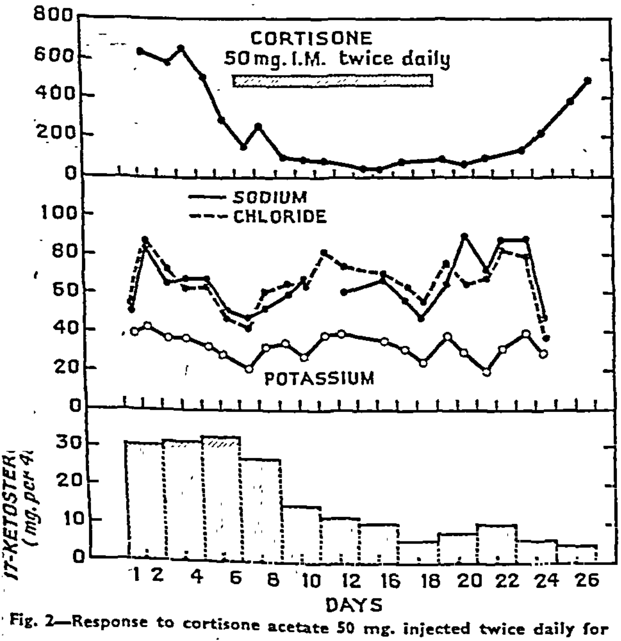

Fig. 2—Response to cortisone acetate 50 mg. injected twice daily for ten days.

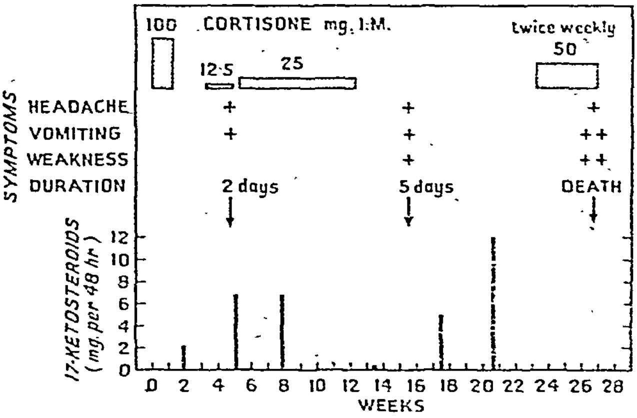

Fig. 3—Response to continuous therapy with cortisone acetate.

DISCUSSION

The clinical diagnosis of adrenal pseudohermaphroditism in this patient was based on the presence of an enlarged clitoris at birth, progressive virilisation with a high 17-ketosteroid excretion, and the advanced state of epiphyseal development. An unusual feature was the presence of separate urethral and vaginal orifices. Wilkins (1950) records only 1 such case, for the usual finding is a urogenital sinus. The degree of normal genital differentiation in this patient suggests that the excessive androgenic stimulus from the adrenals developed later in fœtal life than is usual in such cases.

The natural history of the metabolic disturbance is also unusual, in that there were no symptoms referable to adrenal insufficiency until attacks of vomiting developed between the ages of 2 and 4 years. In view of the child's subsequent progress these attacks were most probably related to adrenal insufficiency. Examination of published reports of 22 fatal cases shows that symptoms of adrenal failure developed within the first month of life in 18, and between the ages of 6 weeks and 7 months in 3 cases; only 1 patient was free from symptoms until the age of $3^1/_2$ years.

The clinical picture of vomiting, dehydration, and collapse that preceded the death of this patient has been described in all the reported cases in which death was due to adrenal failure. The picture is closely similar to that of an addisonian crisis in the adult. As with Addison's disease, a crisis may be precipitated by infection (Thelander 1946) or operation (Allibone et al. 1947), and death may take place despite restoration of the electrolyte balance (Zuelzer and Blum 1949). The biochemical findings have been depletion of sodium and retention of potassium. Few data are available on the blood-sugar levels during a crisis, but severe hypoglycæmia has been reported (White and Sutton 1951). Adrenal failure in the presence of hyperplastic adrenals seems to be very like failure due to destruction of these glands. The published data do not justify the view (Wilkins and Lewis 1948) that this adrenal failure with excessive production of androgen is confined to a lack of salt-retaining hormone. In contrast to this group, most patients with hyperplastic adrenals secreting excessive androgens from before birth undergo progressive virilisation without clinical evidence of adrenal failure. Nevertheless the investigations of Bartter et al. (1951) and Wilkins et al. (1950) show that there is an underlying abnormality of the adrenal cortex common to patients with and without overt adrenal insufficiency.

The case reported here is of particular interest in that studies with A.C.T.H. and cortisone were made when there was no clinical evidence of adrenal failure, and the patient survived a period of very restricted salt intake in the words of the Coalition Government in the British white paper of 1944) that the health of the people was a *responsibility of government*

A hundred years' lag between the expression of a basic principle and its actual application is about average for this country Professor Titmuss attributes the delay in this case to the fact that the present British social services—the Welfare State—had to be built up from below When the old sources of social security—the Church, the parish poor-box, the charity of the lord of the manor—could no longer meet the demands on them, the poor working people began, voluntarily and democratically, to make their own provisions for social security They created, he said, an embryonic Welfare State, resting on the principles of mutual aid In the belief that all should compulsorily stand together to meet the needs of sickness, injury, old age, and unemployment, they built up a vast organisation of friendly societies clubs, and trade unions "The term 'friendly society' is very significant here, positively it expressed the idea—surely a Christian idea—of mutual neighbourly help in the contingencies of industrial, city life, negatively it expressed the working class loathing of a harsh poor-law and authoritarian forms of charity" It was in direct opposition to the doctrine of laisser faire "Every man," John Donne had written centuries before, "is a piece of the Continent, a part of the main any man's death diminishes me, because I am a part of mankind" The working class of the 19th century were not the only ones to experience intuitively this truth there were the great rebels of the humanitarian movements—men and women with a tradition of public service like Lord Shaftesbury, Elizabeth Fry, Octavia Hill Florence Nightingale, and Charles Booth They rebelled, as Professor Titmuss said, "against the excesses of a philosophy of unbridled individualism", and many of their rebellions were successful, because they were based on a passionate desire for social justice They are still with us, the private rebels and reformers, still moved by the same desire and still expressing it in voluntary social service

> "Over 10,000 men and women are now engaged, in a voluntary capacity, in running the present system of hospital boards and hospital management committees under the National Health Service Never before have so many voluntary workers been engaged in constructive work on hospital boards and committees"

The conjunction of two social forces—the working-class ethic of mutual aid, and the educated man's tradition of public service—achieved the social policies of the early years of this century national insurance schemes of sickness benefit, general-practitioner care, unemployment benefit, and workmen's compensation, and the beginnings of school meals, a school medical service, and a maternity and child-welfare service The Boer War, by revealing much physical unfitness among recruits, fostered the revolutionary idea of prevention "It was revolutionary because it spelt publicly sponsored services and a higher income tax"

The second Industrial Revolution—the scientific revolution—aggravated the social problems of the first Children meant poverty and poverty, as always, meant sickness Social services multiplied to meet special needs—"a patchwork," as the Beveridge report said, "of disconnected administrative organs" The second world war taught us still more about basic social needs, and especially the need to get away from a two-standard service—an inferior standard of health care, education, and nutrition for the poorer classes, a higher standard for the better off A civilians' war, we found, must be fought on the principle of "fair shares," and this principle was carried over into the peace and written into the National Health Service, National Insurance, National Assistance, and Family Allowances Acts, and the Education Act In this legislation we can di recognition of the importance of the family a recognition that the costs of unemployment and sick must be a national charge, a greater emphasis prevention, and the backing of scientific medicine the State, so that all may benefit by it The work incomplete, and we have often made mistakes, Professor Titmuss believes that the aims of the Welf State do offer a healthy alternative to either a totalitar State or a system based entirely on materialistic value

INTESTINAL MOVEMENTS

MOVEMENTS of the alimentary canal in man have b studied mostly by radiological techniques, or else by introducing balloons to record pressure changes Both methods have their disadvantages, and neither gives results that are as straightforward as they may seem With balloons changes of pressure due to intestinal movements may be too sluggishly recorded, or if the balloon is so inflated as to distend the walls of the g this may itself initiate movements Code et al[1] at the Mayo Clinic have worked out their own method of recording pressure by means of balloons, but they make it clear that this is inaccurate for contractions recurring more than once in about 5 seconds Contractions of h greater frequency can, however, be recorded by transforming changes of pressure into variations of electric current

Code and his associates agree with earlier workers in describing three types of intestinal movement Type 1 is reflected in low amplitude waves, each lasting seconds, which are very constant for any particular portion of bowel Type-2 waves are of greater amplitude and may last up to 60 seconds In type 3 a change of tonus or "base line," sometimes lasting for minutes, added to waves of type 1 or 2, this 3rd type is seen most commonly in records of the small intestine In patients with ulcerative colitis there may be a further type (type 4) of large single waves, lasting 1–2 minutes, this type seems to be limited to the colon In the small intestine type-1 waves are mainly for "mixing" and type-3 waves for propulsion, type-2 waves are rarely if ever, seen In general the small intestine shows much more continuous activity than is evident in either the stomach or the colon, it is at rest for less than half the twenty four hours, being depressed in sleep when type 3 waves largely disappear

Ingelfinger and Moss[2] have shown that nausea is often associated with generalised contraction of the duodenum, and other investigators have noted duodenal spasm during mental or physical situations which involve distress or pain Many agents reduce or inhibit motility of the duodenum or small intestine one is atropine, while others are such drugs as tetraethylammonium chloride and 'Banthine' It is not, however, so well recognised that transit through the small bowel is also delayed in such conditions as acute bacillary dysentery With obstruction of the small intestine type 3 waves increase, with a gradual disappearance of type 1 ("mixing") waves In observations on an isolated loop of jejunum Jackson[3] found that propulsive waves were most violent when the distal end of the loop was occluded and fluid was introduced into the proximal end Pain however did not seem to be related so closely to the peristaltic waves as to the type of fluid introduced into the loop Thus water or 5% glucose solution caused only slight discomfort, whereas 50% glucose solution caused extremely severe colicky pain referred to the umbilicus—which persisted after peristalsis had ceased in the loop Our knowledge of the sensory innervation of the small intestine is far from complete, but all evidence seem to show that distension is the main—if not the only—stimu

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1 Code C F, Hightower N C Morlock, C G Amer J Med 1952 13, 328
2 Ingelfinger F J, Moss R E Amer J Physiol 1942 136
3 Jackson W P U Clin Sci 1952 11, 209

t complications than do early ones (Lowden 1951, ey 1952, and others).

a paronychia two anomalies are at once apparent. ay in seeking treatment bears no relationship to the ent of the lesion and, as a corollary to this, no relation- to the time required to heal the lesion. It is astonish- how quickly an infection in one case can spread round l under a whole nail, floating it away from the nail l, whereas in another case of longer duration it may duce no more than a little discharge from the base or localised pocket of pus in one corner. An analysis this clinic of 50 consecutive cases according to their lay in seeking treatment and their healing-time after ndard operations, did not show any relationship tween the two. The most outstanding extremes re a case with two days' history which took thirty- ur days to heal, and another which had been established r three months and healed on the eighth day. At at time (1948) an analysis of cases treated with nicillin and those treated without showed no significant fferences. In this clinic in four years the average capacity for subcutaneous infections has been reduced y nearly 40%; and for pulp-space infections by 60%, ut for paronychia, until recently, by little more an 6%.

Pilcher's conception (Pilcher et al. 1948) of paronychial fection is that it starts as a subcuticular infection f the nail fold or the lateral sulcus; on this assumption e maintains that an incision into the subcutaneous issue is not only unnecessary but also may delay healing y infecting an area not previously involved. There are, owever, certain theoretical and practical objections o these views. The most practical objection in this linic was that 107 cases treated by Pilcher's conserva- ive operation averaged slightly longer than 116 cases reated by Kanavel's standard operation (Lowden 1952). Moreover, many cases proved at operation to be ot entirely subcuticular infections, and even mainly ubcutaneous infections, with well-defined paronychial pockets and small extensions or none at all under the nail; and a few had discharging sinuses through the nail fold, showing that subcutaneous tissue was most certainly involved. Those with well-defined subcutaneous abscess cavities alongside the nail fold—a type which Bailey (1952) considers rare—occur quite commonly in this clinic. In the last 34 cases at least 10 have been observed. Why some should develop in this direction, and some remain subcuticular, has not so far been determined, though one's impression is that the subcuticular type occurs predominantly in young people and children. However caused, the subcuticular ones produce a rapid spread under the nail, and pus often extends beyond the nail bed, stripping the cuticle from the finger and extending proximally towards the hand. These cases often take a long time to heal, leaving an impetiginous lesion of the finger which outlives the original lesions of the nail bed by many days.

Finally, it is unreasonable to assume that the infection is staphylococcal by the time it is first seen at a hand clinic—at least, not without further consideration. Cultures taken either at operation (if there is no discharge on first attendance) or on sight (if there is) indicate that some of our cases grow gram-negative bacilli or (what is equivalent for practical purposes) penicillin-resistant cocci. This fact, coupled with the fact that much of the administration of penicillin in earlier days was haphazard, might explain the findings that penicillin-treated cases did little better than those without it. For many months in this clinic it was not considered that penicillin therapy in paronychiæ was worth the expense.

If the results of cultures are assessed according to whether the lesion has discharged on the surface, when the culture is taken, or has remained intact, it is seen that, up to now, the penicillin-resistant organisms, when they occur, are nearly all in the former. The intact lesion is still staphylococcal or staphylococcal and streptococcal (table I). Reliance cannot be placed on figures derived from thirty swab reports, but the fact that these organisms do occur in paronychia is significant. The nature of the infecting organism cannot be correlated with the distinction in clinical behaviour described already. Most of the subcuticular lesions, whether discharging or not, remain staphylococcal. On the other hand, one at least of the *Bacterium coli* lesions was localised and subcutaneous. The original lesion is probably staphylococcal and rupture gives an opportunity (not always taken) of infection by gram-negative or other resistant organisms.

TABLE I—BACTERIOLOGICAL FINDINGS IN PARONYCHIA

Bacteria	Unruptured	Ruptured
Penicillin-sensitive :		
Staphylococcus aureus	12	8
Staph. aureus and hæmolytic streptococcus	3	8
Penicillin-resistant :		
Staph. aureus and hæmolytic streptococcus		2
Coliforms		2
Proteus	1	1

All were chloramphenicol sensitive.

RELATIONSHIP WITH PULP-SPACE INFECTION

Bailey (1952) reports 5 cases in which he described extension into the pulp space, though he remarked that they were more probably cases of pulp-space infection which pointed in the nail sulcus, having tracked alongside the phalanx. No doubt this latter process can take place and has taken place in most of the apparently combined lesions. Very rarely however, a pocket of pus in the sulcus is observed beginning to track into the pulp space. Only by very accurate observation can the classification be precise.

The situation is complicated by the fact that the inexperienced may be tempted to remove the nail in late neglected ("bag of pus") pulp-space infections. Fluctuation (an unreliable physical sign in fingers) under the nail may be detected. In these cases the pus tracks between the phalanx and the nail bed, raising nail and nail bed together; removal of the nail in such a case is mischievous (Lowden 1951).

CHRONIC PARONYCHIA

Bailey (1952) draws an arbitrary line at fourteen days and only considers the "acute" cases. It is convenient to have some such standard, but histories of septic hands are notoriously unreliable, and we have established that many long-standing cases present the same clinical features as more "acute" ones, and are cured as swiftly. Many of them, also, grow typical organisms. "Chronic" paronychia, as distinct from "late" paronychia, may more properly be assessed on its clinical appearance. It is better known to the dermatologist than to the surgeon, and, let it be confessed, often better treated by the dermatologist. The lesions are often multiple. The history is measured in weeks or months rather than days—sometimes in years. There is a little cheesy discharge. The nail fold hangs away from the nail, and the surrounding skin may be macerated. If the dermatologist fails to cure it, which is unusual, a cure may be obtained by removing the bases of all affected nails, carefully excising all loose and macerated tags of cuticle from the nail fold, and treating *daily* thereafter with Castellani's paint. The patients should be admitted to hospital because the operation may take a long time, and to operate on both hands at once is incapacitating. All affected nails should be done at one sitting, if possible, for fear of reinfection.

œsophageal-pulse records which they feel can be interpreted as showing the presence and nature of mitral disease Zoob has obtained similar records but is less confident about their interpretation A cautious attitude may be wise These two groups of workers agree that the œsophageal pulse does not actually measure the left auricular pressure, and furthermore the experience of Wynn and his colleagues,[13] who made direct measurements of auricular pressures at operation, suggests that the interpretation of these pressures in mitral disease is far from easy. The status of the "œsophageal piezocardiogram" is still uncertain, and further direct correlation of it with operative findings would be helpful

"FUNCTIONAL END-ARTERIES" IN MUSCLE

ONE of the more tedious occupations pursued by the student of anatomy is the memorisation of the great system of collateral circulations by which the body safeguards its lines of communication Now that aneurysms are out of fashion the meaning of this system often becomes clear only when he sees a coarctation of the aorta or Blalock's operation The surgery of congenital vascular defects often demonstrates the astonishing extent to which these "by-passes" can dilate in response to need For example, in a case of coarctation Clagett[14] ligated the left subclavian artery above its branches and also the first three left intercostal arteries; the hand was pulseless for some time, yet it showed no sign of gangrene

In other situations, however, collateral circulations are not so successful, and some arteries have won notoriety as "functional end-arteries," implying that if they are blocked the central part of their distribution will die or be severely injured by ischæmia Such a result depends on a combination of factors, among which are the rapidity of the blockage, the oxygen needs of the tissue, and the capacity of the collateral vessels to respond If the occlusion of the artery is gradual, the collateral circulation has time to dilate to the best of its capacity and the tissues may not suffer If, however, the block is sudden, some tissues with a high oxygen demand may be unable to get along with a grossly reduced supply while the necessary permanent dilatation is in progress Again, disease of the collateral vessels may prevent the establishment of an adequate relief circulation in a reasonable time, so that even tissues with less urgent oxygen requirements may die The term "functional end-artery" is therefore a poor one, since there is hardly an artery in the body that cannot be brought into this category by the force of circumstances Thus in arteriosclerosis the lumen of a diseased artery anywhere in the body may be suddenly occluded, and the collateral vessels may be in no condition to meet the demand Even the skin, the traditional home of free anastomosis, is not immune, and Edwards[15] has pointed out that in an arteriosclerotic lower limb the occlusion of an artery supplying the skin may lead to a patch of cutaneous gangrene

Edwards also notes that one muscle occasionally becomes gangrenous while the rest of the limb is comparatively little affected, and suggests that this is due to the lack of adequate communication between the vessels supplying adjacent muscles, some main muscular vessels, in fact, behave as end-arteries Brash[16] has worked on the gross blood-supply of the muscles of the upper limb, but as yet there appears to be no full statement for the lower limb Blomfield[17] has studied the vascular patterns within some of the muscles of the lower limb and finds great variation in the degree of intramuscular anastomosis in different muscles For example, gracilis is well endowed, but tibialis anterior is not He correlates this variation with clinical findings such as the tibialis anterior syndrome,[18] in which the extensor muscles atrophy following exercise Compared with the effort expended on other aspects of muscle physiology, the vascular supply of human and animal muscle has been neglected Le Gros Clark[19] and Blomfield[17] have reviewed their own and other work on experimental ischæmia in animals In rabbits the interruption of a main vessel of supply to certain muscles leads to necrosis of a well-defined region of the muscle despite the existence of intramuscular anastomotic channels It is not known whether this happens because the collateral circulation is anatomically inadequate or because striated muscle can survive only a short time without oxygen

We hope that further clinical work on the lines followed by Edwards will be supplemented by basic observations on experimental ischæmia and on the anatomy of the blood-supply to muscles

SMALL-QUANTITY BLOOD TESTS FOR SYPHILIS

HITHERTO we have had no authoritative evaluation of the various micro serological tests for syphilis Now however, the venereal diseases section of the United States Public Health Service has filled this gap[20–24]

Of the tests described, the micro-modification of the Venereal Disease Reference Laboratory (V.D R L) test requires 0 015 ml of serum, the filter-paper microscopic (F P M) test is done on a saline extract of a drop (0 05 ml) of whole blood dried on a strip of filter-paper, while the Chediak test requires 0 05 ml of whole blood dried on a glass slide These last two tests can be used as "detector" reactions in field operations Five laboratories participated in the comparative tests, and all reactions were measured on the fourth day after the donors were bled

The four modifications of the Chediak test (Chediak Kline, Chediak Mazzini, Chediak-Kahn, Chediak V D R L) proved more specific and sensitive than the original Chediak test itself, but the Chediak-Kahn and Chediak V D R L modifications were much less specific than the other two, and gave a much higher proportion of non syphilitic reactions The Chediak-V D R L modification has the advantage that results can be reproduced in different laboratories

This study seems to show that these micro tests are inferior both in sensitivity and specificity to the usual serum tests, and should be avoided if possible If venepuncture proves impracticable, enough blood for such a test can usually be obtained by the intelligent use of a guarded safety-razor blade Secondly it appears that the micro-V D R L test is superior to the other micro tests, but loss of specimens either in transit or in the laboratory (amounting to 8% in the American investigation) cannot be ignored Thirdly, all varieties of the Chediak test show a loss of sensitivity when carried out on specimens stored for more than 24 hours Fourthly, the F P M test is much less sensitive than the usual serum tests, and its use should therefore be limited to some field operations Finally, the value of micro tests for syphilis is greatest in mass testing of a population remote from a fully equipped laboratory The choice of these tests is influenced by the type of donor, geography, the interval between collection and testing, the capacity of the field laboratory to do the tests, and the fact that with relatively untrained personnel all specimens are likely to be collected successfully s treated by standard methods in the period of stigation.

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THE INFECTING ORGANISM

he old doctrine that "if you take care of the gram-tives, the gram-negatives will take care of them-es" dies hard. It has already been shown (table I) penicillin-resistant organisms play some part, and opinion has been given that these occur mainly in ons which have been discharging before they come treatment. We have often observed also that, if of the factors mentioned above has operated and re is any delay in healing, a penicillin-sensitive anism is superseded by, or changes into, a penicillin-istant one. This is in line with findings by other kers on other types of wound (Summers 1952) and vadays is to be expected. Secondary infection in pital, even if staphylococcal, is very often penicillin-istant.

On all counts, therefore, the first day or two in the atment of paronychia are the crucial ones, and it is ential, to obtain consistently good results, that treat-nt shall be prompt, surgery shall be precise, and other cillary forms of therapy shall be overwhelmingly ective. This forbids one to wait for a bacteriological ort before defining treatment.

The data we have accumulated lead us to suppose it the infection is probably penicillin-sensitive, but y not be so; and that it is almost certain to be sitive to chloramphenicol.

ROUTINE

In this clinic I am not yet prepared to use chloram-enicol systemically for the routine treatment of septic nds, because a penicillin routine is still proving out-ndingly successful in over 95% of cases, because l exhibition is unreliable in outpatients, because of pense, and because of the possible side-effects of oramphenicol (*Lancet* 1952). Nevertheless the topi-use of chloramphenicol, reported as being highly cessful in other wounds (Flint et al. 1952), offers means of attacking those which might defy the nicillin.

Ellis (1951) reported his observations on high initial nicillin dosage, and he used it in the treatment of ronychia (Ellis 1952). He reports 90 to 95% four-y cures by incising alongside the nail fold, evacuating pus, and putting a dry dressing over the incision. does not remove any nail. In the localised unruptured es this appears eminently reasonable; but, since re is a considerable incidence in this area of cases th extensive subcuticular spread ("run-arounds" d "floaters") and of ruptured lesions already possibly ensitive to penicillin, I have been led to use topical loramphenicol, after removal of detached nail, in dition to penicillin in cases which are unlocalised or discharging.

In this way one hopes to anticipate a gram-negative ection while treating for a lesion still predominantly nicillin-sensitive.

The routine operative treatment now adopted may erefore be summarised as follows:

1) All cases have high preoperative penicillin dosage, rt of which, at least, is readily absorbed aqueous penicillin G, d further penicillin on the first postoperative day.

(2) Unruptured well-localised lesions have a small precise ision alongside the nail fold. The pus is evacuated, the jacent nail raised, and any pus dried out, but no il removed. A dry dressing is applied and inspected the second or third postoperative day (the "Ellis" eration).

(3) Ruptured paronychia, or those with much subcuticular ead, have Pilcher's operation and are dressed with a wick chloramphenicol (5%) in propylene glycol. Subsequent dressings of the same may be required on one or two occasions.

(4) All cases not obviously healthy and healing on the third or fourth day are treated by a toilet of the nail fold and with chloramphenicol drops two or three times weekly.

TABLE II—RESULTS OF TREATMENT OF PARONYCHIA

Operation	No. of cases	Incapacity (days)	Postoperative attendance (days)	No. of cases lasting more than 7 days	Longest healing-time (days)
Ellis (penicillin only) ..	20	5·0	4·75	2	11
Pilcher (penicillin and chlor-amphenicol)..	27	5·0	4·5	2	11
Resolution without operation	4	4·2	—	—	5
Others (Pilcher with penicillin only)..	7	8·7	8·7	4	13
Total	58	5·4*	5·1	—	—

* The average incapacity for all cases treated in the corresponding months in 1951 was 11·4 days and in 1950 12·8 days.

It has not been considered necessary to describe or to tabulate all the cases for this report. Note is taken of the type of lesion, and it is put into one of three classes. Bacteriological examination was made in many of the cases (table I). The results shown in table II include all cases coming up for treatment in an unbroken series (except 2 cases in which operation was refused), and no "mitigating circumstances" or "excuses" have been accepted. They include operations by one surgeon, two registrars, and five or six house-surgeons, according to chance. Seven operations done by others not briefed for the experimental period have been included but assessed separately from the foregoing.

CONCLUSION

The table of results is self-explanatory. We have adopted as a routine the principles defined in the later part of this paper. Although the periods of incapacity for the two methods seem to be the same, there is a place for both. Ellis's operation is followed by a more comfortable postoperative course and a quicker return to an uncovered finger, because no nail has been removed: it will be found applicable to a larger proportion of cases than the 30% reported. Nevertheless, a short series of cultures indicates that 15–20% of cases of paronychia may resist the use of penicillin; this incidence is higher than for other septic conditions of the hand. Ellis's operation on an insensitive infection will probably fail. The use of local applications of chloramphenicol, instead of penicillin lactose, with Pilcher's operation, seems to have prevented the occurrence of those refractory cases which previously kept the average high. As a result the recovery period for all cases has been reduced by half.

I have already recorded my constant debt to the nurses and to a succession of enthusiastic residents for their continued interest in the Hand Clinic. I must further pay grateful tribute to Dr. James Wilson and his department of pathology for their bacteriological work, and to record an acknowledgment of the work of Prof. Pilcher and Mr. David Bailey, and of Mr. Maurice Ellis at the General Infirmary at Leeds, whose progressive ideas are a constant stimulation.

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Special Articles

THE FIREGUARDS ACT

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UNDER the Fireguards Act, 1952, it will become an offence for any person to sell or hire (except in certain specified circumstances) an electric or gas fire or oil-burning space-heater which is not fitted with a guard conforming to prescribed safety regulations The Act gives the Secretary of State power to issue these regulations, and to decide when the Act shall come into operation

In framing the regulations the Secretary of State will no doubt be largely influenced by the findings of the British Standards Institution committee, which were set out in the new standard no 1670 (1951) for electric fires, and amendment no 1 to British standard 1250/1946 for the most dangerous types of gas fire

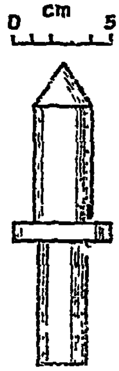


Fig 1—The testing cone. (With acknowledgments to the British Standards Institution)

In the standard for electric fires it was laid down that the safety or otherwise of any particular type should be judged by two considerations

1 *Non accessibility of Live Parts*—This was to be determined by three specific tests, as follows

(*a*) By a dummy finger (preferably connected up to an indicator lamp) of specified dimensions, which, when passed through any apertures *in the case* of the fire, does not reach any live parts

(*b*) By a testing cone (fig 1) which must not be able to pass through any aperture *in the dress guard* and touch the element or elements at any point

(*c*) By measurement of the distance between the element or elements and the guard In the case of reflector fires with spiral wire elements this distance must not be less than 1 in In the case of fires heated by a " fire bar " element (i e , a helix of resistance wire mounted on a fireclay support), the distance must not be less than 2 in at the centre of the element, and $1^{1}/_{2}$ in at the extremities

2 *Heat Intensity at the Face of the Dress guard*—This was to be roughly determined by the effect of the heat upon a readily flammable fabric such as flannelette If a piece of this material laid on the guard with the fire at full heat, does not " smoulder or ignite " within 10 seconds, the guarding is considered adequate (at least for the protection of able bodied adults)

The standard specifications speak at one point (clause 17) of " scorching " of the flannelette, and at another point (clause 25) of " smouldering " It should be noted that the time of exposure needed to produce these two effects is often widely different Moreover, although these specifications have been drawn up by the British Standards Institution, manufacturers are not required by law to conform to them Some manufacturers have announced their intention to do so, but there are already indications that others will not Qu recently (November, 1952) an inexpensive reflector fire (retail price under £2) has been put on the market with a neat wire-mesh guard which is fixed *at only* $^{1}/_{8}$ *in* from the fire-bar, so that it clearly fails to conform to the British standard specifications When this fire and guard was tested for heat intensity, it was found that white flannelette began to scorch at 7 seconds, and was blackened at 10 seconds, but did not begin to smoulder until 18 seconds The fire carried no maker's name The retailer who showed it to me assured me that it would sell much more readily than one with an adequate guard made by a firm of good reputation at a much higher price

The standard for gas fires applies only to " portable gas fires and gas fires fitted above hearth level having exposed flames or radiants " Its safety clauses are similar to those for electric fires, but the one dealing with non-accessibility of the heated element is judged by a cone test only, and in its dimensions differs somewhat from that employed for electric fires The heat intensity test is identical with that for electric fires, but here again the value of the test depends largely upon whether scorching or smouldering is taken as the danger point Since these fires tend to be somewhat hotter than electric fires the margin of safety secured by the B S I specifications for their dress guards is correspondingly less

NEW GUARDS FOR OLD FIRES

The passing of this Act was an important step in the elimination of burning accidents from our homes But it is not enough For the Act takes no account of the (estimated) 4–5 million gas and electric fires already in use in homes, offices, hospitals, and elsewhere in England and Wales—to say nothing of the coal fires, which are believed to number something like 12 million These various types of fires have been involved in, if not entirely responsible for, approximately 2400 severe burning accidents a year since the war—that is, nearly 7 a day About 280 of them each year have proved fatal, and 75% of these accidents have happened to children, to people over 65 years of age, or to epileptics If most of these fires continue in use for some years, as they well may, and continue to be (for the most part) unguarded, in homes where there are children, old people, or epileptics, we must expect that they will still contribute to as many tragic accidents as they have done in the past

It is for the public to deal with this unfortunate situation—the Government cannot do so Many people during the last few years have improvised guards for their electric fires—from cake-trays, wire letter baskets, and the like Others have exercised their ingenuity in devising guards specially suited to the several types of

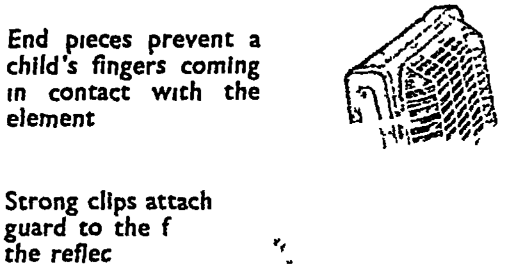

End pieces prevent a child's fingers coming in contact with the element
Strong clips attach guard to the f
the reflec
(a)

Fig 2—Guards for reflector types of electric fires
spring-loaded hooks (a) or by helical cur
fire and fixed to the guard by hooks (b
cleaning of the reflecting surface
filled in, in most recent r

LIVER-FUNCTION TESTS

Date	van den Bergh (mg. of bilirubin per 100 ml.)	Alkaline phosphatase (K.A. units)	Thymol turbidity (units)	Cephalin cholesterol flocculation	Serum-colloidal gold	Total plasma-protein (g. per 100 ml.	Albumin (g. per 100 ml.)	Globulin (g. per 100 ml.)
Normal	*0–1*	*3–13*	*0–4*	*No flocculation*	*No precipitation*	*6–8*	*60–70 % of total*	*30–40 % of total*
uly 6, 1948	10·0	46·0	24·0	3	4	7·0	2·9	4·1
„ 17 „	3·6	42·0	25·0	3	4	8·0	3·0	5·0
„ 27 „	7·5	43·0	20·0	4	5	8·5	3·2	5·3
ug. 4 „	6·2	34·0	20·0	3	5	8·0	3·1	4·9
„ 24 „	4·0	49·0	18·0	4	5	8·6	3·1	5·5
ov. 12 „	11·0	43·0	18·0	3	4	7·4	3·6	3·8
ay 3, 1949	10·2	34·0	22·0	4	5	6·7	2·9	3·8
„ 7 „	Removal of gall-stone from common bile-duct							
„ 20 „	8·9	29·0	20·0	4	5	6·6	3·2	3·4
une 28 „	2·6	27·5	19·2	4	5	6·6	3·0	3·6
ec. 2 „	1·4	23·5	15·2	4	5	6·9	3·9	3·0
Nov. 20, 1951	1·4	16·5	7·0	1	1	6·6	3·9	2·7

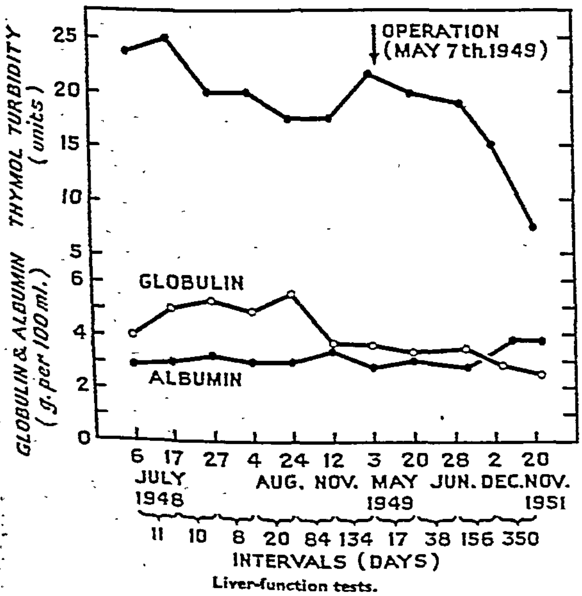
e had upper abdominal pain for two days. In March, 1947, e was seen in a follow-up department, and a note was made at the pelvic mass was unchanged. At this time she was ll complaining of epigastric pain from time to time.

In June, 1948, the niece with whom she lived wrote to say at her attacks were now very frequent, that her face was a astly yellow, and that she looked very aged. She was seen the radiotherapy follow-up clinic and found to have nsiderable enlargement of the liver and spleen as well as ep jaundice. There was some doubt about the diagnosis of etastases, and she was referred to the medical unit for further vestigation. A straight radiograph showed no evidence of ll-stones, and a blood-count showed Hb 70%, 3,890,000 red lls per c.mm., and 6400 white cells per c.mm. (polymorphs)%). On July 16, 1948, she was admitted under the care of e medical unit with a provisional diagnosis of hepatitis. xamination showed a grey-haired woman with xanthoma elow the eyes. There was deep jaundice. The liver and leen were enlarged, and the gall-bladder was not palpable. er blood-pressure was 200/100 mm. Hg. and the urine ntained bile.

During the next four weeks she had four attacks of right bcostal pain with nausea and flatulence, but with no increase the jaundice. After this she improved; the jaundice ecreased, and the stools became coloured.

Ten months later, on May 2, 1949, she was again admitted fter several severe attacks of biliary colic. Her condition was uch the same as on the previous admission, except that she ow had severe pruritus and was feverish and sweating. On ay 7, 1949, she was transferred to the surgical unit and two rge gall-stones were removed, one from the common bile-uct, the other from the gall-bladder. There was pus in the all-bladder and in the bile-ducts. The liver was enlarged, and its surface was nodular; the tissue was friable and bled easily. The spleen was enlarged, and the portal-vein tributaries were greatly distended. There was no ascites. It was thought wise not to take a biopsy specimen. Recovery following operation was satisfactory, but shortly after discharge the patient had to be readmitted with pyrexia. This was considered to be due to cholangitis; it responded well to treatment with antibiotics.

Follow-up.—The patient is somewhat temperamental, and it was difficult to persuade her to attend the follow-up clinic again. In response to several requests she attended on Nov. 20, 1951, when she was of a good colour, very energetic, and eating well. She said that her bowels were a little looser since the operation. The xanthoma under the eyes was thought to be less pronounced. The accompanying table and figure show the completeness with which liver function has apparently returned to normal.



Liver-function tests.

Reviews of Books

Ciba Foundation Colloquia on Endocrinology

Vol. 4. Anterior Pituitary Secretion and Hormonal Influences in Water Metabolism. Editor: G. E. W. WOLSTENHOLME, O.B.E., M.A., M.B., assisted by MARGARET P. CAMERON, M.A., A.B.L.S. London: J. & A. Churchill. 1952. Pp. 591. 45s.

THIS volume is the largest of the four Ciba Foundation Colloquia on Endocrinology so far published, and like the others it includes two separate symposia.

The larger and more recent of these was devoted to the anterior-pituitary gland and was noteworthy for the number of outstanding authorities who participated. They covered the anatomical, histological, and cytological aspects, including the cytochemical localisation of pituitary protein hormones, and the controversial question of the secretory innervation of the glandular cells of the hypophysis. One session dealt with the hypothalamic control of the secretory function of the hypophysis, many of the contributions being concerned with the mechanism of A.C.T.H. release. A paper on *p*-hydroxypropiophenone (which some believe specifically affects certain pituitary functions) heralds further studies of chemical control of pituitary function. The rest of the sessions dealt with the physiology and biochemistry of the six known anterior-lobe hormones. The whole is a fascinating record of recent research.

At the second conference, less ambitious in scope, the theme of hormones and water metabolism revealed the great advances in our knowledge of the relation of steroid hormones and hormones of both pituitary lobes to fluid and electrolyte metabolism. The adrenal cortex is a ubiquitous participant in a bewildering variety of metabolic functions.

This volume is impressive testimony to the excellent work of the Ciba Foundation in promoting an exchange of up-to-date information between workers in various countries. Moreover, it is a well-made book. The records of the discussion following each paper must have undergone some editing, for they are neither disjointed nor scrappy, but they nevertheless preserve the vivid atmosphere of informality aimed at by the organisers of the colloquia.

The old "nursery" type is usually too large for the modern small home, whose kitchen is also the living room The smaller fold-up types are usually devoid of any effective means of fixing them to the fireplace, so that a child can and often does remove them They have also to be removed for re-fuelling or stoking the fire It is to be hoped that it may soon become standard building practice (and enforced by local authorities) to provide staples at the side of the hearth to which guards can be securely hooked

Meanwhile a new design has been introduced which dispenses with the need for such staples and certainly seems worthy of a thorough trial It is the 'Braddell' guard (fig 4), sponsored by the Women's Advisory Council for Solid Fuel, which is now made (for the trade only) by Messrs Duke Waring, & Crisp Co, of London This guard is fixed to the chimney by two strong spring-loaded hooks It has also a large gate, fastened by a strong dog lead type of clip which a child cannot easily undo And it can be folded up and put away when not required

A rather more substantial and larger guard which is favoured by the Edinburgh Accident Prevention Council and the Scottish Department of Health is that shown in fig 5 It allows the fire to be re fuelled through the top, and it is adaptable to grates of different sizes by virtue of the telescopic construction of the front This latter feature also enables it to be folded into a comparatively small space when not in use Guards of this type are hired by the Edinburgh Accident Prevention Council, to householders who cannot afford to buy them, for the sum of 5s a year I am informed that there is a long waiting-list for them

Neither of these guards is spark-proof To make them so it would be necessary to use a guard of much smaller mesh, which would hide the fire Such guards would probably not be used It has therefore been thought better to concentrate on the greater danger—that of direct contact of clothing with the fire

The guards shown in figs 2(*a*) and 3(*c*) are made by Messrs J Broughton & Sons Ltd, of 234, Pershore Road South, King's Norton, Birmingham, 30, under the trade name of 'Lumley' guards Those shown in figs 2(*b*) and (*c*) are sold as 'Ann D' guards and are made by the Kleerun Co, Lane End, High Wycombe, Bucks The illustrations fig 2(*a*) and fig 3 are borrowed, by kind permission of the town clerk of Birmingham, from the leaflet *Advice on Fireguards*, issued by the city council

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THE MEDICAL SERVICES IN THE KOREAN WAR

FROM A CORRESPONDENT

It is now over two years since the British 27th brigade, and later the 29th, joined the fighting in Korea The medical problems of any campaign are those of collection, first-aid evacuation, and definitive treatment of the sick and wounded, but particular circumstances determine what is practicable and the results that can be obtained The relatively static battle lines which have developed during so much of the Korean fighting have been compared to the western front of the 1914–18 war, and the description "Passchendaele of the hilltops" has been used Another comparison was made by a former D D M S of the 5th Corps in Tunisia, who, during a visit to Korea, said that if he had been led blindfold into the forward areas in the British zone it would have been difficult for him to tell that he was not back in Tunisia, at any rate as far as the superficial appearances of terrain and of medical arrangements were concerned The medical services of the British Commonwealth Division have been working for over a year in this setting There are 3 field ambulances—Canadian, British and Indian The Indian field ambulance has attached to it a field surgical team There is a Canadian field dressing station and a Canadian field surgical team These forward units serve one of the new mobile army surgical hospitals (M A S H), in this case a Norwegian unit, and a Swedish Red Cross hospital

LINES OF EVACUATION

From Korea the wounded go to a combined hospital at Kure, in Japan, the British Commonwealth General Hospital, which is staffed by British, Australian and Canadian personnel, and where there is also a convalescent depot Although the British field ambulance deals mainly with the Norwegian M A S H, a proportion of casualties, including nearly all neurological cases are sent direct to American M A S H s which have well equipped neurosurgical teams The consultant supervision of all forward units and all hospitals in Japan is the responsibility of the consultants division of the medical section G H Q, United Nations and Far East Command Certain medical casualties are treated in Korea but all the others are evacuated by air to Japan and then by rail to the Commonwealth hospital Most of the neurosurgical cases pass from the M A S H along the American lines of evacuation to Japan, and are transferred later to the Commonwealth hospital From Japan the seriously wounded come home by air as soon as they are fit enough to travel The flight to Britain takes five or six days A certain number of casualties return by sea

In the early stages of the fighting, when things were going badly for United Nations troops, H M Hospital Ship *Maine* did very valuable work in transporting American and British casualties from Korea to Japan

MOBILE ARMY SURGICAL HOSPITALS

The M A S H has lately been introduced by the Americans It differs from our own casualty clearing station (C C S) in being limited to 100 beds and to surgical cases It is more mobile than the C C S, but it may prove of less general value than the C C S, especially in tropical countries where acute medical conditions are often a big medical responsibility The static lines in Korea are not a thorough test of its value, although the widespread use of antibiotics seems to have reduced the number of medical cases needing admission to hospital

HELICOPTERS

A special feature of the Korean campaign has been the use of helicopters in the evacuation of wounded These aircraft, flying between regimental aid-post and M A S H, have made it possible to give full surgical treatment to serious casualties within one to three hours of the man being wounded It has therefore been necessary to stop giving fluids by mouth in the regimental aid post to those injured who will be taken quickly to the surgeon in this way In one period of ten months 254 serious casualties were evacuated from the British zone by helicopter, 154 of these were wounded, and 100 represented other emergencies, including medical conditions

TYPES OF WOUND

The type of wound sustained in battle clearly depends a great deal on the weapon causing it One analysis of wounds in the Korean campaign was as follows

Mortar wounds	37%
Bomb and grenade wounds	21%
Gunshot wounds	17%
Shell and high explosive wounds	12%
Mines	6%
Battle accidents	6%
Burns	1%

This distribution is not unlike that seen during certain periods of the late war in Europe The risk of burns in battle has increased steadily over the last fifty years, and the low proportion of burns in this list is unusual Accidental napalm burns have shown no clinical differences from burns of equal severity due to other agents

THE LANCET

LONDON: SATURDAY, JAN. 17, 1953

Measles Encephalitis

THE biennial epidemic of measles is in full swing; England and Wales weekly notifications have ached the 30,000 mark. Encephalitis seems to especially liable to complicate measles during pidemics of the disease [1, 2]; its incidence during pidemics has been approximately estimated at 1 per 000 cases admitted to hospital.[1, 3–8] There seems o be no correlation between the severity of the attack f measles and the liability to encephalitis; so a ubstantially similar incidence of encephalitis is to e expected among cases treated at home. Yet erified cases of post-measles encephalitis notified n the years 1950 and 1951 numbered only 73 out of total of 983,900 notifications of cases of measles. t seems likely, therefore, that the reporting of acute ncephalitis under the 1949 Regulations has not yet got into its stride, and that many cases, possibly nild, are not being notified.

Measles encephalitis belongs clinically and pathoogically to the group of post-infectious encephalitis. This group also includes the encephalitis that may follow vaccinia, smallpox, chickenpox, rubella, occasionally mumps, and other virus infections. It usually appears suddenly and unexpectedly when the rash has just subsided leaving staining of the skin—that is, about the 3rd post-eruptive day. It may start, however, at any time between the 4th and the 14th days of the disease or, very rarely, in the pre-eruptive stage.[9] In one series of 74 cases the age-distribution ranged from 14 months to 35 years [7]; but about half the cases are in children aged 5–8 years.[6] The fatality-rate varies from 10 to 30%. The earliest histological lesion, according to APPELBAUM and his colleagues,[7] is cellular infiltration of the adventitia of small and medium veins in the grey and white matter of the brain. In cases where neurological symptoms have been present more than 3 days before death there are, in addition, perivascular demyelination, infiltration of the demyelinated areas with microglial cells, and small areas of softening in the white matter. Usually there is also significant cellular degeneration, and many ganglion cells may be missing. Such changes have been interpreted as inflammatory; and in one case virus was recovered from the brain of a child who died of post-measles encephalitis 9 days after the rash appeared.[10] The alternative interpretation of these changes is that they are an allergic response to the virus of measles; and for this view there is much weighty evidence.

The clinical course is very variable and may include cortical, brain-stem, myelitic, and meningeal signs. Fortunately, in the great majority rapid recovery sets in after 2–3 days of pyrexia, coma, convulsions, or other central nervous disturbance. When coma and other symptoms continue longer, neurological recovery is usually slower; but recovery is progressive and, with some exceptions, virtually complete after weeks, months, or years according to the extent of the damage. The potential reversibility of all the lesions has been emphasised by JENNINGS,[11] who showed in particular that blindness almost always clears up although it may take some years to do so. The electro-encephalogram (E.E.G.) during the acute stage shows gross high-voltage slowing in all leads; judged by the E.E.G., recovery is slower than the apparent clinical recovery, and it is not always complete even after 4 or 5 years.[12]

The ultimate prognosis has now been further examined in a psychological follow-up study by MEYER and BYERS [13] of 16 cases treated in the Children's Hospital, Boston, between 1943 and 1949. This reveals that abnormalities of mental function can be demonstrated by appropriate psychological tests in a high proportion after neurological and E.E.G. evidences of the disease have cleared. Easy fatigability of intellectual function and defects in attention, in perceptual-spatial organisation, and in learning capacity tend to persist for months, or even permanently, in about a third of the children—usually those who have had a long acute stage. When such psychological defects persist, the child has difficulty in acquiring new knowledge, and consequently his intelligence quotient falls gradually over the years. His defective powers of adaptation tend also to produce emotional stress and either a retreat into himself or aggressive rebellion. Such children need to be handled tactfully, affectionately, patiently, and with due allowance for their mental disabilities; they must not be pressed either in school or in the home. The outcome is influenced by age at the time of the attack. Older children, because of their more elaborate foundation, are more likely to remain competitive despite incomplete intellectual recovery than are younger children who must acquire their fundamental learning with defective tools. MEYER and BYERS have stated a good case for detailed psychological assessment of cases of encephalitis where the patient, after apparent recovery, shows behaviour difficulties, personality change, or some loss of intellectual capacity. Thereby a way of life may be planned which will diminish anxiety and tension and improve behaviour.

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1. Peterman, M. G., Fox, M. J. *Amer. J. Dis. Child.* 1933, 46, 512.
2. Reisman, H. A., Rosen, A. S. *Ibid*, 1943, 66, 597.
3. Hoyne, A. L. *Illinois med. J.* 1939, 76, 136.
4. Geiger, J. C., Sappington, E. E. *Arch. Pediat.* 1940, 57, 313.
5. Litvak, A. M. *Ibid.* 1947, 64, 507.
6. Sawchuk, S., LaBoccetta, A. C., Tornay, A., Silverstein, A. Peale, A. R. *Amer. J. Dis. Child.* 1949, 78, 844.
7. Appelbaum, E., Dolgopol, V. B., Dolgin, J. *Ibid*, 77, 25.
8. Banks, H. S. The Common Infectious Diseases. London, 1949; p. 103.
9. Wyllie, W. G. *Proc. R. Soc. Med.* 1934, 27, 1425.
10. Shaffer, M. F., Rake, G., Hodes, H. L. *Amer. J. Dis. Child.* 1942, 64, 815.
11. Jennings, G. H. *Lancet*, 1952, ii, 66.
12. Jacobson, E., Holmgren, B. *Ann. pædiat.* 1949, 173, 231.
13. Meyer, E., Byers, R. K. *Amer. J. Dis. Child.* 1952, 84, 543.

The old "nursery" type is usually too large for the modern small home, whose kitchen is also the living room The smaller fold-up types are usually devoid of any effective means of fixing them to the fireplace, so that a child can and often does remove them They have also to be removed for re-fuelling or stoking the fire It is to be hoped that it may soon become standard building practice (and enforced by local authorities) to provide staples at the side of the hearth to which guards can be securely hooked

Meanwhile a new design has been introduced which dispenses with the need for such staples and certainly seems worthy of a thorough trial It is the 'Braddell' guard (fig 4), sponsored by the Women's Advisory Council for Solid Fuel, which is now made (for the trade only) by Messrs Duke, Waring, & Crisp Co, of London This guard is fixed to the chimney by two strong spring-loaded hooks It has also a large gate, fastened by a strong dog-lead type of clip which a child cannot easily undo And it can be folded up and put away when not required

A rather more substantial and larger guard which is favoured by the Edinburgh Accident Prevention Council and the Scottish Department of Health is that shown in fig 5 It allows the fire to be re-fuelled through the top, and it is adaptable to grates of different sizes by virtue of the telescopic construction of the front This latter feature also enables it to be folded into a comparatively small space when not in use Guards of this type are hired by the Edinburgh Accident Prevention Council, to householders who cannot afford to buy them, for the sum of 5*s* a year I am informed that there is a long waiting-list for them

Neither of these guards is spark-proof To make them so it would be necessary to use a guard of much smaller mesh, which would hide the fire Such guards would probably not be used It has therefore been thought better to concentrate on the greater danger—that of direct contact of clothing with the fire

The guards shown in figs 2(*a*) and 3(*e*) are made by Messrs J Broughton & Sons Ltd, of 234, Pershore Road South, King's Norton, Birmingham, 30, under the trade name of 'Lumley' guards Those shown in figs 2(*b*) and (*c*) are sold as 'Ann D' guards and are made by the Kleerun Co, Lane End, High Wycombe, Bucks The illustrations fig 2(*a*) and fig 3 are borrowed, by kind permission of the town clerk of Birmingham, from the leaflet *Advice on Fireguards*, issued by the city council

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THE MEDICAL SERVICES IN THE KOREAN WAR

FROM A CORRESPONDENT

It is now over two years since the British 27th brigade, and later the 29th, joined the fighting in Korea The medical problems of any campaign are those of collection, first-aid, evacuation, and definitive treatment of the sick and wounded, but particular circumstances determine what is practicable and the results that can be obtained The relatively static battle lines which have developed during so much of the Korean fighting have been compared to the western front of the 1914–18 war, and the description "Passchendaele of the hilltops" has been used Another comparison was made by a former D D M S of the 5th Corps in Tunisia, who, during a visit to Korea, said that if he had been led blindfold into the forward areas in the British zone it would have been difficult for him to tell that he was not back in Tunisia, at any rate as far as the superficial appearances of terrain and of medical arrangements were concerned The medical services of the British Commonwealth Division have been working for over a year in this setting There are 3 field ambulances—Canadian, British, and Indian The Indian field ambulance has attached to it a field surgical team There is a Canadian field dressing station and a Canadian field surgical team These forward units serve one of the new mobile army surgical hospitals (M A S H), in this case a Norwegian unit, and a Swedish Red Cross hospital

LINES OF EVACUATION

From Korea the wounded go to a combined hospital at Kure, in Japan, the British Commonwealth General Hospital, which is staffed by British, Australian, and Canadian personnel, and where there is also a convalescent depot Although the British field ambulance deals mainly with the Norwegian M A S H, a proportion of casualties, including nearly all neurological cases, are sent direct to American M A S H S which have well equipped neurosurgical teams The consultant supervision of the forward units and all hospitals in Japan is the responsibility of the consultants division of the medical section G H Q, United Nations and Far East Command Certain medical casualties are treated in Korea but all the others are evacuated by air to Japan and then by rail to the Commonwealth hospital Most of the neurosurgical cases pass from the M A S H along the American lines of evacuation to Japan, and are transferred later to the Commonwealth hospital From Japan the seriously wounded come home by air as soon as they are fit enough to travel The flight to Britain takes five or six days A certain number of casualties return by sea

In the early stages of the fighting, when things were going badly for United Nations troops, H M Hospital Ship *Maine* did very valuable work in transporting American and British casualties from Korea to Japan

MOBILE ARMY SURGICAL HOSPITALS

The M A S H has lately been introduced by the Americans It differs from our own casualty clearing station (C C S) in being limited to 100 beds and to surgical cases It is more mobile than the C C S, but it may prove of less general value than the C C S, especially in tropical countries where acute medical conditions are often a big medical responsibility The static lines in Korea are not a thorough test of its value, although the widespread use of antibiotics seems to have reduced the number of medical cases needing admission to hospital

HELICOPTERS

A special feature of the Korean campaign has been the use of helicopters in the evacuation of wounded These aircraft, flying between regimental aid-post and M.A.S.H., have made it possible to give full surgical treatment to serious casualties within one to three hours of the man being wounded It has therefore been necessary to stop giving fluids by mouth in the regimental aid post to those injured who will be taken quickly to the surgeon in this way In one period of ten months 254 serious casualties were evacuated from the British zone by helicopter, 154 of these were wounded, and 100 represented other emergencies, including medical condition

TYPES OF WOUND

The type of wound sustained in battle clearly depends a great deal on the weapon causing it One analysis of wounds in the Korean campaign was as follows

Mortar wounds	37%
Bomb and grenade wounds	21%
Gunshot wounds	17%
Shell and high explosive wounds	12%
Mines	6%
Battle accidents	6%
Burns	1%

This distribution is not unlike that seen during certain periods of the late war in Europe The risk of burns in battle has increased steadily over the last fifty years and the low proportion of burns in this list is unusual Accidental napalm burns have shown no clinical differences from burns of equal severity due to other agent ef in 64% of cases; but WALDRIFF and his col-gues rightly emphasise the inadvisability of treating this method acute or subacute vesicular dermatitis widespread dermatitis. MADDEN[11] treated 141 cases various selected dermatoses with 'Thephorin' henindamine hydrogen tartrate) ointment and ported relief in 90%, no change in 5%, and worsening 5%.

ELLIS and BUNDICK[12] received 200 replies to a estionary which they sent to 265 dermatologists in e United States and Canada. 94% of these derma-logists reported that they had used anti-histamine ugs in the past, but only 10% continued to use em often; 50% were using them occasionally, while e remaining 40% were not using them at all. easons for discontinuing their use were the belief at they were ineffective, or liable to sensitise the in, or to aggravate dermatosis. Sensitisation actions were commonest with thephorin, followed tripelennamine ('Pyribenzamine') and diphen-ydramine ('Benadryl'); but thephorin relieved ching the most effectively. It was generally felt hat these substances were useful for anogenital ruritus and neurodermatitis, but that they were of ttle help in moist areas. About a quarter of the ermatologists thought that the local use of anti-istamines was of value; about a third were oubtful; and the remainder (approximately two-ifths) thought they were useless: 29% suggested hat anti-histamines for local use should be taken off he market. The only report of controlled trials has een by BALDRIDGE,[13] who treated 41 patients with % thephorin ointment on one side and with its nmedicated base on the other. These were presented o the patient as "slightly different forms of the same nedication," and the patients were asked to estimate he percentage of relief on the two sides. The areas reated with thephorin were reported on the average s 47% relieved, and the areas treated with the nmedicated base as 49% relieved. These results re a chastening reminder of the powerful influence f suggestion in treatment, particularly when symptoms of emotionally influenced disorders are being ountered, and when remedies are "put across" with enthusiastic expectancy (as they should be in umanistic medicine).

Anti-histamine drugs vary in their skin-sensitising power; but usually 2–6% of cases become sensitised. It is therefore especially important to know whether these are really effective antipruritic agents. It is surely significant that the local use of these drugs is confined almost entirely to the neurodermatoses; for there is increasing evidence that in these conditions the pruritus is produced in the first place by emotional disturbance, though no doubt it is often aggravated by friction and local applications. It seems irrational to expect local applications to relieve a symptom which has been brought about by frustration of emotional expression. The lessening of emotional tension by the abatement or removal of a conflict situation, or by the adoption of a more nearly physiological mode of emotional expression, is the essence of relief in these maladies; and any material treatment given about the same time may undeservedly be credited with the "cure." The dermatologist is familiar, too, with the obstinate and irrepressible neurodermatoses which if relieved at one site erupt at another, indicating the seething unrest beneath; and he is also aware that the scratched and rubbed nucha or wrist may sometimes represent a genteel way of relieving an itchy anus. The value of topical anti-histamines would seem to be "not proven"; and the doctor who thinks of using them should pay due regard to their sensitising power, which is midway between that of the hazardous benzocaine derivatives and the old-fashioned but trustworthy oily calamine lotion.

Annotations

SOCIAL NEEDS: A RETROSPECT

IT is not in man's nature to be unmoved by the acts of his fellows: we are changed, for good or evil, by what goes on around us. In this country, the events of our history and the temper of our people have combined to make us build a State in which the rights and welfare of the individual citizen are particularly honoured; and we are naturally happy that others should profit by our experience, both of failure and success. At the Anglo-German conference arranged by G.E.R.,[1] which has been held in London in the past week or so, speakers surveyed our social insurance, health, and welfare services, in the hope that the German experts who attended might find in them the answer to some of their own problems.

The present scene was set against the stormy background of our history by Prof. Richard Titmuss. Ours, he said, was once a peasant society, as Germany's was; and when a family fell on evil days its needs were met by the Church, by charity, and by the collective efforts of the parish towards the relief of the poor. In a rough sort of way this served very well. This pattern of charitable welfare and collective aid broke down when the amount of social need was violently changed by the first of the Industrial Revolutions, based on the steam-engine. It called into being a great society of wage-earners solely dependent on their labour power; and dependence on this power made them more dependent on the state of their health. Ours became—and still is—a society with no useful place for the sick, the disabled, the substandard, and the old: they have lost their labour power.

> "Simultaneously, this new industrial system based on the wage-earning capacity of the *individual* itself created new hazards to health and new problems in the rearing of children. As a result of the growth of town and city, factory and mine, new dangers to health and sanity appeared; new forms of mass disease arose; new social evils—psychological as well as physical—were generated. The stability of the family unit was threatened when the father left his home for six days out of seven to exchange his labour power for money; it was threatened too by a system of reward which ignored altogether his rôle as a father and his responsibilities for those who were too young or too old for industrial wage-earning work."

The Industrial Revolution, in fact, created social insecurity over the whole span of life, insecurity which the family could not remove by their own unaided efforts. By breaking up the family unit, selecting only those that industry could use and rejecting the rest, it created new problems of poverty and misery with which charity and the poor-law were unable to cope. In the 1840s Rudolf Virchow, the pathologist, led a strong public-health movement in Germany, claiming (almost

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11. Madden, J. F. *Ibid*, p. 673.
12. Ellis, F. A., Bundick, W. R. *J. Amer. med. Ass.* 1952, 150, 773.
13. Baldridge, G. D. *Arch. Derm. Syph., Chicago*, 1951, 63, 260.

[1] A society for promoting Anglo-German educational relations, founded in 1942 to help German refugee teachers and social workers to prepare for post-war educational reconstruction in Germany, and now giving a reciprocal character to its work.

a few minutes each, the methods best suited to their particular subject Dr J Vallance-Owen taught on physical signs in the chest; Dr I McIntyre illustrated a convenient method of determining the alkali reserve, Dr G A K Missen questioned his class on a specimen of bacterial endocarditis from the pathology museum, Mr H H Bentall discussed a swelling in the breast at his ten-minute outpatients, and Dr E S Clarke guided his students through the examination of a man with a neurofibroma pressing on the cervical cord.

Some of the audience found it hard to see and follow all the details, but this was no serious criticism, for the methods used were designed for a more intimate atmosphere than that of the lecture theatre

Discussing the technique of outpatient teaching, Dr R C Mac Keith suggested that a session set aside largely for teaching, with only four patients instead of the usual dozen or more, would help the teachers, who often found it difficult to give students the time they needed to reach their diagnosis On the other hand, Professor Aird thought that the steady stream of patients brought the pages of the textbook to life in a very profitable way Professor McMichael added that a particular value of outpatient teaching was the opportunity it gave for students to see patients who had recovered, often from diseases with a serious prognosis

HEALTH UNDER INDIA'S FIVE-YEAR PLAN

Under India's first Five-Year Plan, approved by both houses of parliament, the health programme embraces the following priorities (1) provision of water-supply and sanitation, (2) control of malaria, (3) preventive health care of the rural population through health and mobile units, (4) health services for mothers and children, (5) education and training and health education, (6) self-sufficiency in drugs and equipment, and (7) family planning and population control The medical and public-health plans of the central and State governments will cost Rs 995 5 million The central government will aid the States in higher education and research and in certain specific schemes

Of the total outlay on medical programmes, more than 50% will be on hospitals and dispensaries, and nearly 40% on medical education and training, in addition to the establishment of the All-India Medical Institute, the completion of new medical colleges in Assam, Bombay, Madras, Madhya Pradesh, West Bengal, and Travancore-Cochin, upgrading of existing medical schools, and provision of training for auxiliary medical personnel including nurses, midwives, and compounders

The execution of these schemes is expected to increase the total number of personnel trained thus

	NUMBER TRAINED DURING YEAR ENDING 1950–51	1955–56	Increase %
Doctors	2504	2782	11 1
Compounders	894	1621	81 3
Nurses	2212	3000	35 6
Vaids and hakims	914	1117	22 2

The increase in the number of hospitals and dispensaries and the number of beds in them is expected to be as follows

	During 1950–51	By 1955–56	Increase %
No of hospitals	201	206	2 4
No of dispensaries			
Urban	1358	1695	24 8
Rural	5229	5840	11 6
No of beds in hospitals	106 478	117,222	10 1
No of beds in dispensaries			
Urban	2013	2233	11 4
Rural	5066	5582	18 2

The expenditure on public-health programmes undertaken by the central and State governments is Rs 503 8 million. Water-supply, drainage, and anti-malaria schemes account for the bulk of the expenditure

Malaria is the most important public-health problem in India and its control is naturally accorded the highest priority Over Rs 170 million has been provided in t plan for malaria control The operational programme the malaria plan is based on the use of insectic residual spraying in rural areas, protecting 200 mill people, and treatment with anti-malaria drugs Th plan also embraces the construction of two D D T pl to ensure sufficient supply of D D T at reduced cos This project is financed jointly by the central and t State governments

Tuberculosis ranks next in importance to malaria a a health problem to India In this case the schem generally relate to sanatoria, hospitals, and clinics, BCG vaccination teams Compared with 1950-51 t plan envisages the following increase by 1955-56

	1950–51 No of institutions	No of beds	1955–56 No of institutions	No o be
Sanatoria	37	4161	46	[illegible]
Hospitals	48	3077	50	[illegible]
Clinics	127	2323	180	[illegible]

Specific recommendations have also been made for t control of venereal diseases, for maternity and ch welfare, for medical education, and for research

The recent steep increase in the population of th country has brought to the fore the urgency of fami planning and population control Family limitation deemed both desirable and necessary for safeguard the health of the mother and for the better care an upbringing of the children The Five-Year Plan provid Rs 6 5 million for family-planning measures It al suggests the constitution of policy and research com mittees, and a population commission at a later date

NEW YEAR HONOURS

The list appearing in our last issue omitted the nam of two members of our profession on whom honours hav been conferred They are

Knight Bachelor

Frank Percivale Montgomery, M C, M B Belf, F F
Consulting radiologist, Down County Infirmary a
Ulster Hospital for Children and Women

C B E (Civil)

Louis Boyd Neel, M R C S
Musical director, founder of the Boyd Neel Orchestra

In the community of Northern Ireland Dr Montgomery holds a leading position won by distinction in several different fields, including that of International rugby, and his public work has latterly included the chair manship *of the Northern Ireland Hospitals Authority*

Medicine and the Law

Fatal Poisoning by Mothballs

A boy, aged 21 months, died the day after he had eaten a number of mothballs which he found in a wardrobe in his home At the inquest at Bromley, Kent, on Jan 8 [1] the pathologist reported that the child died of a respiratory failure which was in keeping with naphthalene poisoning He added that the literature on the subject tended to suggest that the majority of such cases were not fatal Asked whether there was no antidote to mothball poisoning, he replied "As far as we know there is none" The coroner inquired "Assuming the stomach had been washed out early enough and thoroughly enough, could the child still have absorbed the poison?" "Yes The poison could have got into the intestines and affected the liver"

Recording a verdict of death by misadventure, the coroner warned parents to regard mothballs as a dangerous poison which should be kept out of reach of children which gives rise to true "colic." Morphine, which ically brings about constipation as well as relief of ı, seems to increase tone with obliteration of the gut en while greatly reducing propulsive type-3 waves.

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[1] *Manchester Guardian*, Jan 9, 1952

[ovements of the colon differ from those of the small stine in many ways: type-1 ("mixing") waves are frequent in the lower bowel, while type-2 waves, h lasting about 30 seconds, are of greater pressure; s these waves that account for the haustration seen iographically. The so-called mass movement of the n—a very infrequent propulsive wave—is confined the large intestine. In normal people colon motility xtremely variable; periods of activity alternate with iods of inactivity, and both are greatly influenced by emotional state. In patients with chronic ulcerative itis the total colonic activity seems to be reduced, with eneral change from the mixing to the propulsive type movement. In the colon, as in the small intestine, rphine tends to increase the non-propulsive move-nts and to decrease the propulsive.

Ve still do not know the exact relation of absorption food to the frequency and strength of the different estinal movements, nor of the varying rates of absorp-n of different substances to the amount of mixing they dergo in the small intestine. These and allied problems er a fruitful field for further investigations.

STILLBIRTHS AND NEONATAL DEATHS

Two factors in particular seem to have largely counted for the decline in the number of stillbirths d neonatal deaths. These factors are better social nditions and a higher standard of obstetric practice. first both seemed equally important; but with e continued decline in the stillbirth and neonatal death tes their influence became less distinct and their relative portance changed. With the establishment of adequate aternity services and a high general standard of living stetric causes were seen to account for a higher rcentage of deaths.

Workers[1] at Bristol, where the stillbirth and infant ath rates are low and the general standard of living is gh, have compared two series of stillbirths and neonatal aths with two groups of controls. No significant fference was found between cases and controls in cial factors, nor in the *amount* of antenatal care; portant differences were discovered, however, in the *ality* of obstetric care. For instance, many patients ith infants who were born dead or who died neo-tally were not seen by a consultant at any time ring the pregnancy or labour, although the number abnormalities among such patients was far greater an among controls. Commonly the reason for this as that labour began before the 34th–36th week, hen specialist appointments are normally made. It peared that there was a failure to appreciate that me cases may require specialist supervision at a much rlier stage in pregnancy than that normally regarded s routine. 44% of the stillbirths and 60% of the neonatal eaths were of infants with a birth weight below $5^1/_2$ lb. he most common complication of pregnancy was found be toxæmia. This condition, besides occupying first lace as a cause of maternal death, is the most common ondition known to be associated with prematurity.[2] ossibly the early signs of this condition were evident efore the 34th week; and had these signs been recog-ised, and specialist advice sought, some of these remature births might have been prevented.

It would appear that throughout the country antenatal are is often energetically practised along strictly outine lines. Thus patients are commonly weighed t each visit, yet any attempt to control weight-gain by diet is rare. Similarly, iron in tablets is given in large amounts to almost all patients; not always, however, is an attempt made to ensure that such tablets are taken, and that if they are taken the iron is absorbed and the patient's blood picture improves. The mounting list of routine investigations carried out on all patients at every visit to the clinic tends to divert attention more and more from the individual patient and from the true purpose of antenatal care—namely, the early detection of important abnormalities. The Bristol workers have given a timely reminder that much of the standard practice in antenatal care is due for reconsideration. Greater obstetric skill can prevent only a proportion of stillbirths[3]; but this proportion is by no means small.

INTRA-ŒSOPHAGEAL PRESSURE

By means of a modern electromanometer and some fine plastic tubing slipped through the nose, it is easy to record respiratory and cardiac fluctuations in the œsophagus. Recent work on both sides of the Atlantic has been concerned with two different aspects of such records—namely, as guides to general intrathoracic pressure and to certain cardiac events.

Dornhorst and Leathart[4] found good dynamic agreement between the pressures in the œsophagus and in a shallow pneumothorax and concluded that the intra-œsophageal pressure reflected intrathoracic pressure. Such measurements have been helpful in analysing circulatory events—for example, in Valsalva's manœuvre[5] and with pulsus paradoxus[6]—and, combined with a respiratory record, they provide a simple way of investigating the mechanical properties of the lungs and air-passages. The principles of this potentially valuable type of investigation were clearly set out twenty-five years ago by von Neergaard and Wirz,[7] but they have been little exploited because the original method necessitated puncturing the pleura—a possibly risky procedure in patients with pulmonary disease. An American team[8] has now confirmed the agreement between œsophageal and pleural pressures, and has used the method to construct volume-tension characteristics for normal and emphysematous lungs.[9] The further application of this technique—for example, to provide an objective measure of fibrosis in patients with silicosis—should yield information of interest and possibly of diagnostic or prognostic value.

The œsophageal-pressure record, especially when a water-filled system is used, shows cardiac pulsations which vary at different levels of the œsophagus and are often considerably larger than those in an intrapleural record. They must therefore depend on some local action of the heart-beat. It is natural to inquire what information they will yield about events in the heart, and especially in the left auricle which is in direct contact with the œsophagus. This question has been studied by Zoob[10] in this country and by Lasser et al.[11 12] in the U.S.A. A prime object has been to assist in the recognition of mitral incompetence—a diagnosis whose importance has been greatly enhanced by the introduction of valvotomy. Lasser and Loewe[11] showed that in dogs the œsophageal pulse agreed in form remarkably well with the pressure-pulse recorded directly from the left auricle, both before and after the production of mitral incompetence. In patients they have obtained

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8. Fry, D. L., Stead, W. W., Ebert, R. V., Lubin, R. I., Wells, H. S. *J. Lab. clin. Med.* 1952, 40, 664.
9. Stead, W. W., Fry, D. L., Ebert, R. V. *Ibid*, p. 674.
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11. Lasser, R. P., Loewe, L. *Amer. Heart J.* 1952, 44, 531.
12. Lasser, R. P., Epstein, B., Loewe, L. *Ibid*, p. 681.

one of them regularly brought her daughter Of these, Miss H and both the domestic helps developed Q fever in September The family doctor (Dr W) and district nurse (Nurse N) attended old Mrs F before she died, and another doctor (Dr V) and 2 undertakers (Mr B and Mr Z) visited the farm after her death , but these 5 paid only short visits, and none of them developed Q fever

After excluding Mrs F , sen , there were in all 25 people at risk Of these, 5 adults had no clinical or serological evidence of infection, but 4 of them had paid only short visits to the farm One child remained well, but the presence of Q-fever antibodies six months after the outbreak suggested a subclinical infection An adult and 2 children also remained well, but no serological tests were performed All the other 16 adults developed clinical Q fever , this included everyone over the age of twelve who was living on the farm at the time of exposure

CLINICAL PICTURE

Although the attack-rate in this outbreak was unusually high and subclinical infections were rare, the clinical picture was very like that described in previous outbreaks and groups of sporadic infections Sudden onset with severe headache and fever was common to all, but clinical signs of pulmonary involvement were found in only 5 patients (In most cases X-ray examination was carried out too late to be of value) There were the usual wide variations in severity , 9 patients had mild febrile illnesses lasting less than a week, while 7 had more severe attacks lasting between one and seven weeks Symptomatic treatment only was given to most patients, and no noticeable benefit followed the use of a sulphonamide, penicillin, or streptomycin 6 patients were given chloramphenicol in various doses, starting between two and eight days after the onset, and they responded well The 2 oldest patients had the longest illnesses, lasting seven weeks and three weeks respectively, as the following case-histories show

Mrs P , the farmer s mother in law, aged fifty six, was taken ill in Berlin on Sept 7 with severe headache, fever, sweating, and insomnia Her condition improved slightly during the next day, but she became suddenly worse and was admitted to hospital on Sept 12 with dyspnœa, cyanosis, and signs of pneumonia of the left lower lobe Sulphonamides and penicillin produced no response, but on Sept 15 news of the other illnesses at the farm (not then diagnosed) reached her doctor, who immediately suspected Q fever and gave chloramphenicol The patient's temperature promptly fell to normal, but rose again when supplies of chloramphenicol ran out on Sept 24 There were now no radiological signs of pneumonia, but the patient was still very ill, and fever continued until fresh supplies of chloramphenicol became available and were given on Oct 13 The temperature again fell and her condition improved, but there was a further relapse as soon as the drug was stopped on Oct 20 However, after a third course, ending on Nov 2, the patient remained well and was discharged from hospital on Nov 19 The diagnosis of Q fever was confirmed by a rising titre of Q fever antibodies

TABLE III—PIGS ON FARM, WITH DATES OF PARTURITION A RESULTS OF LABORATORY TESTS

Name	Litter born	Serum tested	Result *
Snotch	Aug 10, 1951	Jan 28, 1952	Negative
Blowey	Aug 10, 1951	Jan 28 1952	Negative
Lady pig	Sept 4, 1951	Not tested	—
Flirt	Aug 18, 1951	April 10 1952	Non specific reac
Squib	Not pregnant	Not tested	—
Piglets			
Snotch 1–4	—	Jan 28, 1952	Negative
Snotch 5	—	April 10, 1952	Non specific reac
Blowey 1–4	—	Jan 28, 1952	Negative

* Pig sera were tes[illegible]
the conglutina-
tion test, and
reactions were
in the anti globulin sensitisation test

Mrs D , aged fifty six, one of the domestic helps, felt ill o *Sept 8, but, in spite of a feverish headache with pains in t* neck and limbs, she tried to continue her work On Sept 1 she took to bed, and was found to have signs of a bilater basal pneumonia A diagnosis of virus pneumonia was mad and she was given 0 25 g of chloramphenicol four hourly t to a total of 6 0 g In spite of the low dosage, her temperature fell to normal in thirty six hours, and the signs in her che rapidly cleared, but she remained very debilitated indeed a was confined to bed for three weeks

With the exception of Mrs X , one of the visitors *from London, whose illness was diagnosed on* clinical grounds alone, all the patients had Q fever antibodies in their serum when it was tested later Mrs P 's serum showed a rise in antibody titre from 1 in 128 to 1 in 51 and in the others the titres varied between 1 in 40 and 1 in 320 in specimens taken about one month after the illness The blood of 2 patients was not examined until later, and both showed Q-fever antibody titres of 1 in 20 while serum from Jill T , who was not ill at all, also had a titre of 1 in 20 when tested six months after the outbreak

SOURCE AND MODE OF INFECTION

The explosive nature of the outbreak suggested the exposure of completely susceptible individuals to a single large dose or to an unusually infective strain of *Rickettsia burneti* The peak of the outbreak was reached on Sept 6–8, and the mean day of onset was Sept so that, with the usual incubation period of about nineteen days, infection would have taken place about Aug 19 *This gives a minimum incubation period of* thirteen days for Maureen T , and a maximum of twenty nine days for Mrs C Fortunately 4 of the patients had visited the farm for short periods only during August, which suggested that infection must have occurred between Aug 16 and 19 (see table I and figure) Only 7 of the patients had been to the cottages, whereas all had visited the farmhouse or outbuildings during this period, except for Mrs J , the cowman's wife, who could not remember visiting the farmhouse after Aug 6 However, infection could well have been carried to Mrs J 's cottage by her husband's clothes or in the milk

TABLE II—COWS ON FARM, WITH DATES OF PARTURITION AND RESULTS OF LABORATORY TESTS

	Name	Calved	Pooled milk of Oct 27 1951, tested for *R burneti* by guineapig inoculation	Serum antibody titres, Jan 26, 1952 (complement fixation test)	Whey antibody titres in individual samples	
					Direct agglutination	Anti globulin sensitisation test
In milk Aug 13–26 1951	Dulcie	Dec 13, 1950	—	<1 in 8	<1 in 2	<1 in 2
	Daphne	Jan 14 1951	Negative	<1 in 8	<1 in 2	<1 in 2
	Dot	Nov 29 1950	—	<1 in 8	<1 in 2	<1 in 2
	Dally	Feb 9 1951	Negative	<1 in 8	<1 in 2	<1 in 2
	Ruby	Jan 24, 1951	—	<1 in 8	<1 in 2	<1 in 2
	Dancer	Oct 26, 1950	—	—	<1 in 2	<1 in 2
	Dawn	Jan 30, 1951	Negative	—	<1 in 2	<1 in 2
Dry Aug 13–26, 1951	Dora	Sept 2 1951	,,	—	<1 in 2	<1 in 2
	Dillis	Sept 10, 1951	,,	<1 in 8	—	—
	Diana	Oct 17 1951		—	<1 in 2	<1 in 2
	Dilly	Feb 1 1952*	—	—	1 in 16	1 in 64
	Della	March 24 1952†	—	—	<1 in 2	<1 in 2

* In milk to Aug 5 1951 then dry and pastured 2 miles from farm † Heifer also pastured 2 miles from farm in August, 1951

ACERIN

THE discovery of a new bacteriostatic agent is unlikely arouse more than polite interest today, but a substance ctive against viruses is always news. Fischer[1] has studied e action of an extract from the fruit of the Norwegian aple (*Acer platanoides*) on a bacteriophage and on accinia virus. The active substance in these extracts, which he has given the provisional name "acerin," ppears to have a rapid phagicidal action on a *Bacterium li* bacteriophage in concentrations which do not inhibit he growth of the host bacterium. A small number of xperiments suggest that acerin may also have a virucidal ction on vaccinia virus. Apparently it has no significant ffect on a staphylococcus bacteriophage, and a few xperiments suggest that it is not toxic to mice and abbits in the dosages tested.

This is only a preliminary communication, and clearly uch more information is needed about the range of ctivity, mechanism of action, and chemical structure f acerin before deciding whether it will prove an important chemotherapeutic substance, giving the lead to more f its kind, or merely a laboratory curiosity.

OBJECTIVE TESTS FOR CORONARY INSUFFICIENCY

IN the absence of abnormal signs in the heart and lectrocardiogram, the diagnosis of coronary disease ften depends solely upon clinical interpretation of the istory. The story of angina pectoris is usually characeristic enough, but there are always a few patients with typical chest pain in whom objective evidence of oronary insufficiency would be valuable. Standard ests, based on the well-known capacity of exercise and noxæmia to provoke electrocardiographic changes imilar to those sometimes recorded in an anginal attack, ave been used for some time and found helpful. The xercise test consists in climbing steps either a fixed umber of times[2] or until pain or breathlessness appear.[3] n the anoxæmia test a mixture of 10% oxygen and 90% itrogen is breathed from an anæsthetic apparatus for eriods up to 20 minutes. The electrocardiogram may e affected in several ways: the chief changes are epression of the RST segment, inversion of the T wave, nd, more rarely, shortening of the P–R interval.[4] These hanges are found to a limited extent in apparently ealthy people in response to exercise or anoxæmia, but hen the RST depression in leads I, II, III, and IV totals mm. or more, or when there is inversion of the T wave ccompanied by RST depression of 1 mm. or more in ad I, they are generally regarded as abnormal.[5] [6] urner and Morton[7] have lately confirmed this view and mphasised the importance of using lead IV.

An abnormal response either to exercise or to anoxæmia ay be expected in between a quarter and a half of those ith known angina or with a history of infarction. The echanism of the changes is obscure, for their unpreictable appearance cannot be correlated with the egree of oxygen desaturation of the blood or with the tent of coronary arteriosclerosis.[8] However, provided at the effects of a recent heavy meal, a cold drink, or vere anæmia can be excluded, they may be taken as idence of coronary insufficiency. There is little to oose between the exercise test and the anoxæmia test, d the two are probably best used in conjunction.[9] tisfactory electrocardiograms are less easy to obtain after exercise; on the other hand, the anoxæmia test has caused unpleasant and even dangerous effects, although its advocates believe it to be safe enough provided that a supply of 100% oxygen is immediately available.

Clearly, both tests have disadvantages, especially since negative results do not exclude angina pectoris; but they have a definite place in diagnosis. Turner and Morton suggest that they should be used for those cases of suspected angina without positive signs and where the pain is atypical. They also suggest their use as a method of assessing recovery from myocardial infarction, as a test of fitness for surgical operations, and as an index of the therapeutic action of drugs on the coronary circulation. Nevertheless the limitations of the tests emphasise the importance of adequate history-taking and complete electrocardiographic investigation.

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Riseman, J. E. F., Waller, J. V., Brown, M. G. *Ibid*, 1940, 19, 683.
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Biörck, G. *Ibid*, 1946, 32, 689.

MESENTERIC THROMBOPHLEBITIS MIGRANS

THROMBOPHLEBITIS is a mysterious disorder. Occasionally it manifests itself—nearly always in men under the age of 50—as a series of episodes involving mainly superficial veins but sometimes a vena cava.

North and Wollenman[1] report 3 cases of venous mesenteric thrombosis occurring in series with migratory thrombophlebitis. From their account it is clear that this grave complication has a characteristic clinical picture; and prompt diagnosis and resection of the infarcted segment or segments of gut may be life-saving. A vital clue is the history of an attack, perhaps years previously, of superficial thrombophlebitis with, in about a quarter of the cases, evidence of pulmonary involvement. The actual mesenteric venous thrombosis does not present—like arterial occlusion—as a fulminating catastrophe. The principal disturbance is abdominal pain becoming, over several days, increasingly severe. There is a notable absence of signs of peritoneal irritation, although in the later stages tenderness may be present over the infarcted segment, which is often palpable. The lumen of this segment is not occluded; hence vomiting and distension are inconstant and late. Red blood is often passed per rectum. Operation reveals an imperfectly demarcated infarcted portion of large or small intestine. The veins draining this segment are filled with dark-red thrombi whose uniform age suggests that their extension proximally to the collecting veins is more likely to result from propagation than from intermittent involvement. The arterial bed is not thrombosed.

North and Wollenman point out that resection, while it saves life, has no influence on the disease and further thrombotic episodes are likely. In thrombophlebitis migrans anticoagulant therapy with dicoumarol or ethyl biscoumacetate (‘Tromexan’) should perhaps be continued for many months or even years. The disease may subside as mysteriously as it starts; so the true efficacy of such therapy cannot be gauged.

NUFFIELD CHAIR OF SURGERY: AN APOLOGY

OUR last issue contained an announcement that Professor T. Pomfret Kilner had been appointed to succeed the late Sir Hugh Cairns as Nuffield professor of surgery in the University of Oxford. This announcement was based on a newspaper statement which, though explicit and detailed, was quite incorrect: the position at Oxford remains as it was last October, when we reported that Professor Kilner had been asked to carry on the duties of the Nuffield chair during the current term, and the successor to Sir Hugh Cairns has not yet been chosen. We greatly regret the inconvenience caused by our giving currency to inaccurate information.

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[1] North, J. P., Wollenman, O. J. jun. *Surg. Gynec. Obstet.* 1952, 95, 665.

The Third Quarter in England and Wales

Provisional figures for England and Wales in the September quarter, 1952,[1] show that the death-rate equalled the lowest ever recorded for the country, while the infant-mortality rate and the stillbirth-rate were the lowest ever recorded

The death-rate was 8 9 per 1000 population The infant-mortality rate was 23 0 per 1000 related live births The stillbirth-rate was 21 5 per 1000 total live and still births The birth-rate was 15 2 per 1000 population—the same as in the September quarter of 1951

The estimated total population of England and Wales at June 30, 1952, was 44,166,000 (21,343,000 male and 22,823,000 female)—an increase of 158,000 over the estimate for 1951

Control of Narcotic Drugs

The control of the Permanent Central Opium Board over the licit movement of narcotic drugs is largely based on the information supplied by the governments producing the raw materials It is the more disturbing therefore that in their report for 1952[2] the board deplore the "vagueness which characterises the statistics of the principal non-producing countries" Thus the total world production of opium is not accurately known, while that of coca leaves cannot be conjectured, because Bolivia and Peru, two of the four producing countries, have never submitted statistics of their production But statistics of the use of these substances for medical and scientific purposes are almost complete, and the board draw attention to the "steady and remarkable increase in the production of codeine during the last two decades" In 1951 for the first time codeine was converted into morphine, 26 kg of codeine produced 18 kg of morphine The board suggest that as a result some change in the control exercised over codeine may be called for The board also point out that though synthetic narcotic drugs are being more widely used than ever there is no decline in the use of the chemical derivatives of opium

Cancer Registration in Denmark

On May 5, 1942, the Danish Cancer Register was inaugurated by the Danish National Association for Combating Cancer, with the support of the Danish public-health authorities, the Danish Medical Association, and other bodies The primary object of this register, the first of its kind organised on a national basis, was to investigate the incidence of malignant disease in Denmark and elsewhere It was to be an endemiological or epidemiological investigation not concerned with the results of the treatment of malignant disease

In his survey of the first ten years, Dr Johannes Clemmesen,[3] who is in charge of the register, points out that all the Danish hospitals send in reports of every case of neoplasm, pathological institutes also send necropsy and histological diagnoses Furthermore, the staff scrutinise all the death certificates for Denmark, so account is taken of the fatal cases of cancer not passing through a hospital

During the past decade studies in Denmark of heredity in relation to malignant disease have suggested that it is easier to establish the influence of heredity on cancer of the body of the uterus than on cancer of the cervix The records of the register show that cancer of the left breast is more common than that of the right breast, in the ratio of 111 to 100, and that close relatives of a patient with breast cancer are more likely to develop disease of the breast on the same side than on the opposite side The register has also disclosed a remarkable rise in the mortality from cancer of the lung in males in Copenhagen, where the death-rate from this cause has risen from 5 per 100,000 population in 1931 to 37 in 1950, in the same period the rate for women has only risen from 4 to 5 per 100,000

In England Now

A Running Commentary by Peripatetic Correspondents

ONE day in the pride of my first house-appointment I overheard a stout lady confide to Sister in a hoarse undertone "Ah want tae see a right doctor Thon's ju a laddie" This balanced judgment, I found, made crystallised into words a fairly general feeling, and many of my associates have subsequently been troubled by the suspicion that I may not, in spite of my now advanced years, be a right doctor Since I embraced academic life the suspicion has, for most of them, hardened into a certainty To the layman, the idea that anyone could voluntarily take such a manifestly wrong turning is a strange one "Do you mean people call you Doctor?" they ask, over the weekly canasta table "Oh" they say, "how odd" And a little silence falls, while they glance furtively at the leather patches on my elbows and then stare speculatively at their own husbands When they get home they tell each other how sad it all is

The neighbours have given us up professionally long ago When we first moved in they used to send their children round, attracted by the prospect of a free medical service just over the fence, and a stand had to be taken. "You see, he's not that kind of doctor," my wife explained, "he does research" "Oh," they say doubtfully, "really?" It is only too clear that they don't believe a word of it They have agreed on a harmless convention whereby they refer to me as Doctor when they think I may be listening, and as Mister when they are reasonably sure I am not

Such a reaction does little to alleviate my own distrust of my rapidly receding clinical acumen As a student I once cut myself badly during an access of zeal for the study of anatomy, and confidently approached my preceptor, an anatomist of twenty years' standing, loaded with higher degrees and fellowships "Oh yes," he said hesitantly, peering into the spurting depths, "that's a nasty one, you'd better see a doctor" With what scorn did I relate this tale to my friends, for from whom should one expect surgical treatment if not from an F R C S? The other day came retribution One of the lab assistants, in the course of an argument with our still, burned his forearm slightly and exhibited the lesion to me "Oh yes," I said hesitantly, "that's a nasty one, you'd better " "No," I said, "on second thoughts, reach me down the first-aid box" He is still alive, and in the limited sphere of the lab there is a growing feeling that I may, despite appearances, be a right doctor after all Only yesterday our histological technician asked me if I would pierce her ears

* * *

The clinicopathological conferences that the students have started are going well An interesting case is chosen, particularly where autopsy material is available, and written up in detail, but with some essential points missing These case protocols are circulated to students and staff two days beforehand, to allow them to wrestle with the case and work out the probable diagnosis Groups of students can be seen in the medical school heatedly debating the differential diagnoses At the C P C the "principal performer," who is a member of the staff selected by the students, reads through the protocol and, by deductive reasoning, attempts to reach the correct diagnosis When he has irretrievably committed himself the audience discuss his conclusions The radiologist then steps forward and shows the films Finally the climax is reached as the pathologist uncovers his specimens and shows his slides, to the triumph or mortification of the speaker The atmosphere is so charged with the competitive spirit that the physician or surgeon who appears enters like a gladiator before the crowd For the students it is an ideal and entertaining way of learning One of them said that it was the first time he had heard a physician thinking logically For the staff it is a somewhat harrowing experience, and even the toughest has shown symptoms of nervous apprehension beforehand

* * *

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[1] Registrar General's Quarterly Return No 415 H M Stationery Office Pp 26 2s 6d

[2] United Nations Publication Geneva 1952 XI 11 Pp 75 $0 70

[3] Nord Med Dec 19, 1952 p 1751

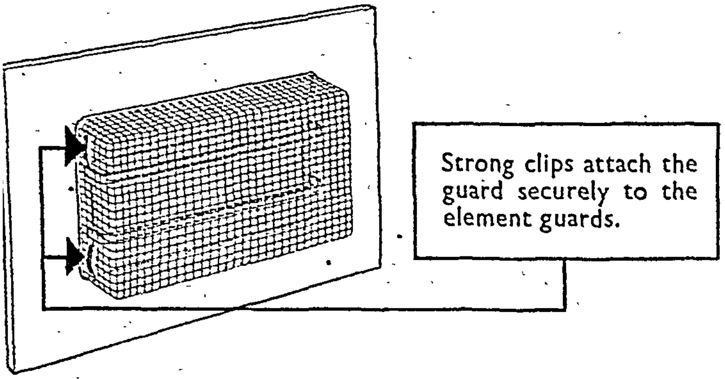
Strong clips attach the guard securely to the element guards.

Fig. 3—Guards for non-reflector electric fires (portable or panel types), attached by means of clips, in such a way that a child could not easily remove them.

electric and gas fire, which could be marketed at a reasonably low price. These new guards are now available, and they will undoubtedly go far to eliminate the most dangerous accidents—those caused by the ignition of clothing and the burning of children's hands. Some of the earliest models were rather unattractive in appearance, but this difficulty has been largely overcome. Moreover it is expected that parents who are concerned about the safety of their children will be willing to make some small sacrifice of æsthetic satisfaction—they will regard a dress-guard as a kind of insurance (and indeed it is so regarded in most other countries). Unfortunately the new guards are not yet widely known, as the firms that have produced them are not in a position to embark upon a nation-wide advertising campaign. This article is written in the hope that many of those connected with the health services—doctors, hospital and district nurses, health visitors, welfare workers, and others—will use such opportunities as they have to make these guards widely known and to encourage their use. It is felt that hospitals, especially, have a responsibility to set an example in this matter. Already a few have acquired guards for the electric fires used in waiting-rooms, side-rooms, sisters' duty rooms, and nurses' homes. It is hoped that all others will follow suit.

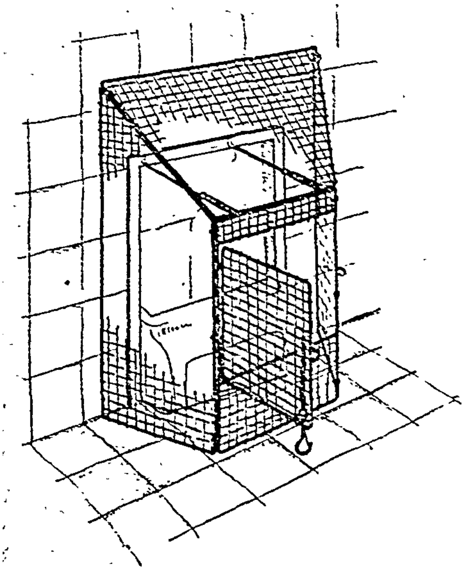

Fig. 4—The Braddell guard.

Is there danger from electric shock associated with the use of these wire guards? As this possibility has sometimes been suggested I have sought expert advice on the point. I was given the following opinions:

(i) Provided the fire is on a proper 3-pin circuit (with nothing disconnected) the use of guards such as those shown in figs. 2 and 3 cannot create any electrical hazard.

(ii) But very often there is some fault in the circuit—e.g., the earth wire is not properly connected up to the socket of the switch, or the earth wire in the plug has got loose, or the wiring of the premises is incorrect, or the earth wire is not connected up properly to a water pipe, &c. In such a case *any* electric fire carries a shock hazard—and the presence of a wire mesh guard will not materially increase it.

(iii) The risk of thermal burning injury associated with an unguarded fire is so much greater than that of electric shock that the balance of advantage is quite clearly in favour of guarded fires.

In view of the possible risks referred to under (ii) both the makers (whose names are given below) emphasise that their guards should be fitted by a competent person, and give explicit instructions as to how they should be fixed.

Guards for reflector types of electric fires appear in fig. 2, and for non-reflector (portable or panel) types of electric fire in fig. 3. Actually the guard shown in fig. 2(*b*), which is made in several sizes, can also be used for non-reflector types. In such cases the guard can be fixed by passing the curtain wires through the horizontal bars usually provided in front of the element and hooking them (with the help of a button-hook) into the front wires of the guard. This method of fixing has the advantage that a child would have more difficulty in removing the guard than when the curtain wire is simply carried round the back of the fire.

GUARDS FOR GAS-FIRES

The guards shown in fig. 2(*b*) and fig. 3 can be applied to those types of fixed gas-fire which carry one or more horizontal bars across the front to which the springs or curtain-wire can be attached. For some of the portable gas-fires (reflector types) at present on the market the guards shown in fig. 2(*b*) will be applicable. In other cases it is hoped that the makers of standard models of gas radiants will be able to supply an appropriate guard.

GUARDS FOR COAL-FIRES

There are so many types of coal-fire—the old-fashioned kitchen range, the bowl fire so widely used in living-rooms, and the closable type of slow-combustion stove—that it would seem to be impossible to design a guard which will be applicable to all of them. And many of the guards which have been on the market in the last fifty years are clearly not very suitable for their purpose.

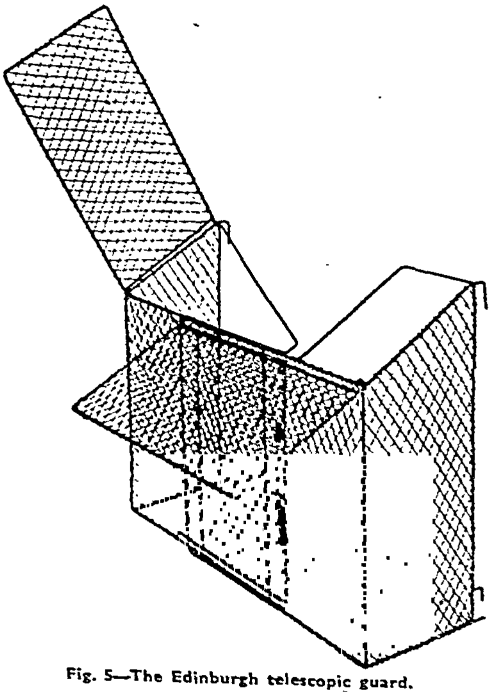

Fig. 5—The Edinburgh telescopic guard.

depression may be well worth while from the patient's standpoint Is he dismayed in a reactive or psychoneurotic way, or is his depression of a kind that might be expected to respond quickly to appropriate psychiatric treatment? In this connection "labels" such as psychosis, endogenous depression, and involutional melancholia still retain a certain meaning Even more urgently is the patient so "depressed and worried about himself" that he may feel prompted to take his life?

And is not Dr Todd a little hard on Service medicine? After all, what could be vaguer than "unfit to fulfil Army physical requirements," a designation under which many are discharged Moreover, his suggested phrase "short fever of undetermined origin" bears a striking resemblance to the "P U O" so familiar thirty-five or more years ago

Definitions, labels, the conception of disease as distinct from disparate disease types—these and kindred matters were dealt with in a Skinner lecture by Sir Henry Cohen [1] with rare and characteristic clarity

> "The first stage in the diagnosis of disease is the recognition of simple quantitative deviations from the normal"
>
> "A complete diagnosis must tell us where disease is, what functional disturbances are present and how these have arisen, and only in so far as diagnosis answers all these questions is it complete"
>
> "There are no diseases, only disease"
>
> "Yet a further function fulfilled by diagnosis, and herein lies the importance of accurate labelling, is that it shall serve as a means of *conceptual shorthand* by which experience can be pooled"

Finally Dr Todd urges that doctors should view their diagnostic problems with humility, and realise how often they are in the dark If anything *can* teach that lesson, it is the practice of medicine

Liverpool S BARTON HALL

SIR,—Rarely is an opportunity missed of echoing Trousseau's "il n'y a pas de maladies, il n'y a que des malades" Dr Henderson (Jan 3) is among many who deride the notion of the "reality" or the "existence" of disease entities "disease names do not represent real *things*" he writes

It is not altogether clear what they mean by "entity," "thing," "real," or "exist" They seem either to assert that diseases are not physical objects, which is a true but not very important observation, or to imply that "entity," "reality," or "existence" can be predicated only of physical objects, which is false Any process, including those we call diseases, that can be seen to be a unity, having a characteristic evolving pattern, can be called a "real entity"

There are both patients and diseases Both exist Precision in diagnosis demands a knowledge of the natural history of diseases, and to think that, like the unicorn, they have no existence is singularly unhelpful

London, W 1 KENNETH STONE

TREATMENT OF BULBAR PARALYSIS

SIR,—With reference to Professor Lassen's interesting article (Jan 3) concerning methods of overcoming the problems created by bulbar paralysis in poliomyelitis, I wish to draw attention to the use of a rectal drip, which I have found very helpful in this condition These patients are not well able to tolerate tubes in the mouth, throat, œsophagus, or stomach Such intubation causes increased salivation and occasionally vomiting, apart from the discomfort, and it increases the risk of aspiration pneumonia On the other hand, fluid is well retained in the rectum, retention being aided by the weakness of the bowel and abdominal wall and the postural drainage position

Waddon Hospital
Croydon. J J LINEHAN

THE ANKLE BLOW-OUT SYNDROME

SIR,—May I congratulate Mr F B Cockett and Elgan Jones on their paper in your issue of Jan 3 consider that this work is as significant in connexion with ulceration about the ankle as was that of Brod 1846 and Trendelenburg in 1891 in connection with treatment of varicose veins They have added preci to what we knew only generally

These incompetent "blow out" ankle veins can felt on firm thumb pressure behind the posterior bord of the tibia 3–6 in above the tip of the internal malleol and more certainly when the patient is lying down the leg is held up vertically The orifices of emergence feel like buttonholes in the deep fascia

Dr Ferdinand Martorell, of Barcelona, has alrea described these important vessels in his book on Var and also the method of block excision of the ulcer a pigmented skin with the superficial and deep fascia ligation of the faulty communicating veins in the He immediately sutures a Padgett skin graft to t defect, and he reports good results, although he admitted to me in September, 1952, that they sometimes bre down In my practice of ligation only, the wound edges have often necrosed after ligation of these inefficient communicating veins, forming yet another ulcer which takes some time to heal this adds support to the block excision and skin graft I regard this procedure ligature of a communicating vein above the ankle as a major one and think that it should be undertaken only by those trained in this work

London, W 1 HAROLD DODD

WATERHOUSE-FRIDERICHSEN SYNDROME TREATED WITH CORTISONE

SIR,—With reference to the article by Dr Breen and his colleagues [1] I think that a case treated by me la October should be put on record

A man, 47 years of age, awoke one morning with general malaise, severe headache, and severe aching pains in all four limbs I saw him at 9 A M and found a temperature of 103°F with moderate tachycardia and no other signs Influenza was provisionally diagnosed, and he was given sulphadiazine 1 g four hourly together with routine symptomatic treatment That evening his temperature was 101°F, but his headache and limb pains continued and he had a bad night

The next morning his symptoms were unchanged, but he had developed a widespread purpuric rash There was no neck rigidity, Kernig's sign was negative His temperature was 97°F and his blood pressure 80/55 mm Hg, normally his B P ranged from 120/80 to 150/95 Arrangements were made for his admission to hospital as a case of Waterhouse Friderichsen syndrome By 2 P M he was given aureomycin as well, and he was given 100 mg of cortisone parenterally

At 5 P M he was seen by Dr J Markell in consultation There were still no clinical signs of meningitis, although a lumbar puncture revealed a turbid cerebrospinal fluid at a pressure of 160 cm of water The cell count was 1170 per c mm, nearly all polymorphs, *Neisseria meningitidis* was present, but culture was sterile At lumbar puncture the opportunity was taken to inject 20,000 units of penicillin in saline intrathecally

At 7 P M the patient became confused and attempted to get out of bed Shortly afterwards he had a fit and entered status epilepticus He never regained consciousness and died in coma at 9 P M

Although the prognosis for a man of 47 with Waterhouse-Friderichsen syndrome is always grave, we were shocked at the sudden deterioration that occurred at 7 P M We came to the conclusion that this rapid deterioration might have been due to the cortisone, especially in view of its known inhibitory effect on fibrosis and healing

After reading the account by Dr Breen and his colleagues, and noting the convulsive episodes in both ich as phosphorus and petrol; and the full thickness of he skin was not invariably destroyed.

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[1] Cohen H The Nature, Method and Purpose of Diagnosis London 1943

[1] Breen G E Emond, R T D Walley R V *Lancet*, 195 i, 1140

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At one of the sessions, Prof. G. PAYLING WRIGHT discussed the balance between teaching and learning. He thought that the emphasis in our medical schools was on teachers teaching, rather than on students learning. The medical student could with advantage be called on for more emotional and intellectual activity during his own education; for the object of his training was to turn out a doctor who could stand alone, independent of his teachers, and who could continue to learn by his own efforts. To keep abreast of medical progress, most doctors had to rely very largely on their reading; and students should be introduced to library work and methods, with which few of them gained any close acquaintance at present. How many students knew, for example, how to use the *Cumulative Index Medicus* or the *Index Catalogue* of the Surgeon-General? If the student spent more time in the medical school library, not in systematically reading the standard textbooks but in following up the conditions he saw in his patients from day to day, he would fortify the intellectual stimulus by the emotional one which sprang from his contact with the patient and his problems.

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Sharing the general concern at the size of the medical curriculum and the stress it placed on the student, Professor Payling Wright suggested that preclinical subjects be taught and examined at two levels, and that the student be given the option of taking, say, either anatomy or physiology at the higher level. Such a provision for specialisation at quite an early stage in his career would relieve the student of some of his burden. Much of the day-to-day teaching of anatomy was given by graduates working for the primary fellowship examination, who tried to raise the student's knowledge to what was, in Professor Payling Wright's view, an unreasonably high level for all to attain.

As a means of improving and maintaining the standard of clinical teaching, Professor Payling Wright commended the staff round which was a regular feature in many American teaching centres. This round, which was generally restricted to senior members of the staff, stimulated enlivening debate among the teachers and so brought out new ideas which were presently reflected in the teaching to students.

Prof. J. MCMICHAEL agreed that the staff conference was the best way of keeping teachers up to date and in tune with one another; and Prof. IAN AIRD, recalling some lively meetings he had attended in the United States, pointed out that the staff round in this country lacked the historical prestige that it enjoyed there, and that in consequence busy consultants were not always ready to set aside two or three hours each week for this purpose.

TEACHING DEMONSTRATIONS

The young men who tackled the discour of teaching before teachers did well to de costal movement and no further improvement during the *next 110 min A pint of whole blood was given The patient's* condition remained satisfactory on 100% oxygen with intermittent gently assisted respirations 20 ml of nikethamide had no effect

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[1] See *Lancet*, 1951, i, 1408.

At this stage feeble finger, toe, and facial twitches were apparent The endotracheal tube was removed, and the patient made ineffective attempts to clear her throat She was obviously recovering consciousness, though still paralysed

Though it normally potentiates the effect, there seem to be some theoretical grounds for giving neostigmine in these cases,[11] and here it was given slowly in dilute solution After a total of 2 0 mg over 3–4 min there was a dramatic response The patient was able to move freely and to talk coherently, and she was safely returned to the ward 5 min later, fully conscious Remarkably, next day she had no recollection of the experience

It is most unlikely that the early small dose of tubocurarine, after which adequate intercostal respirations continued for 40 min, *had any effect on the paralysis that followed 90 min* later and persisted for a further 2 hours The thiopentone and pethidine were also given early and, had either been the cause, 20 ml of nikethamide should have produced some response, for it has been shown to be a most efficient antidote to overdoses of pethidine[12]

Blood taken the day after the operation provided further evidence in favour of a succinylcholine paralysis The Hb was 64% and the serum cholinesterase level was 50 units (normal for this method 130–310 units) A fortnight later it was 45 units, and the Hb was 61%

In this case there was an extremely low plasma-cholinesterase level This is the main factor in all true prolongation of paralysis[13 14] It is not certain, however, whether all the reported cases have had true succinylcholine paralysis, for with the exception of Dr Bourne's cases,[4] information about the serum—not the whole blood—enzyme levels is lacking

Dr Lehmann[14] says that Callaway et al[15] have shown that "there is little chance of encountering such a case" (of low serum pseudo-cholinesterase) "*in an average* sample of the population" As the work quoted is based on the levels found in Servicemen "fit for full combat duty anywhere" and healthy civilian blood-donors, I cannot agree that this is necessarily true of the average "anæsthetic population" Preliminary examination of the figures from the preoperative cases I have collected tends to confirm this opinion Preoperative treatment may indeed mask the effects of chronic malnutrition and anæmia, both of which lower the cholinesterase activity of the blood Regeneration is very slow[16] and cannot easily be corrected in short periods Transfusion of packed red cells does not raise a low plasma-enzyme level, and stored blood has been shown to lose its cholinesterase activity rapidly[17]

Naturally, conditions which cause a low plasma-enzyme level should be avoided Anæmia, liver disease and malnutrition have been mentioned, and I would add patients who have been recently transfused to raise their hæmoglobin to levels otherwise acceptable to the surgeon Dr Barnard also mentions the effect of X radiation

I consider succinylcholine to be a relaxant unparalleled for effect, general flexibility, and lack of side effects, and I have used it successfully in nearly 800 patients, only 2 of whom have given me any anxiety The second patient, though not entirely similar to the first one described here, also took a long time to recover, and had been transfused over a short period from a grossly anæmic state to a superficially safe level In both these cases the choice of the drug was probably unwise and would have better avoided

From Dr Barnard's observations it now seems that anæmic patients may be protected from unexp prolongation of paralysis by the infusion of cholinest concentrate

Portsmouth R J **HAMER HODG**

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[11] *Discussion at meeting of section of anæsthetics*, Royal Society of Medicine, Nov 7, 1952

[12] Romer, C *Brit med J* 1952, ii, 1135

[13] Evans F T, Gray, P W S, Lehmann, H, Silk, E *Lancet*, 1952 ii 682

[14] Lehmann H *Ibid* p 199

[15] Callaway S Davies D R Rutland J P *Brit med J* 1951, ii 812

[16] Grob D Lilienthal J L jun Harvey, A. M, Jones B F *Bull Johns Hopk Hosp* 1947, 81 217

[17] Scudamore H H Vorhaus L J Kark R M *Blood* 1951, 6 1273

ANÆSTHESIA IN WHOOPING-COUGH

SIR,—On May 20, 1951, a *four-year-old child*, who h been suffering from whooping-cough for ten days, f down some steps A large wound of the chin was su and the bleeding arrested under general anæsthesia w ethyl chloride When the child recovered from t anæsthetic the parents noticed that the whooping h completely stopped, though she continued to cou a little for a few days

In November, 1952, I gave ethyl chloride to a f year-old girl with whooping-cough, and the whoop again stopped after the anæsthetic

Royal Hospital, Bagdad **KHALID NA**

THE ACTION OF SODIUM P.A S ON RODENT ULCERS

SIR,—In an account[1] of the treatment of rheumato arthritis and osteo-arthritis with sodium *p* am salicylate (P A S), I described a patient with o arthritis in whom a rodent ulcer, which had been pre for some months on the ala of the nose, disappear during the administration of sodium P A S This pati (case 1 in the accompanying table) had previously h an operation for the removal of a rodent ulcer of th lobe of an ear Since then 4 more patients with rod ulcers have been treated with sodium P A S by mouth In one case the drug produced symptoms of incompat bility, and *local infiltrations of sodium* P A S solutio *were substituted (case 5)*

This report is based on 5 cases in which the diagnosis w made purely on clinical grounds, without biopsy and path logical confirmation of the diagnosis The reason for th was that although the patients were told about the nat of their condition, it was felt that even a minor surg procedure, such as a biopsy, might discourage the pati *from continuing treatment* and delay possible confirmati of the results obtained in the first case

The 5 patients (3 women and 2 men) were all over the a of 60 Details of treatment and results are shown in th *accompanying table*

I understand that investigations on a much larger sca including a study of the pathological changes, are to be conducted shortly at the Royal Adelaide Hospital

Of course a rodent ulcer can be cured more quickl with radium, but these results suggest that there may b

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[1] Brons, M *Med J Aust* 1952 i, 774

RESULTS OF TREATMENT OF RODENT ULCER WITH SODIUM P A

Case no	Age	Duration of lesion (months)	Diameter of lesion (in)	Site of lesion	Duration of treatment	Dose of P A.S by mouth	Result
1	62	6	0 2	Nose	3 months	*6 g daily*	Cured
2	71	8	0 5	Nose	2 months	6 g daily	Cured
3	60	5	0 4	Cheek	4 months	6 g daily	Cured
4	68	5	0 3	Nose	3 weeks	6 g daily	Lesion reduc to half i original si in 3 week, patient th given radi therapy on Cured
5	67	4	1 0	Right temporal region	3 months	6 g daily for 3 weeks then local infiltration of P A S.	

such as phosphorus and petrol ; and the full thickness of the skin was not invariably destroyed.

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[1] See *Lancet*, 1951, i, 1408.

Rubin et al [1] found liver damage with jaundice and (in one animal) a decrease of the erythroid cells in the bone marrow after administration of large doses (25 mg per kg body-weight) of isoniazid to dogs Benson et al,[2] in their long-term experiments with large doses of isoniazid fed to rats, observed a depression of the average leucocyte count and an increased cellularity of the bone-marrow, with a relative reduction in the number of adult neutrophils

It seems that in man there are big individual variations in the sensitivity to isoniazid, even when it is given in the usual dosage for a short period It is debatable what part the streptomycin and P A S played in this agranulocytosis The clinical signs did not appear until three weeks after streptomycin was stopped, it was also at this time that the rapid fall of the granulocytes was discovered These *two facts, together with the* prompt recovery, suggest that streptomycin was not to blame On the other hand, the concomitant jaundice and the restoration of the granulocytes soon after the withdrawal of isoniazid support the view that isoniazid was the cause At all events, the animal experiments I have mentioned and Dr Ferguson's observation indicate that there is a strong case for careful hæmatological control during isoniazid treatment

Department of Pathology,
City General Hospital, Sheffield
S Varadi

Winter Street Hospital,
Sheffield
T D Kelleher

GONORRHŒA IN ANCIENT ROME

Sir,—It is true that clear references to venereal disease are scarce in classical literature Considering the undeveloped state of nosology, the taboo surrounding the subject, and the wholesale destruction of most of the writings of that period, this is perhaps not surprising Even our own acquaintance with venereal disease might appear rather fragmentary to our successors if nothing were left of our literature except a few dozen non-medical books, chosen at random, and half a dozen texts on general medicine

Even so, Dr Vertue (Dec 20) probably wrongs Juvenal in stating that he never mentions gonorrhœa "Podice levi cæduntur *humidæ*, medico ridente, *mariscæ*" may be taken to refer to gonorrhœal condylomata which is the form of the disease which seems to have received most attention from the ancients This is not surprising in view of the climatic and hygienic conditions in classical Rome

Dr Vertue certainly misrepresents Celsus, who devoted most of the 18th chapter of his 6th book to infectious afflictions of the genital organs The apologetic preamble to this chapter provides at the same time a clue to the reticence of classical writers on this subject Lanceraux in his treatise on syphilis quotes Martial, and states that he was embarrassed in making his choice because the epigrams of this writer are so fertile in references to the contagiosity of venereal disease He also mentions in addition passages from Hippocrates, Natalis Comes, Aretaeus, Galen, Aetius, Oribasius, Marcellus Empiricus, and Dion Chrysostome

The Roman argument in favour of prostitution—namely, that it preserved the chastity of the home—has been used by protagonists of prostitution through the centuries and up to our own times, and cannot therefore be adduced as evidence *for the absence of gonorrhœa* The natural history of this disease tends to be forgotten in these days of universal and effective treatment, but there can be no doubt that untreated gonorrhœa will proceed to resolution and cure in the majority of cases Casanova, for example, cured himself again and again by a simple regimen comprising little more than rest, diet, and temperance

In my limited reading of the classics, I have not come across a reference to the acute urethral *stage of gonorrhœa* as convincing as that in *Leviticus* xv but this itself should serve to allay some of Dr Vertue's doubts, for, if the disease was rampant on the eastern side of the Medi ranean, it is entirely improbable that the master r should have been spared

Edinburgh
Erich Geiringer

SPLENOMEGALY IN SCARLET FEVER

Sir,—I was interested in Dr O'Reilly's letter (Dec for I have also noticed splenomegaly quite frequ in scarlet fever On referring to my notes on the l 100 cases of this condition that I have seen, I found th the spleen was palpable in 11 patients Such cases d not seem to be any more severe than those witho splenomegaly Box[1] states that the spleen is rare palpable in scarlet fever

It is, of course, well known that a moderate enlar ment of the spleen may be found post mortem in ca es scarlet fever, as in many other acute infective conditio

Tyntyla Isolation Hospital,
Pentre, Rhondda
M S Pathy

Sir FRANCIS CHAMPNEYS AND THE MIDWIVES ACT

Sir,—In the reports of the festivities to celebrate th 50th anniversary of the passing of the first Midwives Act and the birth of the Central Midwives Board, it is surprising to see so little reference to Sir Franci Champneys, who did so much to promote the Bill a was the first chairman of the C M B from 1902 until h death in 1930 However great his part in promoting th Bill—and I understood from some who worked wi him that his was the main driving force behind it— was his administrative ability, patience, firmness, an tact, as chairman of the C M B, which made possible th implementation of the Act and the development of th great profession of midwives as we know it today

Prior to the passing of this Act, midwives as a whole we drawn from a poor social class, often quite illiterate, and th training was of the scantiest, while, in many instances, th handy woman, without any training, was in charge

The Act of 1902 forbade any woman to attend a confinem unless she was on the register of the C M B and laid down period of resident training in a maternity hospital and th passing of an examination for those who aspired to th To tide over the period until a new generation of bett trained women was available, the old midwives had to b employed and the first register consisted of those who h been in practice as midwives for a year before the passing o the Act Some latitude had to be given, and I think m memory is not at fault in placing the date as Jan 1 190 after which date no woman could be placed on the regis unless she had completed the prescribed training and pa ed the C M B examination

In Manchester, and no doubt in other centres, the fi "inspector of midwives" commenced her duties on this d and it happened that I commenced my 3½ years as resid obstetric officer to St Mary's Hospital, Manchester, on th same day In this post I had the usual responsibilities of senior resident for the hundred obstetrical and gynæcolo beds in the hospital and, in addition, complete responsibilit for a large home district in which 3000–4000 confinements p annum were attended by hospital district midwives, eve one of whom was now on the register by virtue of hav been in practice before the passing of the Act Many of th women had acquired much clinical knowledge and the gr majority were devoted to their patients and their work, b with a few notable exceptions, they were drawn from a p social class with little education Some were almost illiter and incapable of absorbing anything from the cours lectures they had attended while few of the others under the meaning of "sepsis" and "antisepsis" and still pref a little freshly rendered lard as a lubricant

These I think were a fair sample of the midwives of th country, and the task of the C M B was to keep the midwif service of the country functioning while by *slow degrees* th replaced the worst offenders by newly trained midwives a educated the more intelligent of the old ones to a hig standard of practice

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[1] Rubin B Hassert G L jun Thomas B G H, Burke, J C *Amer Rev Tuberc* 1952 65 392

[2] Benson W M Stefko P L Roe M D *Ibid* p 376

[1] Box C R *In* A Textbook of the Practice of Medicine Lon 1950, p 81

Public Health

N EXPLOSIVE OUTBREAK OF Q FEVER

M. G. P. Stoker
M.D. Camb.
LECTURER IN PATHOLOGY, CAMBRIDGE UNIVERSITY

J. F. Thompson
M.R.C.S.
GENERAL PRACTITIONER, WOODCHURCH, KENT

ISOLATED sporadic infections probably account for ost cases of Q fever, but it is well known that severe plosive outbreaks also occur, and indeed their spec- cular nature has often led to the first recognition of the sease in a particular locality. One such outbreak at a ondon hospital in 1949 gave the first definite proof at the disease existed in Great Britain (Harman 1949, acCallum et al. 1949), and, since the source of this utbreak was a fatal case of Q fever from North-East ent (Marmion and Stoker 1950), attention was soon rected to this county, where the disease was discovered be endemic. Many sporadic cases were found (Marmion al. 1953), and in the following year a second outbreak volved 27 students at the Canterbury School of Art. lthough the source of infection was not clearly identified ere, epidemiological evidence suggested that the pening of a packing-case and the removal of straw and ther packing material some nineteen days before the utbreak may have been responsible (Harvey et al. 1951).

This paper describes a third outbreak, distinguished y a remarkably high attack-rate, which took place in eptember, 1951, amongst residents and visitors at a farm n South Kent.

THE OUTBREAK

The farm occupies some 120 acres on high ground verlooking Romney Marsh, and includes a farmhouse, divided into two flats, immediately surrounded by owsheds, a dairy, and pigsties, with two cottages, which ie at the edge of the farm some 250 yards from the house. On land adjoining the farm there is a short row of ouncil cottages, where the two domestic helps at the farm ive; but otherwise the farm is fairly isolated. A dairy herd of tuberculin-tested attested Red Poll cattle and some pigs and poultry form the main business of the farm.

The farmer, Mr. F., and his wife, live on the ground floor of the farmhouse, and a family, comprising Colonel T. (an engineer temporarily home from Kenya), his wife, and two daughters, Maureen and Jill, occupy the upstairs flat. Mr. C., a retired business man, and his wife, who are friends of the farmer, have one of the cottages, and Mr. J. (cowman at the farm) and his wife the other.

On Sept. 1, 1952, Maureen T., aged thirteen, became ill quite suddenly with a headache and fever. Next day her father, Colonel T., who had just returned from five days in Scotland, developed a more severe illness with pneumonia, and he was admitted to Ashford Hospital on Sept. 8. Meanwhile, on Sept. 3, the cowman, Mr. J., became ill, and during the next three days his wife, his neighbour, Mr. C., the farmer himself, his wife, and Colonel T.'s wife also succumbed. By Sept. 7 everyone living on the farm was ill with what was later shown to be Q fever, except for Mrs. C., who did not develop the disease until Sept. 17, and Jill T., aged five, who remained well, but later showed serological evidence of infection. All this came at a busy time, and for a few days there was great difficulty in running the farm; but fortunately many of the illnesses were short and mild.

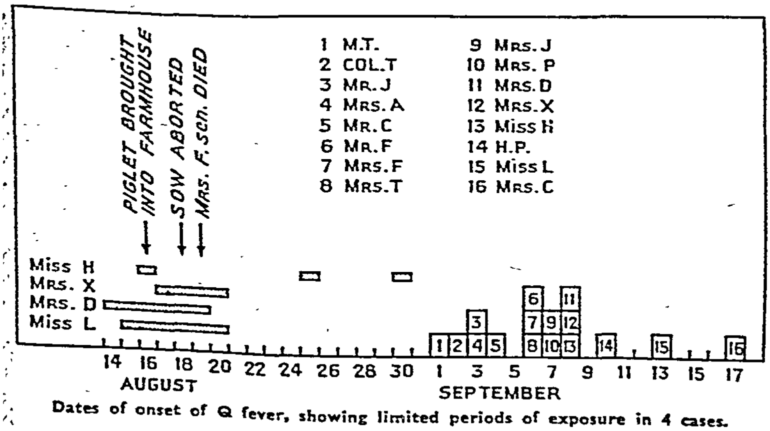
TABLE I—PERMANENT RESIDENTS, TEMPORARY RESIDENTS, AND VISITORS TO FARM FROM AUG. 13 TO 26, 1951

—	Name	Age	Occupation or status	Visits to farmhouse Aug. 13–26, 1951	Onset of Q fever
Living at farmhouse	Mr. F.	48	Farmer	Resident	Sept. 6
	Mrs. F.	32	Farmer's wife	„	Sept. 6
	Mrs. F., sen.	76	Farmer's mother (invalid, died Aug. 19)	„	—
	Mrs. P.	56	Relatives on visit from Berlin (returned Sept. 2)	„	Sept. 7
	Helga P.	8		„	Sept. 10
	Colonel T.	44	Relatives living in upstairs flat	„	Sept. 2
	Mrs. T.	45		„	Sept. 6
	Maureen T.	13		„	Sept. 1
	Jill T.	5		„	—
Living at cottages on farm	Mr. J.	29	Cowman to farm	Daily	Sept. 3
	Mrs. J.	26	Cowman's wife	Aug. 6	Sept. 7
	Mr. C.	45	Retired (friends of farmer)	Frequent	Sept. 4
	Mrs. C.	44		„	Sept. 17
	Mrs. X.	35	Weekend visitors from London (staying with Mr. and Mrs. C.)	Aug. 17–20	Sept. 8
	Bruce X.	10		Aug. 17–20	—
	Miss L.	45		Aug. 15–20	Sept. 13
Visitors to farmhouse	Mr. Y.	58	Casual labourer	Uncertain	—
	Miss H.	42	Friend of Mrs. A.	Aug. 16 and 25	Sept. 8
	Mrs. D.	56	Domestic help	Aug. 14–19	Sept. 8
	Mrs. A.	44	„	Daily	Sept. 3
	Vivienne A.	4	Daughter of Mrs. N.	Daily	—
	Dr. W.	38	Attending Mrs. A., sen.	Aug. 14, 16, 18–20	—
	Dr. V.	51	„	Aug. 20	—
	Nurse N.	46	District nurse	Aug. 13–19	—
	Mr. B.	32	Undertaker	Aug. 20	—
	Mr. Z.	46	„	Aug. 19–20	—

From the dates of onset it seemed likely that infection had taken place sometime in the third week of August. When inquiries were made it was found that there had been 6 extra people living on the farm at about this time (see table I and figure).

Firstly, there had been the farmer's invalid mother (Mrs. F., sen.), who had died of carcinoma of the rectum on Aug. 19. Secondly, his mother-in-law (Mrs. P.) and her granddaughter (Helga P.) had been on a visit from Germany, and they had returned to Berlin on Sept. 2, where they both developed Q fever the following week. Finally 3 visitors from London, Miss L., Mrs. X., and her son Bruce, aged ten, had stayed with Mr. and Mrs. C. at their cottage for a long weekend. Three weeks after their return to London, Mrs. X developed an illness which was assumed to be Q fever on clinical and epidemiological grounds, despite the fact that a specimen of her blood could not be obtained for serological confirmation. Bruce remained well and his serum was not tested, but Miss L. succumbed five days later to a similar illness, and her serum was subsequently found to contain Q fever antibodies.

In addition to the 16 residents, and excluding tradesmen who only made very short visits, 9 other people had visited the farm during the two weeks Aug. 13–26. Miss H., a friend from Rye, spent the afternoons of Aug. 16 and 25 at the farmhouse, and Mr. Y., a casual labourer, worked on the farm. There were two domestic helps (Mrs. D. and Mrs. A.) at the farmhouse, and



Dates of onset of Q fever, showing limited periods of exposure in 4 cases.

red or livid plaques of varying size The lesions were most numerous on the chest and abdomen, and the irritation was unbearable The mucosæ were unaffected

The blood-pressure was 130/90 mm Hg, and X ray examination of the chest showed a normal heart

Laboratory Investigations—Red cells 4,280,000 per c mm, Hb 74%, white cells 5800 per c mm (polymorphs 63%, stab forms 6%, lymphocytes 22%, monocytes 4%, eosinophils 5%), erythrocyte sedimentation rate 108 mm in the first hour (Westergren), blood calcium 9 9 mg per 100 ml, blood cholesterol 224 6 mg per 100 ml The Takata-Ara test was strongly positive The urine was normal Histological examination of the skin showed a non specific inflammatory reaction in the corium with hyperkeratosis We are indebted to Prof Z Kopac, of Sarajevo, for the biopsy report

Treatment and Progress—A diagnosis of herpes gestationis was made The patient was treated with phenobarbitone, antazoline ('Antistin'), and serum from a healthy pregnant woman, but with no success Her condition became desperate, for she was utterly exhausted by the intolerable irritation and lack of sleep, and it was considered justifiable to terminate the pregnancy This was done on April 4, but the disease went relentlessly on

Finally, on April 14, we turned to aureomycin (250 mg every 4 hours) On the second day of treatment she slept better, and the skin lesions became paler and the irritation substantially less On April 21 the aureomycin was stopped because she had severe diarrhœa By that time the skin had cleared except for the legs, where erythema persisted During treatment with aureomycin the eosinophil count rose to 18% on April 16

After aureomycin was stopped, she had vitamin C by mouth and calcium bromide intravenously, but the skin lesions and irritation recurred Starting on April 28 she was given 1 5 g of aureomycin daily for five days On that day the eosinophil count was 6% and the erythrocyte sedimentation rate was 78 mm in the first hour Again the irritation disappeared and the skin lesions subsided On May 5 the eosinophil count was 4% and the sedimentation rate 43 The improvement was maintained and the patient went home on May 9 at her own request She was not completely cured, but she was infinitely better

The association between aureomycin and the improvement in the condition seems clear, but it is hard to see how the drug worked A smaller point which we were also unable to explain was the changing eosinophil count

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TIBOR SALAMON

MUMPS ORCHITIS WITHOUT PAROTITIS

SIR,—In his paper last week Mr Connolly describes a case of testicular swelling in an infant and produces convincing evidence that it was due to mumps It is his opinion that many other such cases have the same ætiology, and that mumps more often causes acute swelling of the testicle than does torsion of that organ

My experience, though admittedly of an older age group, convinces me that his conclusions are wrong —that is, unless he considers mumps to be the commonest cause below the age of 1 year and torsion after that age

Of the 13 cases of torsion that I have now seen, 8 were in patients under 14 years, and among the 11 cases I described,[1] 3 of the 5 I had not seen were under 14 years Further, to the best of my knowledge I have seen only 1 child (aged 4) with acute testicular swelling in whom the diagnosis of torsion was not confirmed Although he was admitted with that diagnosis operation was not advised

While appreciating that Mr Connolly advises exploration in all cases of doubt, I would like to add a warning It is not uncommon for the testicle to undergo spontaneous untwisting This occurred in 6 of the 18 cases of which I have notes In 3 operation was performed very shortly after the pain and swelling suddenly subsided In each there was excess fluid in the tunica vaginalis, and congestion of the testicle, as Mr Connolly describes in his second case In 2 of these there was obvious anatomical abnormality, such as a long mesorchium The sudden subsidence of swelling and pain while the testicle was being manipulated was evidence of the mechanical factor.

I suggest, therefore, that unless there is strong evidence of contact with a case of mumps, all such cases should be explored If the testicle is not gangrenous steps should be taken to fix it to the scrotal tissues If the cause of the swelling were torsion its recurrence would thereby be prevented If it were due to mumps no harm would have been done

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[1] Walton A J *Lancet*, 1952, ii, 211

SUPPORTIVE THERAPY

SIR,—Professor Boyd and his colleagues in their article last week very rightly draw attention to the importance of a rational approach to the development of polymeric substances for use in plasma substitutes No product should be finally accepted until all the recognised important factors have been fully investigated

When more than one such substance is being developed it can always happen that unpublished data are available on one of the polymers which would assist in the assessment of the others, although the ideal molecular [illegible] need not necessarily be the same for every polymer. The results of experimental work on a particular type of polyvinylpyrrolidone, carried out in these laboratories, are being prepared for publication, and some of the conclusions are important in the light of Professor Boyd's paper

I should emphasise that they refer only to the polyvinylpyrrolidone used in 'Plasmosan' In this material the maximum molecular weight is about 100,000 and the peak value about 35,000 Samples of polyvinylpyrrolidone of other molecular weight ranges need not have the same physiological properties as those described here Indeed the differences between the results obtained by us and those on polyvinylpyrrolidone cited by Professor Boyd may easily be accounted for in this way

The excretion of polyvinylpyrrolidone is such that about 40% remains in the body after 24 hours At that time plasma-levels are just less than half of the value immediately after transfusion Detailed interpretation of these results is difficult since the concomitant variation in blood-volume is not known, but they indicate that most of the unexcreted polyvinylpyrrolidone is in the plasma, so that the colloidal osmotic pressure produced can hardly be transient

No histological evidence for the permanent storage of polyvinylpyrrolidone has been found,[1] and this is supported by the following results

Determination of the molecular weight distribution of polyvinylpyrrolidone recovered from the urine of patients receiving intravenous plasmosan has shown that molecules of all the molecular weights present in the infusion are capable of being excreted, and that if a threshold molecular weight exists above which polyvinylpyrrolidone molecules would not be excreted this is considerably in excess of 100,000 The rate of excretion, as would be expected, decreases with increasing molecular weight Consequently, about 14 days after the infusion, when at least 80% of the administered polyvinylpyrrolidone has been excreted, the urine concentration is at the limit of sensitivity of the method of estimation. In but there is no indication that excretion suddenly stops In addition, the residue not accounted for may be excreted by other means—e g, in fæces and sweat—or may possibly be degraded to very small molecules which cannot be estimated by the present experimental methods There is evidence, moreover, in one case studied in great detail, that some such degradation does occur It appears unlikely, therefore, that any appreciable quantity of polyvinylpyrrolidone can remain in the body

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[1] Thrower W R Campbell H *Lancet*, 1951 i, 1096
[2] Campbell, H, Hunter, G *Ibid* (in the press)

e Farm Animals

None of the patients had been bitten by ticks, and re were no sheep or goats on the farm. The most ely source of *R. burneti* was obviously milk, placenta, fæces from one or more of the 12 dairy cows, but the quence of infections among the people on the farm plied that any excretion of organisms by the cows must ve been a new event occurring for the first time tween Aug. 16 and 19. It was therefore surprising to d that nothing unusual had happened in the herd at is time. No new cows had been imported, no calves ere born until Sept. 2, and the same 7 cows had been in ilk for the previous seven months. This milk was used the farmhouse and at one of the cottages. Mr. and rs. C. at the other cottage obtained their milk from a fferent source, but they did occasionally have tea at e farmhouse. The bulk of the milk went to a wholesale iry where it was pasteurised.

Of the 5 cows not in milk, 2 were pastured in a field early two miles from the farm ; 4 of the patients had isited this field on various occasions, but had had no ose contact with the cows.

Various laboratory tests were made on material from e cows during the succeeding months, and the results re shown in tables II and III. We originally intended to ke serum samples from all cows, but foot-and-mouth isease restrictions prevented us doing so. However, it as been shown that there is close correlation between hey and serum antibodies (Stoker and Marmion 1952), nd specimens of whey were eventually tested by the irect agglutination and anti-globulin tests instead. One ow, Dilly, had Q-fever antibodies in her whey, but she as one of the two animals who had been dry and astured in a field two miles from the farm. None of the nimals kept on the farm itself showed any evidence of nfection. The laboratory tests thus support the epidemio-ogical evidence in suggesting that the cows were not esponsible for this outbreak.

There was considerable activity in the piggery during ugust, but although Giroud and Jadin (1951) claim to ave demonstrated Q-fever agglutinating antibodies in igs from the Belgian Congo, these animals have never een shown conclusively to harbour *R. burneti*. Never-heless, it was interesting to learn that two litters of iglets were born at the farm on Aug. 10 and that a sow borted on Aug. 18. One of the piglets was injured by a at, and on Aug. 16 it was brought into the farmhouse or treatment. It was fondled by several individuals who subsequently developed Q fever, including Miss H. who must have been infected on that day or on Aug. 25 see figure). This piglet might have been heavily contami-nated with infected placental fluid from a sow ; so, when he farm was first visited on Oct. 27, sebaceous material was scraped from the piglet's ears and a suspension was noculated into guineapigs and mice ; but *R. burneti* was not isolated. Serum was also obtained from this piglet, from the 3 sows which were delivered in August, nd from 8 other piglets. Pig antibodies are notoriously lifficult to detect by ordinary techniques, and of course positive pig sera were not available for controls ; but the hæmolytic complement-fixation test, the conglutinating complement-absorption test, the direct agglutination test, and the anti-globulin sensitisation test (Coombs and Stoker 1951) all gave negative or non-specific reactions.

As well as the cattle and pigs, there were chickens, ducks, cats, a horse, and a dog on the farm. It was not possible to bleed these animals, but none of them had arrived on the farm in the middle of August.

Other Possible Sources

The body of a patient who has died of Q fever may be highly infective (Marmion and Stoker 1950), and since Mrs. F., sen., died on Aug. 19, there was a possibility that she might have had unrecognised Q fever. On the other hand, there was absolutely no doubt that she died of carcinoma of the rectum with widespread secondary deposits, and there was no evidence of terminal pneumonia. Neither the doctors, the nurse, nor the two undertakers developed Q fever ; and there was no illness at the laundry where the bedding was washed. Another possible source was some furniture and tinned food brought to the farm by Colonel T. from a flat in London which had been vacated after a tenant had died, but this death was later discovered to have been accidental. Lastly, there was a rubbish tip adjoining the farm, but none of the dustmen who used it had been ill at the time of the outbreak.

DISCUSSION

The main interest in this outbreak lies in the very high attack-rate among the people at risk. Of the 15 residents, all the 12 adults and 1 child became ill ; another child may have had a subclinical infection and one (Bruce X.) was not tested. Only 3 of the 9 non-resident visitors developed Q fever, but these were the 3 who probably spent longest in the farmhouse. In fact, with only 1 exception, all the 16 adults who were on the farm for more than brief visits between Aug. 12 and Aug. 26 developed clinical Q fever. The exception was the casual labourer, Mr. Y., whose movements were difficult to trace and who may have been absent at the critical time.

The rate of infection was thus 100% among the residents who were tested and 77% among the total population at risk ; and this is higher than the rate reported for any previous outbreak, except those described by Babudieri (1951) and del Turco et al. (1951) in Italy. It is possible that the individuals at risk were unusually susceptible, but a highly infective strain or the release of unusually large numbers of organisms are more likely reasons for the high attack-rate. It is therefore all the more disappointing that the source of infection was not identified, particularly as the dates of infection were known to within narrow limits. At first sight the cows were certainly the most obvious reservoirs of *R. burneti*, but laboratory tests revealed no evidence of infection in the animals on the farm at the time of infection, and on epidemiological grounds the pigs were far more likely to have been the source, despite the fact that they are not a recognised reservoir of Q fever.

Clinically the outbreak followed a typical course, and it is interesting to note the wide variation in the lengths of the illnesses (the longest being those of the 2 oldest patients) and the rapid response to chloramphenicol.

SUMMARY

In an explosive outbreak of Q fever in South Kent, 13 out of 15 people living on a dairy farm contracted the disease, 1 child had a subclinical infection, and 1 was not tested. There were 3 other cases among 9 visitors to the farm.

Epidemiological findings and laboratory tests did not suggest that the cows were the reservoir of infection. Although there was some evidence pointing to pigs as the source, it was not possible to confirm this in the laboratory.

We are indebted to the owner of the farm and to his wife for their kind coöperation ; to Mr. J. D. Paterson, M.R.C.V.S., of the Veterinary Investigation Centre, Wye, who took the serum specimens from the animals ; to Dr. Krüger, who kindly sent details of his patient from Berlin ; and to Miss Z. Page for valuable technical assistance.

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Notes and News

M.R C RESEARCH POSTS

TODAY the Medical Research Council employs nearly 1500 people of these 153 are doctors (or dentists) and a further 286 are science graduates To these workers the council offers an opportunity for a life time career in research comparable to the academic posts available at universities Would be research-workers, especially perhaps those who do not wish to teach, will therefore study with interest the booklet lately compiled by the council which sets out the opportunities for appointment to its scientific staff Some of the research staff work in the council's own laboratories —the largest is the National Institute for Medical Research at Mill Hill—but others are ensconced in M R C units in hospitals and universities throughout the country The council does not appoint staff centrally, but leaves the director of each unit to recommend that a post should be offered to a particular worker For the guidance of candidates the booklet contains a list of these units and a survey of the council's research programme, and candidates are encouraged in the first instance to write to the director of the unit where they would like to work But the council's headquarters staff is always willing to advise the hesitant as to the unit to which they should apply Copies of the booklet, which also sets out conditions of work and terms of service, may be had from the offices of the council, 38, Old Queen Street, London, S W 1

MEDICAL AND DENTAL DEFENCE UNION OF SCOTLAND

Scotland's own medical defence society has now passed its half century, but the latest report on its activities[1] suggests that it is in the full bloom of vigorous youth In its jubilee year, as in previous years, the membership increased, and at Aug 8, 1952, this stood at 7491, compared with 7189 a year earlier The council remarks that, partly owing to the Legal Aid Scheme, cases taken to court have tended to increase, and furthermore " the Courts are inclined more and more to apply the maxim *res ipsa loquitur* " The report draws attention to the need for care in injecting penicillin or other substances, during the year there were several instances in which an injection of penicillin into the buttock affected the sciatic nerve

CANCER RESEARCH IN INDIA

WHILE inaugurating, on Dec 30, in Bombay, the fifth session of the International Cancer Research Commission, India's health minister also opened the Indian Cancer Research Centre, which is the first of its kind in Asia The central government have borne the main part of the cost of erecting and equipping this centre, and have also undertaken to meet the entire costs of maintenance Dr V R Khanolkar, director of the centre, has been appointed president of the International Cancer Research Committee

The meetings of the commission were attended by delegates from more than 20 countries One of the main subjects discussed was the geographical distribution of cancer It was generally felt that there was need for more scientific investigation in the Orient of differences in diet, which apparently gave rise to varied manifestations of the disease

SWIFT'S MALADY

" THE mystery about Swift is that there ever should have been any mystery about him,"[2] Sir Russell Brain remarked in his address to the Royal College of Physicians of Ireland, when they made him a fellow Adroitly disentangling the evidence about this unfortunate genius, he pointed out that, as far as his physical disorders went, Swift suffered for many years from what was undoubtedly Ménière's syndrome, with vertigo and deafness, and later from cerebral arteriosclerosis and involutional melancholia The vertigo first appeared in 1710, just before his 43rd birthday, the deafness came on four years later Many years afterwards he wrote to a friend, " I walk like a drunken man and am deafer than you ever knew me ' He tried many remedies, and it seems many doctors, without deriving the least benefit from either Spa waters made his legs swell and his vertigo worse, which, as Sir Russell remarked, is not surprising in view of the modern treatment of aural vertigo by restriction of fluid intake The syndrome persisted longer with him than is usual, for it afflicted him for most of the rest of his life—and he d[illegible] But there is nothing mysterious about that for the [illegible] was able to outmatch him with a patient who had the [illegible] order for 50 years, and who also was getting distressin[illegible] of vertigo when he was over 70 As for Swift's [illegible] (which he invited his friends to expect by that [illegible] remark about dying at the top), he showed no s[illegible] suggesting mental deterioration till he was over 70, by [illegible] time he was almost completely deaf, and with [illegible] sight, though he refused to wear spectacles At 74 he still writing rational, if depressed, letters, but dur[illegible] following year he had what Sir Russell believes t[illegible] been a cellulitis of the orbit, which was extremely p[illegible] and possibly caused some thrombophlebitis of the s[illegible] petrosal sinus and of the cortical veins draining [illegible] area, for after it he suffered from aphasia Even the [illegible] cousin (confusingly named Deane Swift) reported "S[illegible] times he will not utter a syllable, at other times he will [illegible] incoherent words but he never yet, as far as I could [illegible] talked nonsense, or said a foolish thing " For the [illegible] years of his life he suffered great despondency and [illegible] talked at all He is said to have died after conv[illegible] lasting 36 hours, and a post-mortem examination [illegible] " much water on the brain "—a likely enough accomp[illegible] of arteriosclerotic atrophy His last bust suggests a r[illegible] palsy, which might well accompany a lesion of Broca's [illegible]

Swift's emotional disorder, displayed in his relation[illegible] Stella, is, Sir Russell suggested, equally devoid of [illegible] " He was a single man of irreproachable morals, [illegible] woman for years and he did not publicly marry her " I[illegible] he did marry her, privately, but if so it makes little di[illegible] to the story He had, Sir Russell thinks—and he s[illegible] the idea with satisfactory evidence—an obsessional pers[illegible] emotionally arrested at an immature level of develop[illegible] A common enough state but in Swift it was combined [illegible] intellectual genius In attempting to reconcile the [illegible] and the emotions, each of us engages in a daily bal[illegible] feat, when the two are widely disparate in their d[illegible] ment the feat becomes impossible, and the unfort[illegible] subject suffers accordingly Swift's emotional immatur[illegible] made married life impossible to him, but he could g[illegible]

" Friendship in its greatest Height
A constant rational Delight '

(an offer made, in fact, not to Stella but Vanessa) Merci[illegible] for him, Stella was able to accept it, though Vanessa wa[illegible]

NEW AUSTRALASIAN RESEARCH FUND

THE Life Offices' Association for Australasia has establ[illegible] a fund to promote scientific and medical research in Au[illegible] and New Zealand Announcing this, the *Medical Jo[illegible] of Australia* (Jan 3) says that about £25,000 per annu[illegible] likely to be spent, sums will be payable either as gr[illegible] in-aid or for research fellowships To begin with, the [illegible] will be used to foster research in cardiovascular diseases.

FILM ON CONTROLLED HYPOTENSION

A NEW film on the reduction of surgical hæmorrhag[illegible] controlled hypotension was shown at the Royal Colle[illegible] Surgeons, London, on Jan 8 This film, produced by M[illegible] May & Baker Ltd, is in colour with sound, and is inte[illegible] primarily for anæsthetists

A brief introduction on the desirability of reducing sur[illegible] hæmorrhage is followed by an animated sequence illustra[illegible] the factors affecting blood flow and blood pressure T[illegible] principles of ganglionic transmission and paralysis are [illegible] lined, and the action of the more usual ganglion paraly[illegible] such as tetraethylammonium bromide, procaine, nicotine, [illegible] hexamethonium bromide, is demonstrated The cli[illegible] section shows in detail the use of hexamethonium bromide [illegible] bring about controlled hypotension and, by suitable positi[illegible] of the patient, postural ischæmia for hemiresection of [illegible] mandible and block dissection of the glands of the [illegible] Further operations illustrate the main benefits from [illegible] technique these include shortened operation time, clear [illegible] vision in difficult operation fields, reduction in the numb[illegible] operations necessary for a particular patient, and some[illegible] reduction of total blood loss

The film was introduced by Sir Cecil Wakeley, P[illegible] Sir Archibald McIndoe emphasised that it dealt prim[illegible] with an anæsthetic technique which was of great valu[illegible] surgery, and particularly to plastic surgery He ad[illegible] however, that this technique should be used only experienced anæsthetists

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[1] Medical and Dental Defence Union of Scotland Ltd, 113, St Vincent Street Glasgow, C 2 Fiftieth Annual Report 1952

[2] *Irish J med Sci*, August 1952, p 337

With rumbling guts
At Rumbling Bridge
Food-poisoned children
Wish their Mums
Had bought
And used
A fridge.

* * *

We medical dons are sometimes envied by the more cessful members of the profession, the real doctors. nice quiet life, they say, for we have it in malt if not [illegible] olidays, of course. True, academic [illegible] he systole of terms with diastoles tween. But what they forget is that for many of us that the vacation means is no lectures, which are er all only a small item of the academic daily round. nmarked examination papers, unfinished research, read proofs still await us: the library committee still eets, and autopsies, on mice or men, go on as usual. And to get down to details, what can anyone make of a nuary holiday? There's Madeira and Marrakeesh, but e can do those only by brochure. I have slithered lf-frozen on the hills, and stumbled over upturned boats the winter darkness of famous promenades. The aster vacation is little better. It is too early for omfort, and in the country your only friend is the lesser elandine. But give me June, Mr. Vice-Chancellor, and ll show you what I can do. He won't, though. Instead, e gives us the heaviest examinations of the year—final onour schools—and students and examiners both weat away in the first heat-wave. July and August nd us still hard at it, for colleagues also need a rest. And so it's September, as often as not truly backendish—histling winds, heavy rain, leaves flying, and officially oo early for fires. No wonder the session starts off with olds and influenza. But October, when the equinoctial ales are over, is often rich in sunshine. By this time, owever, we are up to the neck again—coping with the ew class, addressing the medical societies, and longing or our January break . . .

* * *

She was describing some small brown mobile objects which had been present in her little boy's urine. "I was very stupid at first, doctor," she said, "because I thought they were tea leaves, but now I've just remembered he doesn't drink tea."

* * *

He belonged to a well-known local family of gipsies, and was suffering from lobar pneumonia, after a night spent in a drunken stupor in a cold, damp ditch. I took appropriate action, and he made a rapid recovery. Later when I pointed out to him the probable ætiological significance of his night's exposure, he asked me whether I would allow him to go into the pub at night, to have just one or two beers, as this was an essential part of his job. When I asked for further details he explained that the greater part of his income came from the buying and selling of lead, and the trading was done in the local. So yet another disease is shown to be connected with this unhappy metal.

Driving back that night I mused on the changing pattern of industrial disease. Will the decreased incidence of Crystal-Gazer's Strabismus and Palmar Argyria be counterbalanced by an increase in Lead-Merchants' Pneumonia and Truncheon Coma? Has the gipsy laid down his fiddle to take up another?

* * *

The Physiologists have long been discouraging about alcohol as a restorative after exposure to cold, and the *Medical Journal of Australia*[1] has lately had harsh things to say about St. Bernard dogs and their flasks of brandy. Alcohol causes the skin blood-vessels to dilate, thereby diverting the warmed blood from the more essential inner organs to the surface of the body where it is promptly cooled. So the *Journal* advises the dogs to carry 'Thermos' flasks of hot milk instead. But of course Sydney is a very long way from Switzerland.

* * *

From an insurance report: "Mr. —— was treated in — Mental Hospital by Electroconsultant therapy."

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[1] *Med. J. Aust.* 1952, ii, 379.

Letters to the Editor

PRECISION IN DIAGNOSIS

SIR,—Dr. Todd is always stimulating; he manages to put on paper what most of us only ponder on.

Diagnosis literally means knowing through and through: it is the very fullest statement of every aspect of a case. Of course we always use it to mean the exact reverse; it is the shortest possible summary, the label. So let it be. Medicine has little respect for the classics.

A label is a useful thing. Rightly affixed it gets one to one's destination. Wrongly addressed it can misdirect one seriously. The practical exigencies of medicine will always require such labels. We should make them reflect reality as accurately as possible. To that end I enter a plea for the "serial" diagnosis.

Those of us who do general practice in any form know that it is only a tiny minority of illnesses that can be adequately and honestly covered by a single term like "mastoiditis" or "intussusception." The case has actually carried a series of labels, such as "upper respiratory infection," "N.A.D. earache," "otitis media," "mastoiditis for admission," "recent mastoidectomy"; or instead "collywobbles," "colic with constipation," "intestinal obstruction," "intussusception at operation," "stitch abscess." Which one of these the records officer chooses to select for his returns is of little importance. Each in its time has been the correct diagnosis. Case-records both for general practice and for hospitals should be designed with that in mind. Instead of a ridiculous little box in the top corner, one should have space for half a dozen insertions with their dates.

A wider appreciation of the practical inevitability of serial, rather than single, diagnoses would in my view lessen the need knowingly to invoke phoney pathology, such as the usual "fibrositis," "neuritis," or "gastritis." All diagnoses are temporary; most are tentative. A large number of complaints met in general work never need carry their series of labels as far as the pathological diagnosis. They resolve spontaneously or are of such a nature that the labours and sufferings entailed in going further are not warranted by the prospects of clinical improvement. For such cases it may be that a new category of accepted terms could come into use. How about undifferentiated somatic pain ("U.S.P.") or acute undifferentiated abdominal pain ("A.U.A.P.")? "Lumbago" takes a lot of beating! Such phrases, having no insidious implication of finality, leave the mind open to revise and review, which is surely what serves the patient best. Diagnostic labels should reflect the harassed uncertainty of the clinician, not the euphoric naivety of the morbid histologist.

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NICOLAS MALLESON.

SIR,—Many of the truths and criticisms expressed in the thoughtful article by Dr. Todd (Dec. 27) must of course be admitted; but is the fact that attempts at precision in diagnosis can be overdone sufficient reason for relaxing effort towards that end? His arguments are so forceful as almost to persuade one of the necessity for a return to Hippocratic principles in diagnosis, with their emphasis on description of the patient and his ills.

In reply to Dr. Todd's question "Do not such homely phrases as 'depressed and worried about himself' and 'stupid and self-centred' often give a better understanding of the symptoms?" one feels impelled to answer "No." These are mere descriptive terms the pronouncement of which would not warrant a long, arduous, and expensive professional training. The description of a patient as "stupid" hardly argues understanding in the physician. Secondly, the effort of assessing the significance of a symptom such as

Notes and News

M.R C RESEARCH POSTS

TODAY the Medical Research Council employs nearly 1500 people of these 153 are doctors (or dentists) and a further 286 are science graduates To these workers the council offers an opportunity for a life time career in research comparable to the academic posts available at universities Would be research-workers, especially perhaps those who do not wish to teach, will therefore study with interest the booklet lately compiled by the council which sets out the opportunities for appointment to its scientific staff Some of the research staff work in the council's own laboratories —the largest is the National Institute for Medical Research at Mill Hill—but others are ensconced in M R C units in hospitals and universities throughout the country The council does not appoint staff centrally, but leaves the director of each unit to recommend that a post should be offered to a particular worker For the guidance of candidates the booklet contains a list of these units and a survey of the council's research programme, and candidates are encouraged in the first instance to write to the director of the unit where they would like to work But the council's headquarters staff is always willing to advise the hesitant as to the unit to which they should apply Copies of the booklet, which also sets out conditions of work and terms of service, may be had from the offices of the council, 38, Old Queen Street, London, S W 1

MEDICAL AND DENTAL DEFENCE UNION OF SCOTLAND

Scotland's own medical defence society has now passed its half century, but the latest report on its activities[1] suggests that it is in the full bloom of vigorous youth In its jubilee year, as in previous years, the membership increased, and at Aug 8, 1952, this stood at 7491, compared with 7189 a year earlier The council remarks that, partly owing to the Legal Aid Scheme, cases taken to court have tended to increase, and furthermore "the Courts are inclined more and more to apply the maxim *res ipsa loquitur*" The report draws attention to the need for care in injecting penicillin or other substances, during the year there were several instances in which an injection of penicillin into the buttock affected the sciatic nerve

CANCER RESEARCH IN INDIA

WHILE inaugurating, on Dec 30, in Bombay, the fifth session of the International Cancer Research Commission, India's health minister also opened the Indian Cancer Research Centre, which is the first of its kind in Asia The central government have borne the main part of the cost of erecting and equipping this centre, and have also undertaken to meet the entire costs of maintenance Dr V R Khanolkar, director of the centre, has been appointed president of the International Cancer Research Committee

The meetings of the commission were attended by delegates from more than 20 countries One of the main subjects discussed was the geographical distribution of cancer It was generally felt that there was need for more scientific investigation in the Orient of differences in diet, which apparently gave rise to varied manifestations of the disease

SWIFT'S MALADY

"THE mystery about Swift is that there ever should have been any mystery about him,"[2] Sir Russell Brain remarked in his address to the Royal College of Physicians of Ireland, when they made him a fellow Adroitly disentangling the evidence about this unfortunate genius, he pointed out that, as far as his physical disorders went, Swift suffered for many years from what was undoubtedly Ménière's syndrome, with vertigo and deafness, and later from cerebral arteriosclerosis and involutional melancholia The vertigo first appeared in 1710, just before his 43rd birthday, the deafness came on four years later Many years afterwards he wrote to a friend, "I walk like a drunken man and am deafer than you ever knew me' He tried many remedies, and it seems many doctors, without deriving the least benefit from either Spa waters made his legs swell and his vertigo worse, which, as Sir Russell remarked, is not surprising in view of the modern treatment of aural vertigo by restriction of fluid intake The syndrome persisted longer with him than is usual, for gid[illegible] afflicted him for most of the rest of his life—and he d[illegible] But there is nothing mysterious about that for the [illegible] was able to outmatch him with a patient who had the [illegible] order for 50 years, and who also was getting distressing [illegible] of vertigo when he was over 70 As for Swift's [illegible] (which he invited his friends to expect by that [illegible] remark about dying at the top), he showed no [illegible] suggesting mental deterioration till he was over 70, by [illegible] time he was almost completely deaf, and with [illegible] sight, though he refused to wear spectacles At 74 he [illegible] still writing rational, if depressed, letters, but dur[illegible] following year he had what Sir Russell believes to [illegible] been a cellulitis of the orbit, which was extremely pa[illegible] and possibly caused some thrombophlebitis of the sup[illegible] petrosal sinus and of the cortical veins draining B[illegible] area, for after it he suffered from aphasia Even the [illegible] cousin (confusingly named Deane Swift) reported "[illegible] times he will not utter a syllable, at other times he will [illegible] incoherent words but he never yet, as far as I could [illegible] talked nonsense, or said a foolish thing" For the la[illegible] years of his life he suffered great despondency and h[illegible] talked at all He is said to have died after convul[illegible] lasting 36 hours, and a post mortem examination re[illegible] "much water on the brain"—a likely enough accompa[illegible] of arteriosclerotic atrophy His last bust suggests a ri[illegible] palsy, which might well accompany a lesion of Broca's [illegible]

Swift's emotional disorder, displayed in his relation[illegible] Stella, is, Sir Russell suggested, equally devoid of [illegible] "He was a single man of irreproachable morals, [illegible] woman for years and he did not publicly marry her' [illegible] he did marry her, privately, but if so it makes little d[illegible] to the story He had, Sir Russell thinks—and he [illegible] the idea with satisfactory evidence—an obsessional pers[illegible] emotionally arrested at an immature level of develop[illegible] A common enough state but in Swift it was combined [illegible] intellectual genius In attempting to reconcile the in[illegible] and the emotions, each of us engages in a daily bal[illegible] feat, when the two are widely disparate in their de[illegible] ment the feat becomes impossible, and the unfortu[illegible] subject suffers accordingly Swift's emotional immat[illegible] made married life impossible to him, but he could give

" Friendship in its greatest Height
A constant rational Delight '

(an offer made, in fact, not to Stella but Vanessa) Men[illegible] for him, Stella was able to accept it, though Vanessa was [illegible]

NEW AUSTRALASIAN RESEARCH FUND

THE Life Offices' Association for Australasia has establ[illegible] a fund to promote scientific and medical research in Au[illegible] and New Zealand Announcing this, the *Medical Jo[illegible] of Australia* (Jan 3) says that about £25,000 per annu[illegible] likely to be spent, sums will be payable either as g[illegible] in aid or for research fellowships To begin with, the [illegible] will be used to foster research in cardiovascular disease[illegible]

FILM ON CONTROLLED HYPOTENSION

A NEW film on the reduction of surgical hæmorrhag[illegible] controlled hypotension was shown at the Royal Colleg[illegible] Surgeons, London, on Jan 8 This film, produced by Mes[illegible] May & Baker Ltd, is in colour with sound, and is inte[illegible] primarily for anæsthetists

A brief introduction on the desirability of reducing sur[illegible] hæmorrhage is followed by an animated sequence illustra[illegible] the factors affecting blood flow and blood pressure [illegible] principles of ganglionic transmission and paralysis are [illegible] lined, and the action of the more usual ganglion paraly[illegible] such as tetraethylammonium bromide, procaine, nicotine [illegible] hexamethonium bromide, is demonstrated The cl[illegible] section shows in detail the use of hexamethonium bromid[illegible] bring about controlled hypotension and, by suitable positi[illegible] of the patient, postural ischæmia for hemiresection of [illegible] mandible and block dissection of the glands of the [illegible] Further operations illustrate the main benefits from [illegible] technique these include shortened operation time, clar[illegible] vision in difficult operation fields, reduction in the numb[illegible] operations necessary for a particular patient, and some [illegible] reduction of total blood loss

The film was introduced by Sir Cecil Wakeley, P[illegible] Sir Archibald McIndoe emphasised that it dealt pri[illegible] with an anæsthetic technique which was of great valu[illegible] surgery, and particularly to plastic surgery He ad[illegible] however, that this technique should be used only [illegible] experienced anæsthetists cases after cortisone and the subcortical hæmor- s in the fatal case, I am of the opinion that cortisone responsible for the convulsive episodes in all these . I think that cortisone is contra-indicated in infection, where the mobilisation of the defensive reparative mechanisms of the body are all-important. ture I certainly shall not use cortisone in meningitis its rôle is more clearly established.

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[1] Medical and Dental Defence Union of Scotland Ltd, 113 St Vincent Street Glasgow, C 2 Fiftieth Annual Report 1952

[2] *Irish J med Sci* August 1952, p 337

dney, Australia. BRIAN HAYNES.

ATION OF THE POPLITEAL VEIN FOR THE GRAVITATIONAL SYNDROME

IR,—Mr. Goligher, in his interesting remarks last k about ligation of deep veins for valvular incom- ence, makes the assumption that ligation of either the erficial femoral or popliteal veins will have the same sequences as far as the venous circulation in the lower is concerned.

t is possible, however, that a resistance placed at the let of the calf-muscle pump (which is presumably at ligation of the popliteal vein amounts to) would be re efficient in diminishing reflux during calf diastole n one placed at the groin with a considerable venous ervoir intervening. Further, the resistance offered the two procedures is probably not the same; the n profunda femoris vein provides a by-pass of much ger calibre than any at the knee after popliteal vein ation.

In support of this hypothesis is the finding[1] that pliteal vein ligation in patients with incompetent lves in the deep veins of the leg can reduce the high nous pressure in the foot, measured during exercise, ich exists in such patients. Comparable hydrostatic [illegible] has not, to my knowledge, been shown for e superficial femoral vein.

I do not wish to advocate popliteal vein ligation, but lieve it cannot justifiably be condemned because ation of the superficial femoral vein does not succeed.

niversity College Hospital Medical
School, London, W.C.1. C. J. LONGLAND.

THE SURGICAL TREATMENT OF ULCERATIVE COLITIS

SIR,—I do not wish in any way to detract from the erits of the excellent article on this subject by Mr. ounsell and Mr. Goligher (Nov. 29); but I feel that, ough ileostomy is no doubt often necessary in ulcerative olitis where medical treatment fails, there is still a lace for the older operation of appendicostomy, at least s a trial before resorting to the more serious and utilating one of permanent ileostomy, coupled with olectomy with its mortality of 16%.

Appendicostomy was at one time regarded as a good peration; it clearly cannot succeed if there are ulcers bove the colon, but I feel that this is possibly the xception rather than the rule. The operation fell into isrepute because of Arthur Hurst's dogmatic statement hat lavage of the colon from below is just as effective s lavage with 4 pints of saline through an appendicostomy pening, but I doubt if this is necessarily always so.

Ulcerative colitis is rare in children, in whom it was irst described by Helmholtz at the Mayo Clinic as late s 1923. As a pædiatrician, I can only recollect having een two examples in the last ten years or so, both, of ourse, in older children.

The first of these was not doing entirely satisfactorily after a year of medical treatment; and, being aware of the danger of carcinomatosis supervening even in an older child or young adult (probably about 10% according to American figures), I approached Mr. Henry Stokes with the request that he should do an ileostomy. Even under considerable pressure from me, he held out in his view that an appendicostomy should be tried first. The child washed her colon out daily for a year; and when, after a further trial period of three months during which lavage was suspended, the stools remained normal the appendicostomy was closed. The radiographic appearances returned from the typical "ironed-out" and "string" pattern to the normal one with its characteristic haustrations; and the patient has remained perfectly well for five years. When I saw her recently, she told me that she is now a typist.

The second case, a boy, has done very well so far with an appendicostomy, again after a period of medical treatment had failed. He now has relatively normal stools free from blood, and he has put on 10 lb. in weight since his operation in June.

What applies to a child may not necessarily apply to an adult; but at least one cannot help feeling that this girl's future is likely to be a happier one, from a marital and every other point of view, with a normal body such as she has than with a permanent ileostomy.

National Children's Hospital,
Dublin. R. E. STEEN.

THERAPEUTIC APPLICATION OF PLASMA CHOLINESTERASE

SIR,—Dr. Barnard's letter (Dec. 13) is of great interest, and now that succinylcholine chloride is widely used in anæsthesia the confirmation that plasma "pseudo"-cholinesterase concentrate is an effective and innocuous antagonist of the drug is encouraging. Dr. Barnard says, however, that "some of the observed therapeutic effects . . . remain inexplicable." The same can sometimes be said of the anticholinesterase, neostigmine.

The danger of giving such a cholinesterase inhibitor in the presence of succinylcholine (cholinergic) paralysis is supported by substantial experimental and theoretical evidence. Several writers[1–5] have mentioned the prolongation produced by neostigmine, a powerful inhibitor of the cholinesterase which is responsible for the hydrolysis of succinylcholine. Three cases of paralysis apparently prolonged in this way have been published,[6–8] but Grant[9] described a case in which paralysis persisting until the third day after 80 mg. of succinylcholine was reversed by 1·0 mg. of neostigmine. Ruddell[10] had success with 6·0 mg. of neostigmine in a patient who had had succinylcholine and decamethonium. Other cases have been reported after decamethonium.

The following report tells of another instance in which neostigmine was used successfully.

A woman of 62, weighing 120 lb., had malæna due, it was thought, to a peptic ulcer. 2 pints of packed red cells raised her hæmoglobin from 39 to 62%. Her general condition was fair, and the blood-pressure was 120/90 mm. Hg. She was operated on after a second 2 pints of packed red cells.

Premedication.—Pethidine 100 mg. and atropine gr. $^1/_{100}$.

Induction.—Thiopentone 0·25 g. and succinylcholine chloride 25 mg., followed by intubation.

Maintenance and Progress.—Nitrous oxide and oxygen (65/35%) at 6 litres per min. on semi-open circuit with absorption. Intermittent pethidine (total 50 mg.). Full spontaneous respirations returned before the peritoneum was opened. Thiopentone (0·25 g.) and *d*-tubocurarine (10 mg.) sufficiently relaxed the poorly developed abdominal wall, though adequate respirations remained.

Laparotomy, lasting 35 min., revealed an inoperable carcinoma. For closure, 25 mg. of succinylcholine produced immediate apnœa and relaxation, but unforeseen surgical difficulties led to some delay and closure took 55 min. Relaxation was continued by small doses of succinylcholine, given when weak respiratory efforts reappeared (total 225 mg.).

When controlled respiration was stopped feeble inadequate diaphragmatic respirations returned, but there was no inter-

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1. Walker, A. J., Longland, C. J. *Clin. Sci.* 1950, 9, 101.

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1. Ottolenghi, S. R. Communication to 26th International Congress of Anæsthesiology, London, September, 1951. See *Brit. med. J.* 1951, ii, 668.
2. Thesleff, S. *Ibid.*
3. Scurr, C. F. *Ibid*, p. 831.
4. Bourne, J. G., Collier, H. O. J., Somers, G. F. *Lancet*, 1952, i, 1225.
5. Evans, F. T., Gray, P. W. S., Lehmann, H., Silk, E. *Ibid*, p. 1229.
6. Harper, J. K. *Brit. med. J.* 1952, i. 866.
7. Gray, T. C. *Lancet*, 1952, ii, 40.
8. Mackay, M. L. *Ibid*, p. 145.
9. Grant, G. *Brit. med. J.* 1952, i, 1352.
10. Ruddell, J. S. *Lancet*, 1952, ii, 341.

Award for Research on Infertility

The American Society for the Study of Sterility is offering a prize of $1000 for an essay on infertility and sterility Essays must be submitted not later than March 1, 1953, and further particulars may be had from Dr Herbert H Thomas, assistant secretary of the society, 920 South 19th Street, Birmingham, Alabama

British Council for Rehabilitation

On Wednesday, Feb 4, at the Royal College of Nursing, Henrietta Place, London, W 1, the council is to hold a conference on Speeding Recovery Through the Closer Cooperation of Hospitals and Industry Particulars may be had from the general secretary, at Tavistock House (South), Tavistock Square, W C 1

William Gibson Research Scholarship for Medical Women

The Royal Society of Medicine will make the next award of this scholarship (£200 p a) in July It is open to women doctors who are subjects of the British Empire, and it is usually tenable for two years Further particulars may be had from the Secretary of the Society, 1, Wimpole Street, London, W 1, to whom applications should be sent not later than June 1

A Blood-donor Marathon

Last weekend Montreal had a "blood donor marathon" The *Times* (Jan 12) reports that this started on Saturday morning and continued until midnight on Sunday, and the blood collected was expected to total 1850 pints The Ex-Service Men's Taxi Association provided free transport for donors, and entertainers gave their services in a non stop variety show It was expected that by the end of the marathon 6000 more people would have promised to give blood at a future date

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EMERGENCY BED SERVICE—In the week ended last Monday applications for general acute cases numbered 1758 The proportion admitted was 80 8%

Appointments

BALL KATHLEEN M B Lpool asst maternity child M O, Blackpool
DOW J D M C, M D Glasg, D M R D consultant radiologist, Guy s Hospital London
DUNCAN G D, M B Aberd, D P H asst M O H and asst school M O Burton upon Trent

Births, Marriages, and Deaths

BIRTHS

ATKINSON—On Jan 9 at University College Hospital London, to Iris (née Bowman) wife of Dr Michael Atkinson—a daughter

FAIRLEY—On Dec 20, at R A F Hospital Rinteln Germany, to Dorothy Jean (née Orr) wife of Dr H Barrie Fairley, D A—a daughter

SCOTT—On Jan 3, at Keresley Hospital Coventry, to Gisele wife of Dr James D Scott—a daughter

SLEE.—On Jan 6 at the Churchill Hospital, Oxford, to Joan, wife of Dr Mark Slee—a son

VÉREL—On Jan 2 at the London Hospital, to Agnes, wife of Dr D Vérel—a son

MARRIAGES

BALINT—EICHHOLZ—On Jan 2 in London Michael Balint F R C P F of Devonshire Place, London, to Enid Eichholz of Porchester Terrace London

ROBERTS—WATERS—On Jan 5, at Great Hampden Harold Roberts M R C S to Marian Waters

DEATHS

ABBOTT—On Jan 3, at Vallance Gardens Hove Horatio White Abbott M D Lausanne M R C S, late of Holloway, London

HUGHES—On Jan 4 Leslie Edward Hughes M C M R C S of Cotswold Lodge Cirencester Glos

JEAFFRESON—On Jan 7, at Headingley, Leeds, Bryan Leslie Jeaffreson M D Lond F R C S F R C O G

MARTIN—On Jan 6 at Hampstead Alfred John Martin O B E M R C S aged 43

MELLAND—On Jan 8, Charles Herbert Melland M D Lond F R C P, of Fallowfield Manchester aged 80

RICHARDS—On Jan 1, at Port Talbot Glamorgan, William Jones Richards F R C S, aged 79

TENISON MOSSE—On Jan 7 Cotton Grimley Tenison Mosse B A Camb M R C S of Southminster Essex

WARE—On Jan. 5 Arthur Maitland Ware M D Camb, of Tyting Down Guildford

Diary of the Week

JAN 18 TO 24

Monday, 19th

ROYAL EYE HOSPITAL St George s Circus Southwark, S E1
5 P M Dr T H Whittington Refraction Work in th
and the Old Aphakia
HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4) Dr J van Laer (The E
Auto mutilation of Prisoners

Tuesday, 20th

UNIVERSITY OF LONDON, Senate House W C 1
6 P M Sir Godfrey Thomson D SC Geometry of M
Measurement (First of three lectures)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical M
Keppel Street, W C 1) Mr A S Parkes D.SC. FR
Preservation of Living Cells at Low Temperatures
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
6 P M *Section of Pathology* Prof G Payling Wright
Trunks as Pathways of Infection (Presidential ad
INSTITUTE OF DERMATOLOGY, St John s Hospital Li
W C 2
5 30 P M Prof P B Medawar, F R S Pigmentation
WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Mar
Lane, Welbeck Street, W 1
5 30 P M Mr J Minton Ocular Manifestations in Ne
Disease Part I
SOCIETY FOR THE STUDY OF ADDICTION
8 P M (11, Chandos Street, W 1) Detective sergeant
Lyle Dangerous drugs Traffic in London
SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P M (Bolingbroke Hospital, S W 11) Dr Kenneth Ca
Common Psychiatric Problems in Childhood

Wednesday, 21st

UNIVERSITY OF LONDON
6 P M Sir Godfrey Thomson Geometry of Mental Me
ment (Second of three lectures)
ROYAL SOCIETY OF MEDICINE
8 15 P M *Sections of Epidemiology and Preventive Medi General Practice* Dr E Maurice Backett, Mrs L A
Shaw An Urban General Practice
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver
INSTITUTE OF UROLOGY, St eet W C
4 30 P M Mr J L Sen s of Re
Pain
LONDON ASSOCIATION OF THE MEDICAL WOMEN S FEDERATION
8 30 P M (Royal Free Hospital School of Medicine, 8 Hu
Street W C 1) Sir William MacArthur Histor
Smallpox in the British Isles
MIDLAND MEDICAL SOCIETY
8 15 P M Medical Institute, 154, Great Ch
Street A L M Pearcy Dr A
Nuss Mr Charles Rudd C
sone and A C T H
EUGENICS SOCIETY
5 30 P M (Burlington House, Piccadilly W 1) Mr J D M
PH D Family Environment and Intelligence

Thursday, 22nd

UNIVERSITY OF LONDON
6 P M Sir Godfrey Thomson Geometry of Mental Mea
ment (Last of three lectures)
UNIVERSITY COLLEGE, Gower Street W C 1
5 30 P M Prof F Bergel PH D Chemical Aspects of N
Growth (First of three lectures)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medi
Mr H J Seddon Nerve Repair
ROYAL SOCIETY OF MEDICINE
5 P M *Section of Urology* Mr J P Mitchell, Dr G S Andrew
Clinical Aspects and Pathology of Bladder Neck Obstr
tion Mr M Caine Fate of Bladder Neck and Pros
Cavity Mr Thomas Moore Blad
Neck
INSTITUTE OF Hospital for Sick Childr
Great Orm
5 P M Dr Cough
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Pathogenesis of Tinea Capiti
ST GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Cor
S W 1
5 P M Dr J Hamilton Paterson Neurological lect
demonstration
LIVERPOOL MEDICAL INSTITUTION, 114 Mount Pleasant Liverp
8 P M Dr M K Alexander Case of the Steven-Joh
Syndrome Dr A H Cruickshank Case of Chi
Disease Dr K McCarthy Generalised Vaccinia
UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd Dundee) Prof C
Rob Treatment of Intermittent Claudication
Gangrene of Toes by Arterial Grafting

Friday, 23rd

ROYAL EYE HOSPITAL
5 30 P M Mr Howard Reed Visual Fields
INSTITUTE OF DERMATOLOGY
5 30 P M Dr I Muende Anomalies of Pigmentation

Saturday, 24th

BRITISH ASSOCIATION OF ALLERGISTS
11 A M (1, Wimpole Street, W 1) Annual general meeti

ırtant information to be gained from further investions. For instance, it would be interesting to know the tro reaction of cancer cells to sodium P.A.S.; and conceivable that a biological method of diagnosis ıt be evolved in this way.

Adelaide,
uth Australia.

MICHEL BROUS.

ALMONERS

ɪR,—I fully endorse the last paragraph of your otation on Almoners (Dec. 27) which says: "It would ly be better, as a first step, to consider the factors ch are hindering recruitment of almoners of our sent high standard." Some of these factors are ıtioned earlier, and to these should be added the fact, hasised in the Cope Committee's report on almoners, t there are too few students in social science in the versities to meet the requirements of all professions which this training is the basis, and until this shortage be overcome there does not seem any likelihood of viding adequate numbers of almoners.

t is, therefore, of paramount importance that ioners should be employed only on the medical social rk for which their course of training especially equips m. Any dissipation of their energies to cover administive and clerical duties, such as registration, appointnts, waiting-lists, and transport arrangements, is steful and can only lead to a proportionate lessening of ir value as almoners. Some hospitals have taken a long ie to grasp the value and proper uses of almoners. ıers, regrettably, have not grasped these points yet. e limited number of almoners could be distributed r a much larger number of hospitals if they were all owed to concentrate on medical social work. This in elf is no narrow, restricted field but, according to a ent definition, consists in studying the patient's social ckground and his reactions to illness with a view to isting in the solution of the many personal and ıctical problems which are associated with illness.

The members of the Institute of Almoners have ently been reconsidering this problem in order to see w the available medical social skill can be employed ere it will be best used for furthering the patient's erests. It is understood that they hope shortly to omit a memorandum on this subject to the Minister Health. Meanwhile it cannot be too strongly emphaed that an obvious and immediate way of alleviating present shortage problem is to ensure that almoners engaged only on almoner's work.

North West Metropolitan
Regional Hospital Board,
1A, Portland Place, London, W.1.

H. M. C. MACAULAY
Senior Administrative
Medical Officer.

FRACTURES OF THE NECK OF THE FEMUR

SIR,—With reference to my recent article on a techque for inserting the Smith-Petersen nail for fractures the neck of the femur without moving the patient m his bed,[1] it has been brought to my notice that of. Carl Semb, of Oslo, published a paper in 1938[2] scribing his own technique, which was also designed relieve the patient of disturbance and shock by rrying out all the treatment, including operation, in e patient's own bed.

Although his technique is quite different from my own, e principle is the same. In a personal communication tells me that his method has now been used in over a ousand cases in his department, with excellent results. hat is more important is that he states that this method, cause it is less liable to cause shock, enables him to erate in 90% of cases.

As I emphasised in my paper, the avoidance of shock using a simple technique and avoiding all disturbance the patient makes the operation a life-saving measure as well as a means of treating the fracture. I would like to draw the attention of all those who have to deal with these cases to Professor Semb's paper.

Guy's Hospital, London, S.E.1. T. T. STAMM.

AGRANULOCYTOSIS DURING ISONIAZID THERAPY

SIR,—Dr. Ferguson (Dec. 13) describes a patient with an agranulocytosis whose blood-count promptly returned to normal after cessation of treatment with isoniazid. In this connection the following case is of interest.

A patient, aged 20 years, suffering from diabetes mellitus and pulmonary tuberculosis, received: (1) streptomycin 1 g. daily from Nov. 3 to 20; (2) *p*-aminosalicylic acid (P.A.S.) 12 g. daily from Nov. 3 to Dec. 12; (3) isoniazid 200 mg. daily (3 mg. per kg. body-weight) from Nov. 21 to Dec. 12.

On Dec. 10 he developed fever, followed next day by slight jaundice. The liver was slightly enlarged, but the spleen was not felt. The urine contained bile pigments.

A blood-count on Dec. 10 showed an agranulocytosis. Next day, after all treatment was stopped, sternal puncture showed a maturation arrest at promyelocyte level with a considerable reduction of the number of neutrophil semi-mature myelocytes and complete absence of neutrophil myelocytes and polymorphs.

The details of the sternal-marrow count were:

	Percentage
Neutrophil (segmented)	0
„ (myelocyte)	0
„ (semi-mature myelocyte)	0·5
„ (semi-mature myelocyte in mitosis)	0·25
„ (promyelocyte)	3·0
„ (promyelocyte in mitosis)	0·25
Eosinophil (segmented)	0·75
„ (promyelocyte)	0·25
Myeloblast	1·75
Lymphocyte	8·5
Monocyte	3·75
Promonocyte (? promyelocyte)	2·0
Monoblast (? myeloblast)	2·75
„ (in mitosis)	0·25
Normoblast (orthochromatic or late polychromatic)	36·25
„	18·0
„	0·75
„	5·5
„	0·25
Proerythroblast	0·5
Hæmocytoblast	0·25
Megakaryocyte	0·5
Reticulum cell (macrophage)	5·5
„ plasma cell	1·75
„ lymphoid cell	6·75

There was an increased proportion of monocytes in the peripheral blood throughout the whole agranulocytic episode.

The patient was given penicillin, pyridoxine, aureomycin, and methionine. The temperature (104°F on Dec. 12) fell by lysis, and six days after stopping P.A.S. and isoniazid the granulocytes started to reappear and the fever finally disappeared.

The changes in the differential white blood-cell count are shown in the accompanying table. Hæmoglobin red cells, reticulocytes, and platelets were normal throughout.

DIFFERENTIAL WHITE BLOOD-CELL COUNTS

Date	White cells per c.mm.	Neutrophils (%)				Eosinophils (%)	Basophils (%)	Monocytes (%)	Lymphocytes (%)
		Myelocytes	Metamyelocytes	Stab forms	Segmented forms				
Dec. 10	4200	—	—	2·5	2·5	7·0	—	18·5	69·5
„ 12	—	—	—	—	—	—	—	32·0	68·0
„ 13	5250	—	—	—	—	—	—	18·0	82·0
„ 15	1700	—	—	—	—	—	—	41·6	58·4
„ 16	2300	—	—	—	—	—	—	35·0	65·0
„ 17	2100	—	—	—	—	—	—	46·4	53·6
„ 18	2900	0·8	1·6	6·4	1·6	—	—	49·6	40·0
„ 19	2300	5·6	6·4	10·4	7·2	0·8	—	16·8	52·8
„ 20	4100	3·2	4·0	12·8	14·4	—	—	24·0	41·6
„ 22	5350	1·6	0·8	15·2	21·6	—	—	19·2	41·6
„ 24	7400	—	1·6	16·8	41·6	—	0·8	8·8	30·4
„ 29	9200	—	—	6·5	39·0	—	0·5	15·0	39·0
„ 30	7700	—	—	6·5	49·0	—	1·0	12·5	31·0

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1. Stamm, T. T. *Lancet*, 1952, ii, 59.
2. Semb, C. *Surgery*, 1938, 4, 321.

given, usually producing a stool of 150–200 g with a very low electrolyte content Fæcal losses were therefore ignored As no patient was febrile, except for a short time after operation, sodium and chloride losses in sweat were also ignored In calculating the balances 30 m eq was considered a reasonable allowance for losses of sodium and chloride in the operating theatre

Nearly all the patients were weighed every day, always in the first 2 hours of the period, with the bladder empty, by the same observer using the same scales (Avery, model 1064) Observations could easily be made to within 4 oz, as shown by multiple readings The weight of the dressings (a strip of gauze and plaster) was negligible While on intravenous fluids the patients received no protein and not more than 600 calories in 24 hours (glucose 150 g) during this time, therefore, they would be expected to lose about 1 lb in weight and some 30 m eq of sodium per 24 hours (Gamble 1951)

Results

Our results show that three separable phases of retention can be recognised after operation We have named these primary water retention, early sodium retention, late sodium retention

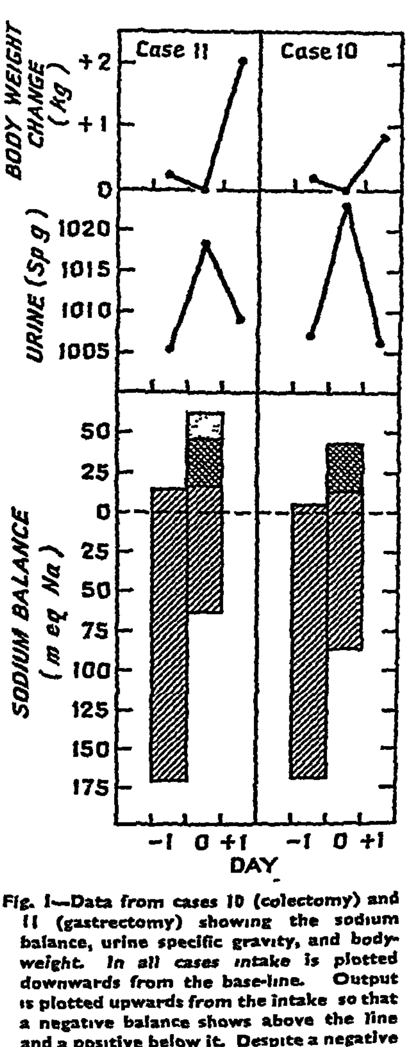

Fig. 1—Data from cases 10 (colectomy) and 11 (gastrectomy) showing the sodium balance, urine specific gravity, and body-weight. *In all cases intake is plotted downwards from the base-line.* Output is plotted upwards from the intake so that a negative balance shows above the line and a positive below it. Despite a negative sodium balance on the day of operation these patients showed the weight-gain of primary water retention

▨ URINE
☐ GASTRIC SUCTION
▩ ALLOWANCE FOR SODIUM LOSS DURING OPERATION

Key to figs 1 3 4 and 5

Primary Water Retention

15 patients were weighed on the morning after operation Every one showed a gain in weight of 1 8–5 1 lb (0 8–2 3 kg), the average being 3 3 lb (1 5 kg) (see table I) This occurred when the calorie intake in the 24 hours was less than 600 calories, was accompanied by oliguria with a raised specific gravity (see table I), it can only have been due to water retention, which was never less than 1 litre This water retention is not due to gastrectomy in itself, nor to the change from oral to intravenous fluids, as cases 10 and 21 show These 2 patients underwent respectively colectomy and herniorrhaphy, the latter receiving oral fluids throughout, yet both showed water retention with characteristic urine changes

In 4 patients (cases 10–13) no sodium was given on the day of operation (save for that in a bottle of citrated blood) The data from cases 10 and 11 are summarised in fig 1, which shows that the weight-gain and high urinary specific gravity occurred despite a ne sodium balance It is evident, therefore, th retention is the primary event This is conf the changes in the plasma-protein and ele concentrations, which indicate dilution of the and extracellular fluid on the day after op (table II)

TABLE II—AVAILABLE FIGURES SHOWING BLOOD CHANGES DURING THE 24 HOURS AFTER OPER.

Case no	Plasma Na (m eq per litre)		Plasma Cl (m eq per litre)		Plasma (g per
	0	0+1	0	0+1	0
2	158	146	112	103	[illegible]
3	144	146	104	99	65
4	155	140	102	94	68
5			109	102	[illegible]
7	142	138	110	105	65
9	150	138	102	100	[illegible]
10	144	144	100	99	63
11	144	136	107	94	67
14	152	144	106	101	[illegible]
15	144	136	100	94	67
16	146	142	102	96	70
18	142	142	95	90	63
21	138	132	103	103	68

In case 10 (colectomy) urine samples were 4-hourly from the indwelling catheter The information obtained is summarised in fig 2, show for nearly 24 hours the urine flow was reduced, specific gravity and chloride concentration the characteristic effects of the release of anti- hormone, and we know of no other physiological nism that produces such a result In only 2 p (cases 1 and 18) was this action prolonged second postoperative period; in all the others, day, the urine specific gravity was below 1 010, and was an increased volume of urine of low sodium chloride concentrations In many cases there was same time a loss of part or all of the weight by water retention on the day of operation, thou some th masked further and water r tion

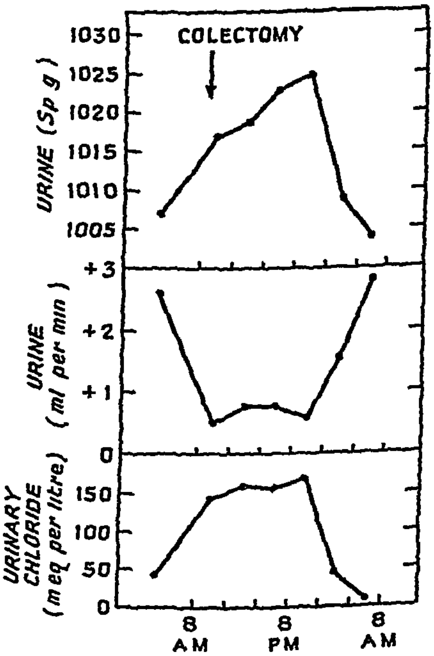

Fig 2—Data from case 10 The first observations were made on the pooled 24-hour specimen for the day preceding operation thereafter 4-hourly specimens were examined The results show the prolonged fall in urine volume and the rise in specific gravity and chloride concentration

Early Sod Retention

The 17 p given sod during the operation showed a po balance for period Lea aside cases 9 21, with a l intake, the r for the o was 70–186 m (average 10 some cases or all of retained sod was excret the next (fig 3)

Coincidin it does wi water retent this early sod retention accompanied a urine of to have removed from the register all who failed to conform modern standards before new ones had been trained would ve created chaos: to have been too lenient and weak would ve failed to bring home to the profession the necessity of provement if they were to retain their registration. Above it was necessary to improve the tests of general education the candidates, to increase the training and, to stiffen the ndards of the examination. Only in this way could a ofession be created which would attract candidates from a her social scale with greater intelligence and better ucation. That this was done gradually without chaos and ith the minimum of friction was due in no small measure the firmness, patience, and breadth of vision of the first hairman of the board, Sir Francis Champneys.

Needless to say the new supervisor of midwives and myself on fell foul of each other when she reported some of my idwives to the board; but soon I realised that the power iven to this board was being exercised with firmness tempered ith common sense and understanding and that the supervisor as encouraged to train rather than to punish. When I ecame conscious of this influence at the highest level I, and obably all others in similar posts, freely coöperated with the upervisor to the great advantage of the midwives and of the ervice. Of all my staff only one had her name removed om the register, and she thoroughly deserved it, though many were reported to the board, admonished by the chairman, and dismissed with a caution, always with good effect.

During the chairmanship of Sir Francis Champneys his despised profession of poorly educated, poorly rained women, grew into the profession as we know it oday. Gradually the period of training and the standard f general education and examination were raised, and with each step a better class of woman was attracted to he service, until now it is one of which the members ere justly proud and with its own college.

This indeed is a fitting memorial to the wise guidance f Sir Francis Champneys through the 28 years of his hairmanship. As there can be few, if any, alive today who saw at such close quarters the work of the C.M.B. nd its chairman, I feel that I must put on record what his service owes to him.

Manchester. **WM. FLETCHER SHAW.**

CHRONIC BRONCHITIS AND BRONCHIAL CARCINOMA

SIR,—During recent hospital experience I have been greatly impressed by the autopsy findings in a number of patients dying after long-continued chronic bronchitis and emphysema. These autopsies confirmed our clinical opinion that death had resulted from terminal bronchopneumonia, but the striking feature (which we had not recognised during life) was the co-existence of primary bronchogenic carcinoma.

Clinical impressions without figures to support them are, I know, apt to be misleading; but they can at least point the way towards valuable research. Therefore I feel that this observation, which may or may not be significant, merits an investigation into whether bronchogenic carcinoma is commoner in patients with long-standing chronic bronchitis and emphysema than in the rest of the population.

If this association should be proved, then we should have to revise the teaching that the possibility of bronchogenic carcinoma must be remembered in patients over 40 years of age with *recent* pulmonary symptoms or signs. Instead, whenever chronic bronchitics took "a turn for the worse" we should have to send them to hospital for detailed investigation.

This observation may have an important bearing on the vexed question of tobacco and lung cancer. We know already that all inveterate smokers sooner or later develop a greater or lesser degree of chronic bronchitis. Is it not possible that this chronic bronchitis, per se, renders the smoker especially prone to lung cancer? The analogy of the pneumoconiotic lung being especially prone to tuberculosis springs to mind.

Heathfield, Sussex. **ADRIAN V. ADAMS.**

CONGENITAL ABSENCE OF THE COMMON BILE-DUCT

SIR,—In their interesting report on this subject (Dec. 20), Dr. Durell and Mr. Halliwell point out that only 21 instances of successful operative treatment had been reported up to 1949. It is likely that the successes not reported would increase this number considerably, but nevertheless the condition is rare and operative relief much rarer.

Thus my recent experience, at the Royal Manchester Children's Hospital, of operating on 3 such cases in one week was unusual, and finding 2 of these cases suitable for treatment was even more so. After an anastomosis between Hartmann's pouch and the duodenum, using 'Nylon' sutures, both patients gained coloured stools and lost their jaundice. 1 infant died three weeks later from respiratory distress, present before operation, the cause of which was not found before or after death. The other has done well.

Since there is always a possibility of operative relief all cases with complete congenital bile-duct obstruction should be surgically explored before the liver is too severely damaged.

Manchester. **HERBERT HAXTON.**

TABLET-IDENTIFICATION BOX

SIR,—A tablet-identification box such as that described by Dr. Russell and Dr. Thorne (Dec. 27) can be very easily manufactured out of a large sheet of cardboard and the strips of perforated cardboard which Messrs. Menley & James send out with some of their proprietary preparations. The tablets can be retained in their individual recessed holes with 'Selotape.'

A tablet-identification box on these lines was of great use in a hospital which was constantly admitting patients in coma, whose relatives said they had swallowed some "tablets the doctor gave her," and also children who accidentally swallowed tablets left lying about the house. Accurate knowledge of the tablets swallowed made treatment much easier.

Winchester. **P. G. CRONK.**

HERPES GESTATIONIS AND AUREOMYCIN

SIR,—In your leading article on the Action of Antibiotics[1] you mentioned that certain effects of streptomycin and the newer antibiotics cannot be attributed to their direct action on bacteria and viruses. Thus, for example, the remissions that have been reported in leukæmia, Hodgkin's disease, disseminated lupus erythematosus, and rheumatoid arthritis cannot be direct antibiotic effects. It is also known that these drugs have some action in diseases such as scleroderma, acrodermatitis, and pityriasis rubra, and that this action cannot be explained by their antibiotic properties. In a letter in the same issue Dr. Barnard[2] discussed the same question, and put forward a hypothesis based on the "indirect" action of streptomycin and other "mycins."

We have given aureomycin to a patient with herpes gestationis and, as the result was a partial success, we think this is an example of the "indirect" action of aureomycin.

History and Clinical Findings.—A woman, aged 42, was the mother of five children. The family and personal history showed nothing of note until 1944, when she became pregnant for the sixth time. During the fifth month, irritating skin lesions developed and persisted throughout the pregnancy. She was delivered at term, but the child died immediately afterwards. The skin changes and the irritation then gradually disappeared. In October, 1951, she became pregnant again. After two months, the same skin changes appeared with severe irritation, and on March 25, 1952, she was admitted to hospital.

At this time the skin of the whole body, except the face, was covered with urticarial and papulovesicular lesions, with

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[1] *Lancet*, 1952, ii, 374.
[2] Barnard, R. D. *Ibid*, p. 387.

TABLE III—DETAILS OF LATE SODIUM RETENTION FOR DEFINITION OF "COALESCENT," "DISTINCT," AND "SEPARATED" SEE FIG 4

Case no	Morning on which body-weight finally fell below preop level	Days of positive Na balance, with low urine Na conc	Relationship between early and late Na retention
1	After 0 +4	0 +1, 0 +2	Coalescent
2	0 +3	0 +1	Coalescent
3	After 0 +6	0 +1, 0 +2, 0 +3, 0 +4, 0 +5	Coalescent
4	0 +4	0 +2 0 +3	Separated
5	0 +6	0 +2, 0 +3, 0 +4, 0 +5	Distinct
6	0 +6	0 +2, 0 +3	Distinct
7	After 0 +5	0 +2 0 +3, 0 +4	Separated
8	After 0 +5	0 +2, 0 +3, 0 +4, 0 +5	Separated
9	After 0 +6	0 +3, 0 +4, 0 +5	Separated
14	0 +2	0 +2, 0 +3, 0 +4	Separated
15	0 +6	0 +2, 0 +3, 0 +4, 0 +5	Separated
16	0 +3	Nil	Separated
17	0 +3	Nil	Separated
18	0 +3	0 +1, 0 +2, 0 +3, 0 +4	Coalescent
19	0 +4	0 +2	Separated
20	0 +4	0 +1, 0 +2	Coalescent

potassium, then it was less both in degree and duration, and coalescence with the early sodium retention occurred less often (table III) Typical cases are illustrated in fig 5

Potassium excretion studies were not carried out, save in case 20, this man was in positive potassium balance during every period except the day of operation, when the typical increased potassium excretion took place

CHLORIDE BALANCES

A positive sodium balance was always accompanied by a positive chloride balance of the same order, but the latter was sometimes the greater for no obvious reason Urinary chloride concentrations paralleled those of sodium

EOSINOPHIL-COUNTS AND THE RATIO OF URINARY URIC ACID TO CREATININE

Daily eosinophil-counts were done on 10 patients All showed a pronounced fall to about zero immediately after operation, but the rate of return to normal was very variable and bore no relation to sodium retention Urinary uric-acid creatinine ratios were estimated in the early cases only, they showed similar, but reversed, changes to those of the eosinophils (fig 6)

NITROGEN BALANCE

Nitrogen balances were studied in 6 cases all showed the usual negative balance after operation

Discussion

Many workers have noted the urinary and plasma changes occurring after operation, in association with water and salt retention Continuous balance studies, with a fixed intake before and after operation, enable the whole phenomenon to be more exactly defined and have shown that it results from the fusion of three clearly separable events—namely, primary water retention, early sodium retention, and late sodium retention Depending on the relationship of these last two, the retention of salt and water after operation may be continuous or interrupted

Most of the earlier work dealt with the postoperative retention of saline However, it was clearly shown by Cooper et al (1949) that immediately after there is retention of water, with a urine of h gravity This was also described by Moyer et al and by Ariel (1951) who also recorded the weight-gain None of these workers, howev defined the duration of this retention or th played in the whole Our own results show th water retention is independent of sodium rete is rarely maintained after the first 24 hours, cases 1 and 18 did it last longer The dilutio extracellular fluid resulting from this retention h noted by many observers, in particular by Zi (1951) Stressing that the oliguria occurred at t time as the fall in the eosinophil count, Hard suggested that its origin was adrenocortical T no reason to suppose, however, that these ev causally connected Indeed, the characteristic of primary water retention (oliguria with high gravity and electrolyte concentration) are not th of a release of cortical hormones, but of the anti hormone, and we believe that this is in fact th of this water retention

That antidiuretic hormone is released as the re anæsthesia was suggested by Burnett et al (1949) An Miller (1950) thought that this might occur during ab operations Habif et al (1951) considered that mor pethidine reduced the urine flow by *stimulating* th of this hormone Moyer et al (1949) thought that factors might be responsible for the reduction in urine There is evidence that emotional and other stimuli potentiated by morphine to produce a prolonged re antidiuretic hormone (Lewis et al 1952)

The normal stimulus to a release of this hormone is a in the osmotic pressure of the plasma (Verney and it is possible that this may occur in some cases operating-theatre However, in case 20 care was ta to give intravenous glucose throughout at such a ra to preclude this The release of antidiuretic hor

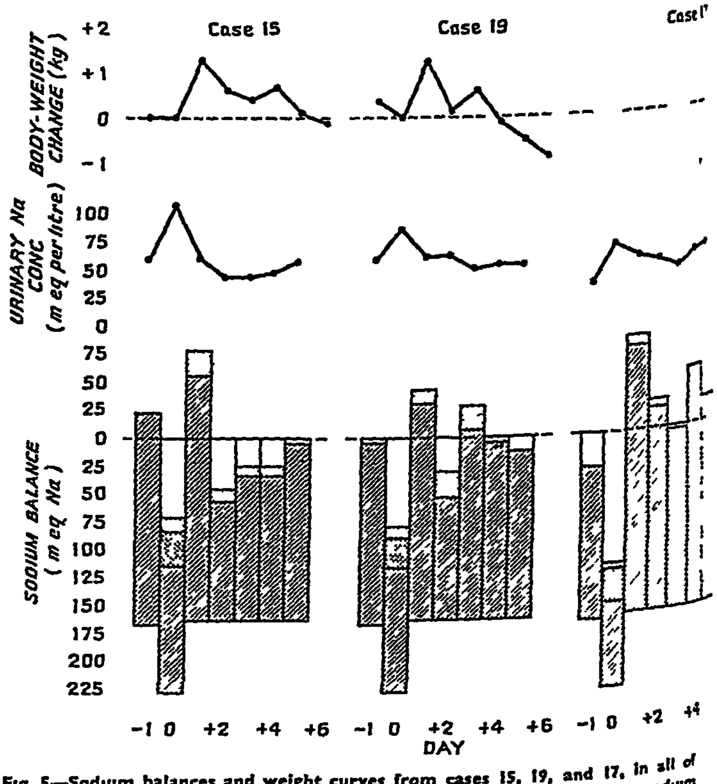

Fig 5—Sodium balances and weight curves from cases 15, 19, and 17, in all of potassium was given In every case primary water retention and early sodium *tion are clearly seen In none of the cases is late sodium retention marke* coalescence is not seen (cf fig 3)

is essential that any substance used in a plasma itute should not interfere with the functioning of normal blood components. In this connection ographic studies have shown that the polyvinyl- lidone used in plasmosan does not form complexes the plasma cations—sodium, potassium, and um—although it forms weak complexes with some valent ions, such as chromium.

full account of these studies, together with their bearing e mechanism of the passage of large molecules through glomeruli, will be published elsewhere. This work was ed out in collaboration with my colleagues, Mr. P. O. e and Mrs. Ingrid G. Ottewill, PH.D.

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Dagenham, Essex.

HUGH CAMPBELL.

Obituary

CHARLES HERBERT MELLAND

M.D. Lond., B.Sc. Vict., F.R.C.P.

r. Charles Melland, consulting physician to Man- ster Royal Infirmary, who died on Jan. 8, was ended from a family of long-living doctors practising he Bakewell area of Derbyshire. His father Frederick a practitioner of great repute who, at the age 0, presided at the gathering of old residents of the chester Royal Infirmary assembled to take farewell he old building in Piccadilly.

orn in 1872, Charles was educated at the Manchester mmar School and the medical school at Owens lege. He qualified in 1894 and held a resident and er hospital posts before he was elected physician to oats and the Northern Hospitals. One of his junior pital appointments was that of director of the infant ical laboratory at the infirmary, a very different post n that of the present day. The director cut the sections l carried out the blood-counts, and it was here that lland began to take an interest in diseases of the blood subject in which he later specialised and on which he te several papers. In 1906 he was appointed medical estigator to the Royal Commission on the care and trol of the feeble-minded. His report on the prevalence pilepsy in Manchester was included in the commission's e-book, published in 1908, and this work led to his ointment as honorary physician to the National ociation for the Feeble-minded.

le was appointed to the medical staff at the Man- ster Royal Infirmary in 1914, but the war intervened l he left to serve in the R.A.M.C. On his return he was appointed lecturer in clinical medicine at the versity. In 1921 he was elected F.R.C.P. He retired m the staff of the Infirmary in 1932, but he continued consulting practice.

V. B. writes: "A good walker and an enthusiastic nper who by no means chose pleasant pastures for the ching of his tent, Melland was keenly interested in university lacrosse and mountaineering clubs. The dents showed their appreciation by electing him sident of the athletic union, and he was president of ir lacrosse club when he died, having held the office ively for many years. Until well over 60 he could be n in an old sports coat and grey flannel trousers, king disreputable but supremely happy, keeping goal the B team courageously and in no unskilful manner. Charlie Melland was a physician of the old school; l, gentle, courteous and friendly, giving a sound nion on a difficult case. With the outbreak of the second ld war, he was recalled to duty at the Infirmary and oughout the war years he held a regular outpatient ic and helped in other ways. Those returning from Forces found him much changed; yet, despite the dicaps of ill health and advancing age, he could be nted on to attend, with a progressively lengthening d, the dinners of the Infirmary medical board and suppers of the lacrosse club. He even continued to h the matches of his beloved team and to help with uragement and sound advice. He was watching a ch at the age of 80 on a foggy December afternoon he day his last illness began. Few octogenarians will be mourned and missed so much by the present generation of undergraduates."

Dr. Melland was predeceased by his wife. He leaves a son and a daughter.

BRYAN LESLIE JEAFFRESON

M.D. Lond., F.R.C.S., F.R.C.O.G.

Mr. Bryan Jeaffreson, gynæcological surgeon to the United Leeds Hospitals, died on Jan. 7, after a short illness, at the age of 56.

He stemmed from the Jeaffresons of Framlingham in Suffolk: many of them were well-known surgeons, and the most famous of them is said to have performed the first successful ovariotomy in England, in 1836. From Hurstpierpoint College he went to St. Bartholomew's Hospital; but he spent two years as a private during the first world war, before qualifying in 1921. After serving at St. Bartholomew's as house-surgeon and resident internal midwifery assistant, he went to Sheffield, where he was senior resident officer at the Jessop Hospital, and to Birmingham, where he held a combined registrarship to the gynæcological department and a surgical unit. At this stage of his career he came under the influence of those great teachers, Miles Phillips and Beckwith Whitehouse. Meanwhile he had taken the London M.D. in 1924 and the F.R.C.S. in 1928. In 1929 he was appointed university tutor in obstetrics and gynæcology at Leeds, and after barely a year he became assistant surgeon to the Hospital for Women. There was no vacancy at the Maternity Hospital until 1934, when he became obstetric surgeon there on Dr. McGregor Young's retirement.

He examined for the Universities of Manchester and Sheffield besides his own, and had for many years been presiding examiner at Leeds for the Central Midwives Board. This was a part of his work that he particularly enjoyed, and he carried it out with skill and sympathy. He served on the council of the Royal College of Obstetricians as a member from 1943 to 1949, and in 1950 he was elected to the fellowship. Last year the organisation of the British Congress of Obstetrics and Gynæcology which was held in Leeds fell mainly on him. But the task was congenial, and when the congress was over letters from colleagues from all over the British Isles and from many other parts of the world bore witness to the signal efficiency of his work.

A. M. C. writes: "Though Bryan Jeaffreson had a keen interest in surgical technique, it was perhaps as a teacher that he reached his greatest heights. His ward rounds and outpatient teachings were always crowded. He had a quiet, clear, and dogmatic way of making his points. He was a keen member of the North of England Obstetrical and Gynæcological Society, and we often travelled to meetings together. The last occasion was last month when the council of the society elected him president for 1953, and he appreciated this election as a great honour, though with typical humility he was doubtful of his capacity to do justice to the duties involved; for despite his considerable talents, he was modest to a fault. No man could have wished for a more loyal or dependable colleague."

Mr. Jeaffreson leaves a widow, a son, and a daughter.

WILLIAM JONES RICHARDS

F.R.C.S.

Mr. Richards died on Jan. 1 at Port Talbot, Glam, where he had practised for many years as a surgical consultant on industrial insurance.

He was born in 1873 and he was educated privately and at St. Bartholomew's Hospital. After qualifying in 1897 he spent a few years in the Middlesex county mental service and then turned to surgery, taking the F.R.C.S. in 1906. He held clinical assistantships at St. Luke's Hospital and the Royal London Ophthalmic Hospital, before he settled at Port Talbot. At the outbreak of the 1914–18 war he joined the R.A.M.C. and he served in a field ambulance at Gallipoli and as a surgical specialist in Palestine with the rank of major.

D. R. writes: "Richards had built a reputation for a sound and fair opinion. He was a man of many interests, always ready to help in local activities provided it did not involve any public office. His loss will be felt in many circles and perhaps most in the Church he served so well."

wards Thus, we do not consider the number of children with "sensitivity" manifestations as any accurate indication of the real number of cases Clinical or radiological evidence of the primary infection was present at some time in 80% of the children traced

But we do think that the number of cases of miliary dissemination, bone disease, or meningitis is likely to reflect the risk of these complications in the children infected at the age of less than 5 years Thus in 1020 infected children 16 (1 5%) developed bone lesions (4 of these after treatment for either tuberculous meningitis or miliary tuberculosis) and 42 (4 1%) meningitis or miliary tuberculosis or both, within a minimal period of observation of two years If the possible range is calculated, we find that the risk is 1–2% for bone disease and 2 9–5 5% for either tuberculous meningitis or miliary tuberculosis We would have liked to be able to take our data further and to calculate the risk in children infected before and after the age of 2 years Certainly 31 of the 42 cases of miliary tuberculosis or of tuberculous meningitis occurred in children infected before the age of 2 years, but we did not know if the remaining 11 had been infected before or after their second birthday If we assumed that all the 11 had been infected afterwards, the calculated risks of the development of tuberculous meningitis or miliary were 1 in 20 at the age of less than 2 years and 1 in 30 at the age of more than 2 years, but this difference was not statistically significant

COMMENT

The chances of developing bone lesions, miliary tuberculosis, or tuberculous meningitis are the greatest hazards following the primary infection with tuberculosis It is therefore important that these risks should be measured, and we can only assume that they are not well known because the conditions for their measurement are difficult to obtain

All writers on childhood tuberculosis are agreed that the risk of illness is greatest with infection in the first year of life, remains high until the age of 2 or 3 years, and then diminishes Authors who have followed large series of children infected in the first year or two presenting in hospital clinics or outpatient departments have found a varying mortality, usually about 10–20% of children within five years (Bernard et al 1925, Asserson 1927, Myers and Kernkamp 1930, Wallgren 1938, Brailey 1940) In the Luebeck disaster, which combined heavy oral infection with extremely young age, there was a mortality of 36% (72 from 251) within a year

None of these investigations, however, represents the risk of development of these lesions in all children infected in a given population under natural conditions We have only been able to find one estimate similar in method to ours Holmdahl (1950), in a follow-up designed to study the prognosis in children who had erythema nodosum at the time of primary infection, found that in children aged less than 7 years there was a 2 9% chance of the development of either tuberculous meningitis or miliary tuberculosis within a year of infection, and 3 8% within two years After two years the risk did not increase

It does appear, therefore, that primary infection with tuberculosis in children aged less than 5 years carries a risk of the development of serious complications of about 3–5% This risk is probably not the same for all children aged less than 5 years and is likely to vary with age at infection, and possibly with other factors, such as genetic resistance, with repeated exposures or the development of other infections As yet we have not the data to make any numerical estimate of these factors

SUMMARY

The known rate of conversion in a group of children representative of the childhood population of a city has been used to estimate the number of primary infection in children aged less than 5 years

4% of all children aged less than 5 years were
—1020 from a population of 25,000

We traced 258 of these children and found that within a minimum of two years from infection, 16 (1 5%) had developed lesions of bone and 42 (4 1%) had developed either tuberculous meningitis or miliary tuberculosis, and that 36 (3 5%) had died of tuberculosis

We wish to thank all our friends, and acknowledge the great help we have received in this study, particularly from the chest physicians of the clinics in Newcastle, and the medical staffs of the children's hospitals

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INFLUENCE OF CARBOHYDRATE METABOLISM ON BACTERIAL ALLERGY

ITS RELATION TO CORTISONE DESENSITISATION

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D A LONG M.D Lond

From the National Institute for Medical Research, Mill Hill, London

HYPERSENSITIVITY to streptococcal allergens, ascorbic acid deficiency persisting into convalescence, and endocrine disturbance have all been suspected of playing significant parts in the pathogenesis of rheumatic fever Based on this broad analogy, a study has been made of bacterial allergy (as represented by sensitivity to tuberculin in B C G infected guineapigs), ascorbic acid deficiency, and the effects of various hormones upon them (Long and Miles 1950, Long et al 1951a, b, and c, Cornforth and Long 1952) The limitations of animal experiments in elucidating human pathology have been repeatedly stressed (Long 1951, 1952) Our present views, to which these limitations strictly apply, may be summarised as follows

It has been postulated that, in B C G-infected guinea pigs, cortisone and alloxan facilitate the formation of dehydroascorbic acid (Long et al 1951c), which, by inhibiting phosphoglucomutase, blocks the conversion of glucose-1-phosphate to glucose-6-phosphate—accumulation of glucose 1-phosphate being associated with diminished sensitivity to tuberculin (fig 1) (Cornforth and Long 1952) Organic phosphates representing the various stages of carbohydrate metabolism were therefore tested empirically Among these, adenosine diphosphate (A D P) was shown to have marked desensitising activity, whereas in comparable doses the closely related adenosine triphosphate (A T P) had none (Cornforth and Long 1952)

It is known that the breakdown of glycogen in the tissues (leading in the first stage to glucose 1-phosphate) is sensitive to the equilibrium between A T P and A D P and to the availability of inorganic phosphate This has been emphasised by Potter (1944), who says "It must be recognised that there is a basal rate of A T P breakdown which is balanced by the resting metabolism and that glycogen may be expected to break down only when there is a sudden shift in the A T P/A D P balance" These observations refer to intracellular metabolism but it is possible that such arguments based on intracellular physiology may apply in the tuberculin sensitive

rsity of London

Jan. 7 the following degrees were conferred :

. *Branch I (medicine).*—P. J. Banks, A. F. Barnett, Herbert Barnett Bass, Mary Bateman, S. I. Cohen, Phyllis M. E. Betty B. Dyer, F. R. Ellis, D. G. Evans, D. M. D. Evans, Felix Davies, I. T. Gabe, P. J. D. Heaf, Cherry D. Heath, Jaslowitz, R. P. V. Jayewardene, A. M. Johnson, J. C. d, Wilfrid E. Medd, L. P. A. Newborne, C. P. Newcombe, C. Nordin, M. A. Pears, Betty E. Powe, S. J. G. Semple, Shorter, K. A. Sowden, C. J. Stevenson, Frank Taylor, Thomson, Brenda D. Van Leuven, B. W. Webb.

). *Branch II (pathology).*—Aleck Bernstein, J. L. Brennan, ia C. Brown, L. H. Collier, H. R. Colquitt, J. C. Crook, Phyllis ll, David Marrack, D. J. O'Brien, F. R. Philps, K. A. Porter, ugh, M. V. Salmon, W. J. L. Sladen, C. S. Treip, S. P. B. Way, Williams, A. L. Woolf, E. A. Wright.

D. *Branch III (psychological medicine).*—A. A. Cashmore, Denham, Aleck Folkson, W. P. Gurassa, Julius Merry, *D. J. H. P. Tarnesby, D. L. C. Thomas, G. C. Turle.

D. *Branch IV (midwifery and diseases of women).*—J. C. Samuel Burke, Frank Denny, James Elstub, G. W. Garland, S. Gordon, J. M. Holmes, Rustam Moolan-Feroze, Elsie M. orpe, N. G. G. Talbot.

D. *Branch V (hygiene).*—J. D. B. Andrews, J. R. Mayers, J. Thomas.

D. *Branch VI (tropical medicine).*—J. C. L. Adams, P. B. ison, A. C. S. Hobson.

* Mark of distinction, university medal.

ersity of Bristol

e dissertations of A. O. Chick and E. J. Field for the e of PH.D. in the faculty of medicine have been approved.

ersity of St. Andrews

Heneage Ogilvie, consulting surgeon to Guy's Hospital, lon, has been appointed praelector in the faculty of cine for 1952–53. During his tenure of office he will take in the teaching and clinical work of the department of ry and deliver a series of open lectures.

al College of Surgeons of England

a meeting of the council held on Jan. 8, with Sir Cecil eley, the president, in the chair, the Cecil Joll prize for was awarded to Mr. Geoffrey Keynes. A Laming Evans arch fellowship was awarded to Dr. Angus McPherson for research into the blood-flow changes in the limbs in omyelitis. A Hunterian professorship was awarded to H. R. Dew for a lecture to be delivered during his visit Sir Arthur Sims Commonwealth travelling professor in 3. Erasmus Wilson demonstratorships were awarded to V. E. Negus, Sir Frank Colyer, and Dr. B. E. Heard, and Arnott demonstratorship to Mr. L. E. C. Norbury.

he following were elected to the fellowship of the Faculty næsthetists :

r. J. G. Bourne (Salisbury), Dr. H. G. Epstein (Oxford), Prof. nando Hudon (Quebec), Dr. J. V. Mitchell (Oxford), Dr. G. xson-Rees (Liverpool), Dr. Arnold Robertson (Brisbane), Dr. A. er (New Zealand), Dr. B. N. Sircar (Bombay).

iplomas of membership were granted to A. G. N. Calder, G. Lupprian, and N. E. Pitts. Diplomas were also awarded, tly with the Royal College of Physicians, to the following :

.C.H.—Anima Banerjee.

.A.—D. E. Argent, Anima Banerjee, D. W. Barron, M. McC. rows, K. B. Chambers, C. C. D. Chandler, H. S. Cohen, E. A. per, J. S. Crawford, D. W. J. Cullingford, L. D. Davidson, H. Egerton, Sam Galloon, Rosalinde J. Harrison, Pamela M. lings, Frances S. Huxley, E. G. A. Jackson, J. W. Latham, A. L. Leatherdale, Samuel McKechnie, A. V. McVey, A. H. B. ison, R. A. Millar, A. C. Milne, P. R. H. Molesworth, Ruth phy, E. J. O'Mullane, Doreen B. Pallot, James Parkhouse, il Pearce, D. J. Pearce, Subramaniam Ponnambalam, L. T. Rees, V. H. Robinson, F. M. Sandford, P. H. Simmons, W. D. Turner, . White.

.L.O.—T. L. Bradbeer, D. C. J. Carter, G. O. Clark, D. A. nents, J. B. David, J. W. T. Dixon, Apurba Kumar Ghosh, V. Jones, Kattesomanahalli Venkatakrishnappa Krishnamurthy, n Lapper, James Littlejohn, Abdessalam Najali, J. S. Martin, W. H. Shepperd, D. W. Stuart, John Konda Suryodayam.

.P.M.—R. H. Boardman, Kunhunni Nayar Kothaneth, T. R. loy, T. L. Pilkington, J. W. Warboys.

.T.M. & H.—Hashim Barakat, Mohindra Singh Boparai, Tahir za.

.P.—J. N. Dearnaley, J. S. Elwood, M. M. Friedman, E. M. k, Jean E. D. Taylor.

yal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Jan. 5, with Dr. Andrew ison, the president, in the chair, Oon Teik Khoo and endra Chandra Mallik were admitted fellows of faculty physician.

ffield Dental Fellowships

One of the aims of these fellowships is to enable graduates medicine and science to undertake teaching and funda- ntal research on dental health and disease. The annual ue of a fellowship is between £500 and £800 a year. Further ticulars will be found in our advertisement columns.

Medical Research Council

The council invite applications for the following fellowships for 1953–54 :

Rockefeller Travelling Fellowships.—These fellowships are intended for graduates resident in this country who have had some training in research work in clinical medicine or surgery, or in some other branch of medical science, and who are likely to profit by a period of work at a centre in the United States or elsewhere abroad, before taking up positions for higher teaching or research in the United Kingdom. Fellowships tenable in the United States will normally carry a maintenance allowance at the rate of $2600 per annum for a single fellow and $3600 per annum for a married fellow. Provision will also be made for travelling and other approved expenses. Applications should reach the secretary of the council not later than March 15.

Eli Lilly Fellowships.—These fellowships, tenable in the United States, are offered on terms and conditions similar to those attaching to the Rockefeller fellowships.

Dorothy Temple Cross Research Fellowships in Tuberculosis.—These fellowships offer opportunities for study or research to British doctors who intend "to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis." The fellowships will, as a rule, be awarded to candidates who wish to make their studies or inquiries elsewhere than in the United Kingdom. They provide for the payment of a maintenance allowance at the rate of £650 per annum for a single fellow and £900 per annum for a married fellow. An allowance will also be made for travelling and other approved expenses. Applications by March 15.

Alexander Pigott Wernher Travelling Fellowships in Ophthalmology and Otology.—These fellowships are intended for medical graduates who are likely to profit by a period of work in ophthalmology or otology at a centre abroad before taking up positions for higher teaching and research in these branches of medical science. They are normally tenable for one year. A maintenance allowance at the rate of £650 per annum is offered for a single fellow or £900 per annum for a married fellow ; in addition, an allowance is made for travelling and other approved expenses. Applications by March 31.

Further information about all these fellowships may be had from the secretary of the council, 38, Old Queen Street, London, S.W.1.

Food and the Future

The second meeting in the series on this subject which is being held by the food group and nutrition panel of the Society of Chemical Industry will be held on Wednesday, Jan. 28, at 6.15 P.M., at the Chemical Society's rooms, Burlington House, Piccadilly, London, W.1, when Dr. G. A. C. Herklots and Prof. John Yudkin will discuss Present Methods of Attack on the Problem.

Positive Health Measure in Industry

The Industrial Welfare Society are holding four weekly lectures on this subject on Thursdays at 6 P.M., at their rooms at 48, Bryanston Square, London, W.1. Dr. Neil Marr will speak on Organisation of First Aid in Work Places (Jan. 22), Dr. P. Fitzsimons on Sickness Absenteeism (Jan. 29), Mr. W. F. Floyd, PH.D., on Posture and Movement in Relation to Industrial Health (Feb. 5), and Dr. F. M. Oldershaw on Health Education in Industry (Feb. 12). Further particulars may be had from the administrative officer of the society.

Nuffield Lodge

The Nuffield Foundation and the Nuffield Provincial Hospitals Trust are moving from 12 and 13, Mecklenburgh Square, London, W.C.1, on Jan. 22, 1953, to Nuffield Lodge, Regent's Park, London, N.W.1 (Primrose 8871–5). The National Corporation for the Care of Old People will also be moving to the same address from 33, Doughty Street, W.C.1. The address of the trust's Investigation into the Functions and Design of Hospitals will be 33, Doughty Street, W.C.1 (Terminus 5288) from Jan. 22 until further notice. Nuffield Lodge is the new name given, with the consent of the Commissioners of Crown Lands, to Grove House (opposite St. John's Wood Church), which the foundation has acquired for the future headquarters of itself and associated trusts.

Anglo-French Exchange Bursaries

Applications are invited for bursaries which will be awarded this year to young British doctors under the exchange scheme arranged by the French Embassy in London between the Institut National d'Hygiène in Paris and the Ciba Foundation in London.

The value of the French grants is 60,000 francs a month tax-free, and they will be awarded for periods of two to four months to doctors who wish to obtain clinical experience or carry out medical research in France. The following are members of the British selection board : Prof. Alexander Haddow, Prof. John McMichael ; *representatives* of the British Council (Dr. Margaret Suttill), the British Postgraduate Medical Federation (Dr. C. F. Hamilton-Turner), and the Medical Research Council (Dr. F. J. C. Herrald) ; joint secretaries, Miss A. M. Vidal-Hall (French Embassy) and Dr. G. E. W. Wolstenholme (Ciba Foundation). Applications should be sent before March 31 to Dr. Wolstenholme, 41, Portland Place, London, W.1.

As in previous work, the diameter of the tuberculin lesions after twenty-four hours was found to be proportional to the logarithm of the dose of tuberculin, and it was possible to estimate the degree of sensitivity by the relative positions of the dosage-response lines fitted to the mean lesion-diameters plotted against the logarithm of the dose Changes in sensitivity are measured in terms of the change in potency of standard doses of tuberculin compared with that in control animals Thus a potency ratio of 0 25 indicates a fourfold decrease, of 4 00 a fourfold increase in sensitivity The probability that ratios differing from unity indicate a significant change in sensitivity is expressed by the value of P in the tables Ratios for which P is 0 05 or less are considered significant

TABLE I—ANALYSIS OF RESULTS OF EXPERIMENTS

Expt	Agent and dose per kg body-weight	Variance ratio*	P	Potency ratio
1	ATP (10 mg) + ADP (2 mg)	< 1	—	0 925
	ATP (2 mg) + ADP (2 mg)	27 59	< 0 001	0 464
	ATP (1 mg) + ADP (2 mg)	56 54	< 0 001	0 252
2	ATP (10 mg)	< 1	—	1 09
	Alloxan (50 mg)	75 05	< 0 001	0 423
	Alloxan (50 mg) + ATP (10 mg)	< 1	—	0 912
	Cortisone acetate (5 mg)	79 81	< 0 001	0 462
	Cortisone (5 mg) + ATP (10 mg)	17 81	< 0 001	1 434
	Dehydroascorbic acid (50 mg)	60 04	< 0 001	0 519
	Dehydroascorbic acid (50 mg) + ATP (10 mg)	—	—	1 000
	Glucose 1 phosphate (0 01 mg)	162 42	< 0 001	0 325
	Glucose 1 phosphate (0 01 mg) + ATP (10 mg)	182 46	< 0 001	0 312
3	Insulin (2 units) injected 0 hours before tuberculin	2 14	>0 10	1 23
	Injected 2 hours before tuberculin	7 42	< 0 05	0 596
	Injected 4 hours before tuberculin	18 99	< 0 001	0 500
	Injected 6 hours before tuberculin	49 18	< 0 001	0 458
	Insulin (2 units) in ascorbic acid deficient guineapigs injected 6 hours before tuberculin	5 03	> 0 05	1 445
	Insulin (2 units) injected 6 + mg) d 6	1 26	> 0 20	1 18
	hours before tuberculin + *ATP (10 mg)*	43 07	< 0 001	2 06
4	Alloxan (50 mg)	51 28	< 0 001	0 466
	Alloxan (50 mg) + insulin (2 units)	< 1	—	1 182
	Cortisone acetate (5 mg)	92 03	< 0 001	0 295
	Cortisone + insulin (2 units)	9 38	< 0 05	1 953
	Dehydroascorbic acid (50 mg)	84 97	< 0 001	0 249
	Dehydroascorbic acid (50 mg) + insulin (2 units)	< 1	—	1 034
	Glucose 1 phosphate (0 01 mg)	53 02	< 0 001	0 366
	Glucose 1 phosphate (0 01 mg) + insulin (2 units)	61 38	< 0 001	0 364
5	Growth hormone (10 mg per kg) injected 0 hours before tuberculin	3 47	> 0 05	0 733
	Injected 3 hours before tuberculin	129 07	< 0 001	0 14
	Injected 9 hours before tuberculin	214 07	< 0 001	0 08
	Injected 12 hours before tuberculin	559 11	< 0 001	0 04
	Growth hormone (10 mg) at 0 hours + cortisone acetate (5 mg)	270 17	< 0 001	0 084†
	Cortisone acetate (5 mg)	25 24	< 0 001	0 545
6	Growth hormone (10 mg) injected 6 hours before tuberculin	163 35	< 0 001	0 279
	Growth hormone (10 mg) + ATP (5 mg)	111 09	< 0 001	0 346
	mg) + *(150 mg)*	*171 94*	*< 0 001*	*0 287*
	mg) +	81 52	< 0 001	0 332
	Growth hormone (10 mg) in ascorbic acid deficient animals	51 82	< 0 001	0 253

* Ratios of "between treatments" variance to error variance

† Cortisone acetate + growth hormone produced effects significantly greater than either alone
Alloxan + growth hormone also produced an effect significantly greater than either alone
These synergistic effects did not occur in ascorbic acid deficient guineapigs

TABLE II—CONDITIONS IN WHICH DESENSITISATION
WITH THE AGENTS TESTED

Agent and dose per kg body weight	Normal diet	Ascorbic acid deficient diet	Reduced glutathione (150 mg per kg)	ATP (10 mg per kg)	[illegible]
Alloxan (25–50 mg)	+	–	–	–	–
Cortisone acetate (5 mg)	+	–	–	–*	–
Dehydroascorbic acid (50 mg)	+	+	–	–	–
Glucose 1 phosphate (0 01 mg)	+	+	+	+	–
Growth hormone (10 mg)	+	+	+	+	–
Insulin (2 units) (compensatory phase succeeding hypoglycæmia)	+	–	–	–*	

+ = desensitisation – = no desensitisation
* Sensitivity significantly *greater* than in controls

RESULTS

Adenosine Triphosphate

The ATP used in these experiments contained a small proportion of ADP which was taken into account when calculating the amounts of the two substances

The simultaneous injection of ATP (1 mg per kg body-weight) and ADP (2 mg per kg) caused a significant fourfold diminution in sensitivity, the effect was halved when the dose of ATP was doubled and abolished by a tenfold increase (experiment 1 table I) Thus, by increasing the ratio of ATP to ADP, desensitisation was prevented

The injection of ATP (10 mg per kg) did not in itself influence sensitivity, but in cortisone treated animals (5 mg per kg), it not only abolished but significantly increased sensitivity to tuberculin, however, it merely abolished the desensitising action of alloxan (50 mg per kg) and dehydroascorbic acid (50 mg per kg), and it did not influence that of glucose-1-phosphate (0 01 mg per kg) (experiment 2). These results, excluding the marked hypersensitivity in animals treated with both cortisone and ATP, had, as already stated, been expected The explanation of these effects may perhaps be inferred by considering the mechanism by which ATP may inhibit glycogen breakdown Stimulation of the hexokinase reaction by ATP leads to the disappearance of inorganic phosphate fixed during the later oxidative stages of glucolysis Cori and Cori (1940) showed that, when the ratio of inorganic phosphate to glucose-1-phosphate falls below a certain level, glycogen splitting (i e, production of glucose-1-phosphate) ceases and glycogen synthesis occurs The reason for the special effect of cortisone may be that (unlike alloxan or dehydroascorbic acid) it induces *synthesis of glucose from protein* Fuel is the provided for the hexokinase reaction and more inorganic phosphate disappears Some of the glucose mobilised by cortisone is known to be converted through glucose-1 phosphate to glycogen, but in the special circumstance under discussion this should not cause accumulation of glucose 1 phosphate, the concentration of which would remain low so long as there was a shortage of inorganic phosphate

Insulin

Insulin (2 units per kg body-weight) injected at the same time as the tuberculin (0 hours) did not significantly influence sensitivity, but injected four or six hour beforehand, it markedly depressed sensitivity (experiment 3) This experiment was repeated and tuberculin sensitivity was *plotted* against blood-sugar levels (fig 3) as hyperglycæmia succeeded hypoglycæmia, sensitivity

TOPERATIVE WATER AND SODIUM RETENTION

P. Le Quesne
A. Oxfd, F.R.C.S.

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many years it has been known that after surgical tions there are changes in the metabolism of water alt. Pringle et al. (1905) first observed the oliguria ing operation. In more recent times interest in the ct was stimulated by the work of Coller et al. (1936) of Avery Jones and Naunton Morgan (1938), and that time numerous studies have been made. ever, from the accumulated evidence no clear picture e nature and magnitude of these changes could be n. We therefore planned to investigate this problem the simplest methods, and maintaining as far as ble a fixed intake of water and electrolytes before, ig, and after operation. This intake was designed as the ideal one for routine use, but to demonstrate uivocally any depression of excretion which might r postoperatively.

MATERIAL

ses of gastrectomy in men form the basis of this , as their study involved the least departure from al routine.

group of 21 routine admissions to a general surgical was studied. Of the 21 patients, 19 underwent otal gastrectomy for benign peptic ulceration, 1 sion of the sigmoid colon for carcinoma, and 1 inguinal iorrhaphy. All the patients were well-nourished ; their average age was 50·5 years, the range being 4 years.

ll the patients were operated on under general sthesia, a wide variety of agents being used. All ived a preoperative injection of either morphine or idine (with atropine or scopolamine), and postatively all received either of these drugs as required. lifference in our results could be detected from these ing combinations.

Methods

alance studies were made from 8 A.M. to 8 A.M. for days before operation and 1–8 days afterwards ; ughout this article the word "day" implies such a nce period. The day of operation is termed day 0. he operation began at 9 A.M. in all but 2 cases, the perative medication was given at the start of a od.

ring the preoperative days the patients were fed solely he following mixture, given by slow drip down a Ryle's for 16 hours out of the 24 :

Casinal	80 g.
Glucose	250 g.
Arachis oil (emulsified with acacia) ..	150 ml.
Ascorbic acid	100 mg.
Water to	3000 ml.

This mixture provided 2600 calories and 70 g. of protein, but no sodium or potassium salts, which were added in a known amount as required. The patients were also given a litre of water to drink in the 24 hours, making the total intake 4 litres per day.

On the day of operation and until they could be allowed to take 4 litres of fluid a day by mouth, the patients were given continuous intravenous fluids—5% glucose, normal saline, and in certain cases (group 3 below) 0·375% potassium chloride or a mixture of potassium phosphates. Oral fluids gradually replaced intravenous in the usual way, the preoperative feeding being resumed by the 4th or 5th day ; during this transition it was impossible to maintain a fixed water intake, but this was never allowed to fall below 4 litres in 24 hours. Apart from the blood given at operation the daily electrolyte intake was accurately maintained as follows :

Group 1.—In cases 1–8 160–170 m.eq. of sodium chloride (about 10 g.) was given throughout. In 1 other (case 9) this level was halved.

Group 2.—In cases 10–13 no sodium was given from the day of operation onwards.

Group 3.—Cases 14–20 received 160–170 m.eq. (about 10 g.) of sodium chloride and 100 m.eq. of potassium. On the day of operation this potassium intake was halved because of the reduced urine volume.

1 patient (case 21) undergoing herniorrhaphy was fed by mouth throughout, the diet containing approximately 85 m.eq. of sodium chloride (5 g.) per day. All patients (cases 1–20), save this last one, also received 500 ml. citrated blood during the operation, giving them an extra 60 m.eq. of sodium, 5 m.eq. of potassium, and 35 m.eq. of chloride in that period.

The volume, specific gravity, and sodium and chloride concentrations of pooled 24-hour urine specimens were estimated, and in some cases the nitrogen, uric acid, and creatinine. The sodium, chloride, and nitrogen content of pooled specimens of gastric juice, removed by routine aspiration, were also estimated. In some cases, during the first 2 hours of each period, 10 ml. of venous blood was drawn into a heparin tube for the following estimations : plasma-proteins, by the method of Phillips et al. (1950) ; plasma-chloride, by the Volhard-Harvey method ; plasma-sodium, by the method of Albanese and Lein (1948) as modified by Chalmers et al. (1951) ; and eosinophils (Randolph 1949).

The following methods were used for urinary determinations : nitrogen, micro-Kjeldahl digestion and nesslerisation ; creatinine and uric acid, King's (1951) modifications of Folin's method and of Benedict and Franke's method respectively. A flame-photometer was used for some of the later estimations of sodium and potassium.

These patients passed almost no fæces on this régime. On the 3rd morning postoperatively a small glycerin enema was

E I.—DATA FROM ALL CASES WEIGHED ON THE MORNING AFTER OPERATION, ILLUSTRATING PRIMARY WATER RETENTION AND EARLY SODIUM RETENTION

Body-weight (lb.)			Weight gain 0 to 0 +1		Urine vol. (ml.)		Urine sp. gr.			Urine Na conc. (m.eq. per litre)		Urine Na excr. (m.eq.)	
0 −1	0	0 +1	Lb.	Kg.	0 −1	0	0 −1	0	0 +1	0 −1	0	0 −1	0
125·3	125·8	130·9	5·1	2·3	3430	975	1·003	1·021	1·009	41	78	143	55
154·0	153·1	156·8	3·7	1·7	2530	950	1·002	1·013		35			47
103·3	102·8	107·4	4·6	2·1	2700	1290	1·003	1·013		17			93
122·6	122·4	126·0	3·6	1·6	2680	890	1·005	1·019		67			87
129·3	129·6	134·3	4·7	2·1	4310	560	1·005	1 [illegible]		50			83
196·0	195·6	197·4	1·8	0·8	3660	1674	1·007	1·01		47			100
128·1	127·6	132·1	4·5	2·0	3240	1000	1·005	1		57			79
148·8	148·4	151·3	2·9	1·3	3700	740	1·003	1		43			59
96·5	96·5	99·4	2·9	1·3	3180	1075	1·004	1		60			114
168·1	168·4	170·9	2·5	1·1	2730	1105	1·009	1		81			80
120·3	120·5	125·4	4·9	2·2	3850	1150	1·005			[illegible]			79
126·9	124·2	126·4	2·2	1·0	3535	1880	1·003			[illegible]			1
131·0	130·5	133·2	2·7	1·2	2750	1300	1·005			[illegible]			
127·1	126·4	129·4	3·0	1·4	3090	1450	1·006			[illegible]			
179·3	179·7	182·1	2·4	1·1	1550	690	1·009						

hormone and of cortisone are brought about by different and synergistic mechanisms *Their site of action is therefore likely to be different* We suggest that, in contrast to the action of cortisone, growth hormone blocks hexokinase activity, and that under its influence the body relies for its energy to a greater extent upon glycogen breakdown, *associated with glucose-1-phosphate formation* This would explain the synergistic effect of growth hormone with both cortisone and alloxan, since blocking phosphoglucomutase in an animal which is breaking down glycogen will cause an accumulation of glucose 1-phosphate and also oppose A T P formation

SUMMARY

Using the response to intradermal tuberculin as a measure of allergic hypersensitivity in albino guineapigs *injected with* B C G, *we find that*

(1) Single subcutaneous injections of adenosine diphosphate diminish sensitivity This desensitising action is first diminished and then abolished by the simultaneous injection of increasing amounts of adenosine triphosphate

(2) Single subcutaneous injections of adenosine triphosphate prevent desensitisation by alloxan, cortisone acetate, and dehydroascorbic acid They do not influence desensitisation by glucose-1-phosphate

(3) Single subcutaneous injections of adenosine triphosphate not only abolish desensitisation by cortisone acetate but actually increase hypersensitivity

(4) Single subcutaneous injections of insulin do not in themselves significantly influence sensitivity The compensatory phase that succeeds insulin hypoglycæmia is associated with desensitisation

(5) The *desensitisation that succeeds insulin* hypoglycæmia is thought to be due to naturally liberated cortisone, since it does not occur in ascorbic-acid-deficient animals, is prevented by injection of reduced glutathione, and is intensified by injection of adenosine triphosphate

(6) Single subcutaneous injections of insulin prevent desensitisation by alloxan and dehydroascorbic acid, they not only prevent desensitisation but intensify sensitivity in animals treated with cortisone acetate, and they are without effect on the desensitising action of glucose-1-phosphate

(7) Single subcutaneous injections of growth hormone depress sensitivity to tuberculin This action was unaffected under our experimental conditions by injection of reduced glutathione, A T P, or insulin, or by ascorbic-acid deficiency

(8) In desensitisation, growth hormone (given in single subcutaneous injections) has a synergistic action with either cortisone acetate or alloxan

Our present hypothesis (see fig 2) provides a convenient summary of these facts We have previously suggested that cortisone facilitates the oxidation of ascorbic acid to dehydroascorbic acid, which inactivates phosphoglucomutase, and thus blocks glycogen breakdown and increases the tissue concentration of glucose 1-phosphate—which is intimately concerned with desensitisation We now suggest that adenosine triphosphate and insulin *oppose* this desensitisation by stimulating hexokinase activity, leading to a disappearance of inorganic phosphate which would otherwise be used for glucose 1-phosphate formation from glycogen This effect is actually enhanced by the glucose formed from protein under the influence of cortisone, more glucose being thus provided for the hexokinase reaction

The desensitisation produced by adenosine diphosphate and by growth hormone is ascribed to the effect of these substances in *causing breakdown of glycogen to* glucose-1-phosphate, with the hormone, at least, this effect is considered to be due to inhibition of hexokinase activity

We are indebted to Dr Knud Tolderlund of the State Serum Institute, Copenhagen, for the B C G, to Messrs Armour, of Chicago and London, for a generous gift of growth hormone, to Dr A Morrison, of Roche Products Ltd, Hertfordshire, for alloxan, dehydroascorbic acid, and red glutathione, *to our colleague Dr R Porter for the m and to Prof F G Young,* F R S, *for some highly p* growth hormone

We are greatly indebted to Miss M V Mussett for stat analyses not only on the experiments described here also on a large number of unquoted confirmatory experim *on which these observations are based*

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THE PREVENTION OF POSTOPERATIVE PULMONARY ATELECTASIS *

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IN the forty years since postoperative pulmonary atelectasis was recognised by William Pasteur at the Middlesex Hospital (Pasteur 1908, 1910) there has been *little change in the incidence of this complication* despite advances made in surgery and anæsthesia and the introduction of antibiotics

The prevention and treatment of this condition is important because atelectatic areas readily become infected, leading to bronchopneumonia (Coryllos 1929, 1930)

Segmental atelectasis is the common postoperative pulmonary abnormality and it was found in 94% of patients who developed pulmonary complications after abdominal operations (Palmer 1952) It results from occlusion of the smaller bronchi by retained secretion and the absorption of air distal to the block (Coryllos 1929, 1930) The lesion is commonly basal and unilateral, but it may be bilateral and involve segments of the middle lobe or lingula (Palmer and Sellick 1952b)

We describe here a method for the *prevention* of postoperative atelectasis It is based on the hypothesis that, if the factors which favour the retention of sputum in patients after operation can be overcome, atelectasis should seldom occur

ÆTIOLOGY

Table I shows that the many factors concerned in the production of atelectasis ultimately have their effect by causing retention of sputum We consider that a deficient expulsive mechanism, a reduction in bronchial calibre, and qualitative or quantitative changes in the bronchial secretion are all of great importance

The cough reflex is the mechanism by which excess secretion is normally removed from the large bronchi (Ballon 1939, Bullowa 1944) After *abdominal* operations coughing is restricted owing to pain from the wound and the cough is rendered weak and ineffective by the semirecumbent posture, impaired diaphragmatic gravity and sodium concentration (fig. 3), these being reversed on the second day. A high sodium concentration therefore coincides with a ium excretion on the day of operation, while rinary sodium concentration may occur with a retion on the next day.

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* Part of this work was included in a thesis for the degree of M D Camb by one of us (K N V P)

lium Retention

ell as this early retention, there was a later, more ed, period of sodium retention characterised by sodium balance, low urine sodium concentration, ter retention with corresponding weight changes. egan on 0+1 or 0+2, and therefore might ier separated from the early sodium retention king the excretion on 0+1, might coalesce with rly phase. It might be maximal on any of t few postoperative days, and its duration was e. These variations are illustrated by cases 7, 5, (fig. 3). *It will be seen that in cases 5 and 1 there* ntinuous postoperative salt and water retention, to the coalescence of three separate events.

t this later retention is primarily one of sodium and water is shown by fig. 4, illustrating the data from 3, in which the patient received no sodium for 4 fter operation. Here the weight fell steadily as the of the low calorie intake, despite the fact that as water was given as in the other cases.

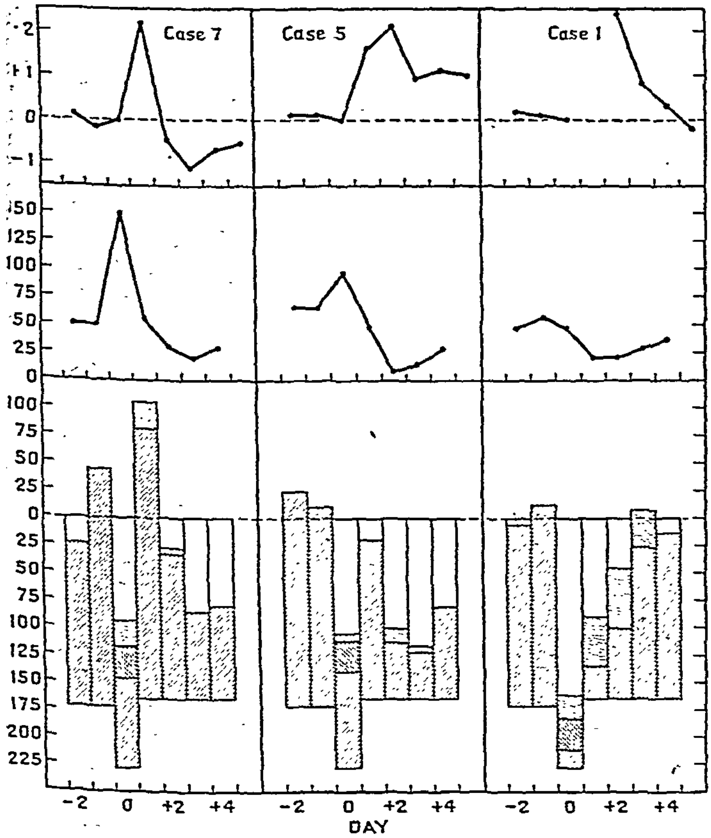
INFLUENCE OF POTASSIUM INTAKE

The effect of giving potassium can be seen by comparing the results in cases 14–20, where this ion was given as described, with those in cases 1–9 where none was given.

Reference to table I shows that "primary water retention" occurred in both groups, though it was slightly less in the group receiving potassium. Applying *the "t" test of significance of the difference* between the means of small samples (Fisher 1946), $n = 10$; $t = 2{\cdot}873$; $P < 0{\cdot}05$, suggesting that the difference between the two groups is significant.

Potassium deficiency has been shown to cause sodium retention (Black and Milne 1952), but our observations on other cases (to be published later) show that the time of this retention is variable. Presumably this was the cause of the preoperative sodium retention in cases 3 and 4, but postoperative retention occurred whether or not potassium was given. "Early sodium retention" occurred in both groups, the average being 95 m.eq. in the group receiving potassium as against 122 m.eq. in the other. Applying the same test as above, $n = 12$; $t = 1{\cdot}74$; $P > 0{\cdot}05$. Even if no allowance were made for loss of sodium on the operating-table, P is still greater than 0·05.

"Late sodium retention" was the only one of the three phases which was greatly modified by giving



—Sodium balances and weight-changes in cases 7, 5, and 1: in all three cases the ght is adjusted to zero on the morning of operation. In case 7 early and late sodium ntion are clearly separated, in case 5 they are distinct, whereas in case 1 they e coalesced.

ary water retention and that secondary to late sodium retention are lected in the weight-changes. In a 5-day period on an intake of only 100 g. icose the normal subject loses nearly 200 m.eq. sodium (Gamble 1951). e urinary sodium excretions on the day of operation and the day after it the reverse of what might be expected from the urinary concentrations, ing to primary water retention followed by water excretion.

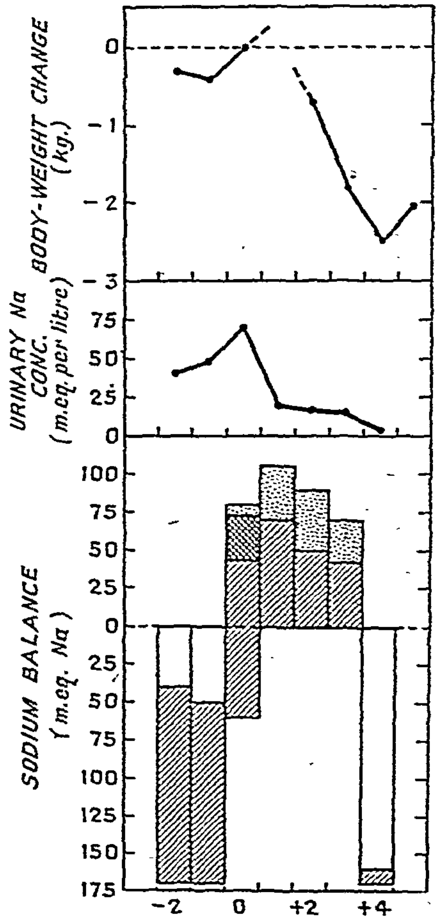


Fig. 4—Full data in case 13, in which no sodium was given after operation apart from that in a blood-transfusion. Although the water intake was maintained throughout at 4 litres per day the weight fell steadily, showing that water is not retained after the first 24 hours in the absence of sodium retention (cf. fig. 1).

tion in patients who develop atelectasis (Palmer and Sellick 1952b)

Preoperative Treatment

(1) Oral inhalation of 1 ml of 1% solution, of isoprenaline ('Neo-Epinine Solution No 1,' Burroughs Wellcome & Co) by means of a hand inhaler three times a day

(2) This is followed by fifteen to twenty minutes' postural drainage The foot of the bed is raised at least 18 in with blocks or a metal stand The treatment consists in clapping and vibration percussion to the chest wall, especially the basal regions, in the expiratory phase of respiration This is done with the patient in the two lateral positions (side-lying) and prone Five to ten minutes' treatment is given in each position This treatment should be continued thrice daily until no sputum is produced when the patient is tipped

Although patients may not confess to a productive cough, sputum is usually produced when they are tipped Many patients with chronic bronchitis have been seen who produced two or three ounces of mucoid or mucopurulent sputum when tipped for the first time After a week's treatment, no sputum was produced, the rhonchi disappeared, and the breathing was much easier Severe cases of bronchitis may require fourteen days' preparation before the operation

All cases should have 1 ml of isoprenaline by inhalation and be tipped immediately before the preoperative injection Very occasionally patients react to the isoprenaline with tachycardia, pallor, and restlessness The first dose, therefore, should be given slowly If there is a reaction, 0 25 ml can usually be given without any side-effect In emergency abdominal surgery postural drainage may be contra-indicated, but the patient should be given a full dose of isoprenaline by inhalation

Postoperative Treatment

(1) As soon as consciousness is regained, the patient should be given an inhalation of 1 ml of 1% isoprenaline, and this is repeated six-hourly

(2) When his general condition permits (usually from six to twelve hours after operation) postural drainage is given six-hourly If the prone position is not tolerated, the treatment should be given in both lateral positions

Treatment is continued as long as sputum is produced on tipping All patients should have at least five days' treatment, and it is essential that during the first twenty-four hours the treatment should be thorough If there is clinical or radiological evidence of atelectasis, it should be given hourly If the affected portion of the lung has not expanded clinically within twelve hours (shown by the return of normal breath sounds) bronchoscopy should be considered

This regimen proved very satisfactory in a small number of high-risk cases in which the patients were not considered fit for operation because of the condition of the chest It was therefore decided to test its efficiency in a controlled series of cases

INVESTIGATIONS

An unselected consecutive series of 180 patients admitted for repair of inguinal hernia or for partial gastrectomy for peptic ulcer were divided into two groups with the help of tables of random numbers (Fisher and Yates 1938) These groups were treated as follows

Group E postural drainage and the inhalation of isoprenaline before and after operation (as described above)

Group O breathing exercises before and after operation

All the patients were given procaine penicillin 600,000 units b d before and after operation as a routine

The sex-incidence and age incidence and the number of smokers, bronchitics, and hernia cases were satisfactorily distributed in the groups (table II) Each patient was examined clinically before operation and thereafter daily The clinical diagnosis of atelectasis is difficult during the first twenty-four hours after operation, when it is most likely to develop (Stringer 1947, Palmer 1952) We have, therefore, relied on ra logical findings X-ray films of the chest were tak before operation and, with a portable apparatu, af the operation Minimal changes, such as promin of the basal markings and slight elevation of the d phragm, which have been reported as normal ra logical findings after abdominal operations (Muller et al 1929), were not considered to constitute any abnormal Only unequivocal radiological evidence of atelecta was accepted, and the films were reported on by t same radiologist, who did not know to which treatm group the patient belonged

TABLE II—COMPARISON OF TWO GROUPS OF UNSELEC PATIENTS

Group	No of patients	No with history of bronchitis	No of smokers	No of females	No of hernia cases	[illegible]
E	90	44	67	19	22	[illegible]
O	90	39	59	13	24	[illegible]
		$\chi^2 = 0\ 56$ n = 1 P > 0 50 Not significant	$\chi^2 = 1\ 69$ n = 1 P > 0 10 Not significant	$\chi^2 = 1\ 46$ n = 1 P > 0 20 Not significant	$\chi = 1\ 17$ n = 1 P > 0 20 Not significant	

Of the group E patients 8 (9%) showed radiolog evidence (table III) of atelectasis, compared with (43%) of group O None of the patients in group E had a productive cough lasting a week or more af operation, whereas this was present in 30 (33%) of group O

This regimen is clearly effective in preventing po operative atelectasis It is successful because it enab the patient to remove secretion from the lungs afte the operation In high-risk cases the amount of sputu is reduced by preoperative treatment

Aronovitch (1945) and Scurr (1951), using a broncho-dilator alone, reported good results in the preventi of atelectasis If atelectasis could be prevented by using isoprenaline alone, the treatment would b simplified An experiment was therefore undertake to determine whether postural drainage with vibrat and clapping percussion alone or isoprenaline by inhalation alone was effective in preventing atelecta

160 consecutive unselected patients undergoing an operation for the repair of inguinal hernia or for partial gastrectomy for chronic peptic ulcer were divided into four groups with the help of tables of random numbers (Fisher and Yates 1938) These groups were treate as follows

Group 1 isoprenaline by inhalation alone before and afte operation

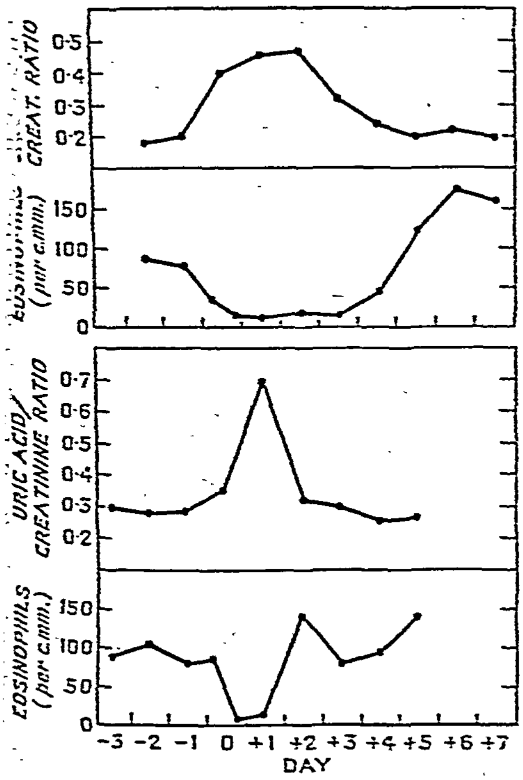
Group 2 isoprenaline and postural drainage and vibrator percussion as described above

Group 3 postural drainage with vibratory and clapp percussion alone before and after operation

Group 4 breathing exercises before and after operatio All the patients were given procaine penicillin and were examined clinically and radiologically before and after operation as in the previous experiment

Table IV shows that there was a satisfacto [illegible] tion of high-risk cases in the groups Much ex

The outcome of this experiment (table V) large bro result of the previous experiment that the ominal op of atelectasis in the group treated with [illegible] pain from the wo by the physiotherapy regimen [illegible] and ineffective by the have arisen by chance (P< paired diaphragmatic motion evidence that either the [illegible] or isoprenaline alone is [illegible]ded in a thesis for the degree exercises in preventing ate (K N V P)



5—Eosinophil-count and urinary uric-acid/creatinine ratio in 2 es undergoing gastrectomy. The characteristic fall of eosinophils the day of operation is shown; but the return to normal was st variable, and bore no apparent relation to the extent or duration sodium retention. The uric-acid/creatinine ratio showed reversed : similar changes.

no less prolonged than in other cases, thus showing : hypertonicity is not the essential factor. Morphine, sthesia, trauma, and emotion are probably the ortant stimuli.

he postoperative retention of salt has often been estigated. In 1944 Coller et al. clearly stressed the ger of giving too much salt in this period, and reported ses made œdematous in this way. Wilkinson et al. 49) related the sodium retention to the postoperative ogen loss, and suggested that both were parts of a plex reaction to trauma—an aspect which has been lied in great detail by Moore and Ball (1952). Search published work has not disclosed any description of separable episodes of sodium retention, though some lished balance studies, particularly those of Howard Mason (1946), show both to have occurred. Indeed, s possible to distinguish in their studies examples of three patterns of sodium retention that we have cribed (separated, distinct, and coalescent retention). he evidence that postoperative sodium retention is ely adrenocortical in origin is considerable (Moore Ball 1952). In particular, the increased excretion of assium and nitrogen, the fall in circulating eosinophils, rise in the uric-acid/creatinine ratio, and the increased nary excretion of glycogenic corticoids are all conent with this hypothesis. Since our results show that ium retention often occurs in two phases, some dification of this hypothesis appears necessary.

t is possible that the hypotonicity resulting from ter retention during the early part of the day of ration stimulates sodium retention later in this iod, and so causes the early sodium retention. But lland and Stead (1951) have shown that hypotonicity uced after pitressin injection does not cause sodium ention. Hæmodynamic factors may be largely responle for early sodium retention. Coller et al. (1943) have shown that the glomerular filtration-rate falls during anæsthesia, and this in itself will reduce the sodium excretion (Chalmers et al. 1952). But the glomerular filtration-rate rapidly returns to normal after operation (Habif et al. 1951, Ariel and Miller 1950), and the period of depression may not therefore account for more than a part of the retention observed. Moreover, the excretion of potassium which has been shown to take place on the day of operation is one of the most characteristic features of the onset of adrenal stimulation (Bartter and Fourman 1951), and it is difficult to believe that the latter plays no part in causing this sodium retention. It therefore seems likely that early sodium retention is due in part to hæmodynamic factors and in part to adrenocortical release.

Late sodium retention occurs at a time when the sweat sodium concentration is falling (Johnson et al. 1950); and this again is known to result from the salt-retaining action of corticoids, suggesting that the late retention is cortical in origin. If, then, cortical release is partly or wholely responsible for both periods of sodium retention, it is difficult to see why they should ever be separated by a day of negative balance. The most likely explanation appears to be that the adrenal salt-retaining mechanism becomes fully effective only after a day or two, and that the early sodium retention is largely due to other factors. The whole postoperative disturbance of salt and water metabolism is probably due to three factors—namely, a release of antidiuretic hormone, renal hæmodynamic factors, and adrenocortical release; during the first 48 hours after operation the effect of the last is overshadowed by that of the first two, but becomes clearly apparent thereafter.

As mentioned above, potassium deficiency by itself can cause sodium retention, and there is little doubt that this has been partly responsible for the postoperative retention observed by many previous workers. However, potassium deficiency is not the main cause of postoperative sodium retention; it merely augments it.

It is possible that the period of relative starvation following operation might in itself cause sodium retention. Newburgh (1942) found that some cases of obesity failed to lose weight initially when put on a low-calorie intake, and suggested that salt and water retention was responsible for this. However, this only occurred in some cases; and Duncan et al. (1948), who gave a salt mixture to 2 patients during starvation, observed a negative sodium balance under these circumstances.

It is not clear whether the water and sodium are retained in the extracellular or intracellular compartment. Our data are insufficient to allow calculation of the exact amount of water retained; but a reasonable estimate could be made in many cases, and in all of these correlation with the sodium balance suggested that the retention of both was largely extracellular. Moreover, the fact that the chloride retention was usually greater than that of sodium also suggests that the retention was in the extracellular space. Indeed this discrepancy between the sodium and chloride balances even suggests that there may be a shift of sodium from the intracellular to the extracellular compartment. This hypothesis—that there is a considerable enlargement of the extracellular space after operation—is consistent with the findings of Lyon et al. (1949) and of other workers that the thiocyanate space is greater at this time. In addition, Levitt and Bader (1951) have shown that the administration of either A.C.T.H. or cortisone leads to an enlargement of the extracellular fluid volume, with a shift of sodium from the cells.

There are important practical applications of this work, which will be discussed in detail elsewhere. In planning the postoperative intake it must be borne in mind that the patient's ability to excrete salt is greatly reduced in this period, and that there is a similar inability to excrete water during the first 24 hours after operation.

Either a bronchodilator—e g, isoprenaline—alone or physiotherapy regimen (postural drainage and vibratory and clapping percussion) alone was not more effective than breathing exercises in reducing atelectasis in 160 patients undergoing operations for inguinal hernia or for partial gastrectomy

It is concluded that postural drainage with vibratory and clapping percussion to the chest wall and a bronchodilator in combination are necessary for the prevention of postoperative atelectasis The reasons for this are discussed

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PRACTICAL PENICILLIN

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It is hoped that this paper may do something to reduce the long stream of patients with minor sepsis entering the casualty departments of hospitals, shorten the time lost to the patient and the community by ill health, and be of practical help to general practitioners It is written to show that procaine penicillin in aqueous suspension is a very serviceable weapon against acute infections

Previously I showed (Cohen 1950) that 300,000 international units of procaine penicillin in aqueous suspension will almost always give an effective blood-penicillin level for twenty-four hours, and that a single daily injection of such a suspension has big advantages over the three-hourly injection of aqueous solutions of crystalline penicillin (soluble penicillin) From the literature it was clear that large doses of procaine penicillin in *oily* suspension could be given without ill effect (Thomas et al 1951), and Cannon et al (1951) stated that twice-weekly injections provided a very effective blood-penicillin level, but when these workers used an aqueous suspension they could not depend *on an effective level after twenty-four hours* In my experience, however, this objection does not apply to the suspension now widely used I have found that, after a single injection, penicillin is present in the blood for three or four days, and that this is a basis of sound treatment not only in the outpatient department of a hospital, but also, and particularly, in general practice

TABLE I—RESULTS OF TREATMENT WITH 5 ML. OF PROC PENICILLIN AQUEOUS SUSPENSION IN HOSPITAL CAS DEPARTMENT

Condition	No of cases	Length of treatment (days)			No incised	No injected more than once
		Ave	Max	Min		
Abscess						
Axillary	9 (*4 5%*)	7	13	2	4 (*44 4%*)	
Breast	2 (*1 0%*)	8	8	8	2 (*100%*)	
Cervical	4 (*2 0%*)	11	20	3		1
Face and scalp	8 (*4 0%*)	7	23	2	1 (*12 5%*)	
Perianal	2 (*1 0%*)	5	5	4	1 (*50%*)	
Boil	32 (*16 0%*)	7	33	2	5 (*15 6%*)	1
Burn	1 (*0 5%*)	2	2	2		
Bursitis	7 (*3 5%*)	8	16	3	1 (*14 3%*)	1
Carbuncle	3 (*1 5%*)	8	10	7		
Cellulitis	4 (*2 0%*)	12	28	3	2 (*50%*)	1
Sepsis						
Arm	14 (*7 0%*)	7	16	2	2 (*14 3%*)	1
Dental	1 (*0 5%*)	4	4	4		
Hand	83 (*41 5%*)	7	34	2	31 (*37 4%*)	2
Leg and foot	30 (*15 0%*)	7	13	2	5 (*16 7%*)	2
Total	200				*54 (27%)*	9

Long et al (1950) have pointed out that, in using an antibiotic, the aim should be to bring the infection under control as quickly as possible, which necessitates adequate doses This is especially important in the treatment of severe or *fulminating infections* The same workers warn against overtreating the patient when the infection is controlled, treatment should be discontinued "Remember," they say, "in most instances the response should be prompt"

TREATMENT IN HOSPITAL CASUALTY DEPARTMENT

With these precepts in view, blood-penicillin levels were estimated at the intervals shown in fig 1 after the administration of 1 5 mega-units of procaine penicillin in aqueous suspension, in these experiments 'Distaquaine Suspension' was used The injection is one of 5 ml, but this volume can be given with little or no discomfort into the triceps or the gluteal region

Having found an adequate blood penicillin level three or four days after the injection of 1 5 mega units

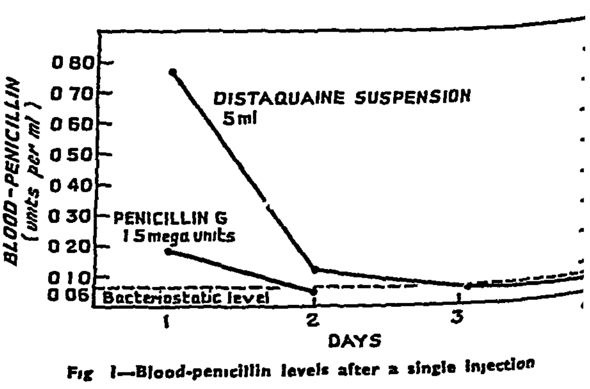

Fig 1—Blood-penicillin levels after a single injection

I—TUBERCULIN CONVERSIONS IN NEWCASTLE CHILDREN 1947–52

of ren	No. tested	No. of conversions	Total	Increase in each round (%)*
nths	960	17	17 (1·8%)	1·8
rs	900	30	47 (5·1%)	3·3
rs	810	13	60 (6·7%)	1·6
rs	800	6	66 (7·5%)	0·7

ne tuberculin testing has been done with Old reculin jelly, followed in doubtful results by an dermal test of 10 T.U. of Old Tuberculin. The ts of these tests (table I) show a conversion-rate of , at the age of 15 months, rising to 7·5% at that of ars. In table II the sample has been adjusted to the of each year and the standard error of the percentage ılated.

ıe estimate of the number of children aged less than ears tuberculin-positive in Newcastle at any given has been calculated in table III from a percentage ulated for the middle of each year. The range ıin which the true figure may fall is, however, siderable; and, though we give 1020 as an estimate, variation may be anything from 720 to 1330. It is to say, however, that in Newcastle at present nearly of the children have been infected by the end of r second year and between 7% and 8% at the end heir fifth year.

ur figure may be checked by the data published by Medical Research Council (1952). In that report children were all of school age attending State ools and not a sample of the population, and the erculin tests used were rather different—a modified ur-paper technique was used with tuberculin jelly as a t test, and as a second test 100 T.U. of Old Tuberculin s injected intradermally. These tests are both stronger ın ours and may perhaps have given a positive ction when the 10 T.U. or the application of Old berculin jelly to the cleansed skin would not have ıne so. In the two areas nearest to Newcastle, Durham tanley U.D.) had 10·6% positive reactors in the sixth ar, and Leeds 9·8%. From Hull Hardy (1950) has ported that, in a tuberculin survey of 4000 children ged 5–15, 10% were positive at the age of 5 years. e does not, however, state the composition of the oup examined or the test used. Parkes (1952), using flour-paper technique, found in Wolverhampton during 50 6·3% positive in 2923 school entrants tested with lly.

BLE II—TUBERCULIN CONVERSIONS IN NEWCASTLE CHILDREN

ge of ildren (yr.)	Tuberculin-positive (%)	Standard error of percentage	Range ± 2 S.E.	
			Minimum	Maximum
1	1·4	0·4	0·2	2·2
2	3·2	0·6	2·0	4·4
3	5·1	0·7	3·6	6·6
4	6·7	0·9	5·0	8·4
5	7·5	0·9	5·7	9·3

We therefore consider that our figure of conversion-ıtes based upon repeated testing of the same unselected ımple of the infant population of the city gives a valid asis for our estimate that 4% of all children aged less ıan 5 years were infected—about 1020 in a population f 25,000 children.

MORTALITY AND MORBIDITY FROM TUBERCULOSIS

After a careful and thorough search of all records we raced 258 of the estimated number of 1020 children ho had acquired primary infection with tuberculosis. Thus only 1 in 4 of the children were traceable at hospital or in tuberculosis contact clinic in a city where there is constant interest in childhood tuberculosis, all children in hospital have routine tuberculin tests, and all children aged less than 5 years who are in contact with a known case of tuberculosis in the family are carefully examined.

The 258 children were found through the following sources: 98 notified cases, 21 hospital cases not notified, 134 household contacts from observation clinics, and 5 other outpatients. In 201 we knew, and in another 30 cases could infer, the source of infection. All but 3 of the notified patients were in hospital, and it is unlikely that we would have missed children with recognised tuberculosis. Unless, therefore, which again is unlikely, a substantial number of children were ill and untraced, about 750 children passed through their primary infection in these five years either without illness or with so slight or temporary a disturbance of health that its nature remained undetected.

TABLE III—ESTIMATED NUMBER OF NEWCASTLE CHILDREN AGED LESS THAN FIVE YEARS TUBERCULIN-POSITIVE AT ONE TIME

Age (yr.)	No. of children	Positive at mid-point of year (%)	Estimate
0–2	10,000	1·6	160
2–3	5000	4·2	210
3–4	5000	5·9	295
4–5	5000	7·1	355
Total ..	25,000	4·1	1020

The 258 tuberculin-positive children comprised two very distinct groups: 117 admitted to hospital, most of whom were notified; and 141 who remained under outpatient supervision, few of whom were notified. More than half (170) of the 258 had been found tuberculin-positive during attendance at the contact clinics.

To the end of 1951, 39 of the 258 had died, 36 (14%) certainly from tuberculosis, and in the remaining 3 there was a strong presumption of tuberculosis. In all the fatal cases, except 4 caused by progressive primary lung lesions, the immediate cause of death was either tuberculous meningitis or miliary tuberculosis. When considering this mortality we should remember that 1949 was the first year in which streptomycin was generally available and B.C.G. vaccination started. Today this mortality of 3·5% within two years would be lower but not by more than half, and even with streptomycin available the present mortality-rate would be about 2% of children infected at less than 5 years of age.

The lesions found in the 258 children are set out in table IV, but the numbers under the various headings are obviously not of equal value or importance. Whereas we are not likely to have missed more than one or two, if indeed any, cases of miliary spread, meningitis, or bone disease, there must have been many cases of "fever of onset," temporary ill health, or failure to gain weight or loss of weight, and perhaps a few of conjunctivitis, wheezing, or even "silent" pleural effusion in young children who did not reach the hospital outpatients or

TABLE IV—LESIONS PRESENT IN 258 TUBERCULIN-POSITIVE CHILDREN AGED LESS THAN 5 YEARS

—	No. of cases
No evidence other than positive skin test	55
Primary lesions (clinical or radiological evidence):	
Chest 180, abdomen 6, cervical glands 15, skin 2 ..	203
Sensitivity manifestations:	
Erythema nodosum 8, phlyctenular conjunctivitis 10, pleural effusion 4	22
Progressive chest lesions	8
Bone and joint lesions (including 4 cases developing after tuberculous meningitis or miliary tuberculosis)	16
Miliary tuberculosis	23
Tuberculous meningitis	35
16 children had both miliary tuberculosis and tuberculous meningitis, making 42 children affected	

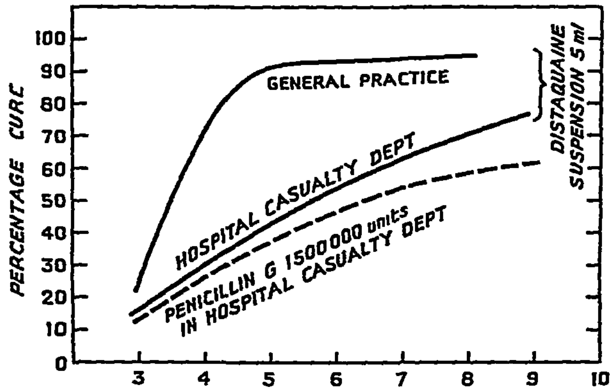

Fig 2—Percentage rates of cure

with a septic finger) had the finger opened with a needle in the surgery All the other cases treated resolved without requiring the help of hospital treatment, and 91 of the 100 cases followed up were cured at the end of five days with one injection and salt-water dressing (see table IV)

The relief on the children's faces, when they were told one injection only would be required, was sufficient reward in itself A large number of ear cases were treated Some had been discharging for months, these dried up but required more than one injection Single-injection therapy, as shown by tables I, II, and III, is not adequate in all cases Should injections subsequent to the first be necessary they should be given every fourth day

Fig 2 and table IV show the day-by-day percentage cure in the three divisions of this trial

COMMENT

The established facts show how important it is to begin treatment early, and it emphasises that the place to begin treatment is in general practice It is better to give an unnecessary injection than to wait and see whether the infection will clear up without it

When all clinical requirements are fulfilled, cost becomes important The cost of this single-dose therapy compares favourably with that of the dressings, ointments, &c, so often prescribed for the types of infection treated in these trials Of the utmost importance is the freeing of the casualty departments of busy general hospitals from the need to attend to many chronic and difficult infections It is important to the nation that workers be able to return to work quickly after absences due to minor acute infections, but the social aspects of these trials need not be emphasised in what is essentially a clinical report

SUMMARY

Trials showed that 1 5 mega-units of procaine penicillin in aqueous suspension would maintain an effective blood-penicillin level for three or four days, and that the same dose of crystalline sodium penicillin G (benzylpenicillin sodium salt) in aqueous solution was effective for twenty-four hours only

Clinical trials showed that this dose of the aqueous suspension of the procaine salt was more effective in combating infection in the outpatient department of a general hospital than was a similar dose of crystalline sodium penicillin G in aqueous solution

Moreover, a single injection of 1 5 mega units of the procaine-penicillin aqueous suspension, given by the general practitioner when the patient was first seen, led to cure of 91 cases out of 100 by the fifth day Only 1 case out of 135 required incision at hospital

In addition to the facts that only 1 patient had to go to hospital and that only 1 patient's finger, that of a baby, had to be opened, the time factor should be sidered The patients are returned to work quickly, and in some cases may altogether avoid ' ping off" Patients themselves can judge whether septic lesion is getting worse, and they can be asked report back if the necessity arises The doctor's is saved, for an injection of this type can be given in couple of minutes

My thanks are due to Mr R Kennion, Mr J B and Mr S V Unsworth, surgeons of the United Hospitals, on whose patients I have undertaken this to Dr J Sytner and his partners for allowing me the facil of their general practice, to the Distillers Company chemicals) Ltd, for the use of their laboratories and for penicillin preparations used in this work, and to Mr Grainger for his invaluable help in the laboratory

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SIMULTANEOUS AORTIC AND AXILLARY EMBOLISM

SUCCESSFUL TREATMENT FOLLOWED BY MITRAL VALVOTOMY

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WE report this case because no similar successful multiple embolectomy seems to have been published, and no other case of similar ætiology seems to have been carried to a logical conclusion by subsequent valvotomy

CASE-RECORD

Mrs A, a thin, nervous, but coöperative housewife of 41 was admitted to the Norfolk and Norwich Hospital on Dec 1 1951, under the care of Dr Branford Morgan, with congestive heart failure complicating rheumatic mitral stenosis She had been admitted several times previously for similar episodes In 1945 she had had an embolic right hemiplegia, from which she gradually and almost completely recovered

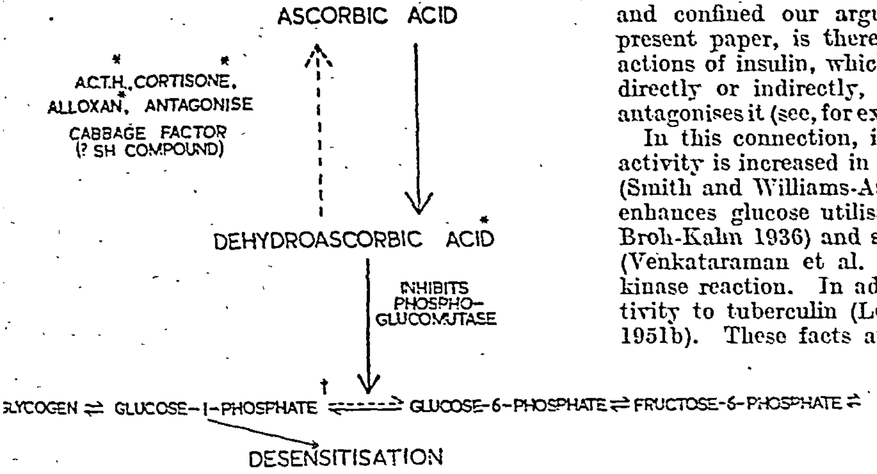
The present attack of failure was typical, with a conspicuous malar flush, rapid auricular fibrillation, and signs of mitral stenosis Under medical treatment, including full digitalisation, she progressed well, and on Dec 29 she was allowed up in a chair for the first time On this day also she developed some nausea and vomiting, due probably to digitalis

On Dec 30 at about 11 A M sudden numbness came on in the left arm and leg, and shortly afterwards in the right leg also There was little pain Both lower limbs were pulseless from the groins down, and the left brachial and radial pulses were also absent Sensation and movement of all the affected limbs were much impaired Although cold and frightened, the patient was in fair general condition fibrillation was present A diagnosis was made of multi-arterial embolism, arising from the fibrillating left auricle, and surgical help was obtained within thirty minutes of the onset of symptoms

Operation

Operation was undertaken four hours after the first symptoms appeared The anæsthetic, given by Dr B G Forres was thiopentone followed by nitrous oxide, oxygen and minimal ether, with fractional doses of gallamine ('Flaxedil')

First, the inert and spastic femoral arteries were exposed in each groin and occluded with Crile clamps Then, with the patient in the Trendelenburg position the abdomen was opened through a generous left lower paramedian incision The aortic bifurcation and the few centimetres of trunk be



* Desensitising action prevented by reduced glutathione.
† Desensitising action not prevented by reduced glutathione.

Fig. 1.

ineapig to the actions of metabolites injected extrallularly; that the extracellular injection of A.D.P. ay cause glycogen to be converted to glucose-1-phoshate and so diminish sensitivity; and that the simulneous extracellular injection of A.T.P. and A.D.P., preventing a shift in the A.T.P./A.D.P. balance, may event desensitisation.

In the present paper we show that, as the ratio of tracellularly injected A.T.P. to A.D.P. is increased, the esensitising action of A.D.P. is first diminished and then olished; in addition, injected A.T.P. inhibits the esensitising action of alloxan, cortisone, and dehydrocorbic acid, but not that of glucose-1-phosphate. hese facts are consistent with our hypothesis; for if T.P. has inhibited glycogen breakdown, blocking hosphoglucomutase will not increase the concentration the tissues of glucose-1-phosphate. On the other and, the concentration, and therefore the desensitising ction, of injected glucose-1-phosphate will be indeendent of these factors. Thus the results we expected n the basis of intracellular metabolism were achieved. t seems more probable that these organic phosphates, njected extracellularly into tuberculin-sensitive guineaigs, influence normal intracellular carbohydrate metaolism than that they produce a hypothetical series of harmacological coincidences associated with like effects. lucose-1-phosphate is a normal metabolite, but its ôle as intermediate in an important biological process ay mean that, unless the balance of the process is ppropriately disturbed, it is never free from the enzyme omplex; so even minute quantities introduced from utside may produce an effect out of proportion to the otal amounts involved in glycogen metabolism. It is ossible that cell permeability is increased in guineapigs ndergoing a severe tuberculin response, and that the rgument holds only for this condition. However, we onclude that in B.C.G.-infected guineapigs, glycogenoysis (glycogen breakdown), with resulting glucose-1-hosphate formation, is associated with diminished ensitivity to tuberculin; that injected A.T.P., by timulating glucolysis (glucose breakdown) and inhibiting lycogenolysis, antagonises this action and so prevents esensitisation; and therefore, that hexokinase hyperactivity and hypersensitivity on the one hand, and hexokinase hypoactivity and desensitisation on the other hand, are associated phenomena.

Fortunately, the actions of certain hormones upon carbohydrate metabolism in general, and upon hexokinase activity in particular, are not subject to the restrictions imposed by these problems of intracellular-extracellular relationship which have hitherto handicapped and confined our argument. The latter part of the present paper, is therefore devoted to a study of the actions of insulin, which stimulates hexokinase activity directly or indirectly, and of growth hormone, which antagonises it (see, for example, Wright 1952, Young 1948).

In this connection, it is noteworthy that hexokinase activity is increased in the tissues of thyrotoxic animals (Smith and Williams-Ashman 1951), and that thyroxine enhances glucose utilisation in the tissues (Mirsky and Broh-Kahn 1936) and stimulates the formation of A.T.P. (Venkataraman et al. 1950), which initiates the hexokinase reaction. In addition, thyroxine increases sensitivity to tuberculin (Long and Miles 1950, Long et al. 1951b). These facts are consistent with, and support, our present contentions.

The argument is strengthened by our findings (reported here) that growth hormone, which inhibits hexokinase activity, depresses sensitivity to tuberculin, whereas insulin, which stimulates hexokinase activity, antagonises the desensitising actions of cortisone, alloxan, and dehydroascorbic acid, but not of glucose-1-phosphate. Moreover, the compensatory phase that follows insulin hypoglycæmia—a phase for which the adrenal cortex is largely responsible (see, for example, Wright 1952)—is associated with desensitisation. As might be expected, this compensatory phase of desensitisation, like that produced by cortisone, does not occur in animals previously injected with reduced glutathione nor in ascorbic-acid-deficient guineapigs (cf. Long et al. 1951a and c). In addition, it can, like cortisone desensitisation, be prevented by injected A.T.P. In this connection, the observation of Kersley et al. (1951) that insulin hypoglycæmia is succeeded in rheumatoid arthritis by symptomatic relief comparable to that obtained with adrenocorticotrophic hormone (A.C.T.H.) is noteworthy.

From our experiments with organic phosphates and hormones, we conclude that sensitivity to tuberculin in B.C.G.-infected guineapigs depends on a balance between hexokinase-stimulating and hexokinase-depressing hormones, with the adrenal cortex controlling the metabolic process most intimately linked with sensitivity—namely, the concentration in the tissues of glucose-1-phosphate. Although part of the argument is based on results obtained with extracellularly injected carbohydrate metabolites, the remainder and major part is not subject to this limitation, and yet points to the same conclusions.

METHOD

Albino guineapigs of the Hampstead strain, weighing 350–550 g. and fed on a pelleted diet (Bruce and Parkes 1947) supplemented with unlimited cabbage, were injected with B.C.G. vaccine, and sensitivity to tuberculin was estimated by the method of Long and Miles (1950).

All drugs tested, except glutathione, growth hormone, cortisone acetate, and insulin, were dissolved in 1 ml. of normal saline and injected subcutaneously two hours before the tuberculin. Reduced glutathione was dissolved in gas-free distilled water and adjusted with sodium bicarbonate solution to pH 6; approximately 150 mg. per kg. body-weight, in a volume of 2 ml., was injected intraperitoneally two hours before the tuberculin. Cortisone acetate was suspended in 1 ml. of normal saline and injected six hours before the tuberculin. Growth hormone, partly dissolved, partly suspended, in 1 ml. of normal saline, was injected in the doses, and at the time-intervals, detailed in the experiments. Insulin was dissolved in 1 ml. of normal saline and injected subcutaneously at the time-intervals detailed in the experiments; the batch did not contain detectable quantities of hyperglycæmic factor. Animals treated with insulin received no food on the day of the experiment.

In this connection it is interesting to note that Ewing (1950) examined the abdominal aorta and iliac vessels from his second case on the patient's death 12 months later the terminal aorta and common iliac vessels were much narrowed and blocked by clot, high enough to include the origin of the inferior mesenteric artery Section of the thrombus suggested that it was "probably over 6 months old"

In spite of the failure to restore the pulses in the present case, the operation cannot be branded as useless or unnecessary McClure and Harkins (1943) believed the prognosis without operation to be nearly hopeless Rothstein (1935) found the recovery-rate to be only 4% from conservative measures as against 32% from surgery Ewing (1950) thinks that even these few successes without surgery are probably cases in which either the diagnosis is doubtful or the clot has broken up and passed distally In our patient the circulation in the lower limbs is so adequate that the internal iliac arteries may well have remained patent, thus giving a circulation via the gluteal vessels

The case for removing the axillary embolus rests on less secure grounds In healthy people the third part of the axillary artery can usually be interrupted without jeopardising the limb Nevertheless the clot here, as in the aorta, was several centimetres long, and must have covered the mouth of at least one major branch The brisk retrograde bleeding that followed its removal lent support to the idea that the procedure would materially enhance the safety of the limb by improving the collateral circulation It is also felt that the main vessel might for a short time maintain the nutrition of the limb while the collateral channels were developing Had the patient's condition been too precarious to allow axillary embolectomy, however, conservative measures would have had a fair chance of success

Prognosis and After-treatment

Besides the 27 successful aortic embolectomies reviewed by Taylor (1951) 2 have been reported by Ewing (1950), 1 by Dalgleish and Taylor (1951), and 1 by Shipman and Goodwin (1951) The present case brings the total to 32

Of the 32 patients at least 13 are known to have died within 3 years of operation, and several others have not been followed up This major vascular catastrophe occurs almost always in patients with crippling cardiovascular disease, by which the end-result should be measured Some workers have attacked the problem of recurrent arterial embolism by operations on the left auricular appendage, where the embolising thrombus often forms The feasibility of amputation of the appendage in dogs was demonstrated by Hellerstein et al (1948) The operation was performed in man by Madden (1949) Of his 2 patients one survived, but the other after a successful aortic embolectomy, died 9 days after the second operation Baronofsky and Skinner (1950) simplified the operation by substituting ligation for resection of the appendage, and published 3 cases without fatality These operations, however, do nothing to improve the basic heart condition According to Taylor (1951) 78% of the successful aortic embolectomies have been in cases with mitral stenosis or with auricular fibrillation, or with both On general principles one would expect the more recently developed operation of transatrial mitral valvotomy to have a place in the cases with mitral stenosis In their report on mitral valvotomy Baker et al (1952) say

> "We now regard such a history (of embolism) as one of the indications for valvotomy in the hope that less stasis in the atrium will discourage clotting"

It was on precisely such reasoning that the present case was referred to the cardiac surgical unit Many more cases and some years' observation will be necessary to determine whether the prevention of recurrent by such means is anything but a pious hope

SUMMARY

A case is described of simultaneous embolism axillary artery and at the aortic bifurcation

Multiple embolectomy was successful in sam patient and the affected limbs, and some po technique are discussed

Mitral valvotomy was subsequently performed where, with a view to improving the cardiac and preventing further embolism

Our thanks are due to Dr Branford Morgan for the case and for help in the postoperative management

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THE METATARSAL FORMULA IN RELATION TO MARCH FRACTURE

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M A, M B Camb, F R C S

J R Napie
M R C S

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THE relative protrusion of the first and second tarsal bones in the normal human foot is a much disp subject Morton (1927) is of the opinion that relati "shortening" of the first metatarsal is abnormal and potent source of foot disorders A similar view has be advanced by Bruce (1937), who states that in the norm foot the head of the first metatarsal is "on the sa transverse plane, or even a little more distal, than t of the second" On the other hand, Wood Jones (19 in discussing the metatarsal formula, denies that t so called "short" first metatarsal is in any wa abnormal, and maintains that "it is normal in man f

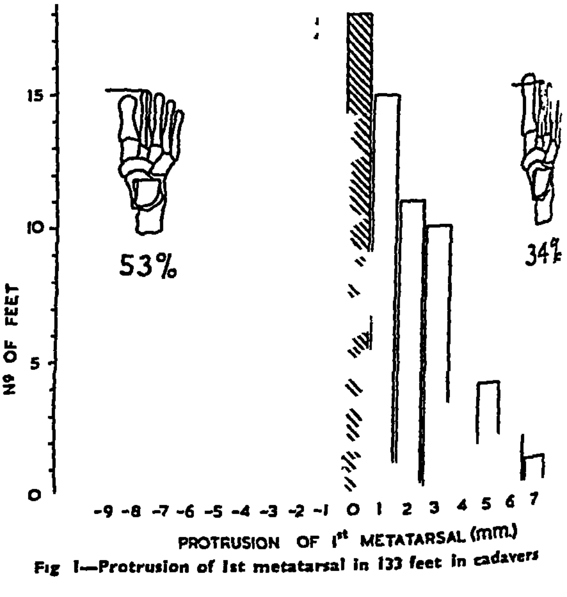


Fig 1—Protrusion of 1st metatarsal in 133 feet in cadavers

. This compensatory hyperglycæmic phase is attribut-
e to hyperactivity of adrenal cortex and medulla
, for example, Wright 1952), and consistent with
s view, the desensitisation associated with it did not
ur in guineapigs previously injected with reduced
tathione, or in ascorbic-deficient animals (experi-
nt 3) (cf. Long et al. 1951a and b). It is noteworthy
t, as in cortisone-treated animals, injected A.T.P.
used a significant increase in sensitivity (experiment 3)
ble II).

The immediate effect of insulin, during the phase of
poglycæmia, is shown consistently by a slight increase
sensitivity. In only one experiment was this increase
tistically significant; the result given in experiment 3
typical. Insulin, by stimulating hexokinase activity
d increasing glycogen storage, might be expected,
the basis of our hypothesis, to antagonise desensitisa-
n by *cortisone, alloxan, and dehydroascorbic acid.*
sulin is thought to stimulate phosphorylase and so
omote the conversion of glucose-1-phosphate to
ycogen (see, for example, Young 1948). Such an effect
as not apparent in our experiments, extracellularly
jected glucose-1-phosphate proving fully active in
nimals treated with insulin (experiment 4). Insulin
evented desensitisation by alloxan and dehydro-
corbic acid, and significantly increased sensitivity in
rtisone-treated animals (experiment 4) (table II).

Presumably this effect, like that of A.T.P. under similar
nditions, is due to the hexokinase-stimulating activity
insulin, reinforced by glucose derived from protein
nder the influence of cortisone.

owth Hormone

Growth hormone antagonises insulin and depresses
xokinase activity (see, for example, Young 1948).
proved a powerful desensitising agent in a dose of
) mg. per kg. body-weight, increasing in effectiveness
p to twelve hours, beyond which time it was not tested.
n-cabbage-fed but not in ascorbic-acid-deficient guinea-
igs, it had a synergistic action with cortisone and also
lloxan (experiment 5). The desensitising action of
rowth hormone is not influenced by injected A.T.P.,
educed glutathione, or insulin; or by ascorbic-acid
eficiency in the diet (experiment 6) (table II), all of
hich, as already stated, prevent cortisone desensitisa-
on. The experiments quoted here were carried out with
single large batch of growth hormone provided by
essrs. Armour; they were confirmed with a highly
urified preparation provided by Prof. F. G. Young.
his latter preparation, tested at eight hours, had
pproximately twice the desensitising potency of the

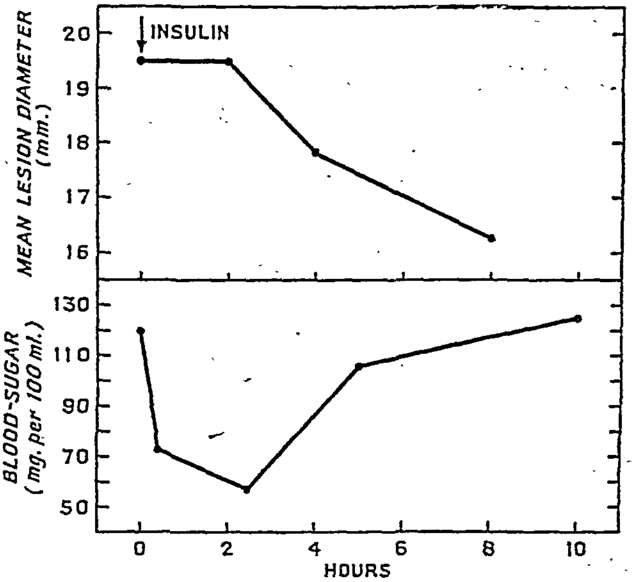


Fig. 3—Effect of insulin on blood-sugar level and tuberculin hypersensitivity.

Armour preparation, possibly owing to its greater solubility.

DISCUSSION

The idea that insulin, the adrenal steroids, and growth hormone influence hexokinase activity is not new. The Coris suggested, on a basis of in-vitro experiments, that the adrenal steroids and the anterior pituitary inhibit hexokinase activity, and that insulin antagonises the actions of these hormones and so allows hexokinase activity to be resumed (Cori and Cori 1946, Colowick et al. 1947). But the Cori contentions are at variance with the facts. Excess of anterior pituitary and adrenocortical hormones are known to influence blood-sugar in a manner comparable to that associated with insulin deficiency. But insulin, which would be expected from the Cori hypothesis to be inactive in the hypophysectomised or adrenalectomised animal, shows instead enhanced activity. It seems improbable that adrenal steroids, in times of emergency, would stimulate the formation of glucose from protein, only to block its oxidation and moreover the oxidation of glucose from other sources. The idea that growth hormone inhibits hexokinase activity is more acceptable and does not depend only on in-vitro evidence. Growth hormone increases the formation of tissue protein, a process associated with a decrease in the amount of amino-acids in the blood and a decrease in nitrogen excretion in the urine; serum alkaline phosphatase and cell lipids are increased in amount, but reserve fat is decreased; calcium and phosphate retention are associated with growth of bone.

These build-up processes, particularly of protein, depend upon the maintenance of a normal level of blood-glucose. If this level falls, adrenal steroids facilitate protein conversion to glucose; thus growth hormone, by blocking hexokinase activity, would be expected to maintain the blood-sugar level, prevent protein breakdown, and assist growth. In the present paper, we show that the desensitising actions of growth

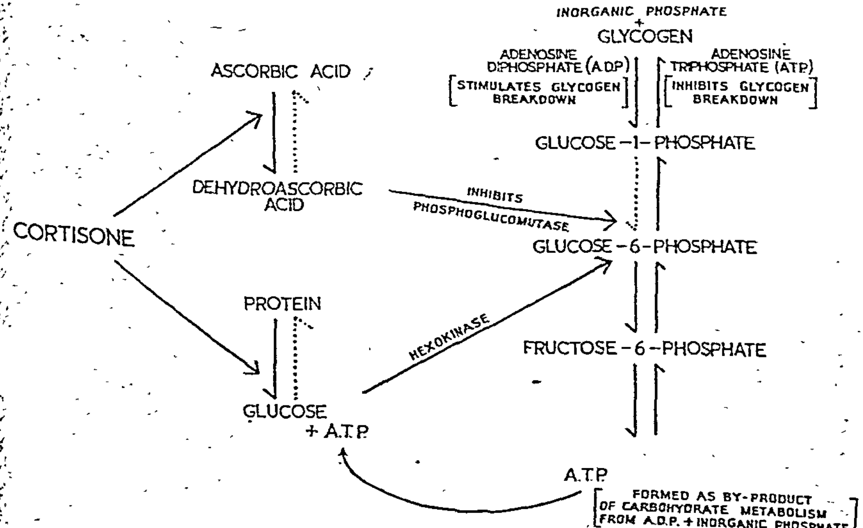

INORGANIC PHOSPHATE
+
GLYCOGEN
ADENOSINE DIPHOSPHATE (ADP)
STIMULATES GLYCOGEN BREAKDOWN
ADENOSINE TRIPHOSPHATE (ATP)
INHIBITS GLYCOGEN BREAKDOWN
ASCORBIC ACID
GLUCOSE-1-PHOSPHATE
DEHYDROASCORBIC ACID
INHIBITS PHOSPHOGLUCOMUTASE
CORTISONE
GLUCOSE-6-PHOSPHATE
PROTEIN
HEXOKINASE
FRUCTOSE-6-PHOSPHATE
GLUCOSE
+ A.T.P.
A.T.P.
FORMED AS BY-PRODUCT OF CARBOHYDRATE METABOLISM FROM A.D.P. + INORGANIC PHOSPHATE

Fig. 2.

TABLE I—ANALYSIS OF 989 BIRTHS

Births	Mother's influenza history	Male births			Female births			Total b	
		Pregnancy order			Pregnancy order			Pregnancy o	
		1st	2nd and over	Total	1st	2nd and over	Total	1st	2nd a ove
Total	I	56	32	88	35	41	76	91	73
	NI	195	255	450	172	203	375	367	458
Stillbirths	I	2		2	1	1	2	3	1
	NI	3	2	5	4	3	7	7	5
Stillbirths per 100 total births	I	3 6		2 3	2 9	2 4	2 6	3 3	1 4
	NI	1 5	0 8	1 1	2 3	1 5	1 9	1 9	1 1
Deformed stillbirths	I	1 (anencephalic)		1				1	
	NI	2 (2 anencephalic)		2	1 (spina bifida)	2 (1 anencephalic) (1 I V D)	3	3	2
Live births	I	54	32	86	34	40	74	88	72
	NI	192	253	445	168	200	368	360	453
Deformed live births	I		1 (absence of kidney)	1	1 (club foot)	2 (1 club foot) (1 spina bifida)	3	1	3
	NI	2 (2 hare lip)	1 (mongol, cardiac defect)	3	4 (2 club-foot) (1 ventral hernia) (1 septal defect)		4	6	1
Deformed live births per 100 live births	I		3 1	1 2	2 9	5 0	4 1	1 1	4 2
	NI	1 0	0 4	0 7	2 4		1 1	1 7	0 2

I = mother had, and NI = mother did not have, influenza during first four months of pregnancy

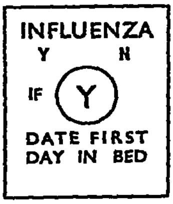
TABLE II—MOTHERS WHO HAD INFLUENZA ALL PREGNANCY ORDERS

—	1st month			2nd month			3rd month			4th month			Total	
	M	F	T	M	F	T	M	F	T	M	F	T	M	F
Normal live births	19	16	35	19	18	37	23	21	44	24	16	40	85	
Deformed live births					2 (1 club foot) (1 hydrocephalic)	2	1 (absence of kidney)		1		1 (club foot)	1	1	
Total live births	19	16	35	19	20	39	24	21	45	24	17	41	86	
Normal stillbirths	1	1	2					1	1				1	
Deformed stillbirths													1* (anencephalic)	
Total stillbirths	1	1	2					1	1				2	

* Date of last menstrual period unknown

bed, the first day of the illness falling between Dec 15 and Jan 31 inclusive"

The antenatal record of the mother would be stamped with a special stamp, which would be marked by the obstetrician concerned


INFLUENZA
Y N
IF Y
DATE FIRST
DAY IN BED

On the completion of the pregnancy, the result would be classified by the pædiatric staff of the hospitals, or by the medical officers of the maternity and child-welfare service, as "normal stillbirth," "deformed stillbirth," "normal live birth," or "deformed live birth"

A total of 989 births were recorded in this way (table I)

Table II sets out in slightly more detail the 164 births to mothers who had influenza it shows the month of pregnancy in which the infection occurred

Although the incidence both of stillbirth and of deformed live birth is rather higher in the "influenza" group than in the control group the difference is in each case slight and cannot be regarded as significant.

CONCLUSION

A group of mothers who had influenza (A-prime type) in the early months of pregnancy, and a similar group who did not have influenza, were observed during pregnancies

The findings do not suggest that influenza in the months of pregnancy adds appreciably to the stillbirth or fœtal abnormality

This report could not have been made without the cooperation of the staffs of the hospitals concerned and of maternity and child welfare service of Belfast Corpora who compiled the bulk of the records The investigation made under the general direction of Prof F M B Prof C H G Macafee, and Prof A C Stevenson Tab. and II were prepared in the Department of Social Preventive Medicine, Queen's University, Belfast

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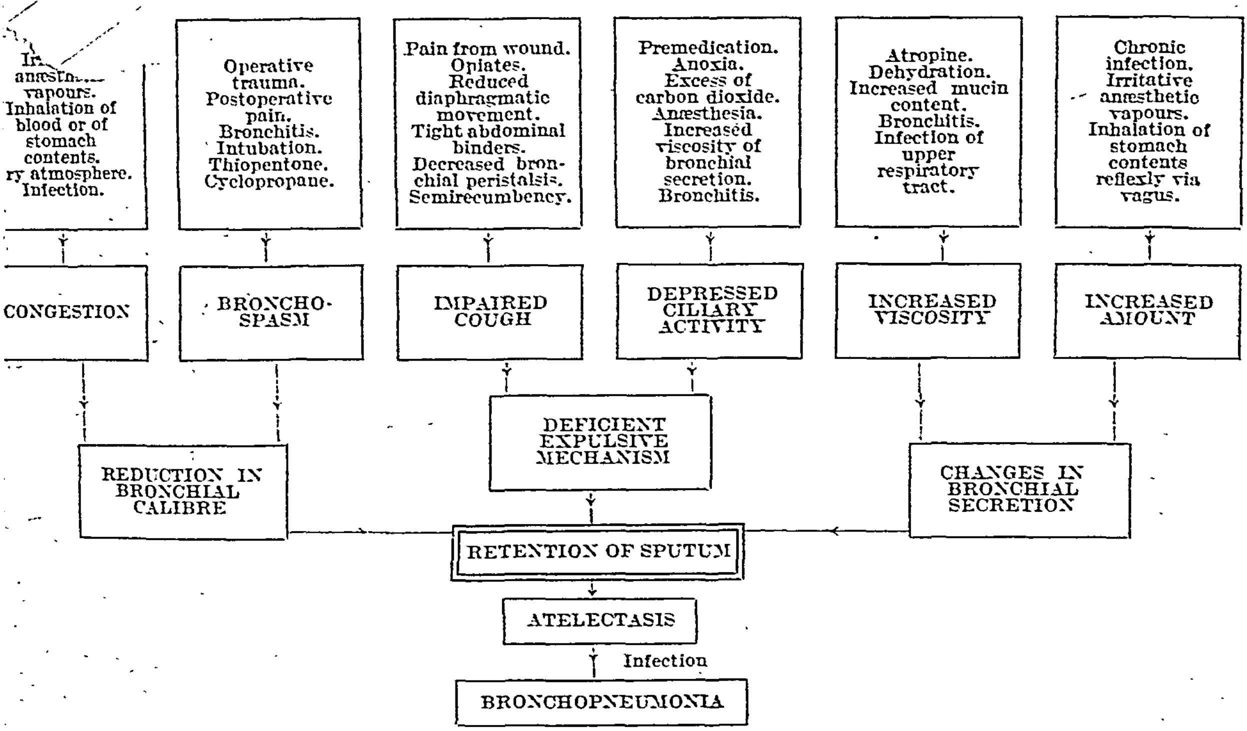
"informed opinion is moving away from the death rates or even of sickness rates as a measure of 'hea in the highest sense of that word It may be asked how of the citizens of Cardiff are enjoying that state of spark or 'positive' health that it is a joy merely to be alive continuing joy not dependent on momentary external

Some of us have known that 'joy-to be alive' feel we came out of the sea on our summer holidays, but ho of it have we retained since we returned to everyday li Unfortunately the nation has become so obsessed with idea that to *cure* all is the end all and the be all of ex that the higher ideal of 'positive' health becomes a receding goal The idea seems to be that if you only enough people of illness there will be no illness left therefore only health will remain"—Dr J Gr WILSON, medical officer of health for Cardiff, in his report 1951

TABLE I—FACTORS INVOLVED IN PRODUCTION OF POSTOPERATIVE ATELECTASIS


Ir anæsth vapours. Inhalation of blood or of stomach contents. ry atmosphere. Infection.
Operative trauma. Postoperative pain. Bronchitis. Intubation. Thiopentone. Cyclopropane.
Pain from wound. Opiates. Reduced diaphragmatic movement. Tight abdominal binders. Decreased bronchial peristalsis. Semirecumbency.
Premedication. Anoxia. Excess of carbon dioxide. Anæsthesia. Increased viscosity of bronchial secretion. Bronchitis.
Atropine. Dehydration. Increased mucin content. Bronchitis. Infection of upper respiratory tract.
Chronic infection. Irritative anæsthetic vapours. Inhalation of stomach contents reflexly via vagus.
CONGESTION
BRONCHO-SPASM
IMPAIRED COUGH
DEPRESSED CILIARY ACTIVITY
INCREASED VISCOSITY
INCREASED AMOUNT
REDUCTION IN BRONCHIAL CALIBRE
DEFICIENT EXPULSIVE MECHANISM
CHANGES IN BRONCHIAL SECRETION
RETENTION OF SPUTUM
ATELECTASIS
Infection
BRONCHOPNEUMONIA

ent (Muller et al. 1929, Howkins 1948), and the judicious use of abdominal binders (Churchill and cNeil 1927). Opiates, moreover, reduce the desire cough.

Secretion in the smaller bronchi is normally moved the activity of the ciliated bronchial epithelium ackson and Jackson 1933, Boyd et al. 1943). Anæs-ietics, lack of oxygen, excess of carbon dioxide, and creased viscosity of the bronchial secretion reduce liary activity (Hill 1928, Negus 1933), thereby favouring ie retention of sputum in the smaller bronchi.

Congestion of the bronchial mucosa and bronchial iasm reduce bronchial calibre. Under these conditions ry small amounts of secretion may produce bronchial clusion and atelectasis. Bronchial spasm may occur the induction period if an endotracheal tube is introiced into an insufficiently anæsthetised patient, and hen anæsthetics such as cyclopropane (Rovenstine 942) and barbiturates (Burstein and Rovenstine 1938) e used. It may be caused during the operation, rough rough handling of the viscera and traction on ie mesentery (De Takats et al. 1942), or after the ieration if there is severe pain (Lucas 1950). Patients ith chronic bronchitis are especially liable to develop onchospasm after operation. Congestion of the onchial mucosa may be produced by irritant anæsietic vapours or by the aspiration of irritant-material ito the lungs. The inhalation of stomach contents iay follow frank vomiting, but of greater danger is ie silent regurgitation which may not be noticed until ie mask is removed at the end of the operation (Culver ; al. 1951).

The amount of bronchial secretion is increased by ifection and irritation of the bronchi and by stimulaion of the secretory glands of the bronchi reflexly via he vagus (Florey et al. 1932, De Takats et al. 1942). n increase in the viscosity of bronchial secretion resultig from dehydration, chronic bronchitis, or large doses f atropine (Thomas et al. 1938) or scopolamine (Hibma nd Curreri 1942) is also an important factor in the roduction of atelectasis; for, when the viscosity of ronchial secretion is increased, secretion is not removed from the smaller bronchi by ciliary movement, or from the larger bronchi by coughing.

Thus, after operation, the normal mechanisms for the clearance of bronchial secretion are seriously impaired and changes in the bronchial secretion may take place. For these reasons sputum is retained in the lungs, leading to atelectasis.

Therefore the prevention of postoperative atelectasis depends essentially on preventing retention of sputum, and on recognising those cases in which this is especially likely.

We have found that the risk of a patient's developing atelectasis is high when one or more of the following factors is present:

(1) A history of even minimal bronchitis—e.g., recurrent productive winter cough.

(2) Clinical or radiological evidence of bronchitis.

(3) An infection of the upper respiratory tract in the 14 days preceding the operation.

(4) Abdominal operations, especially partial gastrectomy and cholecystectomy, and repair of inguinal hernia.

Thus atelectasis is particularly liable to develop in patients who, by reason of chronic infection or irritation of the bronchial tree, produce a viscid bronchial secretion. Smokers and elderly men are high-risk cases because they commonly have bronchitis, and those undergoing abdominal operations because they have most difficulty in expectorating secretion after operation.

METHODS

The present regimen was developed because the routine measures in this hospital—procaine penicillin and breathing exercises before and after operation—were failing to prevent postoperative atelectasis (Palmer and Sellick 1952a). The method we now adopt consists in (*a*) postural drainage with vibratory and clapping percussion and (*b*) inhalation of isoprenaline before and after operation. Isoprenaline has a powerful bronchodilator and vasoconstrictor action on the bronchial mucosa, and it is given to overcome the spasm and the congestion of the bronchi which are thought to be responsible for the rhonchi often heard after the opera-deficiencies and infections There are useful appendices on colloid chemistry, isotopes, thermodynamics, and acids and bases One of the most valuable and novel chapters is that on genetics, the biochemical implications of which are fast expanding, and the authors are not afraid to speculate on the relation of protein structure to the mechanism of memory and imagination, or to discuss smell and taste in terms of enzyme inhibitors The basal metabolic rate in cases of Simmonds's disease is erroneously given as "minus 50 or less," and leukæmia is omitted from the list of conditions with a raised blood uric acid, but there is little else to criticise and much for the clinician to respect and value in this book

Gynäkologische Strahlentherapie

Indikationsstellung, Methodik und Ärztliche Betreuung Dr Med Richard Kurt Kepp, professor of obstetrics and gynæcology, University of Gottingen Stuttgart Georg Thieme 1952 Pp 232 DM 26

This book from the gynæcological department of Gottingen University gives a long and detailed account of the radiotherapeutic methods used in many benign and malignant conditions

The first section deals with menopausal and premenopausal hæmorrhage and lays emphasis on two different effects—one obtained locally by the irradiation of the endometrium, the other produced by the radiation received by the ovary—and gives techniques designed to obtain one or the other effect Several techniques not in ordinary use in this country are described, such as irradiation of the hypophysis for menopausal symptoms attributed to hormonal disorder, using two fields 6×8 or 8×10 cm., and giving doses of 150–200r on two or three occasions with a further course after 3–6 months Other endocrine glands are also irradiated to alter their activity, and excessive bleeding in young girls is treated by irradiation of the spleen

With malignant disease of the uterus, operation is usually chosen for patients whose tumour is in a favourable position When radiotherapy is preferred much reliance is placed on intracavitary treatment with X rays generated at 60 or 100 kilovolts The method is ingenious, and if the vagina is roomy and not severely distorted by tumour a good distribution of the radiation can be obtained For the treatment of cancer of the uterine body the uterus is packed with radium tubes Carcinoma of the vulva treated by radiation receives fractionated superficial X radiation, and fast electrons generated at 4 MeV are beginning to be used as an alternative Cancer of the breast is included because it is regarded, in Germany, as coming within the province of the gynæcological department Both preoperative and postoperative radiation is used, mainly with two tangential fields to the breast area and with single fields to axilla and supraclavicular fossa, and palliative techniques are used for inoperable cases There is a useful chapter on the treatment of post radiation complications, but there are no statistics giving the results obtained by the use of the methods described There is a long bibliography.

Psychosurgical Problems

Editor Fred A Mettler, M D, professor of anatomy, College of Physicians and Surgeons, Columbia University London Routledge & Kegan Paul 1952 Pp 357 42*s*

This is a companion volume to the Columbia Greystones Associates' earlier report on selective partial ablation of the frontal cortex Here the results of cortical venous ligation, thermocoagulation of the cortex, surgical thalamotomy, and transorbital lobotomy are considered Besides reviewing the over all psychiatric results, attempts were made to study changes in general medical condition, including autonomic functions, the neurological state, detailed psychometric tests, and psychological functions such as memory, learning, "attitude," and certain perceptual and motor abilities Apart from the clinical psychiatric sphere, few changes were observed—except for transient neurological disorders, following venous ligation The fact that this evidence was negative implies no criticism of the work, because assessment of this kind of therapy must of course, call for much negative finding The length and method of recording it, however, seem pretentious and out of proportion to the results It is on the whole a more disappointing volume than the preceding one, though it few useful facts for those who are prepared to wakefully its wastes of turgid prose

Abraham Trembley of Geneva

Scientist and Philosopher, 1710–1784 John R M A, D PHIL, D SC Oxfd, lecturer in zoology, U of Oxford London Edward Arnold 195 35*s*

Today, when grafting is a normal part of practice and a very great deal is known ab regeneration of damaged tissues, it is interestin back a couple of centuries to the time when the study of these subjects was just beginning In days many biologists were engaged in static obs The dynamic Trembley was another kind of p was, above all, a student of processes, especi of growth and reproduction

Trembley was the first person to show that certain can be artificially multiplied by division, the first permanent grafts of animal tissues, the first to rigorous experiment that asexual reproduction occurs in animals, and the first to witness cell divi fascinating book is Trembley's first full scale biogra reader shares the excitement of the experimenter first cut a hydra in two in order to determine wh was a plant or an animal To his amazement into a normal specimen, indistinguishable from the He then cut up his hydras in a variety of ways, b regeneration always took place Having made the able discovery—that an animal could be mult division—the patient and observant Trembley set solve the inverse question could two polyps be tr into one ? He made the first successful graft in said he owed his discovery to a happy chance, but think that such chances only occur to those worthy of

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British Encyclopædia of Medical Practice (2nd London Butterworth Medical Publications 1952 Vol Pp 718 Vol 12 Pp 738 65*s* each)—The las volumes of their task completed in good time for a Chr breather, the general editor, Lord Horder, and his sultant and associate editors will have had a little which to stand back and look at twelve sparkling go red volumes on the shelf, and to receive the congratu they and their contributors have earned so well The pair round off the dozen and the alphabet by goin rheumatic infection (an article by Dr Douglas H to yellow fever (by Sir Philip Manson Bahr), the editors extracted all Z's secrets under earlier letters A co analytical index is to follow (each volume already has its individual index), and this will put the finishing touch work of high merit

The Autonomic Nervous System (3rd ed Lon Henry Kimpton 1952 Pp 569 90*s*)—It is eleven since the last edition of this standard work on the auto nervous system, by Dr James C White and Prof Re H Smithwick, was published In this period early enth hopes about the value of extensive sympathectomies in treatment of hypertension have been modified, and experience has clarified the position of sympathectom causalgia In this third edition, the two original authors been joined by Dr Fiorindo A Simeone The observatio the intervening years are fully considered, and the au besides dealing with the disorders in which operation autonomic nervous system may be of value, and with technical details of operation, fully discuss anatomical physiological factors, and assess the value of drug trea in modifying autonomic activity

German-English Medical Dictionary (New York London McGraw Hill 1952 Pp 586 102*s*)—I Louis De Vries, who holds the chair of modern langua Iowa State College, is an old hand at compiling Ger English dictionaries Ably supported by medical exp has set about this latest work with a zest Some p we are told, get by well enough with altogether 400 but in this technical dictionary *Aal* is separated from *plasma* by 40,000, and even this, Professor De Vries in a preface, may not be enough Unhappily the p the book will be more than enough for most woul translators

DISCUSSION

Many factors are involved in the production of post-ative atelectasis (Band and Hall 1931, Brock 1936). have grouped them together in table I to provide etter understanding of the way each acts in causing retention of bronchial secretions.

We found that isoprenaline and postural drainage with ratory and clapping percussion together prevented electasis, but that either singly was less effective.

We think this is because changes in bronchial calibre, deficient expulsive mechanism, and changes in bronchial cretion are present in most high-risk patients after eration, and that, unless treatment is directed to the lief of these factors simultaneously, atelectasis is not evented.

When the physiotherapy regimen (postural drainage nd vibratory percussion) is given alone, secretion does ot get to a part of the lung where the cough reflex is icited. because spasm and congestion of the bronchi old the secretion in the peripheral parts of the lung. When spasm and congestion of the bronchi are relieved y isoprenaline, secretion is brought to the larger bronchi hen the patient is tipped, and it is removed by coughing.

Isoprenaline alone fails to prevent atelectasis, because, lthough spasm and congestion are relieved, secretion not brought to the larger bronchi where coughing is ffective in its removal.

This concept is supported clinically by the following ase:

A man, aged 50, was admitted in April, 1952. for a partial astrectomy for chronic duodenal ulcer. He was a heavy moker and had chronic bronchitis and emphysema. He was treated before the operation with postural drainage and ibratory percussion, with improvement in the productive ough. This treatment was continued postoperatively, but ittle or no sputum was produced, and radiography of his hest twenty-four hours after the operation showed an area f atelectasis at the left base. There were generalised onorous rhonchi and prolonged expiration. When the ostural drainage and vibratory percussion were repeated fter the inhalation of isoprenaline, 4 oz. of viscid mucoid putum was produced, and the area of atelectasis expanded.

TABLE III—RESULTS OF TREATMENT OF TWO GROUPS OF UNSELECTED PATIENTS

Group	No. of patients	No. with segmental atelectasis	No. with productive cough for 1 week or more
E	90	8 (8·9%)	0
O	90	39 (43·3%)	30 = 33·3%
		$\chi^2=27{\cdot}69$ $n=1$ $P<0{\cdot}001$ Significant	

Although all these main mechanisms operate in most ases, rarely one factor may be predominant. Atelectasis as been noted during operation (Cassells and Rapoport 1944), and the bronchoconstrictor and bronchosecretory reflexes described by De Takats are probably responsible. These reflexes may also explain those cases in which no occlusion of the bronchial lumen is found at necropsy.

Bronchial secretion after operation is often extremely viscid. A reduction in viscosity of the bronchial secretion aids removal from the lungs by increasing ciliary activity. Isoprenaline renders the bronchial secretions more fluid in asthmatic patients (Gay and Long 1949), and we are undertaking experiments to determine whether isoprenaline reduces the viscosity of the bronchial secretion in patients after operation.

Baker et al. (1951) used intravenous sodium iodide twice daily to prevent atelectasis and reported successful results. Iodides increase bronchial secretion and reduce its viscosity (Basch et al. 1941), thereby facilitating expectoration. Atelectasis did not occur in any of 100 consecutive patients treated prophylactically before and after operation by this method, but the risk of atelectasis was not great in all these cases. for in 58 the operation did not involve laparotomy. Moreover, only severe degrees of atelectasis were considered.

We have found this treatment of value where the bronchial secretion is extremely viscid, but its routine use is not advised, for the copious secretion produced by sodium iodide may, in the presence of an ineffective cough reflex, lead to retention of sputum and atelectasis.

We favour the use of steam inhalations in conjunction with isoprenaline and postural drainage where the secretion is extremely viscid, because steam reduces the viscosity of the bronchial secretion (Basch et al. 1941) without increasing the amount.

TABLE V—COMPARISON OF RESULTS OF DIFFERENT TREATMENTS IN FOUR GROUPS OF UNSELECTED PATIENTS

Group no.	No. of patients	No. with segmental atelectasis
1	40	15
2	40	4
3	40	13
4	40	17
		$\chi^2 = 11{\cdot}74$ $n = 3$ $P<0{\cdot}01$ Significant

SUMMARY

A deficient expulsive mechanism, reduction in bronchial calibre, and quantitative and qualitative changes in bronchial secretion are considered to be of great importance in leading to retention of sputum and the development of atelectasis in patients after operation.

A regimen for the prevention of postoperative atelectasis is described. This consists in the inhalation of isoprenaline and postural drainage with vibratory and clapping percussion to the chest wall before and after operation.

The incidence of atelectasis in 90 patients undergoing abdominal operations who were treated by this regimen was 9%, compared with 43% in 90 similar patients treated with breathing exercises before and after operation. All the patients received procaine penicillin before and after operation.

TABLE IV—COMPARISON OF FOUR DIFFERENT GROUPS OF UNSELECTED PATIENTS

Group	No. of patients	No. with history of bronchitis	No. of smokers	No. of females	No. of hernia cases	Average age (yr.)
	40	19	32	4	11	49·3 S.D.13·3
	40	20	29	7	14	48·8 S.D.10·9
	40	22	34	6	15	51·1 S.D. 9·9
	40	20	29	4	15	47·9 S.D.11·3
		$\chi^2 = 0{\cdot}47$ $n = 3$ $P>0{\cdot}9$ ot significant	$\chi^2 = 2{\cdot}58$ $n = 3$ $P>0{\cdot}5$ Not significant	$\chi^2 = 1{\cdot}38$ $n = 3$ $P>0{\cdot}7$ Not significant	$\chi^2 = 1{\cdot}19$ $n = 3$ $P>0{\cdot}7$ Not significant	

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ronchial secretion is increased

with assisted postural drainage Their well-designed trial leaves no doubt that these measures largely *prevented postoperative radiological* change and productive cough They were applied before operation until no more sputum could be produced, thus no patient was operated on until any bronchitis present had subsided Since postoperative chest complications are uncommon in patients who are completely free from cough before the operation, one wonders how far the success of these measures is due to their preoperative use and how far they affect the established condition when applied later But PALMER and SELLICK did not set out to answer these questions, which have theoretical as well as practical implications

While nearly everyone agrees that a combination of viscid sputum and reduction of respiratory effort and cough by pain or opiates is the cause of the bronchial obstruction, the precise timing and course of events is still uncertain The term "atelectasis" is used rather vaguely by many radiologists Certainly many shadows so reported are due to pneumonia in a moderately shrunken area of lung, rather than to absorption of air alone, and one may sometimes see typical "jib" shadows clear without re-expansion, as shown by the position of the fissures and other landmarks, leaving the area of uncomplicated collapse quite inconspicuous Indeed it seems likely that the uninfected stage of lobular or segmental collapse can be radiologically invisible Moreover, it is very unlikely that such lesions cause pyrexia or constitutional upset until infection supervenes The point of these considerations is that it is difficult to demonstrate the earliest stages of the lesions or to define the onset of the process There is some evidence that it starts earlier than is often supposed STRINGER[7] found that of 13 patients who developed radiological opacities, 5 had abnormal films as early as four hours after operation CASSELS and RAPOPORT[8] described pulmonary collapse occurring during operation, but these were instances of massive collapse producing immediate signs, and it is probable that the segment or the lobule can collapse without being noticed If in fact the blockage of the bronchus and the absorption of air commonly begin during the operation, the preoperative state and the anæsthetic technique may well be more important than the postoperative treatment A factor worth attention is the effect of anæsthetic mixtures on the rate of air absorption DALE and RAHN[9] have shown that collapse following bronchial occlusion is accelerated sixtyfold when pure oxygen is breathed in place of air The oxygen content of an anæsthetic mixture might thus determine whether a region of lung distal to a bronchial obstruction was or was not airless when the patient recovered consciousness and started to cough, and complete airlessness must greatly decrease the chance of early dislodgement of the obstruction PALMER and SELLICK's results suggest a substantial prophylactic advance, and we hope that their valuable analysis will be continued to explore further the corollaries to their encouraging news

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[7] Stringer P *Ibid* 1947 i, 289.
[8] Cassels W H, Rapoport, A E *Anesthesiology* 1944, 5, 174
[9] Dale, W A, Rahn, H *Amer J Physiol* 1952, 170, 606

Tuberculosis Mortality

SINCE 1850 the Registrar-General has published year by year the mortality-rate from tuberculosis in each sex by age groups Those figures reveal a great fall in the mortality in all age-groups, and most people agree that this must have been due to improved environmental conditions Apart from this general fall the most interesting feature is the change in the age-distribution, and there is now a very distinct difference between the sexes for females the death rate is greatest in early adult life, whereas for males it is greatest at about the end of working life

FROST,[1] who has since been followed by others, suggested that this late peak in males could be better understood if it was studied in relation to the earlier higher rates experienced by the same group of men when young adults, an entirely new picture emerged when the rates were studied for "cohorts" instead of calendar years or decennia This view was reinforced by SPRINGETT,[2] who showed that, if it were accepted that the mortality curve for females followed a more acutely peaked pattern, the postponement of the age *of maximum mortality of males, and not of females,* could be explained mathematically While largely accepting this reasoning, McDONALD[3] has suggested that the late peak of mortality in men is associated with environmental conditions at work He bases his view on differences between various occupational, social-class, and geographical groups in England and Wales in the present century, but he does not discuss the possible influences of "migration," not only geographically but also from one occupation to another and from one social class to another Possibly, as McDONALD concludes, environment at work is partly responsible for the present high mortality in older men, but the fact that single women engaged in employment have the same pattern of mortality as married women (though with a rather higher death rate among the employed) does not suggest that this influence can be very strong Furthermore, a century ago, when men worked under far worse conditions and their wives were for the most part at home, the greatest mortality for each sex was in young adult life

RUSSELL[4] has approached these mortality rates in a rather different way He points out that the grouped data used by previous workers, based on 10-year age-groups and decennia, are not an exact guide to the tuberculosis mortality of cohorts He has accordingly estimated the general and the tuberculosis mortality of twenty-four cohorts of females born in 3-year periods from 1851–53 to 1920–22 His results confirm the great fall in tuberculosis mortality and the general constancy of the pattern of mortality in cohorts, except when disturbed by such gross influences as the first world war and the influenza epidemic of 1918–19 He confirms also the fact, first recorded by PICKEN,[5] *that by the cohort method of analysis,* as well as by the conventional calendar-year method, the age of maximum mortality for women is passing to younger age groups RUSSELL states that previous investigations based on the cohort method of study have emphasised the dependence of pulmonary taquaine suspension, I instituted clinical trials. The lty officer on duty saw the patients, and those whom onsidered should have penicillin were given 5 ml. mega-units) of distaquaine suspension, after which lowed them up in a re-dressing clinic. The cases, fore, were not selected by me. Notes were taken 0 consecutive cases. In most cases the dressings paste of magnesium sulphate (*B.P.C.*) or saline ion for the open sepsis, and glycerin of ichthammol *.C.*) for the closed infections.

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[1] Frost, W H *Amer J Hyg* 1939, 30, 91
[2] Springett V H *J Hyg Camb* 1950, 48, 361
[3] McDonald J C *Brit J soc Med* 1952, 6, 259
[4] Russell W T *Med Offr* 1952, 88 269
[5] Picken R M F *Publ Hlth*, 1940, 53, 145

e results are shown in table I. In 191 cases one tion alone was required. Cure was effected in seven n days. In the remaining 9 cases a second injection required and was given on the fourth day of treat- t. When there is no improvement by the fourth , the organisms are probably penicillin-resistant. accords with the tenets of Long et al. (1950) that response should be prompt. Further, I believe that large dose of penicillin kills off or weakens the invad- organisms in the first few days, while the patient's bodies are being built up, with the result that, when penicillin has disappeared on the fourth day, the ent's own defence mechanisms can dispose of any aining infection.

he usual indications were followed in assessing the essity for incision; these were made when required, he belief that penicillin is given to help the surgeon not to take his place.

o see whether 1·5 mega-units of crystalline sodium icillin G (soluble penicillin) in aqueous solution would e the same effect, blood-penicillin levels were measured . 1) after injecting it dissolved in 3 ml. of distilled water. caused slightly more discomfort than did 5 ml. of the caine-penicillin suspension. The blood-penicillin levels nd suggested that excretion was slow enough to rrant a clinical trial; so 100 cases were treated with the same control being used as procaine penicillin. e results are shown in table II.

LE II—RESULTS OF TREATMENT WITH 1·5 MEGA-UNITS OF PENICILLIN G IN HOSPITAL CASUALTY DEPARTMENT

lition	No. of cases	Length of treatment (days)			No. incised	No. injected more than once	Reactions
		Avg.	Max.	Min.			
..	7	8	15	3	2 (28·6%)		None
n ..	2	12	13	10			None
sis:							
m ..	3	17	33	7	2 (66·7%)		None
illary	3	6	8	5	1 (33·3%)		None
ntal	1	7	7	7			None
e ..	1	7	7	7			None
ce ..	10	7	12	4	1 (10%)	2	None
ot ..	3	10	17	6			None
nd ..	59	9	27	2	21 (35·6%)	4	None
g ..	10	8	19	2		1	None
rianal	1	4	4	4			None
otal..	100	..	..	..	27 (27%)	7	None

lthough a similar proportion of cases required a further ection—7% for crystalline sodium penicillin G cases npared with 4·5% for procaine-penicillin suspension— average time of treatment with crystalline sodium nicillin G was somewhat longer, and the disability ring treatment rather more severe. Œdema did not tle so quickly, pain was not relieved so rapidly, and re attendances in the outpatient department were quired.

With procaine-penicillin suspension little improvement her than the relief of pain was noted in the first twenty- ir hours. During the next twenty-four hours the lema subsided, and carbuncles that were open truded a septic core on that day or the next; those that were not open began to diminish in size and redness, the inflammation appearing to subside by resolution.

TABLE III—RESULTS OF TREATMENT WITH 5 ML. PROCAINE-PENICILLIN AQUEOUS SUSPENSION IN GENERAL PRACTICE

Condition	No. of cases	Length of treatment (days)			No. incised	No. injected more than once	No. sent to hospital	Reactions
		Avg.	Max.	Min.				
Boil	20	4	7	3		1		None
Burn	1	2	2	2				None
Carbuncle ..	1	4	4	4				None
Chest.. ..	4	4	7	2				None
Pemphigus ..	1	2	2	2				None
Sinus.. ..	3	4	4	4				None
Tonsillitis ..	4	4	5	2				None
Sepsis:								
Axillary ..	1	11	11	11	1		1	None
Breast ..	1	12	12	12		1		None
Cellulitis ..	1	5	5	5				None
Dental ..	3	4	4	4				None
Ear	19	7	32	3		2		None
Eye	9	4	5	2				None
Face and neck	12	4	6	3				None
Hand ..	8	3	5	2	1			None
Leg	9	4	8	3				None
Perianal ..	3	5	6	5				None
Total ..	100	..	..	..	2	4	1	None

TREATMENT IN GENERAL PRACTICE

The treatment of patients reaching hospital having thus been shortened, investigation was transferred to general practice. It was hoped to treat patients on their first appeal for medical help. Through the courtesy of Dr. J. Sytner and his partners, I was privileged to attend evening surgery in a general practice until 100 cases had been discharged. This meant that 135 cases were treated, only 100 of these having reported back to be seen when cured.

Here again the choice of cases was left to others, this time to the general practitioners; and, as these attended in three consulting-rooms simultaneously in the same building, it was easy to control the cases without inconvenience to doctors or patients. This group practice is in probably the poorest part of Liverpool, the houses being overcrowded, with few amenities, and in bad repair from war damage. It was chosen for these very reasons, in the belief that this repository penicillin therapy should undergo a really stern test.

I injected 5 ml. (1·5 mega-units) of procaine-penicillin suspension into patients over one year of age, and 2·5 ml. (750,000 I.U.) into those under one year (the youngest was aged eleven days). The dressings were lint soaked in "a teaspoonful of salt to a cup of water, warm but not hot." If the sepsis was closed, glycerin of ichthammol was applied. I believe that local penicillin is without efficacy; so no penicillin was applied locally. The results are shown in table III.

Out of the 135 patients seen only 2 required incision; 1 received the incision in hospital and was healed in eleven days, the other (a child, aged fourteen days,

TABLE IV—PERCENTAGE RATES OF CURE UP TO 10 DAYS

Treatment	Days							
	3	4	5	6	7	8	9	10
Hospital outpatient department:								
Procaine-penicillin suspension	16	26	43	52	61	72	75	80
Penicillin G	13	26	37	44	56	59	61	67
General practice:								
Procaine-penicillin suspension	23	68	91	93	94	95	..	..

with assisted postural drainage Their well-designed trial leaves no doubt that these measures largely prevented postoperative radiological change and productive cough They were applied before operation until no more sputum could be produced, thus no patient was operated on until any bronchitis present had subsided Since postoperative chest complications are uncommon in patients who are completely free from cough before the operation, one wonders how far the success of these measures is due to their preoperative use and how far they affect the established condition when applied later But **Palmer** and **Sellick** did not set out to answer these questions, which have theoretical as well as practical implications

While nearly everyone agrees that a combination of viscid sputum and reduction of respiratory effort and cough by pain or opiates is the cause of the bronchial obstruction, the precise timing and course of events is still uncertain The term "atelectasis" is used rather vaguely by many radiologists Certainly many shadows so reported are due to pneumonia in a moderately shrunken area of lung, rather than to absorption of air alone, and one may sometimes see typical "jib" shadows clear without re expansion, as shown by the position of the fissures and other landmarks, leaving the area of uncomplicated collapse quite inconspicuous Indeed it seems likely that the uninfected stage of lobular or segmental collapse can be radiologically invisible Moreover, it is very unlikely that such lesions cause pyrexia or constitutional upset until infection supervenes The point of these considerations is that it is difficult to demonstrate the earliest stages of the lesions or to define the onset of the process There is some evidence that it starts earlier than is often supposed **Stringer**[7] found that of 13 patients who developed radiological opacities, 5 had abnormal films as early as four hours after operation **Cassels** and **Rapoport**[8] described pulmonary collapse occurring during operation, but these were instances of massive collapse producing immediate signs, and it is probable that the segment or the lobule can collapse without being noticed If in fact the blockage of the bronchus and the absorption of air commonly begin during the operation, the preoperative state and the anæsthetic technique may well be more important than the postoperative treatment A factor worth attention is the effect of anæsthetic mixtures on the rate of air absorption **Dale** and **Rahn**[9] have shown that collapse following bronchial occlusion is accelerated sixtyfold when pure oxygen is breathed in place of air The oxygen content of an anæsthetic mixture might thus determine whether a region of lung distal to a bronchial obstruction was or was not airless when the patient recovered consciousness and started to cough, and complete airlessness must greatly decrease the chance of early dislodgement of the obstruction **Palmer** and **Sellick**'s results suggest a substantial prophylactic advance, and we hope that their valuable analysis will be continued to explore further the corollaries to their encouraging news

Tuberculosis Mortality

Since 1850 the Registrar-General has published year by year the *mortality-rate from tuberculosis* for each sex by age-groups Those figures reveal a [illegible] fall in the mortality in all age-groups, and people agree that this must have been due to improved environmental conditions Apart from this great fall the most interesting feature is the change in age-distribution, and there is now a very [illegible] difference between the sexes for females the death rate is greatest in early adult life, whereas for men it is greatest at about the end of working life

Frost,[1] who has since been followed by others, suggested that this late peak in males could be better understood if it was studied in relation to the earlier higher rates experienced by the same group of men when young adults, an entirely new picture emerged when the rates were studied for "cohorts" instead of calendar years or decennia This view was [illegible] by **Springett**,[2] who showed that, if it were accepted that the mortality curve for females followed an acutely peaked pattern, the postponement of the age of maximum mortality of males, and not of females, could be explained mathematically While [illegible] accepting this reasoning, **McDonald**[3] has suggested that the late peak of mortality in men is associated with environmental conditions at work He bases this view on differences between various occupational, social-class, and geographical groups in England and Wales in the present century, but he does not discuss the possible influences of "migration," not only geographically but also from one occupation to another and from one social class to another Possibly, as **McDonald** concludes, environment at work is partly responsible for the present high mortality in older men but the fact that single women engaged in employment have the same pattern of mortality as married women (though with a rather higher death rate among the employed) does not suggest that this influence can be very strong Furthermore, a century ago, when men worked under far worse conditions and their wives were for the most part at home, the greatest mortality for each sex was in young adult life

Russell[4] has approached these mortality rates in a rather different way He points out that the grouped data used by previous workers, based on 10-year age-groups and decennia, are not an exact guide to the tuberculosis mortality of cohorts He has accordingly estimated the general and the tuberculosis *mortality of twenty-four cohorts of females* born in 3-year periods from 1851–53 to 1920–22 His results confirm the great fall in tuberculosis mortality and the general constancy of the pattern of mortality in cohorts, except when disturbed by such gross influences as the first world war and the influenza epidemic of 1918–19 He confirms also the fact, first recorded by **Picken**,[5] that by the cohort method of analysis, as well as by the conventional calendar-year method, the age of maximum mortality for women is passing to younger age-groups **Russell** states that previous investigations based on the cohort method of study have emphasised the dependence of pulmonary ɔrigin of the inferior mesenteric artery were easily and ɔly displayed by dissection of the pre-aortic peritoneum, ɔathetic fibres, and areolar tissue. The vessel was pulsating ially to within 1 cm. of the bifurcation, below which ; only transmitted thrust was palpable. Beyond, the non iliac arteries were pulseless. The aorta, clamped and d proximally, was next incised vertically for about 1·5 cm. ediately above the bifurcation. Much thrombus was ed from each common iliac artery but was unfortunately preserved. The free retrograde bleeding which followed controlled by digital pressure while the aortic incision being closed with interrupted mattress sutures of fine ded 'Nylon.'

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[2] Springett, V H *J Hyg Camb* 1950, 48, 361

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hen the aortic clamps were released, strong pulsation ted in all the visible distal vessels except the left external and femoral arteries. The left femoral artery was there- opened, and a fine soft suction catheter was passed ximally. After this there was a faint left femoral impulse. ·5% solution of papaverine was applied to the exposed sels, as recommended by Kinmonth (1952), and the wounds e closed, leaving fine 'Polythene' tubing down to the ious arteries that had been handled.

s the patient's condition was still fairly satisfactory, the axillary artery was exposed through a curved incision, cave downwards, on the front of the shoulder. The outer t of the clavicular head of the pectoralis major muscle s detached from the clavicle, and the muscle was divided r its brachial attachment. The pectoralis minor was cut ough, the axillary sheath was opened, giving an extensive osure of the artery. The level of cessation of pulsation s in the third part near the crossing of the medial root of median nerve. The nerves were held aside on tapes, and ch thrombus was milked from a 1 cm. vertical incision in non-pulsating segment. The suction catheter was also d. Although free retrograde bleeding took place, no sation returned after the arterial incision was sutured, even er the application of papaverine. The wound was repaired layers round a fine polythene tube.

The operation lasted about two hours.

stoperative Course

The patient was nursed in an oxygen tent overnight. paverine was instilled at intervals through the polythene es. No anticoagulant was given. After causing some xiety for the first few hours the patient improved, and overy was uneventful apart from an episode on the 13th y, when abdominal pain and distension, with some shock peared and lasted about 48 hours. The cause was uncertain it might have been intraperitoneal rupture of a small ri-aortic hæmatoma. No pulse could be felt at any time in y of the affected limbs, but their vitality was never in ubt.

alvotomy

In view of her poor cardiac prognosis and the repeated abolism, Dr. Branford Morgan was of the opinion that lvotomy should be considered. Accordingly the patient as transferred on the 32nd postoperative day to the thoracic it of St. Bartholomew's Hospital at Hill End, where on arch 24, 1952, she underwent mitral valvotomy by Mr. O. S. ubbs. We are indebted to Mr. Tubbs for permission to include tracts from his notes.

"The auricular appendage, which was large and broad, lt quite soft. The base of the appendage was injected with % amethocaine and a Brock clamp applied. The incision the appendage was made from above downwards with the cape of fluid blood. There was no clot inside the appendage ad the endocardium appeared quite smooth. The clamp was omentarily released and no clot was discharged, only fluid lood. A purse-string suture was not employed as the appen- age was so large. A finger was now inserted through the pening. There was no regurgitant stream palpable. An area f calcification in the anteromedial cusp was felt. There was ome difficulty in finding the actual stoma as it was so small. he lateral commissure split easily, but the medial com- nissure could not be made to split. There did not appear to e any calcification at the margins of the opening. After the ateral commissurotomy the stoma would have admitted about ne and a half fingers. The clamp was then reapplied, the tip f the appendage removed for section, and the opening obliter- ated with interrupted mattress sutures and continuous sutures long the border. The chest was closed with an intercostal rain in the posterior axillary line. The patient was returned o the ward and kept in an oxygen tent for the first 24 hours after operation. Her convalescence was smooth and she was discharged from hospital on April 17, 1952.

"*Pathological report.*—The specimen consists of an auricular appendage measuring 3 × 2 × 1 cm. and showing some slight subpericardial hæmorrhage, but otherwise no macroscopic abnormality. Section shows considerable hypertrophy of the muscle-fibres and some organising endocardial thrombus. In one area of the myocardium there is a focus of chronic inflammatory cells, mostly lymphocytes, but there are no specific rheumatic nodular lesions."

Follow-up

The patient was readmitted to the Norfolk and Norwich Hospital on May 2, 1952, looking an entirely different woman. The cyanotic malar flush was gone, as had the dyspnœa, and she could walk up and down stairs with ease. Apart from a flicker in the left radial artery, no pulsation was palpable in any of the affected limbs.

When last seen on Jan. 14, 1953, she had maintained her improvement, and had gained about 7 lb. in weight, felt better than for years, and could do her housework. She could climb stairs without breathlessness and could walk at least a mile at an ordinary pace without fatigue or claudication. She had some pain in the soles of her feet on walking; this took about two hours to pass off, and may have been structural rather than circulatory. The peripheral pulses were still absent, and the feet were cold, with very slight postural blanching.

The patient will remain under observation.

DISCUSSION

Operative Technique

In view of previous papers there is no need to discuss technique in detail. A few points, however, deserve mention—mainly steps which we now consider to have been errors committed in the atmosphere of unusual emergency.

1. It was almost certainly a mistake to expose and clamp the vessels in the groin before opening the abdomen. Our object was to avoid distal migration of portions of detached thrombus, but this danger is likely to be considerably less than that of spasm and intimal bruising caused by the clamping. Temporary occlusion of the common iliac vessels during extraction of the clot has been described by Linton (1945). If any doubt exists about the diagnosis of aortic saddle embolus, it may be correct to explore a femoral vessel first, as in the case described by Fraser and Goldberg (1951).

2. The use of suction tubes, however soft, is inadvisable. According to Linton (1945) gentle handling of tissues and avoidance of intimal injury are cardinal points of technique. External milking followed by momentarily unchecked bleeding should in most cases obviate the need for endarterial manipulations.

3. The arterial incision is probably best placed in the relatively dilated segment just above the point of impaction of the embolus. The contracted segment at and below that point is already sufficiently damaged and narrowed without having to suffer further insult. Failure to observe this point in the case of the axillary artery probably explains the non-return of pulsation in that vessel immediately after the embolectomy.

4. To the general surgeon, his familiarity with the simple transperitoneal approach, and the good exposure it affords, are invaluable when he is called on to tackle this unusual though not unduly difficult emergency (Linton 1945, Ewing 1950).

Effect of Embolectomy

In none of the affected limbs were normal peripheral pulses restored, although, as has been noted, strong pulsation returned in most of the major distal vessels after removal of the aortic clamp. The failure of the vascular tree to return to normal was probably due to a combination of spasm and thrombosis following over-manipulation of the vessels. Even so, it must be emphasised that they were by no means roughly handled; obviously extreme gentleness is required, together with avoidance of endarterial manœuvres.

THE PAINFUL SHOULDER

SHOULDER pain can be a baffling diagnostic problem, as Furlong[1] has lately reminded us The pain may not arise in the shoulder at all it may originate in a neighbouring structure, or it may be referred from a more distant region, such as the neck or thorax True shoulder pain is felt immediately distal to the acromion process, and it often radiates diffusely down the lateral aspect of the upper arm, usually to about the junction of its middle and lower thirds, it seldom extends below the elbow It is almost invariably associated with physical signs in the shoulder, such as local tenderness, swelling, or increase of warmth, impairment of mobility *in one or more directions*, exacerbation of pain on movement, or crepitation Pain of somewhat similar distribution may be caused by lesions involving the brachial plexus or its roots, such as prolapsed cervical disc, osteophytic outgrowths in cervical osteo-arthritis, and tumours in the spine, neck, or thoracic inlet But pain from these causes often radiates throughout the length of the limb to the forearm and hand, it may be associated with neurological signs; and the shoulder itself shows no abnormality It is worth remembering, also, that pain in the shoulder may be a prominent feature of diaphragmatic irritation (for example, from an inflamed gall-bladder) and of angina pectoris Nelson[2] has lately given an admirable account of the differential diagnosis of shoulder pain

Once it is established beyond reasonable doubt that the pain arises in the shoulder-joint, the next step is to consider each of the possible causes Apart from recent injuries, the number of recognised affections of the shoulder is fairly small, and their differentiation is usually not difficult Like other joints, the shoulder is subject to the common forms of inflammatory arthritis (acute suppurative, rheumatoid, tuberculous) Unlike other large joints it is only rarely affected by osteo arthritis (presumably because it is seldom subjected to thrust-stresses) On the other hand it is commonly the site of affections that have no true counterparts in other joints The chief of these are the supraspinatus, or painful-arc, syndrome, rupture of the musculo-tendinous cuff (often termed, less accurately, the "rotator" cuff), and "frozen" shoulder

The *supraspinatus syndrome* is common, clinically distinctive, and satisfactorily explained by the structural relationships in the upper part of the shoulder During the mid-phase of shoulder abduction the non-articular part of the upper end of the humerus passes close beneath the coraco acromial arch, the clearance just suffices to accommodate the structures that lie between them—the supraspinatus and adjacent tendons blending with the capsule, and the flimsy walls of the subacromial bursa Consequently if any tissue in this area is swollen and tender it will be nipped between humerus and coraco-acromial arch during the critical mid-phase of abduction, thereby causing the painful arc of movement characterising this syndrome Five distinct lesions may be primarily responsible minor rupture of supraspinatus tendon fibres, supraspinatus tendonitis (a localised degenerative lesion), calcified deposit in the supraspinatus tendon, subacromial bursitis, and a minimally displaced avulsion fracture of the greater tuberosity

Rupture of the musculo tendinous cuff raises problems of applied anatomy, of diagnosis, and of treatment The classical picture of a major tear of the supraspinatus and adjacent tendons is well known there is inability to abduct the arm through the early part of its range, though if the limb is abducted passively the position can often be sustained against gravity without assistance But theoretically the deltoid muscle should be sufficiently powerful to abduct the arm against gravity without the aid of the supraspinatus, and it is not fully why it usually cannot do so The most explanation is that the *supraspinatus* normally the articular surface of the humeral head closely to the glenoid fossa, thereby ensuring a stable of movement Without supraspinatus action the head tends to be pulled upwards away from the fossa by the deltoid, and the stability of the fulcrum is lost Early diagnosis of major tears of the cuff is difficult because certain other painful of the shoulder *can cause* temporarily a similar loss abduction, through reflex inhibition Yet prompt nosis is important because operative repair is and more likely to be effective in the early stages Ell has recently called attention to two aids to diagnosis—the procaine-injection test and contrast arthrography By injection of procaine into the area of tenderness pain is temporarily abolished if the patient is enabled *to abduct the arm actively against* gravity a major tear is unlikely Arthrography will demonstrate a communication between the shoulder joint and the subacromial bursa if a communication is present the tendinous cuff must be torn These tests can be of real practical value, but without special skill and experience in their performance and interpretation the results may be equivocal Effective treatment of these major tears of the *cuff presents further difficulties In general* the results of operative repair are poor, it seems that simple suture will often be unsuccessful because the tendon is usually degenerate Possibly attempts by other means to provide a stable fulcrum, whereby the deltoid could take over the sole control of abduction, might be more successful one possibility would be to establish a new joint surface between the upper end of *the humerus and the under surface* of the acromion

"*Frozen*" *shoulder* presents some of the most baffling of all shoulder problems. For no clear reason, and typically without preceding injury, the shoulder becomes painful and stiff There is a proportionate limitation of all movements, which are often reduced to as little as 20–30% of the normal range Yet there is no clinical evidence of an inflammatory arthritis, and there are no radiographic changes The underlying lesion is uncertain Reports of the appearance of the joint in the relatively few cases where operation has been undertaken are conflicting Thus Codman[4] found congestion over the supraspinatus tendon in the floor of the subacromial bursa Lippmann[5] found adhesive tenosynovitis of the long tendon of the biceps, and believed this to be a causative factor Simmonds[6] reported chronic inflammatory changes in the musculo-tendinous cuff, and to a slighter extent in the whole of the capsule, but stated that the biceps tendon was *unaffected* He believed that "frozen" shoulder could be correlated with degenerative lesions of the cuff Others, however, regard it as an independent clinical entity Arthrographic studies have shown defective filling and reduced capacity of the synovial cavity, but the significance of this finding is not yet clear, most observers agree that the interior of the joint itself appears normal at operation[7] In the face of this conflicting evidence it must be admitted that we have no certain knowledge either of the cause or of the pathology of "frozen" shoulder

Nor is the relation of the *ordinary* "*frozen*" shoulder to the "shoulder-hand" syndrome clear In the latter condition the development of a stiff and painful shoulder is followed after an interval by similar *stiffening* of the hand and fingers, which assume a position of flexion and become progressively more useless, with cold glossy

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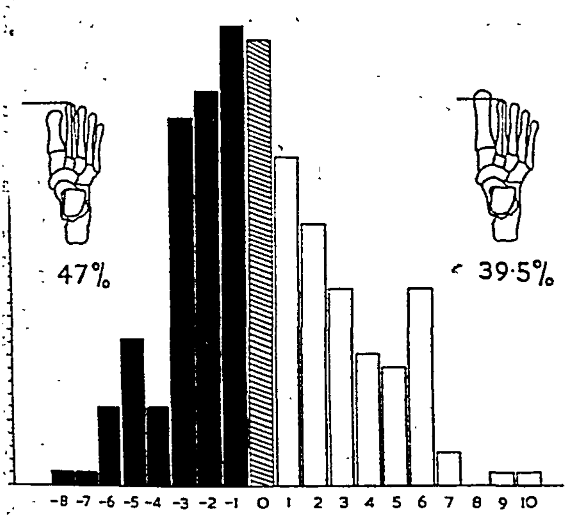

—Protrusion of 1st metatarsal in 249 radiographs of feet of normal people.

head of the second [metatarsal] to be the most nced member of the series.”

view of these conflicting statements the following rvations, made on cadavers during an investigation ie human ankle-joint, may be of interest, especially here does not seem to have been any similar stical inquiry into this subject.

OBSERVATIONS

the cadaver 133 feet were measured by a standard edure. The toes were amputated at the metatarso-langeal joints, and the perpendicular distance was sured from the head of the first metatarsal to a line wn through the tip of the second metatarsal at right les to its long axis. This assessment of the relative minence of the two bones accords with Morton's hod, which, although open to criticism (Harris and th 1949, Hardy and Clapham 1951), is the one most ely used and is moreover the method adopted by protagonists in this controversy.

here were two possible sources of error in the series: the subjects were all elderly, many showing minor t disorders, and (2) the muscles had been dissected y and consequently a partial collapse of the medial gitudinal arch was sometimes found. To estimate the ct of muscle stripping, 18 feet were radiographed ore dissection. The measurements obtained from the iographs did not differ materially from those made m the specimens after dissection. To assess whether had any effect, 249 radiographs of normal people, st of whom were between the ages of 16 and 20, were asured by Morton's method. These radiographs were ained by a standard technique and have been fully lysed by Hardy and Clapham (1951). Their method recording metatarsal protrusion differed from that pted in the present investigation, however.

he findings in the two series are illustrated by histo-ms. The first metatarsal was less prominent than the ond in 53% of dissected feet (fig. 1), and in 47% of radiographic series (fig. 2). Statistical analysis shows significant difference between the two sets of data. therefore seems justifiable to combine the two sets figures and to state that the first metatarsal is less ominent than the second in about half the total of 382 t.

The relative protrusion of the first 2 metatarsal heads not only of academic interest, for Morton's views on mechanics of human gait are based on the supposition at the two bones normally extend to the same transverse line. Before any foot disorder can legitimately be ascribed to “shortness” of the first metatarsal, the normal anatomical variation must be recognised. For example, in the 15 feet showing march fractures recorded by Flavell (1943) the variation in metatarsal protrusion does not differ significantly from that found in the present series of normal feet. In a large series of fractures of the second metatarsal bone analysed by Leveton (1945) this bone protruded beyond the first in 49 out of 87 cases. Leveton tentatively concluded that “if the second metatarsal is longer and protrudes beyond the other segments it is apt to be the site of fracture,” but this statement is valid only if there is a higher incidence of protrusion of the second metatarsal in the pathological series than in a normal one. In fact, statistical analysis indicates no significant difference between Leveton's figures and the normal incidence described above. At present there is insufficient evidence to incriminate protrusion of the second metatarsal as the important predisposing factor in the ætiology of march fracture.

SUMMARY

133 dissecting-room feet, and radiographs of 249 normal people, have been measured by Morton's technique. In about half of them the first metatarsal was less prominent than the second. This normal variation should be borne in mind when considering the ætiology of march fracture.

We are indebted to Prof. H. A. Harris, Prof. M. F. Lucas Keene, and Prof. J. Z. Young for allowing us to study material in their departments; to Dr. R. H. Hardy for his generosity in placing his radiographs at our disposal; and to Dr. D. A. Sholl for statistical advice.

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INFLUENZA IN EARLY PREGNANCY

EFFECTS ON THE FŒTUS

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A FAIRLY severe epidemic of influenza (A-prime) in Northern Ireland in December and January, 1950–51, afforded an opportunity to discover whether influenza in the early months of pregnancy produces fœtal abnormalities, in a manner similar to rubella.

A meeting of obstetricians, pædiatricians, and public-health medical officers was held; and, since retrospective inquiry, after delivery, into the illnesses of early pregnancy is liable to yield inaccurate information, this meeting decided that the inquiry should be prospective. A small committee * drew up the following plans:

The survey was to include, as far as possible, all mothers attending the antenatal clinics of the Belfast City Hospital, the Royal Maternity Hospital, Belfast, and the maternity and child-welfare service of Belfast Corporation, the first day of whose last menstrual period was between Sept. 1, 1950, and Jan. 31, 1951.

Each of these mothers would be asked whether she had influenza, defined as “a febrile illness with a sharp onset, characterised by pains in the legs, back, or head, and sufficiently severe to require that the patient went to of protein Dock's[4] experiments with Winton's technique of perfusion of kidneys with ice cold serum suggest that the glomerular capillaries resemble those of the choroid plexus in filtering a fluid containing some 15–20 mg of protein per 100 ml This modest leakage of protein would lead to heavy proteinuria but for tubular reabsorption The results of analysis of fluid obtained by glomerular puncture in animals have been equivocal on account of technical difficulties, but on the whole they point to glomerular filtration of protein Injection of proteins foreign to plasma, such as hæmoglobin, leads to their appearance in the urine only after a plasma "threshold" level has been reached—a fact best explained on the supposition that at such a plasma level the tubular reabsorptive capacity has been saturated Protein reabsorption appears to occur in the proximal convoluted tubule, and may give rise to hyaline droplet formation (athrocytosis) in the tubular epithelium when the reabsorptive mechanism is being overloaded

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* The committee consisted of Prof. A. C. STEVENSON, Dr. H. A. WARNOCK, Mr. W. S. CAMPBELL, F.R.C.S., and Mr. G. B. GIBSON, F.R.C.S.

One innocent type of proteinuria is that related to exercise Javitt and Miller[5] attribute this to increased glomerular leakage of protein which, they say, is due to the acidæmia of exercise that is supposed to have a softening effect on the intercellular cement substance of the glomerular capillaries, a potentiating factor may be anoxia from reduced renal blood-flow The degree of proteinuria is not related to the pH of the urine, which does not affect tubular reabsorption of protein This is not surprising, since the urine is acidified in the distal convoluted tubule In 3 normal persons studied by Javitt and Miller, albumin/globulin ratios of exercise proteinuria were less than unity Obviously, molecular weight is not the only factor in determining passage through the capillary membrane, and thought must be given to such other factors as the relative amounts of each class of protein in the plasma, molecular structure, and molecular electrical charge

Other types of innocent proteinuria, and also the proteinuria of organic renal disease, require further study along such lines as those followed by Javitt and Miller. Investigators should beware of fallacies, one of which has lately been uncovered by Doxiadis and his colleagues[6] These workers have proved that physiological proteinuria does not occur in the newborn infant, belief that it did had been based on false results from the highly concentrated urine, containing large amounts of urates, that may be passed in the first week of life

ALOPECIA AREATA

THERE has been remarkably little progress in our fundamental knowledge of the causes of loss of hair since the description in *Leviticus* of the differences between leprotic and non-leprotic forms of alopecia We recognise an androgenic alopecia in both males and females and we recognise loss of hair from various scarring diseases affecting the scalp But what of alopecia areata? Is it caused by an infection, is it a "trophoneurosis," or is it a symbolic expression of inadequacy, usually sex-based?

Anderson[7] in a study of 114 patients with alopecia areata found that there had been an emotional shock before the onset in 23%, and various degrees and forms of mental disturbance in another 22% A further 28% had some kind of infection, general and local, or vague ill health before their hair began to fall, but the remaining 27% were apparently in perfect physical and mental health The condition often affects children, and Brown[8] found that in 300 patients 57% of first attacks occurred under the age of 21, and only 9% over 40 The focal-infection and eye strain theories have largely been counted, and opinions now seem divided between explanation of emotional symbolism and that a hypothetical virus or toxin which causes a t neurosis, but no single theory seems to fit all cases

Ignorance of the cause leaves treatment in an state of uncertainty The rubefacient effect of u violet irradiation applied by a physiotherapist is g believed to be more effective than a similar result p duced by the patient's own efforts with "[illegible] If this is true it suggests that the kindly presence of t physiotherapist has more influence on hair growth th the remote figure of the doctor symbolised by the b on the mantelshelf Feeny[9] reported that local app tions of thorium-X were effective, but other wor have found that, while it succeeds in some pat others remain unchanged or even become worse Wh different people obtain such different results, the influ of enthusiasm and confidence must be weighed on t one hand against casualness and scepticism on the oth Many endocrine substances have been used with success Walker and Rothman[10] examined 230 patie with alopecia areata, and came to the conclusion that i the overwhelming majority there was no evidence o endocrine abnormality to be found from phy examination or laboratory tests They neverthe thought that endocrine factors might play a small pa because alopecia areata is often more severe wh begins before puberty, because regrowth may o during pregnancy[11 12], and because some example alopecia areata begin at the same time as thyrotoxic They had no success with large doses of oestro progesterone, lactogenic hormone, and deoxycort

Wilson[13] has now described regrowth of hair in 1 patient with alopecia areata and in 3 with alopecia universalis 8–10 days after the beginning of treatm with adrenocorticotropic hormone (A C T H) He co cluded that this effect might be due to the influence o A C T H on inflammatory exudates, to inhibition of t allergen, to increased local blood-supply, or to a specific adrenal hair-stimulating hormone Dillaha a Rothman[14] have described partial regrowth in 16 out o 22 patients treated with cortisone (100–150 mg daily In 14 the regrowth occurred 3–4 weeks after the star of treatment It was usually only patchy but sometim the cosmetic result was satisfactory The axillæ and th pubis were most resistant to the effects of cortisone I 3 patients new patches of baldness developed during th treatment The average duration of alopecia in the fail cases was 11 7 years (with a range of 4 to 20 year compared with 4 7 years in the successful cases (3 mont to 14 years) Alopecia starting at puberty seemed to have a bad prognosis One patient also had nail changes and these improved as the hair regrew, but both hair and nails relapsed soon after treatment was stopped Similarly, Wainger[15] has illustrated successive improvements and relapses in a patient with alopecia universalis during and after treatment with A C T H and cortisone Dillaha and Rothman conclude that cortisone may act by bringing about some change in the local chemical *milieu* which perhaps influences sebaceous gland function or keratinisation However, they emphasise strongly that they do not recommend this form of treatment for general use

Regrowth of hair during treatment with A C T H or cortisone seems to be a direct result of the treatment and not of suggestion, for it regularly begins 3 to 4 weeks

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[10] Walker S A, Rothman S *J invest Derm.* 1950 14 403
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[13] Wilson, R A *Ibid* p 646
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Medical Societies

MANCHESTER MEDICAL SOCIETY

Cerebral Abscess

a meeting of the pathology section of Manchester al Society on Nov. 12, Dr. G. K. TUTTON said that aprovement in the results of surgical treatment racerebral abscesses was due to the control of ial infection by antibiotics and the avoidance of traumatising drainage procedures. A 20-year y of the cases seen in the Manchester University surgical unit showed an increasing number of cases diminished death-rate since the use of penicillin 15. The mortality for treated cases of all types up years ago was 60%; for 68 cases since then it had to 29%, or 13% (in 54 cases) excluding 14 untreated its in whom the condition was undiagnosed during

cteriological examination was of paramount impor-, since this indicated the correct choice of antibiotic. liagnosis and localisation great use had been made ctro-encephalography, which showed a characteristic delta activity with a delta focus very close to all lying supratentorial abscesses. Air ventriculo-ty was rarely used, but occasionally carotid ography was of value.

these means abscesses could be so precisely localised aspiration was feasible. Excision, either early or was practised only in certain cases where aspiration ailed.

scesses were due either to direct or to vascular d, either from extrathoracic sources or from sup-tive chest lesions. Of 8 patients with cerebral sses from extrathoracic sources none had died; of 10 patients with abscesses from thoracic lesions d died. In the latter group the diagnosis was ed less quickly, and here antibiotics were the most rtant therapeutic factor. 3 patients with multiple ral abscesses had had successful pulmonary resec-. Of 23 patients with frontal or occipital lobe esses, mostly from direct spread of infection, none died. Of 12 patients with temporal otogenic abscesses d died; and of 7 with cerebellar otogenic abscesses d died. Of 12 patients with abscesses, vascular in n, in the parietal lobe 3 had died.

the last 37 cases of cerebral abscess, 21 had penicillin-tive organisms and were sterile after two aspirations instillation of penicillin; 2 needed more than three ations, and 2 never became sterile so that excision necessary. The remaining 16 cases, which had cillin-resistant organisms, were otogenic. In peni-t-resistant cases there was no really suitable anti-c for local instillation; for streptomycin has a limited on, and chloramphenicol and aureomycin were rela-y insoluble. Polymyxin has been tried in 1 case only. cases due to resistant organisms local application of a 000 solution of hydrarg. perchlor. had proved useful.

r. LEWIS PARKER referred to 68 cases of brain ess, 60 of which had been examined bacteriologically. n the initial specimens of pus 61 strains, from 10 ies or groups of associated species, of bacteria were ted. The commonest organisms were *Staphylococcus genes* (15), *Proteus vulgaris* (11), and non-hæmolytic ptococci (9). This wide range of bacteria underlined need for careful bacteriological examination.

r. Parker outlined a comprehensive technique of mination, including stained film of the pus; blood-r plate culture incubated under aerobic, micro-philic, and anaerobic conditions; and broth culture Brewer's thioglycollate medium, glucose broth, and tley's broth.

he bacteria found in an abscess were related to the terial flora at the primary source of infection. Thus abscesses in the temporal lobes or cerebellum, due to direct spread from the ear and associated structures, were mainly due to gram-negative bacilli, *Proteus vulgaris* being the commonest; anaerobic organisms had been found on several occasions. Abscesses in the frontal lobe following direct spread from the frontal sinuses were due to normal inhabitants of the upper respiratory tract, mainly gram-positive cocci.

Abscesses arising through direct-spread from osteomyelitis of the skull or through fracture of the skull were usually due to *Staph. pyogenes*. Hæmatogenous spread from the chest was due mainly to non-hæmolytic streptococci and the bacteroides group of organisms; in 5 of these 12 cases no organisms had been isolated from the pus. Other workers had also experienced this high proportion of negative findings.

The sensitivity of the organisms to antibiotics was determined by the dried-disc and by the serial-dilution techniques. Local administration of the appropriate antibiotic was necessary when the abscess was encapsulated. Penicillin and streptomycin were given most commonly. In many cases the abscess was rapidly sterilised, but in some the organism proved resistant to these antibiotics, and in 4 of such cases chloramphenicol or aureomycin had been used locally with good results. The combined administration of two or more antibiotics had been considered in recent cases, but this had not been found necessary in any of the cases investigated.

Reviews of Books

The Science and Art of Joint Manipulation

Vol. 2. *The Spinal Column.* JAMES MENNELL, M.A., M.D. Camb., consulting physician in physical medicine, St. Thomas's Hospital. London: J. & A. Churchill. 1952. Pp. 264., 42*s*.

PERHAPS science and art should be transposed in the title of this book, which complements Dr. Mennell's earlier volume on the extremities. On such topics as the "binding" of joints and sacro-iliac strain he sets out at length individual views which may not be universally accepted. And yet, as in other fields, such is the importance of close attention to the patient, in sum and parts, that the application of a particular skill may yield empirically the most satisfactory results. Of the practical value of Dr. Mennell's methods there can be no shadow of doubt, even if some of his therapeutic arrows succeed by reaching quite other than their ostensible targets. And who will not applaud the comment that "It is not a great thing to ask that, when symptoms do not conform to routine diagnosis or do not respond to treatment, the joints corresponding to the region of the symptoms should be examined"? Errors in diagnosis will persist until the technique of joint examination takes its proper place in medical and orthopædic training. Meanwhile, we can refer to Mennell.

✓Biochemistry and Human Metabolism

B. S. WALKER, M.D., PH.D., professor of biochemistry, Boston University School of Medicine; W. C. BOYD, PH.D., professor of immunochemistry, Boston University School of Medicine; I. ASIMOV, PH.D., assistant professor of biochemistry, Boston University School of Medicine. Baltimore: Williams & Wilkins. London: Baillière, Tindall, & Cox. 1952. Pp. 784. 68*s*. 6*d*.

THIS outstanding book contrives to present modern biochemistry, without undue simplification, in the main fields which touch on clinical medicine, and it also tells the biochemist about the medical significance of his subject. These things it does in a style so free that it is a pleasure to read. The organisation of the contents is unusual for a textbook of biochemistry: it deals first with structure, pride of place being rightly given to proteins, and then with control by enzymes and hormones, with growth (with consideration of nucleoproteins, cancer, and heredity), with metabolism, including nutrition, digestion, respiration, excretion, and electrolytes, and finally with the pathology of vitamin

Special Articles

SOME PRACTICAL CONSIDERATIONS IN THE CARE OF THE OLD*

NANETTE H NISBET
M D Glasg
SOMETIME CHRISTINA HANSEN RESEARCH FELLOW IN THE UNIVERSITY OF GLASGOW

> "You are old, Father William," the young man said,
> "And your hair has become very white,
> And yet you refuse to remain in your bed
> Do you think, *at your age*, it is right ?"

THE attitude of doctors and administrators towards sick and infirm old people has been discussed many times in recent years Reports from various parts of the country reveal what can only be described as a state of widespread apathy for the plight of old people in need of medical care These reports emphasise the need to provide opportunities for medical students and doctors to work for a time, at any rate, among old people Not the least important advantage of this kind of experience is that the doctor becomes aware of the far-reaching effects of the social policy of a community on the standards of medical practice In my own experience of institutions for old people I have heard the remarks that indicate the unimaginative outlook Here are some of them

"These patients are sent here to die, nothing can be done for them If it could, it would have been done in the hospitals they came from"

"Nothing must be done for them, for the nursing staff are employed on that understanding, and they will refuse to work here if any treatment is begun"

'If the lay administrators could sign death certificates there would be no need for a doctor"

"If you make this place too attractive, too many will want to come in"

"There is no use in re educating the patients to walk if they cannot be discharged, for no hospital beds will be released thereby"

'Anyhow they have been in bed too long, and are all confused and senile"

"The food cannot be as bad as that, or someone would have complained before"

"Clothes cannot be supplied to hospital patients, anyone who is fit to be out of bed is fit for Part III accommodation."

A Survey in a Hospital

A survey at a former poor-law institution was made between September, 1949, and February, 1950, and concurrently reforms were proposed At the time of the survey there were 622 patients in the hospital, 207 women and 415 men They could be grouped in the following categories

(*a*) Those who could walk but were not fit to live alone or in part III accommodation 79 women (38% of the 207 women) and 145 men (35% of the 415 men)
(*b*) Those who needed constant help, or re education in walking 60 women (29%) and 176 men (42%)
(*c*) Those who were unlikely to walk again and needed nursing care 68 women (33%) and 94 men (23%)

Only 45% of the men and 30% of the women had been in the hospital for less than a year, that is, the majority had been an unconscionable time a-dying How much longer were they likely to live ? The fact that elderly people are likely to die within the next ten, twenty, or thirty years seems to be no good reason for leaving them untreated—unless we wish to follow Osler's jocular suggestion that everyone should be quietly disposed of with chloroform on reaching the age of 60

In view of the régime to which the nurses had become accustomed, it was to be expected that they would at first be sceptical about proposed reforms They echoed —not smugly but regretfully—the prevailing note, saying "These patients have been in bed too long for anything to be done now" They feared to be held responsible "if anything happened" to a patient when up (anything that happened as a result of lying in bed was a venial offence), and regarded "letting a patient fall" as a nursing crime to be avoided at all costs To some people it is axiomatic that falls are always the result of a nurse's carelessness, but in point of fact they can happen even when a nurse is standing close to the patient's chair The nurses had also noticed the transient spells of unconsciousness in the elderly which are discussed below, and were reluctant to allow patients out of bed except on the most definite and specific instructions from the doctor.

In that they were perfectly right There are some who regard rehabilitation as a nursing affair "Tell the nurses to get them up, that's all." But it is not the business of a nurse to decide that a patient is to get up, or how he should be got up, and for how long If an elderly patient who has been in bed for years is suddenly dragged out and stood on his feet, he may become unconscious, or feel so ill that he subsides on the floor and makes no effort at all

A doctor, about to tackle Mrs McA, was told that she had been up once before and had been most uncoöperative: she had been lifted out of bed and helped to her feet, and—according to the ward sister—she just sat on the floor and screamed According to the patient she felt "dreadful" and thought she was going to die This patient had been years in bed, and her hæmoglobin was only 6 3 g per 1

The nurses, however, as soon as they saw what could be done, and realised that it was for the good of the patients, offered no opposition to the new plans, and their attitudes ranged from interested toleration to extreme enthusiasm Even the most conservative sisters were soon uttering the accepted dogmas of geriatrics The sister in whose ward rehabilitation was first begun possessed a fine pioneering spirit, and the policy "let bad alone lest worse should befall" was obviously abhorrent to her nature In spite of the most distressing criticisms levelled at her from some quarters she never wavered in her enthusiasm and loyalty The nursing staff was far too small for a geriatric unit, and unsuitably distributed, the nurses were much hampered by domestic duties of polishing and dusting, and the lack of some of the usual nursing aids, such as trolleys, and they had—until the patients were regrouped in October 1950—very difficult heterogeneous wards, with a further admixture, in winter, of acutely ill adults and infants But by their brisk and intelligent cooperation they made possible far greater progress than would ever have been accomplished by twice the number of apathetic nurses

Given the requisite enthusiasm, many of the initial steps in rehabilitation can be taken without waiting for elaborate equipment or physiotherapists—this hospital of course had neither The absence of certain basic necessities, however, was an almost overwhelming drawback The shortage of clothes, armchairs (there were neither padded chairs nor cushions), and outdoor shoes (which are much better than slippers for those relearning to walk) greatly retarded progress The cold draughty wards, the slippery hospital floors, and the lack of hand-rails and wheel-chairs made it unnecessarily difficult to induce the patients to make a real effort When rehabilitation first began there were not even enough dressing gowns to go round, and the patients had to be got up in relays When a dressing gown went to the laundry several patients had to be kept in bed until it returned Those who were up had to take turns of the few armchairs Although there had been some improvement since September, 1949, when the general survey was begun, in the first half of 1950 there were only [illegible] armchairs and 61 frocks available for 108 female "up

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* Based on a thesis submitted to the University of Glasgow for the degree of M D

THE LANCET

LONDON: SATURDAY, JAN. 24, 1953

Experimental Teratogenesis

OUR attitude towards congenital malformations d fœtal death is now changing greatly. There was a ne when tragedies of this kind were regarded as a tribution for some maternal sin of omission or comission. MENDEL's work, however, and the birth of e science of genetics, made it possible to regard onsters as a matter which was finally decided at the oment when conception took place. From this ate of mental resignation we were aroused in 1941, hen the clinical work of GREGG[1] on the association maternal rubella with fœtal cataract suggested that en brief interference with the environment of the etus during its development sometimes produces ngenital abnormalities. Since then other clinical idence has accumulated.

For the last fifty years the experimental embryogists, led by SPEMANN, have been producing monsters aquatic creatures by interfering with the embryo. he number of agents used successfully for this urpose is very large, and it appears that the precise ature of the agent may be less important than the iming and the magnitude of the interference. For bvious reasons such methods could not all be applied o the relatively inaccessible mammalian embryo; nd a new technique had to be adopted by which the aternal-fœtal system as a whole was exposed to the gent under investigation, the mother conveying this gent indirectly to the developing tissues. Thus ALE[2] was led to suggest that lack of vitamin A in he maternal diet could cause anophthalmos in pigs nd since then other workers have investigated in odents the teratogenic effects of other vitamin eficiencies and of many physical and chemical agents. mong these agents was anoxia, which is easily tandardised and readily applied; and we owe to NGALLS and his co-workers at Harvard[3] the idea of using the mouse for a systematic study of the results of maternal anoxia at different stages of pregnancy.

Mice at a known stage of pregnancy were exposed to a low atmospheric pressure for a single period of five hours; and the litter was subsequently delivered by laparotomy on the nineteenth day of pregnancy. Control pregnant mice maintained at normal atmospheric pressure were treated in the same way. The fœtal death-rate was significantly greater in the experimental group than in the controls; and among the living embryos in the test series there occurred gross malformations, such as septal cardiac defects, irregularities and fusions of ribs and vertebræ, cleft-palate, and anencephaly. In the controls some of these defects were not observed at all, and the incidence of others was negligible. INGALLS and his colleagues believe that the genetic strain of the mice used may partly determine the site and incidence of the defects; but the degree and timing of the anoxia are also important. Mice exposed to a pressure equivalent to a height of 27,000 feet produced more deformed fœtuses than those exposed to a "height" of 25,000 feet, and the deformities were more severe. Again, exposure during the ninth or tenth days of gestation caused malformations of the ribs and vertebral column; but the same exposure at other times produced quite different forms of damage. They suggest that anoxia affects the tissues which at the time of exposure are rapidly differentiating and therefore have a high oxygen demand.

This study is undoubtedly of clinical interest. Brief acute anoxia can produce fœtal deformities in mice. What, then, of anoxia in man? There is some fragmentary evidence, summarised by INGALLS and his associates, that among peoples living at high altitudes the incidence of congenital deformities and the fœtal death-rate may be higher than at sea-level. It might also prove valuable to pursue the possibility (already raised by a case-report by OLIM and TURNER[4]) of an association between congenital defects and maternal anoxia from cardiac conditions or acute anæmia. Much more important, however, is the broad concept that lies behind this work. Anoxia is merely a convenient example of what is fashionably called a "stressing agent"; and if, as seems possible, congenital defects can be produced, even though perhaps only in susceptible people, by non-specific maternal stress, a whole new field will at once be opened up for quantitative as well as qualitative study. The problem is a long-term one, especially since experimental results must be correlated with parallel clinical research; but in the end it may be, as INGALLS and his colleagues suggest, "that intelligently conceived measures to protect the fragile embryo or the vulnerable fœtus will ultimately be devised." It is a sound objective.

The Postoperative Chest

POSTOPERATIVE chest troubles are still common enough to disturb the abdominal surgeon. It is true that many of the incidents are trivial and appear as a mere exacerbation of pre-existing bronchitis; but at the best they add to the patients' discomforts, and even minor episodes may carry a risk of bronchiectasis or other permanent damage.[5] The usual lesion is an infected area of collapse—commonly of a patchy lobular, or segmental, distribution, but sometimes involving a lobe or a whole lung. Prophylactic breathing exercises and penicillin are still widely used, though PALMER and SELLICK[6] could find nothing to recommend them. However, in an article in this issue they describe very different experiences with inhalations of a bronchodilator, used in combination

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[1] Gregg, N. McA. *Trans. ophth. Soc. Austr.* 1941, 3, 35.

[2] Hale, F. *Amer. J. Ophth.* 1935, 18, 1087.

[3] Ingalls, T. H., Curley, F. J., Prindle, R. A. *Amer. J. Dis. Child.* 1950, 80, 34; *New Engl. J. Med.* 1952, 247, 758.

[4] Olim, C. B., Turner, H. B. *J. Amer. med. Ass.* 1952, 149, 932.

[5] Morle, K. D. F., Robertson, P. W. *Brit. med. J.* Jan. 17, 1953, p. 130.

[6] Palmer, K. N. V., Sellick, B. A. *Lancet*, 1952, i, 345.

Walshe (1946) states that the term "vasovagal" was originally coined by Gowers for attacks (described to him by patients) of a growing sense of precordial and *abdominal discomfort and a feeling of impending death*, the extremities and the face grow pale but consciousness is not lost Nothing is known of the heart action in these attacks which develop slowly and pass off slowly, lasting as long as half an hour Pickering (1951) writes that he finds it particularly difficult to accept the idea of cerebral arterial spasm to explain attacks of transient paralysis in patients with essential hypertension There is usually no precipitating factor and *consciousness is not lost* He has seen similar attacks in patients with mitral stenosis and auricular fibrillation, which may be attributed to blockage by an embolus, therefore similar attacks in hypertension may also be due to organic occlusion of a cerebral artery—by thrombosis, or hæmorrhage into the wall, or by sudden expansion of the wall (arteriolar necrosis) Further investigation of the "wee turn" is obviously necessary

Falls in the Elderly

There are many causes of falls in the elderly and the results of even a very minor fall can be serious Some complain that they could "trip over a pin" this may be due to incoordination, weakness, or shuffling gait, but the inability to recover balance quickly—as a younger person would—is the real disability Slippery or uneven ground and poor vision may also add to their troubles, so that they feel very unsure of themselves, and the exclamations of well-wishers to "watch" and "take care" only add to their anxiety Quite often a *patient, when questioned after a fall, will admit to* having felt off colour and shivery all day, and is found to have pneumonia—the cause, not the result, of the fall Some find that their unsteadiness increases in confined spaces, as in parkinsonism, or after prolonged sitting, or in unfamiliar surroundings Sheldon (1948) found vertigo an important and distressing symptom, it was present in one form or another in 51 6% of his cases He suggests as causes, changes in blood-pressure, and diseases of the ear, but considers that "senile degeneration of the labyrinth" is most likely especially as the incidence increases with age This vertigo may be severe enough to make standing impossible, and is often induced by looking up This is also noted by Critchley (1948) Alcohol and sedatives naturally increase any *tendency to unsteadiness Platt (1950)* emphasises that dizziness is not invariably present in hypertension, it is not rotatory as in labyrinthine upset, but is more a light-headedness after stooping Sudden extreme weakness, with or without unconsciousness, usually occurs at rest but may result in the patient's falling off his chair Similar attacks are common where the stool type of commode is used, the fall may be due to loss of balance, or to a sudden cerebral anæmia caused by straining or sudden defæcation Another cause of falling is sudden weakness of the legs, similar to that at the onset of cerebral thrombosis but affecting the legs only and of very brief duration Though remaining fully conscious, the patient may be completely helpless and quite unable to rise Sheldon suggests that the whole *central* mechanism subserving postural tone is liable to sudden failure More definite causes of falling are the sudden onset of cerebral hæmorrhage or thrombosis with immediate onset of paralysis and in some, a complete loss of consciousness A substantial proportion of such attacks pass off in a few days

Of the patients at the hospital I have been describing 5% complained of dizziness or unsteadiness Sheldon found a liability to fall in a third of his cases, and that it increased with age and was commoner in women, the younger age groups complained of a feeling that they might fall

Often a fall, especially in the street, results in a to hospital, this was the original reason for admission 8% of the females and 6% of the males in the hosp at the time of my survey McEwan and Laverty (19 found falls to be the cause of admission in 6% of the cases and a liability to falls in a further 4% Only a of the patients admitted after a fall were found to ha some definite lesion, such as hemiplegia or fractur femur, but all except a very few were appar destined to languish in bed for the rest of their li Certainly, as Sheldon remarks, a fall may precede general break-up But that is a terminal condition, a it is only too common to find a patient who fell ten yea ago, and who has no demonstrable lesion as the cause result of the fall, still confined to his bed

When rehabilitation began a few patients objected getting up lest they might fall, but it was usu found that relatives or nurses had advised staying in Such excessive caution is partly due to humane motiv but partly to that fear of responsibility which been alluded to before True even a simple fall may disastrous for the elderly patient, but it would be even worse disaster if fear of falling were regar as a good reason for keeping so many people in bed

Treatment of Incontinence

It is easier to prevent incontinence than to cure once it has become habitual A patient who finds h incontinence accepted by the nurses comes to consi it inevitable, and ceases to try to prevent it For th *reason a patient should never be told that he is necessaril* incontinent because he has had a stroke Tho Thomson (1949) asserts that there is general agreem *that incontinence cannot be avoided by bedpan roun* at frequent intervals, there are some patients who remain continent if given a bedpan at frequent regu intervals or immediately on asking If the patient incontinent at night, he should be wakened some tim before the incontinence has occurred and encourage to pass urine It is always worth while to try th *effect of reducing the fluid intake in the later part of th* day, though not always effective, this expedient mak all the difference in some cases Some patients wou benefit if a bedpan were offered not only after meals bu before meals An adequate number of bedpans an urinals is essential, for some cannot pass urine to orde Male patients can often be kept continent if there is urinal within easy reach and if care is taken to emp it frequently The urinal holder described by Ingha (1951) should be more widely used Patients of eith sex may find the bedside commode easier to use tha the bedpan, even if they have to be lifted out of be *It is recognised that the bedpan is difficult to use in be* and it has been *proved* that patients expend mo energy *on* it than on the bedside commode (Benton et a *1950) Malcolm Donaldson (1948) noting that his ow* device of a bedpan below the bed with a special mattre and drawsheet is considered too elaborate, feels that th bedpan should be redesigned to make it deeper and mo stable

A rubber bedpan seems ideal, but is not popular wi nurses because of the difficulty of cleaning rubber and i perishable qualities The use of a bedside commode condemned by some as being æsthetically unpleasan But where there are feeble patients with frequenc and precipitancy, the presence at the bedside of a com mode, which they can manage to use unaided—withou having to attract the attention of a nurse or mak their way to the toilet—prevents much incontinenc especially at night, in understaffed wards, and al allows the patients to preserve some feeling of ind pendence For those who are feeble and slow at walkin the thought of having to walk some distance to the toil perhaps along a cold passage or up or downstairs, mak erculosis mortality in adult life on that experienced the same group in *childhood*. This is not entirely ect: the most distinct relation shown by vious workers is between the tuberculosis mortality young adult life (15–24 years) and that of later age- ups; in fact the childhood, and especially the ler-5-year, rates do not fit at all well with the iort pattern. **Russell** has calculated the correla- ns between four variables: childhood environment, ldhood tuberculosis infection, adult environment, d adult tuberculosis mortality. The correlations tween these variables would be of great importance the indices taken as representing them were fully ceptable. **Russell**, however, measures adult environ- ent by the adult mortality from all causes other than berculosis. **Kermack** et al.[6] have shown that ortality from all causes tends to be determined by e childhood experience of the cohort. Hence the gh degree of correlation shown by **Russell** between pulmonary tuberculosis mortality and general mortality in the same 5-year age-group cannot be ascribed solely to the dependence of tuberculosis mortality on contemporary environmental conditions. **Russell** confirms **Hill**'s[7] earlier finding that there is no statistical evidence from the national figures that the decreasing tuberculosis mortality under 15 years of age is associated with any rise in tuberculosis mortality in older age-groups.

Both **Russell** and **McDonald** doubt whether the behaviour of tuberculosis mortality in later life can be fitted completely into the cohort pattern; and it is obvious that the mortality of females accords with this pattern less closely than does that of males. The strongest evidence of the importance of contemporary environment is the response of tuberculosis mortality of all age-groups to gross influences, such as war. Let us hope that the considerable falls in mortality since the introduction of chemotherapy will distort the cohort pattern in the opposite direction.

Kermack, W. O., McKendrick, A. G., McKinlay, P. L. *Lancet*, 1934, i, 698.

[7] Hill, A. B. *J.R. statist. Soc.* 1936, 99, 247.

Annotations

REMOTE CONTROL OF EPIDEMICS

The epidemiologist is very like the detective both in s way of reasoning and in his working methods. Like e detective, too, he may be either the armchair type r the man who runs about looking for clues. Usually he anages to find the cause of his disease close to the site f the crime, but two interesting reports suggest that me diseases may operate from a distance.

The first is Murray Valley encephalitis, a disease which roke out in Northern Victoria and New South Wales arly in 1951.[1] Workers in Melbourne isolated the ausative virus[2] and showed by serological tests that a arge number of healthy people, horses, dogs, and wild irds must have been subclinically infected.[3] At the ame time workers in South Australia[4] isolated from a atal case near Adelaide a virus which was identical with he Melbourne virus and closely related to the virus of Japanese B encephalitis. Now, Miles and Howes[5] report he results of further investigations into the epidemiology f this strange disease. Sera taken from aborigines in the Northern Territory in the absence of a recent epidemic howed as high a prevalence as sera from the Murray Valley; and this suggested that the disease might be ndemic in Northern Australia. Presumably the nfection is, like Japanese B encephalitis, primarily one f wild birds, and infection of man is an unfortunate ccident. Murray Valley encephalitis is clinically and pathologically indistinguishable from the mysterious Australian "X" disease, of which three epidemics have been reported. Miles and Howes suggest that Australian "X" disease is in fact an endemic infection of birds in the Northern Territory and Queensland which periodically spills over into Central and Southern Australia to produce epidemics in man. In Western Australia, and presumably also in Northern Australia, the breeding of birds does not depend so much on the time of year as on rainfall. Accordingly, meteorological data from the Northern Territory and Queensland for the past forty years were examined, and a most impressive correlation was found between years of high spring rainfall and epidemics of Australian "X" disease or Murray Valley encephalitis. In seasons with exceptionally early rains birds breed early, and young birds move to the south at a time when mosquitoes and locally bred birds are numerous. As a result, epizootics start in the newly infected area and cases appear in the neighbouring human population. If this reasoning is correct—and it seems reasonable—further outbreaks of Australian "X" disease can be expected when the rainfall in remote Northern Australia is high in the spring. It may be well, however, to remember C. H. Andrewes's comment that epidemiologists have their greatest successes in spotting cycles of past epidemics, and that they are often less successful in prediction.

The second disease that may operate from a distance is poliomyelitis. This infection is commonly supposed to spread by direct contact via infected pharyngeal secretions, although the demonstration by Kling et al.[6] that the virus can be recovered from sewage raised the possibility of fæcal transmission. Fæcal transmission may prove commoner than many people think if epidemiologists are as vigilant as Huss et al.[7] These workers investigated an outbreak of poliomyelitis in Malmö in 1949. They noticed that the incidence of cases was much higher in Malmö than in other Swedish cities, and that the first ten cases occurred at about the same time in people who had had no contact with one another. The possibility of a common source of infection was investigated; and, surprisingly, samples of drinking-water were found to be contaminated with fæcal bacteria. The complex water-supply of Malmö was explored and the infection traced to an uncovered reservoir. A 15-litre sample of this water was concentrated, treated with ether to remove bacteria, and inoculated into monkeys; these animals developed paralysis and histological evidence of poliomyelitis. Virus was found in a second sample of water taken four months later—a result that is in keeping with the known stability of poliomyelitis virus. But how did the virus get into the reservoir? Contamination from sewage pipes was excluded; but the reservoir is close to the sea, into which sewage is discharged, and wild duck and gulls, which had been seen on the reservoir, may have passively carried sewage from the sea. Huss and his co-workers hope that in further experiments they will add the final links to this chain of evidence.

To those who like epidemiological stories there will be the same fascination in these investigations as in a detective story. But perhaps it is best not to confess to too much amazement lest the epidemiologist should retort: "Elementary, my dear Watson."

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1. See *Lancet*, 1952, i, 501.
2. French, E. L. *Med. J. Aust.* 1952, i, 100.
3. Anderson, S. G., Donnelley, M., Stevenson, W. J., Caldwell, N. J., Eagle, M. *Ibid*, p. 110.
4. Miles, J. A. R., Fowler, M. C., Howes, D. W. *Ibid*, 1951, i, 799.
5. Miles, J. A. R., Howes, D. W. *Ibid*, Jan. 3, 1953, p. 7
6. Kling, C., Wernstedt, W., Petersson, A. *Z. ImmunForsch.* 1912, 12, 316.
7. Huss, R., Kling, C., Norlin, G. *Ann. Inst. Pasteur*, 1952, 83, 755.

For suitable patients the procedure is as follows ·

The patient lies on his back on a 'Dunlopillo' mattress placed on three adjustable wooden sections which have a concavity made to suit the curves of the body The perineal region lies over a hole in the rubber mattress, and all excretions pass through this hole by a funnel to a receptacle placed on a rack below If the patient remains in position there should be no soiling of the rubber surrounding the hole, and the patient's skin should never be in contact with his excreta Thus the drawsheet can be given up, and with it the sluicing of the soiled linen, but the patient's back has to receive the usual four hourly attention from the nurses, and the funnel has to be cleaned If the patient does alter his position, the rubber may have to be washed each time Some apparently completely helpless patients even succeed in getting their hands soiled, and their habits make necessary a complete change of linen and the washing of the whole mattress

THE ARNOTT GOWN

The problem of coping with the elderly bedridden patient who constantly and repeatedly contaminates the hands with fæces is of serious moment to nurses Many such patients appear to be perfectly sensible and agree when remonstrated with that their habits are foul In some hospitals the device is used of making them keep their arms outside the bedclothes, but this cannot be done unless the wards are reasonably warm and there has to be sufficient staff to enforce the rule For patients who are sensible enough, occupational therapy is of benefit as a means of keeping their hands employed Some nurses apply a drawsheet like a baby's napkin, but the persistent patient can circumvent any such barricade, and it has the further disadvantage of acting like a kind of fæcal poultice, causing the skin of the back to deteriorate The use of sedatives is effective and justifiable in the insanely filthy, but the doses have to be high, in fairly sensible patients sedatives do more harm than good and by causing mental confusion give them some excuse for their habits The weekly enema is found to be of great benefit and prevents *constant* soiling in those who are well enough to stand it Sister A Arnott has devised a modification of the ordinary hospital nightgown, which can be used in an ordinary bed or with the Brocklehurst bed, and this has been completely successful (Arnott and Nisbet *1952*) When wearing this gown, the patient feels much warmer and her hands remain clean

PREVENTION OF SMELL

Some of the people who live or work in the ward may become accustomed to the smell of an incontinent ward, but not all do, and certainly visitors to the wards are bound to be disgusted if measures are not taken to deodorise the atmosphere A great deal can be done by the regular, frequent, and complete changing of linen and washing of the skin which is carried out in a well-run ward But even so there are bound to be times when some smell is unavoidable, and it is at its worst just after a "purgative night" or an "enema day," when the bowels of many patients move at about the same time

The odour of fæces appears to vary considerably in different patients Nurses report that some patients always have extremely malodorous stools, in others they are offensive only after some digestive upset or when the stools are loose Attempts to overpower the smell by spraying the ward with some strongly scented liquid are not as a rule very effective On the contrary, the combination of an offensive odour with a perfume is often particularly sickening Adequate ventilation is important, but elderly patients seem to have a curious dislike of open windows The use of the Bohmansson toilet chair cannot solve the problem in the incontinent vegetable type of patient, or in very contracted or very heavy patients who cannot easily be got out of bed One solution appears to be to fix the malodorous gas, as with Prof Stanley Alstead's deodorising device, charcoal blanket (Alstead 1942) But that unfortunately is not suitable where there is such danger of its being soiled Moreover, fæcal odours are largely attributable to the presence of sulphuretted hydrogen, and gases with a low molecular weight and high degree of volatility, such as this, are not readily adsorbed on activated carbon Ammoniacal odours, too, easily penetrate a screen of activated carbon, and the charcoal blanket is therefore of no value in minimising the nuisance of this particular kind of smell from incontinent patients Chlorophyll tablets, taken by mouth, which are said to destroy the smell before it reaches the open air, are still on trial

Retention of Urine

In the treatment of retention of urine in the male a few of the more domestic procedures should be carried out before catheterisation is attempted, or the patient transferred to hospital Getting the patient out of bed, hot applications to the lower abdomen, hot drinks, hot baths, the reduction of a hernia, and the administration of an enema should all be tried Carbachol has sometimes an effect but is considered inadvisable when there is much distension and the prostate is enlarged When these measures have failed, the treatment depends on the ease of getting the patient into hospital and the type of treatment advised by the surgeons there

Unfortunately at our hospital there was no close liaison with a urological surgeon, and when emergency admission was impossible, catheterisation had to be carried out to relieve the patient's symptoms Once he had been admitted to a surgical ward, he returned only too often with a suprapubic cystostomy

Wilson Hey (1946) says that the suprapubic tube should be relegated to the museum of medieval prostatectomy and advocates primary suprapubic prostatectomy as being the only clean approach to the prostate He thinks that slow decompression is not only harmful but also unnecessary and that postoperative uræmia is due to infection He advises that the patient should be out of bed every day after the operation even if only for a few minutes Walters (194 too, advises immediate prostatectomy for urinary retention He states that there is no need for gradual decompression with its dangers of infection, either by catheter or suprapubic tube

Riches (1949), however, advises gradual decompression to avoid intrarenal hæmorrhage (A restless patient, confused by pain often disconnects or removes the catheter) He regards suprapubic catheterisation as better than cystostomy and prefers a two stage to a one stage operation He states that the mortality should not exceed 5%

Stewart (1949) reports on 1960 prostatectomies with a 3 01% mortality He describes catheterisation for acute retention after the injection of sterile water soluble lubricant as an alternative he suggests suprapubic aspiration, and he believes that repeated catheterisation has no place in modern treatment Prostatectomy in those suffering from cerebral softening is apt, he says, to cause further mental deterioration. But we can add that suprapubic cystostomy, too, undoubtedly leads to mental deterioration

Jacobs (1948) holds that the establishment of permanent suprapubic drainage as a method of relieving prostatic obstruction is highly undesirable and indeed must be regarded as a confession of failure It may be used as a temporary measure while the effects of renal impairment are treated He describes the numerous methods of prostatectomy—suprapubic, retropubic (Millin), Wilson Hey's immediate prostatectomy, and the transurethral route In a review (Jacobs 1951) of 500 cases of retropubic prostatectomy he found a 6% mortality, in the 80 (16%) patients over the age of 75 the mortality was 8 7% He reports an excellent functional result with ease of micturition, clear urine, complete control, absence of residual urine, and little nocturnal disturbance

This selection from many references gives some idea of the number of methods that can be employed with excellent results, without having resort to suprapubic cystostomy Admittedly these patients with

The elbow and wrist joints remain unaffected. table difference between the two conditions is that, eas the ultimate prognosis of “ frozen ” shoulder is , the “ shoulder-hand ” syndrome may cause re permanent disability. Whether the shoulder-d syndrome is closely allied to the common type rozen shoulder or is a distinct entity has yet to arnt.

BED REST AND REST ETERNAL

HE more we learn about the human body the surer are that it should be kept up and doing. The old, cially, should profit by the hymnist's advice and dread grave as little as their bed ; or as much. Dr. Charles er,[1] however, in reminding us of the dangers of the , is careful also to point out that confinement to it not be beaten as a means of forcing the overtired to . Few of those sentenced to this form of imprisonment plain much after the first day ; for leisure, as we all w, is a drug of addiction. “ There may be restlessness a few days, but then complacency arrives, in the ond week laziness sets in, and later the difficulty may l be to get the patient moving again.”

ut for the old and enfeebled bed rest spells such ngs as loss of tone in the muscles, decline of muscular rdination, stiff joints, postural deformities, pressure es, and hypostatic pneumonia ; while the slowing of peripheral circulation favours venous thrombosis l the risk of pulmonary embolism. Even when they gin to get up they may experience a transient “ effort drome ” because the reflex adjustments of the heart l circulation have become sluggish with disuse. After ong period in bed the aged may never fully readjust mselves, even if their minds have not suffered from diminished mental stimulation which such confinement entails. But by far the worst feature of bed rest a chronic ward, Dr. Baker says, is the loss of hope of y personal independence, to which is often added terness at filial neglect. The geriatricians have hieved a great thing by getting their patients out of d and moving.

The danger of venous thrombosis is now so well preciated that surgeons and obstetricians vie with ch other in getting their patients early out of bed. ysicians, of course, are not so well placed to apply the inciple, but they, too, are less anxious to keep the sick cumbent than they used to be. As Dr. Baker points t, it is not just being in bed that slows the circulation leg veins : it is the fact that the legs are so often *mobile* in bed. The venous flow, it has been shown, increased by even very small movements of the feet. rong normal people kept in bed move their legs, and aintain a normal rate of flow. But patients after erations keep still from fear of pain, and old and feeble ople, as often as not, cannot move because the bed-othes are tucked in too tightly. It seems appropriate urge once again, as we have often done before, that ery patient in a hospital bed should be nursed with a ge over his feet, so that his legs are not pinioned by the eight and tension of their coverings. Nurses are not wedded to the idea of neatness that they will put it efore the well-being of their patients. In a case like is they only need convincing of the value of the measure apply it ; though they will probably not be able to et the necessary equipment without the support of the edical staff. Dr. Baker insists that if patients must main in bed they should be encouraged to move their et ; but adds that this does not absolve their doctors om the duty of examining the legs for painful spots, calised œdema, or localised pain on movement. “ Early rombosis can easily be missed if we look only at the xposed end of the patient or are too chary of disturbing he tidiness of the lower end of the bed.” An active diaphragm, also important in maintaining a good venous circulation, can be ensured by breathing exercises.

He is as convinced as everyone else of the value of bed rest in heart-disease, but offers cogent reasons for not making it absolute. When we are lying, our cardiac output is greater, by as much as a third, than when we are erect. The normal heart, he says, rapidly adjusts itself to recumbency, but this is not so with the failing heart : the patient, when lying, has to cope with increased blood volume and venous pressure, and with relatively hampered respiration. When he is sitting up in bed, with legs extended, his cardiac output is much less, and so is his respiratory embarrassment. But it is a tiring position to maintain, and patients find they sleep best and most comfortably with the body upright in a high-backed chair. He reminds us how patients with left-sided heart-failure ease their discomfort if left to themselves : they prop themselves up with extra pillows, sit up in bed when breathless, and if this is not enough hang their legs over the side—thus diminishing the venous return to the right heart, which is pumping blood into the already congested lungs. In severe attacks they get out of bed and stand up until relief comes, often spending the rest of the night in a chair. “ What unquestioning faith they have in us when we insist on treating their complaint by not letting them out of bed at all.” It is good practice, he says, to advise them to sleep in a chair, especially in the early stages of treatment ; and he emphasises that the best way to treat the acute emergency of pulmonary œdema is to get the patient on to a firm chair. Right-sided failure, with congested neck veins, enlarged tender liver, and general œdema, has usually been preceded by left-sided failure ; so the lungs, as a rule, are congested as well. It is safer and more comfortable, he points out, to have fluid in the legs than in the lungs. The patient with right-sided failure should therefore certainly have periods of sitting in a chair. “ The few steps to and from the chair and a daily visit to the toilet give the heart little extra work, lessen the danger of pulmonary infarction, and pay a rich dividend in improving the patient's outlook.”

Even in coronary thrombosis, he finds, the duration of bed rest may be reduced in mild cases to four weeks ; and it need be absolute only during the initial period of shock. After this he recommends the use of a commode in the bedroom, for it has been well shown that this causes less effort and strain on the heart than the use of the bedpan.[2] Patients and relatives, who are apt to fear that death may result from the slightest movement, can be told that coronary thrombosis most often occurs when the patient is at rest, often in bed, and that the reason for rest is to allow the heart to deal with what *has* happened rather than with what *might* happen.

MECHANISM OF PROTEINURIA

SOME textbooks of general and applied physiology still teach, in Cushny tradition, that in health the renal glomeruli deliver to the tubules a protein-free plasma filtrate, and that proteinuria need only be considered in terms of abnormal permeability of the glomerular capillaries. Monographs of renal physiology, however, mention the alternative, or “ modern,” theory that normally some glomerular filtration of protein takes place and that there is constant tubular reabsorption of filtered protein. Proteinuria could then be due to increased glomerular filtration of protein with saturation of a normal tubular reabsorptive capacity, to diminished tubular reabsorption of a normal protein load, or to a combination of glomerular and tubular defects.

This matter has been debated since the 19th century ; but the balance of evidence, reviewed authoritatively by Rather,[3] *increasingly favours normal glomerular filtration*

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[1] *Guy's Hosp. Gaz.* 1953, 67, 11.

[2] *J. Amer. med. Ass.* 1950, 144, 1443 ; and see *Lancet*, 1951, i, 222.

[3] Rather, L. J. *Medicine, Balt.* 1952, 31, 357.

That sacrosanct pathway of shining linoleum is a busy thoroughfare for shuffling feet There is Mrs A, an old woman of 87 and nearly blind, who used to be kept in bed and was very despondent now she is cheerfully helping a much younger rheumatoid to dress Here comes Miss B, a long-bedridden disseminated sclerosis, bowling along happily in her wheel-chair, to show the doctor the marvellous tea cosy she has just completed And Miss X, that enormous and in every way difficult woman who required four nurses to move her, is pottering round the ward with two Warral sticks, lamenting her six lost years in bed The old "chronic hospital" has emerged from the doldrums

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COLINDALE

Hub of the Public Health Laboratory Service

In opening the new building of the Central Public Health Laboratory at Colindale, London, on Jan 15, the Minister of Health, Mr Iain Macleod, traced the origins of the Public Health Laboratory Service, paid tribute to the work it has already done, and expressed his confidence in its future It has, he said, grown up in a characteristically British way, and a great deal of its success has been due to the happy liaison between the Medical Research Council and the Ministry

A GROUP OF LABORATORIES

The building itself is a plain but well-proportioned brick structure four storeys high (including the ground floor) It has a copper-covered roof, a central square tower, and a semi-basement, in one or other of which are housed most of the essential services, including, for example, compressors for cold rooms at 4°, —30°, and —70°C, air filters, and a gas-fired incinerator The building is about 170 feet long and 40 feet wide, it contains some 60 working laboratories Its design allows great flexibility for making alterations such as removing or constructing partition walls The basic design of each floor is the same there is a corridor running the whole length of the building with rooms leading off on either side Each floor has a preparation room, sterilising-room, and media making facilities for its own special needs There are main and emergency staircases and three lifts—one for passengers and two for services

The third floor of the new building is occupied by the *Virus Reference Laboratory* This, under the direction of Dr F O MacCallum, has of late years given increasingly valuable help in the investigation of virus infections both in the laboratory and in the epidemiological field. The new building should remove many of the difficulties and dangers which have hampered virus work in the past. Great care is being taken to prevent contaminating organisms from penetrating into the virus research laboratories and virus-infected air from reaching the outside atmosphere One of the two service lifts, for example, is intended to travel non stop between the ground floor close to the virus animal-house and the third floor of the new building Cold rooms at 4°, −30°, and −70°C are situated on this floor conveniently close to the virus laboratory

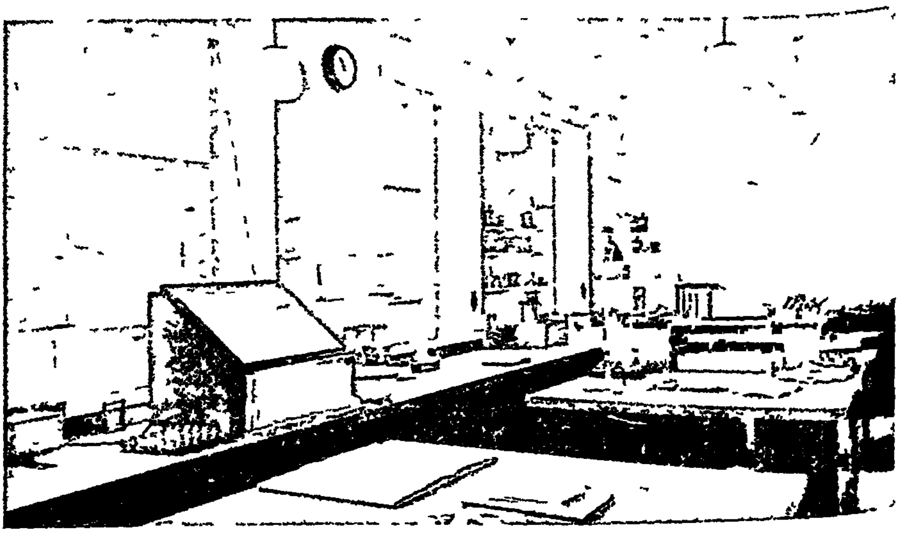
The second floor is devoted to the *Air Hygiene Laboratory* directed by Dr R E O Williams The work here will be done in three main sections

The *streptococcal laboratory* acts as the main reference laboratory for the serological typing of streptococci This has come to be recognised as an indispensable weapon in the laboratory control of streptococcal infections both in epidemic and in inter epidemic times Typing of streptococci is now carried on not only at Colindale but also at some of the regional centres

The *staphylococcal laboratory* undertakes the typing of staphylococci from cases and outbreaks of pemphigus, surgical and other cross infections, and food poisoning, to mention a few of the common sources Typing of staphylococci has proved especially valuable recently in tracking down outbreaks of food poisoning caused by staphylococcal toxins

The study of *air hygiene* will be greatly helped by the provision of special rooms for investigating problems of ventilation and of air disinfection Here, under properly controlled conditions, it should be possible to make real progress in solving some of the baffling problems presented by epidemics of respiratory infections

The first floor is devoted to the bacteriology of food and food-borne infections The *Salmonella Reference Laboratory*, directed by Dr Joan Taylor, has built up a world-wide reputation in the identification of organisms of the salmonella and coliform groups and has also investigated the bacteriology of infantile gastro enteritis On this floor, too, is the *Food Hygiene Laboratory* directed


Virus Reference Laboratory : part of a routine laboratory

starting treatment, and it invariably relapses when treatment stops. But these observations do not carry us very far. Is the action on the hair bulb, the blood-vessels, the autonomic nervous system, or the thalamus? Does it involve a virus, a toxin, or an attitude of mind? An effective answer seems unlikely in the immediate future; but at all events the latest news is hopeful, and promising prospects are opened up by the research tools, A.C.T.H. and cortisone.

THE WORLD'S SOCIAL CONDITIONS

RECENTLY we welcomed a small pamphlet entitled War on Want, issued by the Association for World Peace, as "a sober account of world poverty."[1] A large monograph[2] on this subject has now been prepared by various United Nations special agencies at the request of the General Assembly. This deals with population problems, health conditions, food and nutrition, housing, education, conditions of work and employment, and general levels of income and welfare. There are special chapters on social conditions in Latin America, the Middle East, and South-east Asia. Such a great mass of factual information has been assembled and critically examined that the book is likely to become a standard reference work for students of any social subject who are interested in world affairs.

An introduction discusses the effect of modern scientific technology on our outlook. In the basic ethics of all great religions it has always been recognised that the rich must help the poor: now arising "from this deep impulse of human charity and consistent with voluntary help and personal giving" governments have accepted the principle that the rich countries must help the poorer countries to develop their material standards of living. Such well-doing is "enlightened self-interest." All over the world fatalistic resignation to poverty and disease is being superseded by a demand for a better life, made possible by scientific discoveries. This demand is at the back of nearly all the political unrest in the world today. Unfortunately it is only too often exploited by wicked and ignorant men; nevertheless, as this report abundantly shows, there is often real justification for "unrest," which needs to be directed into creative channels.

The chapter on health, prepared by W.H.O. staff, provides striking contrasts. A map shows the present world-wide distribution of malaria, and the results of modern control methods are described. In the Himalayan Terai, in the Uttar Pradesh State of India, there is a fertile tract of over 2000 square miles; here over a thousand years ago the cultivators were driven out by malaria and the jungle was allowed in. Now, however, malaria control has already enabled man to throw back the jungle and so provided thousands of fertile farms for new immigrants. Most of the cost is falling on federal and State governments, but W.H.O., UNICEF, and F.A.O. are providing some material aid in addition to much technological skill. The effects of malaria control on productivity are immense. In Greece D.D.T. has had the effect of adding an equivalent of between 100,000 and 200,000 healthy workers a year to the labour force. The report makes it clear that in the fight against mass diseases, such as malaria, yaws, tuberculosis, and schistosomiasis, most countries need not only more doctors, nurses, and equipment, but also more and better food and educational services to combat ignorance and age-old superstitions and prejudices. The chapters on other social problems must fascinate the medical reader; for they show how much medicine has to contribute and how closely it is linked with technical problems of food-supply, education, industrial welfare, and housing. The report repeatedly illustrates causal bonds between poverty and disease.

The report is concerned more with statements of general problems than with details of methods for their solution. Accounts are, however, given of many successful ventures in scientific international coöperation, which "may be a means of solving problems that appear insoluble when viewed within the frame of national resources: and thereby the vast gap between the more-developed and the less-developed countries may be reduced. Many pioneer projects and demonstrations are under way." The campaign against yaws now being undertaken by several governments in South-east Asia with the help of W.H.O. and UNICEF is an excellent example. The early successes of the technical U.N. agencies (F.A.O., W.H.O., UNESCO, and I.L.O.), though still small in relation to the problems before them, give rise to a subdued optimism, which runs right through the report. At this time, when the failures of the United Nations on the political side are obvious and are widely publicised, we should remember the successes of the specialised agencies in promoting technical advances in many parts of the world. Scientists are developing techniques for international coöperation which politicians may perhaps copy.

A JOURNAL FOR PRACTITIONERS

IN transforming itself from a weekly into a monthly the *Medical World*[1] has become a very different journal. It ceases to be the official organ of the Medical Practitioners' Union, and its editorial pronouncements will henceforth be independent. A supplement expounding the policy of the union and edited by its general secretary will be sent to every member with his copy of the *Medical World*; but the journal itself, which now bears the aspiring subtitle "the journal of general practice," will be addressed to a wider audience. With the coming of the National Health Service, the issues before the practitioner have become less controversial, but are no less important: "general practice in Britain is about to find itself in the forefront of medical and social evolution," and there is much need to describe and discuss the merits and demerits of new patterns of practice and new ways of organising the work. The *Medical World* also wants to encourage research by publishing the original work of practitioners:

> "It is to fill a gap in British medical literature, to provide a journal written for and, as far as possible, by general practitioners. That is not to say that the specialists and consultants will be excluded from its pages; but they will be admitted as equals, with experience and knowledge to exchange, and not as superiors to pontificate and condescend."

The journal sets its tone in a series of able editorials, written in this vigorous way, and if its contributed articles maintain the level they reach in the first number it will attract and keep a great many interested readers. The accessory items, such as its letter from France, its Impressions of Parliament, and its literary musings, are highly readable—which some authorities regard as the first journalistic virtue—and it offers solid benefit in such articles as the one describing the group practice at Skipton which has lately been visited by the Minister of Health.[2] Here a main surgery was constructed in 1939 from a row of four small houses, and the five partners are now able to tell us how, with the aid of seven ancillaries (definitely excluding wives), they have preserved both their standards of work and their private life. Certainly a most encouraging example, and one which justifies the editorial belief that "we have certainly not heard the last word on the planning of general practice by practitioners. This is not the end but the beginning."

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1. *Lancet*, 1952, ii, 323.
2. Preliminary Report on the World Social Situation. United Nations, Department of Social Affairs. New York, 1952. Pp. 180. 12s. 6d. Obtainable from H.M. Stationery Office.

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1. Edited and distributed from 55, Russell Square, London, W.C.1. Annual subscription £2 2s. (post free). Single copies 4s.
2. *Yorkshire Post*, Jan. 5, 1953.

fortable armchairs has been followed since with new curtains, bed-jackets for the women patients, a regular supply of picture papers and other periodicals, a grant for a library, a piano for a convalescent home, a piano-accordion for a blind patient, and wireless installation with headphones in each ward An annual outing has been arranged for patients who are strong enough to enjoy it, and there are monthly bus rides for others, films are shown in the wards, and visits arranged to the pantomime and to Bertram Mills's circus (the Mills brothers, it seems, are great friends of the hospitals) Services for different denominations are held on Sunday evenings and are broadcast to the wards Thus, as the Minister said, is a wonderful record, which can be matched by those of many other local leagues

But the pattern of social effort is uneven over the country In many hospitals there are problems which could easily be solved by a league of friends, and he drew attention specially to the plight of the mentally ill, of the chronic sick, and of the young chronic sick, who so often live out their lives among the aged and dying He would dearly like to see voluntary effort concentrate on these groups, and if it is not yet possible to find a body of friends for every hospital, then let the friends find their way into the old barrack-like hospitals first He recalled a saying from a King's Fund report—that as people grow older their world grows smaller, and each pleasure and each grievance is correspondingly magnified Loneliness is the worst misfortune of age, and it is in the hands of the local leagues to allay that He reminded the meeting that there is a tremendous field waiting in the mental hospitals, for 42% of beds in this country are for the mentally sick, and the waiting-lists are formidable Occupational and art therapy, he suggested, offer opportunities for helping such patients, since—to quote Cowper—

> "Absence of occupation is not rest,
> A mind quite vacant is a mind distress'd"

Here the league, as he reminded his audience, can call on the experience of Mr Adrian Hill, the pioneer of art therapy, who is among its vice-presidents

The Minister was able to reassure the league about a number of matters on which it has been feeling anxiety Thus, far from regarding it as wrong for the chairmen of hospital management committees to form or initiate local leagues of friends, he is fully in favour of it It does not matter who forms these groups as long as they are formed Nor is there any objection to their holding meetings in the hospitals they are befriending, on the contrary the closer the contact between the friends and the hospital the better Again, there is no reason in the world why the matron and other hospital officers should not come to the meetings, and every good reason why they should Hospital management committees are appointed by the regional hospital boards, but he saw no reason why the boards should not consult the league when making their appointments, or why the league should not submit names to the boards for consideration The regional boards themselves, and the boards of governors of hospitals, are appointed by the Minister, but the National Health Service Act requires him to consult various specified bodies (such as the universities) and also those bodies which appear to him to be interested Mr Macleod had that day added the name of the National League to the wide range of bodies to be consulted

The prestige of the league with the Ministry is thus evidently high It has been further raised by the consent of H M Queen Elizabeth the Queen Mother, to become the Patron, as was announced by Mr J P Wetenhall, the chairman, in the course of the meeting A graceful and appropriate emblem has been designed for the league by Mr Adrian Hill

Medicine and the Law

Death Due to Butazolidine

At an inquest on a 44-year-old woman in Nott on Jan 15, the city coroner recorded a verdict of " from bronchopneumonia following agranulocytosis by butazolidine therapy"

Dr H M Rice, senior pathologist at Nottin General Hospital, said that during the past butazolidine had come to the fore as a drug for diminishing or abolishing rheumatic pain People were undoubtedly benefiting by it, 100,000 patients had been treated in this country alone Toxic reactions were, however, being reported, and of these the most serious was agranulocytosis He was of the opinion that the drug should only be administered in hospitals with facilities for daily blood counts by trained staff

Dr Rice said that the medical profession was placed in an extremely difficult position when the general public saw articles in the popular press describing new drugs that were only in the experimental stage "The public think these drugs are cure alls and demand them from their doctors, who must warn their patients that the drugs are not free from risk The patients reply that they have suffered pain for twenty years and are prepared to take a small risk to get rid of the pain It is a difficult ethical problem"

Public Health

Maternity and Child Welfare in Glasgow

Dr Stuart Laidlaw, medical officer of health for Glasgow, in his report for 1951 discusses the downward trend in infant mortality

"Within the past two years," he says, "there has been a tendency for certain writers, particularly politicians, to assume that the marked reduction in infant mortality now implies that the maternity and child welfare work has attained its ends and can now be maintained by a caretaker staff The truth is that the present reduction is really due to the elimination of the most easily preventable deaths and the service is now faced with the more difficult task of maintaining the present standards and improving them in many directions That further improvement is possible is shown by the fact that Glasgow's figures are still nearly double those prevailing in Aberdeen, for example Of course, our problem of gross overcrowding is unique and is unquestionably a major factor in the relatively high infant mortality rate in the city Among the many causes of infant deaths in which considerable further reduction could be attained are prematurity, gastro enteritis, burning accidents, and overlaying Prematurity is still responsible for more than half the neo natal deaths, and although the number of deaths from this cause has been reduced the reduction has been achieved at relatively great expense by special provision for the care of the premature child both in hospital and at home The prevention of prematurity is our aim, and this is closely allied to the ante natal care of the mother Infant mortality from this cause can be still further reduced by a standard of maternal care which ensures that the expectant mother receives optimum ante natal supervision with proper attention to diet and general hygiene Pre natal dietary carelessness is still far too common, and education of the expectant mother to avail herself of the facilities provided and to follow the advice given is still vitally necessary

" a closer liaison between the general practitioner and the maternity and child welfare department would benefit both the curative and preventive services It is disappointing that little advantage is being taken throughout the city by general practitioners of the clinic and other facilities provided for the examination of the blood from expectant mothers There is no excuse for the deaths (approximately twelve annually) which are due to failure to ascertain the Rhesus factor during the ante natal period Yet only half the mothers are tested for Rh" ients, and 33 armchairs and 176 suits available for male "up" patients. There were no wheel-chairs, rt from uncomfortable dilapidated bath-chairs. The rds were as cold and draughty as ever, and fires were nounced unnecessary for people who should either be bed or in part III accommodation.

These circumstances were easily reconciled with the despread desire to preserve at all costs the status quo. it the work still went on; the "up" patients increased ily in number, and were to be found even in the wards the most conservative and fastidious sisters. Hardness seldom encountered among nurses who actually work ith patients: what is proved to be good for the human ings under their charge is incontrovertibly good in eir eyes, and they do it with all their might.

The "Wee Turn"

The elderly are liable to sudden transient episodes of unconsciousness of varying duration, whose occurrence ends to cause the patient to be kept in bed. The different ypes described below may not be varieties of the same ondition with the same ætiology (whatever it is), but they have been seen in the same patient at different imes.

The briefest variety usually occurs when the patient s sitting in a chair; he is noticed to look vacant for a moment and may drop anything he is holding, then quickly returns to normal—a description suggestive of petit mal. Or he may become very pale, lose consciousness, and slide off his chair; but recovers immediately and completely when returned to bed, knowing nothing of what has happened. A recent meal, getting up in the morning, proximity to the fire, a warm close atmosphere (as during a film show), or excitement (at film show or ward party), may be precipitating factors; but attacks indistinguishable from these may occur on getting up for the first time after many years lying in bed, in gross anæmia, severe nausea, vomiting, diarrhœa, or internal hæmorrhage (confirmed by the subsequent appearance of hæmatemesis or melæna). Sometimes a patient may have several such attacks on successive days and then be free from them for weeks.

There are also attacks of longer duration than those just described. The patient remains unconscious for a longer period and recovers more slowly. He is very pale, sometimes slightly cyanosed, with cold extremities and feeble or imperceptible pulse, but neither tachycardia nor bradycardia. The breathing is quiet; there is no twitching, and no evidence of a lesion of the central nervous system. Sometimes there is incontinence of urine or of a very loose stool. He usually recovers gradually when returned to bed, and improves if given brandy as soon as he can swallow. He is as a rule rather vague at first, but may say that he felt dizzy or very sick, and sometimes vomits on regaining consciousness. A few patients, however, with exactly the same signs, die a few minutes later, before or after regaining consciousness, without further clinical sign or symptom—presumably of a coronary thrombosis.

Occasionally the appearances are exactly as above, but the patient does not immediately recover consciousness, though the pulse becomes palpable again and the colour improves. On examination he is found to have a definite flaccid hemiplegia. The blood-pressure is usually at the patient's normal level—of about 160/90 mm. Hg. The appearances are those of a cerebral thrombosis, but the breathing is quiet, not stertorous. The patient may remain unconscious for as long as twelve hours, then regains consciousness and is found to have no evidence whatsoever of a hemiplegia; he is usually up and about as usual within twenty-four hours. This may be repeated in the same patient several times.

Transient hemiplegia is also seen, accompanied by unconsciousness, flushing of the face and twitching of one side of the body; in such cases the pulse is unaltered. These patients often develop a permanent paralysis after several such attacks.

There is also the sudden weakness, especially of the legs, which occurs when the patient is either standing or sitting and which makes him completely helpless; it is not accompanied by loss of consciousness or alteration in the volume of the pulse, but he sometimes becomes rather pale, and reports that he felt "completely done." Such attacks are usually transient, but are on occasion the reason why old people living alone are found on the floor having lain there many hours or even for days, because they were unable to rise.

The following case-histories illustrate some of these attacks.

Case 1.—Mrs. B, aged 84, was a very pale woman with a hæmoglobin level of 7 g. per 100 ml. She had several brief attacks of unconsciousness, usually on rising in the morning, with quick recovery on return to bed. Since her anæmia has been corrected she has ceased to have such attacks.

Case 2.—Mrs. C, aged 76, has a slight right hemiplegia. For four years she has had brief attacks of unconsciousness when sitting up in a chair; she becomes pale and pulseless and recovers gradually when returned to bed. These attacks were the reason for her being kept in bed for many years. Often she has none for weeks or months, then several in one week. She is not anæmic and her blood-pressure is 150/90.

Case 3.—Mrs. D, aged 80, on several occasions became very pale when sitting in a chair after dinner. Her pulse was impalpable and her extremities very cold. She recovered gradually when returned to bed but was rather vague in manner; she could only say that she felt very sick; on one occasion she was doubly incontinent. She eventually died suddenly one night when convalescing from pneumonia.

Case 4.—Mrs. E, aged 72, is a diabetic and is blind. One day when sitting in a chair after dinner she became deeply unconscious and fell from her chair. She was very pale, but not cold, her pulse very feeble (70 per min.) and her breathing quiet. There were signs of a complete flaccid left hemiplegia. She remained unconscious for twelve hours; twenty-four hours later she appeared to have recovered completely; there was no sign of any paralysis and she was able to walk as before. The blood-sugar at the time of the attack was 200 mg. per 100 ml. There has been no recurrence (in 12 months).

What is the ætiology of these attacks in the elderly? Some are so transient that little or no investigation can be made. The pallor, the cold extremities, and the imperceptible pulse suggest a primary cardiac condition (possibly caused by vagal inhibition) with secondary cerebral anæmia leading to unconsciousness, and in some cases signs of paralysis. The patients have no obvious signs of heart-disease, their blood-pressures are not excessively high; their pulses are of a normal rate and rhythm.

Sir Thomas Lewis (1946) divided "attacks of fainting" into the following:

Postural Faintness.—Temporary giddiness or transient loss of consciousness on rising, usually in middle-aged or elderly people, especially on rising from a chair after a full meal in an overheated room.

Vasovagal Attacks.—Seen especially in the young in poor health, fatigued or fasting. It is a brief attack causing a sinking feeling in the abdomen, nausea, loss of consciousness, pallor, and imperceptible pulse. A similar attack occurs in those with aortic regurgitation.

Cardiac Syncope.—Rare compared with the other causes of fainting. He considered that most are cases of chronic heart-block; a few are due to temporary heart-block; and there are a few rare cases in which the whole heart stops beating for a few seconds. Sudden death is probably due to fibrillation of the ventricles.

Of the differential diagnosis of fainting he wrote:

> "Postural giddiness and vasovagal attacks in middle-aged or elderly people are apt to be attributed to cerebral arterial disease and regarded as attacks premonitory to apoplexy; such cases are differentiated by the absence of profound pallor or heavy sweating, the unaltered pulse, and the association of loss of memory, paresis or aphasia."

Letters to the Editor

CHILD-WELFARE CLINICS

SIR,—I read with considerable interest the contribution by Dr George, Dr Lowe, and Professor McKeown in your issue of Jan 10 Their account of the work done at clinics, and the reasons for attendance, accords with my own experience, and I agree wholeheartedly with their principles and conclusions But I cannot endorse their suggestion that an increased capitation fee should be paid for children on the lists of general practitioners prepared to provide a full child-health service from local-authority clinics

In an urban area such as Birmingham, the children attending any one clinic are patients of several practitioners If all these doctors elected to provide a full child-health service it would be impossible to organise a clinic session for each of them On the other hand, if only one or two doctors undertook the service, they would be seeing children at the clinic who were patients of their colleagues and for whom they would not be responsible outside clinic hours—a perpetuation of the present unsatisfactory system

The analogy with midwifery is clear, and in midwifery we have seen a marked reduction in attendances at antenatal and postnatal clinics It was never the intention of the National Health Service Act that all general practitioners should practise midwifery and carry out their antenatal examinations in their surgeries, but the incentive to do so has been too great

Because some practitioners' lists will now have to be reduced to the agreed maximum of 3500, the present is a very suitable time for a general revision The following scheme would, I believe, solve many problems and have a fair chance of success Since

(a) the supervision and treatment of children can be conducted more satisfactorily from a local authority clinic or health centre than from a general practitioner's surgery,
(b) it would not be practicable to arrange clinics for all general practitioners at which each practitioner could see his own patients, and
(c) it is undesirable that a doctor at a clinic should treat children who are on other doctors' lists,

the following proposals are made

1 All children under 5 years of age should be removed from practitioners' lists
2 Only those doctors willing to provide a full health service for children, including clinics and domiciliary practice, should be allowed to take children on their lists The capitation fee would be greater than that paid for other patients, the increase being refunded to the executive councils by the local authorities, which would no longer have to pay the salaries of assistant medical officers
3 Inclusion of children on a doctor's list would be made at the clinic to ensure that so far as possible the children would be identified with a doctor and a clinic serving the area There would of course be a free choice of clinics by the mother
4 The present clinic medical officers would be allowed to take children on to their lists provided they were prepared to provide a full health service including domiciliary care They are at least as well qualified as their colleagues in general practice to undertake this work

It will be objected that this scheme is inimical to the concept of the family doctor In many families, however, the individual members are on different doctors' lists, and this is especially the case with children, the mother stating that she takes her children to Dr A because he understands them better than her own Dr B Again, not all doctors are keen on work among children, and many would be glad to hand it over to their colleagues

It is significant that, of the mothers questioned a clinics, "the remainder (almost half) gave suggesting dissatisfaction with their general pra service the surgery was too far away, a surgery was no place for a child, afternoon cons was more convenient, or the doctor was abrup or too busy to make even a cursory examin Long waiting periods are another frequent ca complaint

I was interested to learn that some general prac do their antenatal and postnatal work at local an clinics In my area many practitioners would see their maternity cases at the clinics, but our insuperable difficulty has been that the patients at on any particular clinic day are on the lists of as as six different doctors Possibly a solution c found along the lines outlined above for child clinics—i e, that only those practitioners willing t full antenatal and postnatal care to their pa from local-authority clinics should be allowed t maternity cases

If both child-welfare and maternity clinics were conducted as suggested, it should be reasonable to arrange for periodic consultant sessions, o and pædiatric, with all the advantages these bring Obviously the integration of these services have been simplified had health centres been avail but the above scheme would be applicable with ex facilities and could be continued and improved t the health centres of the future

H TABB
Oldbury Area Medical Of

MITRAL STENOSIS

SIR,—In your annotation of Jan 10 about our pa on the dynamics of mitral valvular disease yo several pertinent questions

Firstly, the more benign clinical course of pat developing massive left auricles is of great intere is probable that the most important single factor in production of symptoms in mitral disease is pulmo congestion A massive left auricle, large enough to do the capacity of the pulmonary venous reservoir, wo tend to lead to lower pressures and also to pre sudden large increases of pressure Furthermore, th patients generally fibrillate early, and this also tend lower pulmonary pressures Tricuspid insufficiency, diminishing right ventricular efficiency, may well in the same way

Secondly, it does not seem surprising that Broc and others should find at operation that the orifi of the stenosed valves are of a fairly uniform size T in-vitro experiments of Gorlin and Gorlin[3] have sho that, for a given flow, the area of an orifice is inver related to the square root of the pressure gradient acr the orifice multiplied by a constant of 31 If there is incompetence (and gross incompetence, at any rate, probably excluded by selection), a small difference area will lead to a large difference in pressure gradie Thus, for a given output of 6 litres per minute, increase in the area of the valve orifice from 1·04 1 27 sq cm leads to a fall in pressure gradient fr 30 to 20 cm of water Such a difference in pressure make a considerable difference to the degree of pulmo congestion, but it is doubtful if the exploring fi of the surgeon would detect a difference of one or millimetres on the major or minor axes of an irreg elliptical valve orifice

It is more difficult to accept Brock's contention in slight symptom-free cases of mitral stenosis the la is an oval of not more than 1 5 by 0 75 cm

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[1] Wade G Werkö L Eliasch, H, Gidlund, A, Lagerl Quart J Med 1952 21 361
[2] Brock, R C *Brit Heart J* 1952 14, 489
[3] Gorlin R Gorlin, S G *Amer Heart J* 1951 41, 1

om delay going until it is too late. Many patients our hospital were admitted incontinent from part III commodation for this reason, but were perfectly ntinent in hospital. Toilets should therefore be easy access and warm, and there should be sufficient handils on the way to them. The use of commodes for mi-ambulant patients during the day should be voided if possible; they should be helped to get to he toilet or wheeled in the Bohmansson toilet chair Bohmansson and Malmros 1947). Ideally all commodes hould be permanently screened, but this arrangement ould bewilder many of the frail elderly, and some would ip over the feet of the ordinary ward screens, or try o support themselves by holding on to them. Nevertheless it may be a fact that certain patients are deterred rom using commodes because of the lack of privacy.

In patients with fæcal incontinence, examination may eveal a loaded rectum, causing retention with overflow; epeated enemata should then be given until the bowel s clear (Cosin 1947, Warren 1950). For those who are egularly incontinent of fæces, some ward sisters find hat a regular weekly enema is useful (advised also by Adams 1949 and Amulree et al. 1951); apart from one day there is little soiling; it may however be several weeks before the benefit is apparent. The weak and frail cannot be treated in this way, for some of them become cold and collapsed after an enema. For those who, in spite of routine enemata, have filthy habits and who cannot be got out of bed, sedatives may be the only possible form of treatment; patients of this type who are up and about should be kept in the ward if possible as their habits are often better in public than in the privacy of the toilets. There are also those who have no reason to be incontinent and appear perfectly sensible: they sometimes improve after a serious talk during which extreme disgust is shown and the question of their sanity raised. It is important that such patients should not be mixed with the very degenerate as they seem to take the view that they have as much right to be incontinent as the others. This has been noted also by McEwan and Laverty (1949).

Patients who suddenly become incontinent of urine should be examined to see if the bladder is distended, or if they have a urinary infection. Though in some the treatment of a urinary infection does not alter the incontinence, there are many in whom the incontinence is simply a result of frequency and precipitancy, and the pain caused by trying to suppress the desire to micturate. In some patients a week's course of a sulphonamide is sufficient to stop the incontinence, even though the infection microscopically and bacteriologically persists.

Those who become incontinent as a result of a general infection, cerebral thrombosis or cardiac insufficiency, should not be relegated to incontinent wards, as the condition is often only temporary; and in fact the cessation of incontinence usually indicates general improvement. Wilson (1948) found that many cases improved as a result of gradual distension of the bladder with fluid and inhibitory re-education training. This, however, requires a coöperative interested patient, anxious to overcome the distressing disability. Wilson quotes Allen as writing in 1733 that "in old persons incontinence is altogether incurable unless hot baths relieve them."

Many expedients devised to cope with the problem of incontinence are purely palliative and do not constitute a cure. They accept and in fact condone the patients' failure to remain continent and are intended to make things easier both for the patient and for the nurse. In the male patient, the urinal can be strapped between the thighs. This may lead to excoriation if the skin is not washed often enough. Amulree et al. (1951) recommend condom drainage in men, either in bed or up in a chair. Chapel (1951) describes a modification of this as the 'Simplic' bed incontinence appliance. Incontinence appliances such as the "frequency bag" for ambulant male patients can be of value if the patient is intelligent and of clean habits.

Incontinence appliances for women are usually unsuccessful, and cause pressure sores and areas of excoriated skin. Some who have merely a little dribbling benefit from a napkin, but if there is too much the skin again suffers. Amulree et al. (1951) advised sitting on a commode chair on a rubber ring; again there is the difficulty of giving the skin adequate attention.

Many drugs have been tried for the relief of incontinence—usually of the belladonna, ephedrine, or muscle relaxant type, but without consistently good results (Brocklehurst 1951).

Fortunately, getting the incontinent patient out of bed usually stops the incontinence. Cosin (1947) remarks: "Get them up in a suit of clothes, sit them up to the table at meals, take them to the lavatory at frequent intervals—and they will relearn the habits of childhood." Adams (1949) states that most respond when up, even if only in a chair, though the incontinence often recurs at night. Crockett and Exton-Smith (1949) found that incontinence largely disappeared with the awakening of the patients from a state of mental apathy.

At our hospital these findings were confirmed. Only a few patients were occasionally incontinent when up, and most of these were unable to walk; and instead of being very wet, as in bed, were merely a little damp. A few were incontinent when they were assisted to rise from a chair or when they failed to get to the toilet in time. Those who forget should be taken frequently and regularly in spite of protests. Incontinence in bed at night usually persists for a longer time, but with increasing mobility and lessening of apathy this too disappears. The few "accidents" that occur in the initial stages of rehabilitation are apt to discourage the nurses. But soon, forgetting this initial prejudice, they begin to tell the doctor that *of course* such and such a patient is not incontinent when up. Victory may be regarded as won when a nurse volunteers the information that "We were so short of staff at the weekend and the clean linen was almost finished, so we just *had* to get the patients up." In one ward where formerly 48 drawsheets and 48 short gowns had to be sent to the laundry every day, only 11 drawsheets and 5 short gowns were used daily after four months' rehabilitation of the patients.

Of 58 female patients who were always incontinent (31 doubly) in bed, and who are now up in chairs or walking about, 52 are never incontinent when up; 6 are occasionally incontinent of urine when up; 23 are completely continent even in bed and asleep.

It has been found that it is usually those who are unable to walk who are incontinent when up; and a good nurse will often blame herself and say that she was too busy to assist the patient at the right time. Those who remain incontinent in bed have either not been ambulant for very long or are of the bovine apathetic type.

THE BROCKLEHURST BED

The Brocklehurst bed accepts the incontinence as incurable, and makes a virtue of immobility. The patient must be able to lie flat on his back, and must be sufficiently helpless or apathetic not to roll or turn from side to side or shift his position up or down; he must not have more than a slight degree of contracture of the lower limbs. Once the principle of rehabilitation has been accepted, it is found that there are remarkably few patients with the above qualifications; and most of those who are irremediably bedridden and incontinent have contracted knees. These will in any case become fewer as the teaching of geriatrics advances.

TERRAMYCIN IN SALMONELLA INFECTIONS

SIR,—I feel that Dr Watson's letter (Jan 3) may give rise to undue optimism regarding the value of terramycin in these infections

Recently, I treated a *Salmonella typhi murium* carrier, aged 5 years, with this drug The dose used was 400 mg thrice daily to a total of 5 g—i e, approximately 4 days' treatment This dosage in a boy weighing 46 lb is comparable to the dosages cited by Dr Watson and was the maximum amount I could obtain from the South London Blood Transfusion Depot for the treatment of a boy of that age The organism was absent from the stools 6 days after completion of treatment, but 2 days later it was again present His stools have since remained persistently positive

Similar temporary reversion in the carrier state may be obtained by use of chloramphenicol

One of my patients—a carrier of *S enteritidis*—did become permanently negative after a course of terramycin The evidence of the beneficial effect of terramycin was in this case vitiated by the fact that immediately before treatment the number of organisms decreased spontaneously There is a risk of giving too much credit to drugs exhibited when natural recovery from the carrier state is taking place

Waddon Hospital,
Croydon
J J LINEHAN

SIR,—Recent correspondence on the value of terramycin in salmonella infections prompts me to record the following case

A male child, aged twenty months, was admitted to hospital with enteritis due to *S paratyphi B* He was treated with chloramphenicol ('Chloromycetin Palmitate,' 4 fluid drachms, followed by 2 fluid drachms six hourly for eight days, and 1 fluid drachm six hourly for a further six days) Though he improved clinically, he continued to excrete the organism in his fæces He was then given a combination of sulphathiazole and penicillin, and later streptomycin by mouth, but without effect

The organism was shown to be sensitive to terramycin, though unfortunately a quantitative result was not given

Three months after admission, the child was given terramycin 400 mg, followed by 200 mg four-hourly for eight days Four successive rectal swabs were then negative for *S paratyphi B*

During a recent epidemic of paratyphoid B in this area, it was found that though there was a fairly rapid clinical improvement in cases treated with chloramphenicol, many of these patients continued to pass organisms in their stools, often for two or three months and even after a second course of the antibiotic Terramycin may be of value in these cases

Llwynypia Hospital
Rhondda
M S PATHY

MARASMUS TODAY

SIR,—May I thank you for your exposition (Jan 10) of renal acidosis and idiopathic hypercalcæmia as causes of marasmus, and may I ask that in the differential diagnosis the effect on infants of the absence of maternal care be included

Chapin [1] prevented deaths from marasmus by placing infants in foster-homes instead of institutions, that wise pædiatrician, Brennermann,[2] had a rule that babies in his hospital were to be picked up and carried around several times a day, Bakwin [3] showed how infants in hospital showing successive infections and progressive loss of weight became afebrile and gained weight from the day they returned home to their mothers, in this country Sir James Spence and Prof Alan Moncrieff have for many years taught the importance of humane care of babies in hospital

I would like to think that failure to thrive from this cause does not exist today in this country, but it does, for I see the results at times, so that it is wort naming "loneliness in infancy" as a cause of ma in infancy

Guy's Hospital
London, S E 1
RONALD MACK

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[1] Chapin H B *Trans Amer pediat Soc* 1915 27 180

[2] Brennermann J *Amer J Dis Child* 1932 43, 577

[3] Bakwin H *Ibid* 1942 63 33 *J Pediat* 1949 35 512

THE ANKLE BLOW-OUT SYNDROME

SIR,—I would like to cross swords with Mr C and Mr Elgan Jones over their conclusions concerning the ætiology of leg ulcers

Their careful observations agree substantially those of most workers except at one point Th that incompetence of the valves is strictly loca the lower perforating veins, and that the valves in the deep veins are healthy (figs 6 a I would not quarrel with their findings on th but the anatomical presence in the cadaver of a rently healthy valve may not correspond to a fun valve in the living patient Large series of phleb in fact indicate that the deep veins do often extensive valvular incompetence, nor do the radi published by Mr Cockett and Mr Elgan Jones ex this possibility in their own patients

On general pathological grounds, one might expect incompetence to be extensive rather than strictly l to the lower perforating veins, since recanalisati thrombosis is so often the cause Nevertheless, in cases there is no theoretical reason why it should no What, then, is the accompanying pathology? Mr C and Mr Elgan Jones state that infection constantly with each of the four groups of factors leading to ulce with local thrombosis rapidly supervening The sup part of a perforating vein in the base of an ulcer can escape the thombosis—operation amply confirms th tion The deep part of the communicating vein remains patent as a blind diverticulum of the deep but a superficial block is no less effective for being so, all the cutaneous tributaries are likewise involved block, being in effect akin to the local ligature op proposed by Mr Cockett and Mr Elgan Jones, mi expected to cure the ulcer if there were no valvular i petence elsewhere That self cure does not occur in way suggests that we are arguing from a false hypot and that, contrary to the authors' assertion, there mu valvular incompetence elsewhere

Like any other form of reciprocating pump, the mus venous pump in the leg is only effective in the presen adequate valves It is further not just one but a ser pumps in line from below upwards, each consisting segment of vein with an inlet valve at its lower end and outlet valve at its upper end The diastolic pressure at t lower end of each is limited to the height of the column blood contained in each segment—i e, a few inches of w The systolic pressure is a function of the muscular f applied laterally to the walls and the resistance above outlet valve Mr Cockett and Mr Elgan Jones cite a f of 100 mm Hg, but it must be noted that a raised sy pressure will only be recorded in the upper two thirds of t leg, where the muscle bellies provide the necessary f Only if the deep veins show incompetence of their va *in this portion of the leg can a raised systolic pressure* transmitted to the lowest third of the leg

Now Mr Cockett and Mr Elgan Jones emphasise th incompetence is only found in the lower perforating ve and that these "are situated just *below* a powerful mu pump" They specifically draw attention to the fact t in their dissections valves are always "present in veins posterior tibial bundle" (fig 7) In these circumstan systole cannot affect the pressure in the veins *below* pump, whatever the state of the valves there Similar the diastolic pressure in the lowest third of the leg transmit through a perforating vein cannot show a rise due to incompetent valve greater than the difference in le between that valve and the next functioning valve at —i e, no more than an inch or so if the authors' content are correct That in fact both systolic and diastolic ve pressures are considerably raised in leg ulcers suggests th the valvular incompetence is far more extensive than admitted in their paper, involving the deep veins in th upper two thirds of the leg and higher tostomies do not figure as operative deaths: they discarded to chronic institutions, still attached the bed by means of tube-and-bottle. They endure existence made wretched by the debilitating effects a chronic urinary infection and the repeated pain bladder washouts and changing of tubes, in an ever- ting smell of heavily infected urine and rubber tubing. eir whole life becomes centred on the wound and the be; their habits deteriorate; they gradually curl , often under the sheet, and usually die within a year operation. Surely it would be preferable to give such tients a chance of survival, even if it were only a slight e. It is possible to get a few of them up soon after eration with a special belt and bag, and train them to ok after it themselves in a hygienic manner. They ay even go home for a time and have the tube changed a district nurse; though they usually return with mptoms of ascending infection and uræmia.

Case 5.—Mr. F, aged 69, in part III accommodation, found fficulty in passing urine one morning, but did not mention to anyone, because he was very anxious to go out on pass. was a very cold day and he had several drinks "to warm mself up." He returned at night with acute retention of ine. A hot bath and an enema gave no result and he was ansferred that night to a surgical ward in another hospital. ive weeks later he was returned to our hospital with a prapubic cystostomy. He was kept in bed to allow the be to drain continuously. His habits deteriorated. When en six months later his knees were contracted, his urine avily infected, and bladder washouts and the changing of e catheter were causing him much pain. He died nine onths after the operation, with signs of uræmia.

Fractures

Flemming (1951) states that the rules governing the eatment of fractures in the old do not differ from those niversally applicable to the treatment of injuries in eople of all ages. Too often it is found that a lower tandard of treatment is given to the old than to the oung, because it is not thought worth while to restore mperfect function. He points out that the object of the urgeon is to restore to the patients that degree of ctivity which they enjoyed before the accident, and iot some measure of activity which they enjoyed many years earlier: it is wrong to assume that, because they annot be made fit to walk three or four miles, there is no point in enabling them to potter about their room and do an occasional bit of shopping; and there is no justification for fobbing off the elderly with second-rate [illegible] Besides, if the patient enjoyed only a very [illegible] range of activity before the accident, he cannot afford to lose any of it. On the other hand treatment must not be too academic. Thus, in general it is a sound rule not to allow weight-bearing in a fractured femur after pinning until the bone has united; but this delay can render an old person bedridden.

Another reason often given for refusing proper treatment is that the patients occupy much-needed beds for a long time, and may never recover sufficiently to leave. Yet if they are left untreated, they take a very long time to die. They are not, as is so often stated, overwhelmed by hypostatic pneumonia; they linger on for months in a state of suspended but noisy animation. Of the last 50 inpatients (over the age of 75) whom Flemming had treated for fractures, only 2 failed to return home. The argument that they do not stand an anæsthetic is completely unfounded. A patient has to be far tougher to lead a useful life with a painful unreduced fracture than to withstand the stress of reduction; and patients left with untreated dislocated shoulders and Colles fractures develop nerve palsies.

The commonest fractures in the aged are intertrochanteric and pertrochanteric fractures of the neck of the femur. Flemming advises skeletal traction with a Steinmann's pin through the crest of the tibia; or as an alternative a triflanged nail with vertical plate; this second operation is moderately severe and he reports that the results are no better than with traction, except that the patient can be got out of bed sooner. But he considers that each case has to be judged on its own merits. He emphasises that it is very important to make every effort to return old people to their homes; in general hospital wards, they become noisy and deteriorate mentally and physically. Because fractures of the femoral neck are common in the elderly and because they often fail to unite, it has been quite wrongly assumed that fractures of long bones in the old will not join.

Cosin (1947) thinks that an operation for a fractured femur produces less shock than being bounced on and off a bedpan several times daily and having the bed-linen often changed. He states that immobilisation is a waste of the nurses' time, and causes an increase in joint stiffness, respiratory complications, and venous thrombosis. Many other references are available advising operation and discussing details of technical procedure.

The following case-histories of fractures in patients are instructive:

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Conclusion

The task of rehabilitating old people is never easy, and it is particularly difficult when they have lain neglected in an old "chronic" hospital; but it is most rewarding work. At first the difficulties seem to be insurmountable—the opposition of the diehards, the fears and the conservative attitude of the nurses, the frail physique of the patients, and the unsuitable nature of the traditional "bedridden wards." Only the knowledge of equal difficulties overcome elsewhere, and of the spectacular results achieved, can give the beginner courage to go on. When the first tentative steps are made, progress—if any—is at a snail's pace. The patient is got out of bed for ten minutes and sat in a chair: she slips off in a "wee turn" and has to be hastily tucked in again. Next day she seems stronger, and is more lively and interested: but the examination of her crooked knees gives new cause for despondency. Yet surely the effort is worth while, for at worst she may be taught to get about in a wheel-chair; and at best she can be unbelievably improved by remedial exercises and she can succeed in walking again unaided. The Balkan beam is brought along, bed-end exercises are begun, and a few steps are taken pushing a chair; or else the patient is launched with the help of the walking-machine from which she proceeds to two Warral sticks and then, if we are lucky, to a plain walking-stick with a rubber end. All this work is slow and laborious for patient, nurses, and doctor, and there is little perceptible change each day. But if one looks around the wards a year later—or even sooner—the transformation is startling. The hospital has ceased to be a stronghold of apathy and gloom. The great majority of the patients are out of bed for some part of the day. (In our hospital only 15% of the female patients are now bed-ridden compared with 95% in 1949.)

viously described by Thrower and Campbell to 10 ml of the P V P solution, 0 1 ml of a 0 1 *N* iodine solution in 0 1 *N* potassium iodide is added, and the optical density is measured after 10–15 minutes The concentration of P V P present is found by using experimentally determined calibration curves

The urine, plasma, or serum must be pretreated, as previously described, before the above measurements are made An alternative method of removing proteins by acetic acid [2] has been found satisfactory

A fuller account of this method will be published later

Research Laboratories,
May & Baker Ltd., Dagenham Essex
H CAMPBELL

Electro medical Research Unit,
Stoke Mandeville Hospital,
Aylesbury, Bucks
G HUNTER

SUPPORTIVE THERAPY

SIR,—I was interested in the Manchester article of Jan 10 describing an improved type of dextran Will someone please tell me why this material is dissolved in physiological saline solution? Has 6% dextran no osmotic pressure at all? I feel that it is almost impertinent to remind you, Sir, that the normal serum chloride level is equivalent to a 0 58% solution of sodium chloride, and that physiological saline contains (usually) 0 9% of sodium chloride, a somewhat unphysiological excess of chloride

Pathological Department,
Whipps Cross Hospital
London E 11
W W WALTHER

BOVINE TUBERCULOSIS AND HUMAN TUBERCULOSIS

SIR,—In reply to Mr Daw (Dec 27) I should like to say that population variations were taken into account in every county mentioned in the figures given in my letter (Dec 6) The increase or decrease in the number of notifications is per 100,000 population Mr Daw states that "something more than an apparent statistical relationship is required before any such hypothesis can be accepted" In my view, when 10 out of the 11 Scottish counties, with more than 50% of cattle attested, show an increase in human pulmonary tuberculosis, and when 10 out of 11 Scottish counties, with less than 16 5% of cattle attested, show a reduction, the one result is the consequence of the one cause

I gave the figures for the 11 Scottish counties with the highest and lowest proportions of attested cattle The 10 counties with proportions between those of these two groups would show no significant alteration

Mr Daw also says "I find Mr Pitcher's argument unconvincing" It has long been assumed that bovine tuberculosis increases human tuberculosis What I have tried to show is that the elimination of bovine tuberculosis does not decrease human infection, but very substantially increases it

Turning to the points raised by Dr Bradshaw (Jan 10), I applied in every case to the county medical officer of health for notifications of pulmonary and non-pulmonary tuberculosis for the years 1920 (before tuberculin testing of cattle) to 1950 (when the attested cattle scheme had been in existence for fourteen years, although tuberculin testing of cattle was being practised to a fairly wide extent before 1936, especially in Scotland) I simply took the average for the first five years and compared it with the average for the last five years, taking into account the number of people notified as having pulmonary tuberculosis In some cases, where figures for the full period were not obtained, the earliest five years were contrasted with the latest five years

The significant feature in Scotland is that until about 1936 all the Scottish counties were showing a reduction in tuberculosis notifications, and this reduction has continued in the counties with relatively few attested cattle, whereas the reverse is taking place in co

with 50% or more of attested cattle

Dr Bradshaw's suggestion that the final fig

West Lothian should be +119 and Dumbarto

correct, but this alteration merely emphasises my

In the matter of Glasgow, Dr Bradshaw p

my error, and I must confess to having conf

Burgh of Glasgow with the Port of Glasgow,

The final figures of notifications of pulmonary t

losis for the Burgh of Glasgow per 100,000 pop

should be 1930–34, 150, 1946–50, 248 There h

relatively little alteration in the population,

corrected figures further endorse my point

Dr Bradshaw remarks "there is a fundamental

in the logic of Mr Pitcher's argument" in

sidering whether *living* tubercle bacilli are

My belief is that the milk of a dairy cow infected

tuberculosis (tuberculosis of the udder and hence

of the milk is an extremely rare condition) con

substance which I have called "tuberculin" which

ingested by human beings, increases their resist

the human bacillus I am not prepared to say

this substance is a secretion or excretion or both

bovine bacillus, but its existence is supported b

figures I do not believe that pasteurisation would

any effect on the antibody value of this "tuberc

High Wycombe
L PITC

INTRATHECAL PENICILLIN

SIR,—I have read with interest Dr Haynes's

last week concerning the death of his patient

Waterhouse-Friderichsen syndrome, following the

thecal injection of penicillin, and also the letter

Dr Aronson and his colleagues (Dec 20) concern

danger of intrathecal penicillin to which phenol h

added Other cases have lately been described[1]

It is with regret that I record the death, some

years ago, of two patients with pyogenic men

following the intrathecal injection of 20,000 unit

crystalline penicillin to which no preservative had

added A few hours after the injection, as in Dr Hay

case, convulsions were followed by death

Since then I have not used penicillin intrathe

Perhaps those with greater experience can tell us

frequency of this complication I saw no mention

in the report of the recent discussion on the treatment

non tuberculous meningitis held at the Royal Society

Medicine

Maidstone, Kent
RONALD LA

CONGENITAL ANOMALIES OF THE BON THORAX AND LUNGS

SIR,—I have examined miniature fluorograph

18,570 soldiers, aged 22–28, and I have found

following abnormalities of the bony thorax

(1) Supernumerary cervical ribs	31 (0 17%
Bilateral	7 (0 04%
Unilateral (rt sided 18, lt sided 6)	24 (0 13%
(2) Synostosis of ribs	14 (0 07%
Between the 1st and 2nd ribs	12
Between the 1st, 2nd, and 3rd ribs	1
Between the 8th and 9th ribs	1
(3) Rudimentary 1st thoracic ribs	3 (0 02%

There were thus 48 (0 26%) rib anomalies in all

These figures, although they refer to young men

agree quite well with those previously published

None of the 31 men with cervical ribs had any symp

attributable to the condition, though they were all accusto

to strenuous exercise In 12 cases the radial pulse disapp

when the hand was raised above the head and bent towa

the opposite side

Steiner[2] found 6 cases of tuberculosis among 59 people wh

had anomalies of the ribs, but in only 1 of my cases was th tostomies do not figure as operative deaths: they discarded to chronic institutions, still attached the bed by means of tube-and-bottle. They endure existence made wretched by the debilitating effects a chronic urinary infection and the repeated pain bladder washouts and changing of tubes, in an ever- ting smell of heavily infected urine and rubber tubing. eir whole life becomes centred on the wound and the oe; their habits deteriorate; they gradually curl , often under the sheet, and usually die within a year operation. Surely it would be preferable to give such tients a chance of survival, even if it were only a slight e. It is possible to get a few of them up soon after eration with a special belt and bag, and train them to ok after it themselves in a hygienic manner. They ay even go home for a time and have the tube changed a district nurse; though they usually return with mptoms of ascending infection and uræmia.

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[2] Hunter, G *Canad J Res* 1949, E27, 230

[1] Edmunds V Porter R J *Brit med J* 1952, ii 668 Go
C H *Ibid* p 777

[2] Steiner, H *Radiology*, 1943 40, 175

Case 5.—Mr. F, aged 69, in part III accommodation, found fficulty in passing urine one morning, but did not mention to anyone, because he was very anxious to go out on pass. was a very cold day and he had several drinks "to warm mself up." He returned at night with acute retention of ine. A hot bath and an enema gave no result and he was ansferred that night to a surgical ward in another hospital. ive weeks later he was returned to our hospital with a prapubic cystostomy. He was kept in bed to allow the be to drain continuously. His habits deteriorated. When en six months later his knees were contracted, his urine avily infected, and bladder washouts and the changing of e catheter were causing him much pain. He died nine onths after the operation, with signs of uræmia.

Fractures

Flemming (1951) states that the rules governing the eatment of fractures in the old do not differ from those niversally applicable to the treatment of injuries in eople of all ages. Too often it is found that a lower tandard of treatment is given to the old than to the oung, because it is not thought worth while to restore mperfect function. He points out that the object of the urgeon is to restore to the patients that degree of ctivity which they enjoyed before the accident, and ot some measure of activity which they enjoyed many ears earlier: it is wrong to assume that, because they annot be made fit to walk three or four miles, there is no oint in enabling them to potter about their room and lo an occasional bit of shopping; and there is no ustification for fobbing off the elderly with second-rate herapy. Besides, if the patient enjoyed only a very imited range of activity before the accident, he cannot fford to lose any of it. On the other hand treatment nust not be too academic. Thus, in general it is a ound rule not to allow weight-bearing in a fractured emur after pinning until the bone has united; but his delay can render an old person bedridden.

Another reason often given for refusing proper treatment is that the patients occupy much-needed beds for a long time, and may never recover sufficiently to leave. Yet if they are left untreated, they take a very long time to die. They are not, as is so often stated, overwhelmed by hypostatic pneumonia; they linger on for months in a state of suspended but noisy animation. Of the last 50 inpatients (over the age of 75) whom Flemming had treated for fractures, only 2 failed to return home. The argument that they do not stand an anæsthetic is completely unfounded. A patient has to be far tougher to lead a useful life with a painful unreduced fracture than to withstand the stress of reduction; and patients left with untreated dislocated shoulders and Colles fractures develop nerve palsies.

The commonest fractures in the aged are intertrochanteric and pertrochanteric fractures of the neck of the femur. Flemming advises skeletal traction with a Steinmann's pin through the crest of the tibia; or as an alternative a triflanged nail with vertical plate; this second operation is moderately severe and he reports that the results are no better than with traction, except that the patient can be got out of bed sooner. But he considers that each case has to be judged on its own merits. He emphasises that it is very important to make every effort to return old people to their homes; in general hospital wards, they become noisy and deteriorate mentally and physically. Because fractures of the femoral neck are common in the elderly and because they often fail to unite, it has been quite wrongly assumed that fractures of long bones in the old will not join.

Cosin (1947) thinks that an operation for a fractured femur produces less shock than being bounced on and off a bedpan several times daily and having the bed-linen often changed. He states that immobilisation is a waste of the nurses' time, and causes an increase in joint stiffness, respiratory complications, and venous thrombosis. Many other references are available advising operation and discussing details of technical procedure.

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Obituary

FRANK KEITH HAYMAN

M B Lond., F R C S

Dr Hayman, who died on Jan 9 at his home at Sharnbrook, Bedfordshire, at the age of 59, had spent most of his medical working life at Yarmouth, and he was consulting surgeon to the Great Yarmouth General Hospital

His father and grandfather had both practised dentistry in Bristol, and he was educated at Clifton School and Bristol University He took his M B Lond in 1916 and then served abroad with the R A M C On his return he took the F R C S in 1920, and the following year he settled in Great Yarmouth as a partner in an old-established practice Within five years he was appointed assistant surgeon to the Great Yarmouth General Hospital and he became full surgeon in 1927

L L, a colleague at Yarmouth, writes "Keith Hayman was always cheerful and unassuming, and perhaps his chief characteristic was his equanimity, which in the war rose superior to several bombing attacks in his neighbourhood, and one very large bomb which exploded within a few yards of his house His holidays were spent in a motor-drawn caravan, which he had built himself, for the hands of the surgeon could be adapted at will to another skilled craft"

In 1945 ill health forced Hayman into at any rate semi-retirement After he left Yarmouth he held a Ministry of Pensions appointment until his love of clinical work led him to return to general practice in Bedfordshire

A W A, a friend from schooldays onwards, writes "Keith was notably gifted with his gadgets and always making or acquiring or inventing In sports he excelled at swimming and diving, in the arts he was a keen exponent of the piano Always he was a man of deed not word, and what he wanted he usually effected His independent enterprising character led him to start practice on the East Coast, and medicine there gained, what Bristol has missed, a doctor who sought the precise truth in diagnosis and hated humbug and self-deception He tended his patient with a gentle, kindly, human skill His self-effacing nature accorded with his slight regard for ceremony and convention, and was combined with reliability and an intrepid spirit"

Births, Marriages, and Deaths

BIRTHS

EDDY—On Jan 12 to Margaret Joan, wife of Dr Angwin Eddy, of Aldborough, Norwich—a son

EVILL—On Jan 10, to Judith wife of Dr Christopher Evill of Willow Lodge, Kempsey, New South Wales—a son

HORSFALL—On Dec 13, in Cairns Queensland, to Mary (née Sidgwick) wife of Dr W R Horsfall—a daughter

LEWIS—On Jan 11, at Oxford, to Evelyn, wife of Dr Charles Lewis—a daughter

WATKINS—On Jan 14 at St Luke's Hospital, Guildford to Alison (née Carington) wife of Dr P F A Watkins, of Hazel Cottage, Peaslake—a daughter

MARRIAGES

HOPWOOD—ERB—On Jan 14, at Raghunathpur, Bihar India, Gerald Maxwell Hopwood, M R C S, of Whetstone, London, to Margaret Erb of Ontario, Canada

LEWIS—BATTEN—On Jan 17 at Fulham Cross Edward Claude Lewis, M B to Rosemary Batten

DEATHS

BROWNE—On Jan 13 at the Bristol Royal Infirmary, Frederick William Browne, M A B M Oxfd of Shirehampton, Bristol

COOPER—On Jan 15 at Packhorse Cottage Bessels Green, Sevenoaks, John Gerald Cooper, M B Camb aged 78

ELSNER—On Jan 12, at Heighington, Darlington Colonel Otto William Alexander Elsner, C B E, D S O L R C P I D P H, R A M C retd aged 81

HAYMAN—On Jan 9, at Sharnbrook Bedford Frank Keith Hayman M B Lond, F R C S, formerly of Great Yarmouth, aged 59

MARCH—On Jan 14 Charles March M B Glasg, of Gerrards Cross, Bucks aged 40

RAHILLY—On Dec 30 in Southborough near Tunbridge Wells, John Maurice Bisdee Rahilly, O B E, M B Lond, lieut colonel R A M C retd

TINDAL-ATKINSON—On Jan 14 Wilfred Percy Tindal Atkinson, M R C S of Fair Green Sawbridgeworth Herts aged 68

WILSON—On Jan 14 at Cheltenham Sarah Wilson (née Kaye), M B Lond, aged 85

Notes and News

W H O EXECUTIVE BOARD

WHEN the 11th session of the executive board of th Health Organisation opened in Geneva on Jan. 12, t man, Lieut Colonel M Jafar, director general o Pakistan, expressed grave concern at the orga financial position Because of action by the United Technical Assistance Board, he said, "we are to be have already been asked to cut down expenditure existing projects, and reduce them as much as possi future This reduction is bound to have serious Speaking of governments participating in health the chairman said "It would be an impossible p tell them now that W H O cannot meet its c any more The U N Technical Assistance *as we are all aware, was planned to bring in the* international assistance, as against bilateral An ference with it at this stage will mean a reversal of th which has encouraged national governments a great far" The chairman went on to declare that it seem health had been given a back number in the sphere and economic development "If this is the attitu very difficult to understand how development in agr food production, industrialisation, or the availa healthy labour can go ahead without proper develop the field of health" The chairman remarked that very important item on the agenda was the nomina *new director-general to succeed Dr* Brock Chisholm, retiring in July The board is to meet privately on to decide on a nomination for the post, this nom will be placed before the sixth World Health As which opens in Geneva in May

At a later session Dr A T Shousha, director Eastern Mediterranean Region, reported that the committee had been unable to meet since 1950 because political situation, the Arab League had decided th regional meeting at which Israel was represented sho attended by its member governments

SIXTH INTERNATIONAL CONGRESS FOR MICROBIOLOGY

THE first International Congress for Microbiology was in 1930 in Paris The second, planned for Berlin in 1933, to be postponed because of political events, and it was ev ally held in 1936 in London At the outbreak of September, 1939, the third congress took place in New the fourth was in Copenhagen in 1947, and the fifth Rio de Janeiro in 1950 The next congress is to be held year from Sept 6 to 12 in Rome, and the preli *programme has now been issued by the organising*

Membership of the congress is open to "all persons inte in the subject of microbiology" There is a registration of 12,000 lire, or 10,000 lire for members of a scientific soc Registrations should be sent to the secretary of the congre Instituto di Igiene "G Sanarelli," Città Universitaria, Rom before May 31

The congress opens on Sunday, Sept 6, at 10 A M, there be scientific sessions from 8 30 A M to 12 30 P M and 3 30 to 6 6 30 P M each day except Thursday, Sept 10, which is free for an excursion The closing session will be on Saturd Sept 12, at 4 P M, followed by the official banquet (5000 l at 9 P M

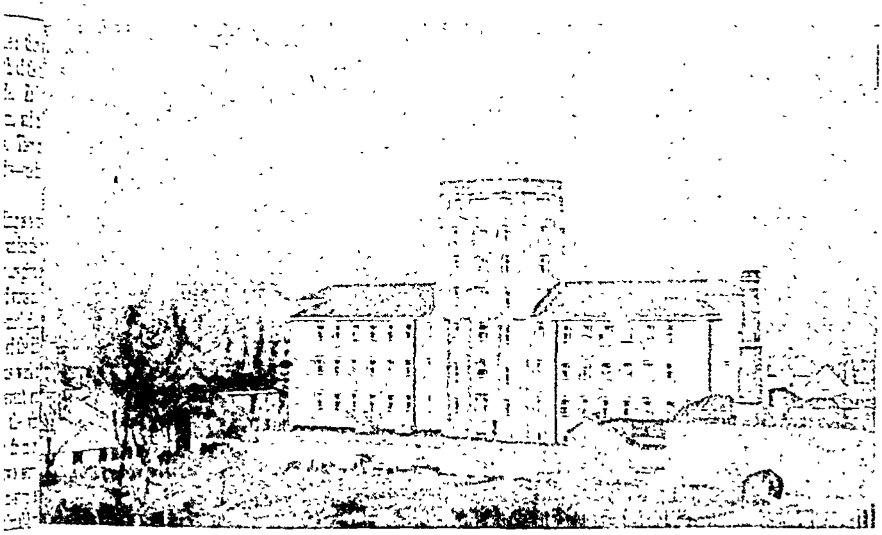
Any member may give a paper to a section, and he sho submit the title and two copies of an abstract (not more th 500 words) to the secretary before April 30 Fifteen min will be allowed for each paper

Lectures by invited speakers will be given on bacte cytology, microbial metabolism, nutrition and growth facto growth inhibitors and chemotherapy, morphology, biol and systematics of the actinomycetales, and host interactions

MEDICINE IN THE SUDAN

THE report of the Sudanese medical services for 19 is an excellent skeleton The bare bones of accomplishme in preventive medicine, in medical education, in research, in the hospitals are shown in 34 tables supported by a factual text

For a population of just under 9 million people there health budget of over £2 million and an established med staff of 1275 people, of whom 116 are British and about



View of the new building.

Dr. Betty Hobbs, while Dr. Patricia Carpenter is in arge of the *Dysentery Reference Laboratory.*

The ground floor houses a number of activities. There a photographic department, some individual research boratories, and a suite of rooms for Dr. W. Charles ckburn's *Epidemiological Research Unit.* Much of the ork of the Public Health Laboratory Service involves idemiological surveys, requiring coöperation with the edical officer of health—for example, the successful ials of whooping-cough vaccine recently carried out ider the direction of the Medical Research Council.

But the new building, though it is by far the largest gle unit of the Central Public Health Laboratory, es not accommodate by any means all of its activities. he work of the laboratory has been severely handipped in the past by lack of space, and the new building ow makes it possible both to rearrange work already eing done and to open up new lines of work. The old ain building will continue to be the headquarters of the irector, Lieut.-Colonel H. J. Bensted. Colindale, in ddition to all its other activities, is also a public-health boratory in its own right and deals with the bacteriology f the surrounding area. The routine laboratory is to emain in this block, together with the *Standards Laboraory for Serological Reagents* under Colonel Bensted's irection. The Standards Laboratory issues diagnostic era and bacterial suspensions and other biological eagents not only to other public-health laboratories ut to hospital laboratories throughout the country.

The old main building still houses the *Central Enteric eference Laboratory and Bureau* directed by Dr. Felix, F.R.S. This is an international as well as a ational laboratory, devoted to the study of methods of dentifying typhoid bacilli, defining new types or subypes, and maintaining a register of known typhoid arriers, besides undertaking research on many of the roblems raised by the method of bacteriophage typing.

In another building is the *National Collection of Type ultures* under the direction of Dr. S. T. Cowan. A large ollection of reference cultures is maintained here, many f them in the dried state, so as to reduce bacterial ariation as far as is possible.

There is another building for the library, suitable also for holding conferences, and others for stores and canteen. There are several separate animal-houses, arranged so as to give the least possible risk of infection and cross-infection.

FUNCTIONS OF THE SERVICE

This in bare summary is an outline of present activities, whose scope will be greatly extended by the completion of the new building. Colindale is quickly becoming one of the main centres in the world in the field of public-health bacteriology and epidemiology. Its reference laboratories are a vital part of the Public Health Laboratory Service, which now possesses, in addition to Colindale, several regional laboratories and 46 area laboratories. From all of these laboratories Colindale receives cultures for precise identification by special methods. The value of these reference laboratories has been proved already in the investigation of numerous outbreaks of different kinds, and many intricate and fascinating epidemics have been unravelled with a speed which would not have been achieved in any other way. It is important to note, too, that this service is not confined to laboratories within the Public Health Laboratory Service. Hospital and other laboratories call upon it for help, and the new accommodation should make possible an increase in this important work.

Though the Public Health Laboratory Service has been described as "about the only section of the National Health Service which receives only *praise and no criticism,*"[1] its many-sided activities are still not as widely known as they should be. It has grown in thirteen years from a small compact organisation of some dozen laboratories to its present outstanding position in preventive medicine. From those modest origins there has been a steady expansion which has culminated in the building now completed. The outstanding success of the service has been due at first to the genius of men like the late Prof. W. W. C. Topley, Dr. W. M. Scott, and Dr. F. Griffith, and in more recent years to the farsighted policy and tireless enthusiasm of its director, Dr. G. S. Wilson, and its chairman, Dr. A. Landsborough Thomson. Under their guidance the service has achieved efficient central direction without sacrificing individuality at the periphery. The new building at Colindale is proof of the initiative and courage of those who have managed in these days of frustration and delay to carry it through to completion.

Congratulations are due to all those who have played a part in this project, and to the architects, Messrs. Maxwell Ayrton & Partners, for a building which combines utility with dignity. Colonel Bensted and his colleagues can look forward to enjoying the use of premises worthy of the high standards which their work demands.

FRIENDS OF THE HOSPITALS

THE voluntary tradition in this country, like the small flame of the lighted touch-paper of a firework display, runs ahead sketching an outline which presently will spring into activity and light. The National League of Hospital Friends is not yet four years old but it has already pointed to many ways in which the lot of patients in hospital can be improved.

At the annual general meeting held at St. Bartholomew's Hospital on Jan. 14, Mr. IAIN MACLEOD, the Minister of Health, could hardly have encouraged the work of the league in stronger terms. He recalled the record of a local league formed in 1948 in Aberystwyth, which decided that the first call on its funds should be a former public-assistance institution for the aged and chronic sick. The first and immediate gift of 20 com-

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1. Daley, W. A. *Amer. J. publ. Hlth,* 1952, 42, 1232.

College of General Practitioners

By Jan 15 over 1000 doctors had joined the newly formed college The address of the college is 14, Black Friars Lane, Queen Victoria Street, London, E C 4

British Association of Urological Surgeons

This association's annual meeting is to be held in Leeds on June 25–27 The proceedings are to include a discussion on *Urinary Tuberculosis*, which will be opened by Mr J Cosbie Ross

Laboratory Animals Bureau Congress

The sixth congress of the bureau is to be held at the Royal Veterinary College, London, N W 1, on Friday and Saturday, March 27 and 28 Sir Harold Himsworth, secretary of the Medical Research Council, will give the opening address

Oxford Graduates Medical Club

The winter dinner of this club will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W C 2, on Friday, Jan 30, at 7 P M, when Sir Rudolph Peters, F R S, will be in the chair Tickets (30s) may be had from Mr Selwyn Taylor, 3, Roedean Crescent, Roehampton, S W 15

Psychology of Eating

The Scottish group of the Nutrition Society will hold a meeting on Saturday, Jan 31, at 1 20 P M at Marischal College, Aberdeen, when this subject will be discussed The speakers will include Prof W M. Millar, Prof C F W Illingworth, Dr C F Rolland, Dr J M Walker, and Dr C G Kennedy Further particulars may be had from Dr E C Owen, Hannah Dairy Research Institute, Kirkhill, Ayr

King Edward VII's Hospital for Officers

Lieut Colonel Claude Shepherd has compiled, at his own expense, an historical record of the first 50 years of this hospital for Service officers, which was founded by Miss Agnes Keyser during the Boer War Copies (*2s 6d*) may be had from the hospital, Beaumont House, Beaumont Street, London, W 1, and all proceeds will go to the funds of the hospital

French Exchange Scholarships

Under a reciprocal arrangement with the Centre National de la Recherche Scientifique, the Medical Research Council invite applications from British workers in medical science, excluding clinical medicine, for two scholarships tenable at research institutions in France during 1953–54 The stipend of the scholarships will be 45,000–90,000 francs a month, according to qualifications and experience, and married men will receive a supplementary allowance Forms of application may be had from the secretary of the council, 38, Old Queen Street, London, S W 1, with whom applications must be lodged by March 31, 1953

Appointments

ANDERSON, A B, M B Lpool asst school M.O Stoke on Trent
ARTHUR, W D, M R C S *appointed factory doctor, Wellingborough* Northamptonshire
ELLIOTT C G B.M Oxfd appointed factory doctor, Aylsham, Norfolk
LITTLE, D CRAWFORD M B Manc, M R C P, D C H asst chest physician (S H.M O), Caernarvon and Anglesey H M C
MURRAY, C P, M B Aberd airport M.O London and Northolt *airports for control service (Middlesex County Council)*
MURRAY F J A, L R C P I, D P H asst M O and M O H, Stone urban district
O CONNOR, NORA, M B N U I, D P H, D C P asst *pathologist*, Boston General Hospital.
PILKINGTON T L M R C S D P M. asst psychiatrist Middlewood Hospital, Sheffield
SHAW PATRICIA M D *Lond*, *D P H*, *barrister at law senior M O* Nottingham
THOMSON W N M B Aberd, F F R, D M R D consultant radiologist Edinburgh northern hospitals
WARWICK ELSPETH, M B Edin D.P H deputy M O H, *Nottingham*

Newcastle Regional Hospital Board

DOBERMAN, HENRY M B Durh, M R C O G consultant obstetrician and gynæcologist (asst), Sunderland H M C group
DUGGAN KEEN G E, M R C S, D P.M medical superintendent *and consultant psychiatrist* Winterton Hospital Sedgefield
GORDON, HELEN M B Aberd D A consultant anæsthetist, North West Durham H M C
HELLER A D M D *Zagreb*, M D, D.P M Prague asst psychiatrist Prudhoe and Monkton mental deficiency hospital
TELS J F M R C S, D A consultant anæsthetist North West Durham H M C

Diary of the Week

JAN 25 TO 31

Monday, 26th

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denm S E 5
5 30 P M. Dr E Stengel *Psychiatry lecture demons*
MEDICAL SOCIETY OF LONDON 11, Chandos Street, W 1
8 30 P M Mr W J Dempster, Mr B W Rycroft Schofield *Homologous Tissue Transplantation.*
MANCHESTER MEDICAL SOCIETY
5 P M (University of Manchester) *Section of* Prof Wilfrid Gaisford *Oral Pædiatrics*
9 P M *Section of General Practice* Dr S Almond Cardiovascular Fallacies

Tuesday, 27th

UNIVERSITY OF LONDON, London Hospital Medical College, Street E 1
5 30 P M Prof A Claude (Brussels) Technical Cell Research (*First of two lectures*)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Keppel Street W C 1) Sir Frederic Bartlett, Nature and Place of Thinking in Medicine
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
8 P M *Sections of Medicine and General Practice* Spence, Dr R J F H Pinsent Brigadier G F *Roberts* Function of the Hospital Outpatient Dep
INSTITUTE OF DERMATOLOGY, St John's Hospital, Li W C 2
5 30 P M Dr P Wade Treatment of the Epithelioma
WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Lane, W 1
5 30 P M Mr J Minton Ocular Manifestations in Disease Part II

Wednesday, 28th

ROYAL SOCIETY OF MEDICINE
5 P.M *Section of Endocrinology* Dr J W Litchfield *Peart, Mr A Dickson Wright Phæochromocytoma*
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Precancerous Conditions of the
INSTITUTE OF UROLOGY, St Paul's Hospital, Endell Street, W.C
4 30 P M. Dr R Thomson Laboratory Aids to Diagnosis
ILLUMINATING ENGINEERING SOCIETY
6 P M (Royal Institution Albemarle Street W 1) Prof E Adrian O M, F R S Nervous Reactions of the (Trotter Paterson lecture)
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLA 242, St Vincent Street Glasgow C 2
5 P M Prof E J Wayne Heart in Endocrine Disease (Fi son lecture)

Thursday, 29th

UNIVERSITY OF LONDON
5 30 P M Professor Claude Morphological and Bioche Aspects of Cell Structure and Function (Second of *lectures*)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medi *Sir Alexander Fleming*, F R S *Recent Progr* Antibiotics
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Child Great Ormond Street, W C 1
5 P M Mr H S Sharp Upper Respiratory Tract Disorder
ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P.M Sir Geoffrey Todd Modern Methods in Treatment Pulmonary Tuberculosis
ST GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Cor S W 1
5 P M Sir Paul Mallinson Psychiatry lecture demonstratio
UNIVERSITY OF EDINBURGH New Buildings Teviot Place, Ed burgh
5 P M Prof Jean Fiolle (Aix Marseilles University) Embo of Arteries of the Limbs
UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee) Prof J Mackintosh Medical Care Tomorrow

Friday, 30th

UNIVERSITY COLLEGE, Gower Street, W C 1
5 30 P M Prof F Bergel, *PH D* Chemical Aspects of Growth (*Second of three lectures*)
INSTITUTE OF DERMATOLOGY
5 30 P M Dr G B Mitchell Heggs Acne Vulgaris, Excoriée and Dermatitis Artefacta

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EMERGENCY BED SERVICE —In the week ended last applications for general acute cases numbered 1700 The prop admitted was 83 97%

Dr A W C Bennett, who has been medical officer to the for Great Western Railway and the western region of British Railwa at Swindon for the past 23 years retired on Dec 31

In England Now

unning Commentary by Peripatetic Correspondents

looks as if the long word has had it. The cult of the one. started, or at any rate revived, by the Fowler iers. has had a strong boost in the works of Sir st Gowers, that formidably unprevaricating arch-gonist of antisesquipedalianism. The jet age has ime for arabesques in language or in art, and the que and rococo are gone with the wind.

vay with such useless lumber as adjectives, articles, unctions and prepositions! Let's see the naked ity of the noun, especially the monosyllabic one, ulable in a trice as we and the train we must catch e simultaneously at the station bookstall. Let's our magazine *Life*, *Time*, *Girl*, *Mind*, *Brain*, or *d*. Take for instance that old stage-coach the *ceedings of the Society for Experimental Biology and licine*: dare we suggest *Frog* as a breath-saver? l would the *Journal of Pathology and Bacteriology* template *Death* or entertain *Bugs* as an alternative? *nily Doctor* would soon be out of the red with a title h as *Pep*, *Zip*, or *Zest*, and the *Provincial Medical and gical Journal* might shed its interim guise of *British lical Journal* and appear as *Doc*. Our senior clinical rnals would take a new lease of life under names like e or *Pain*, *Cut* or *Slash*, and *Womb* or *Birth*. To the tro-enterologists we commend *Tripe* or *Guts*, to the sical medicine men *Rub* or *Tap*, and to the rheumatosts *Damp* or *Wet*. The social medicine people may be teful for *Fog*, and the hospital administrators for *pe*.

o far as we can see, the only catch about all this is risk of getting something you don't want, for pubers and detergent makers are running neck and neck. erefore be sure to buy at a bookshop, otherwise you y get soap for the body or its wrappings and not for mind. Don't forget there's a world of difference ween *Time* and *Tide*.

* * *

Five years ago, before coming to Warwickshire, I was ptical of the influence of microclimatology upon ease. A bracing climate meant, I thought, a keen evailing wind, and a relaxing climate a tendency to gs and a still atmosphere, neither of which I believed uld affect more than the psychological health of the sidents. I am now sure that I was wrong and that the health from catarrhal respiratory illness at all ages considerably greater along the Avon valley than it is, r example, in London. It is not so much that infections e more frequent, as that they last longer, and are prone produce complications, such as bronchitis and sinusitis, which the victims are unused in other places. The planation is a riddle. Popularly, damp, fogginess, and "stagnant atmosphere" (whatever that means) are amed, though the humidity of a river valley does not ach that of seaside areas, and there is more particulate atter in London air than there is here. It is not oticeably colder, nor is there so much overcrowding ere as in healthier parts, indeed the reverse, nor are hanges in temperature any more extreme or sudden.

So I think that a purely physical effect of climate on eople is unlikely. After all, mucous membranes cannot e expected to react in very many different ways; they an be chilled or warmed, caused to secrete more or ss, and to become congested or bloodless. There is ttle subtlety in this and we should look elsewhere for he explanation of a general susceptibility, perhaps to the ffect of climate on the growth and virulence of the rganisms that cause our repeated catarrhs. A study of bacterial ecology in relation to the soil and climate of different parts of this island could show that a winter differing from elsewhere by only one or two degrees of average temperature, where the soil contained critical races of certain elements, would provoke luxuriantly malign growth of common pathogens. In other words that the fertile Vale of Evesham is also a bacterial market garden; that not only its fruit and vegetables but equally its micro-organisms flourish exceedingly. And may it not follow from this, knowing the general antagonism between animal and vegetable kingdoms, that for men to be healthy they should seek places where other animals thrive, but that if they choose to live in a vegetable paradise they will become the constant prey of parasitic vegetables?

* * *

"'Ello Luv!" The lady addressing me had attended my outpatient session that morning. The scene of our reunion was the savings bank, where—as a consultant without merit—I do most of my business. As the queue moved slowly up to the counter, I realised more than ever how like the O.P. the bank is. At both, you hand in your book at point A. Your little job needs privacy: you go to point B, a cubicle where you absent-mindedly start to undress. The job done, you are discharged in public at point C. It all takes time—the trajectory described took me a good half hour—and I was attended to by a probationer into the bargain.

Self: "I'd like my interest for the year."

Clerk: "Do you want something out?"

Self: "No! thanks, I just want my interest put in my book. And I'd like some Savings Certificates, please."

Clerk: "What are those?"

Self: "The things the Government keeps asking you to buy."

Clerk: "You'll have to go through that door."

Self: "It's the tenth issue I want; I've got the others."

Clerk: "There isn't a tenth; there's only the ninth."

Self: "The ninth, then. How many can I have?"

Clerk: "Seven hundred."

Self: "The extra ones, I mean. I'll give you a cheque."

Clerk: "Oh no, you have to take it out of what you've got in."

Self: "May I have my book, please?"

Clerk: "You can't have it back here—you have to go through the door to where it says Don't Come on Saturdays."

Discharged at last, I reflected that I had indeed had my interest for the year.

* * *

A friend of ours recently returned from a somewhat trying social weekend spent at a house where they keep a herd of yellow cats for decorative purposes. The doyen of the establishment, a large and cynical tom, had of late taken to looking on the place merely as a sort of second-rate hotel serving indifferent meals. He now lived in the rafters of a disused outhouse, and visited the house at rare intervals, speaking to no-one. It was generally felt that the animal was not pulling its weight, and our friend, stamped as an animal fancier because of his knowledge of the internal economy of the Wistar rat, was deputed to catch the cat and take him to the vet to be destroyed. Physiologists are brave enough in a reckless sort of way, and our friend accepted the commission. Armed only with a cardboard hatbox and his personality, he approached his quarry during its siesta by means of a long ladder. The cat observed the operation dreamily, and such was the lethargy induced by its excesses of the previous night that, after a purely formal protest which caused our friend to fall headlong down four rungs and nearly lost him the sight of one eye, it suffered itself to be placed in the hatbox, secured with string, and settled on the back seat of the car.

By the first traffic lights it had become clear that the cat, though tolerant of hatboxes, thought nothing of cars, and was taking itself to task for allowing itself to be imposed upon. At the second traffic lights our friend looked round in response to a sinister tearing noise and observed a yellow eye regarding him balefully through a jagged hole in the hatbox. Before any steps could be taken, the animal had become fully abreast of the situation and emerged as if propelled by a blasting charge. Our friend tells us that the car became full of cats, thereby causing him to reconsider his views on mammalian parthenogenesis in hatboxes; he counted at least fifteen as they flashed past, upsetting ashtrays, disrupting upholstery, and dismantling armrests. Finally one of the multitude landed squarely on the top of our friend's head and shot out of the driving window, leaving the car empty. By the time he had staunched his shredded scalp and returned home the cat was once more in residence in the outhouse and taking a well-earned nap.

The atmosphere at supper was rather chilly, and our friend's reputation as an animal fancier is now confined to the Wistar rat.

hypertrophy and a little unfolding and calcification of the aortic arch, the skull was normal Nothing abnormal was found in the urine

Fasting blood sugar (F B S) levels of 60 mg per 100 ml were recorded on Oct 7 and 12, 1950, but were not considered low enough to explain her peculiar mental state On Oct 13, 1950, an insulin tolerance test was made with 1 9 units of insulin (a third of the standard intravenous dose) 60 minutes after the injection the patient became unconscious, but she responded quickly when the test was terminated with intravenous glucose Blood sugar levels were F B S 42 mg per 100 ml, 30 minutes after insulin 20 mg per 100 ml, 60 minutes after insulin 26 mg per 100 ml It was only then that we connected her drowsiness and surliness with spontaneous hypoglycæmia, and the insulin-tolerance test would not have been made if we had suspected such a low F B S

On Oct 22, 1950, she became fevered and lost consciousness and was found to have a heavy pyuria Her blood-pressure fell to 64/38 mm Hg but was easily restored Although the blood sugar was not estimated before treatment was started, it was thought that the coma was due to spontaneous hypoglycæmia During the two days she was in coma she lay with rigid limbs and tight jaws and abdominal muscles, her arms flexed at elbow and wrist and crossed on the chest, her knees drawn up and adducted, with extensor plantar reflexes, several flexor spasms occurred The spasticity disappeared when she recovered consciousness For the next few weeks she was in a state of confusional insanity, and there were minimal signs of a left hemiparesis Three months later she had made a complete recovery

Four years after the menopause, pituitary insufficiency came on gradually and for no apparent reason It was thought that spontaneous hypoglycæmia was the cause of intermittent mental confusion, and of a coma which lasted two days, was accompanied by flexed spastic limbs and flexor spasms, and was followed by temporary insanity and temporary neurological abnormalities

Postpartum Lesions

Certain features were common to some or all of the patients of this group all were married women, in cases 3–6 the patients had Sheehan's syndrome, they were bled white in childbirth, and the resultant shock was of appalling severity in cases 3–5, only case 3 had a blood-transfusion, puerperal sepsis ensued in cases 3 and 5, in case 7 the symptoms date from a confinement which may have been complicated by puerperal sepsis but was otherwise normal, this patient has pulmonary and cutaneous tuberculosis

After her last confinement each patient became a different person, afflicted by unaccustomed inertia and frailty Case 4, dull by nature was remarkably free from psychical upsets The others complained of a decline in memory and in powers of concentration, they " couldn't be bothered with anything," and did not want to mix with other people, they were prone to fits of dejection, and pent-up feelings of irritability would explode now and then in little storms of temper The passage of time brought ever increasing slowness of thought and responses, but not peace of mind Cases 3 and 5 often felt anxious and insecure, and case 6 became immersed in terrible waves of gloom and had " awful spells of crying " in a mute submissive way these people seemed grieved by the change in themselves By contrast, case 7 held on to a stubborn grumbling independence in the face of great physical infirmity and the misery of constant family squabbles

All dreaded cold and clung to the fireplace but cases 4 and 5 were relieved of this symptom when they took thyroid extract All spoke of constant tiredness and sleepiness, yet cases 5 and 6 did not sleep well at night Bodily strength waned case 4, the most active, was exhausted on washing days, case 3 had to send the washing to the laundry, cases 5 and 6 became unfit for any household tasks, and case 7 became too feeble to stand Menstruation ceased abruptly except in cases 5 and 7, whose subsequent bleedings are noted in the case reports Libido was lessened in case 4 and lost in the others None had menopausal flushings All lost axillary and pubic hair, cases 3, 4, and 5 recalled that their scalp hair thinned greatly after the delivery and then grew in again Case 3's teeth were extracted before her pregnancy, cases 4, 5, and 6 did not lose the last of their teeth until from five to ten years after the last confinement, and case 7 still had ten decayed stumps I could not obtain accurate information about previous body-weights, cases 3 and 4 lost weight after obstetric shock (case 4 thinks about $3^1/_2$ stone) and regained it in a year or so, cases 5 and 6 grew stouter, but case 5 returned to her usual build when she took thyroid extract Subsequent weight changes were not remarkable, except in case 7, who has tuberculosis and whose appetite was very poor She thinks she weighed 12 stone before her last pregnancy and gradually came down to 6 stone in the next twenty years Cases 3 and 5 did not enjoy their food, case 4 had chronic cholecystitis, the others had no abdominal discomforts, cases 3, 5, and 7 were constipated All complained of breathlessness on exertion, cases 3, 5, 6, and 7 had angina pectoris, and cases 3 and 5 calf claudication Raynaud's phenomena occurred in the fingers of cases 3, 5, and 6 Case 5 complained of transient dizziness on getting out of bed in the mornings, she was the only one who did not have dull headaches Case 7 was troubled by severe leg cramps at night None had urinary symptoms, and all were remarkably free from the common acute respiratory infections

Physical characteristics—Case 4 was dull and unconcerned, whereas case 7 was irritable and hurled enfeebled defiance at her medical attendants, the others were slow gentle people, at once self-pitying and self reproachful, and they rarely smiled Mostly they spoke slowly and quietly, cases 4 and 5 with a little of the thick broken intonation of myxœdema, a contrast to the weak high pitched complaint of case 7 Case 3 was timid and anxious to please, with spare delicate features and a thin weak mouth Case 4, sombre and big-boned, had heavy features and thick lips There was some puffiness of cheeks and eyelids in case 5 The face of case 6 was round and shiny with swelling, and her reddened eyes were sunk in boggy lids, she was utterly miserable and wept silently, without effort Case 7 had a little withered bird like face, with a small receding lower jaw, and a remarkable coarse facial wrinkling made her look old No such impression of senility was given by the others, case 3 actually looked younger than her years in spite of fine facial wrinkling Whatever the facial contours, all seemed curiously fragile, an effect made up of their weakness and unusual pallor The *pallor* was greater than the moderate anæmia would explain, it was spread evenly over the face and, case 6 excepted, it was the more prominent for being unrelieved, it was a milky whiteness in cases 3, 5, and 6, accentuated by the swollen face in case 6 and setting off the red glow on her nose and cheeks, in case 7 it was mixed with grey, in 5 and [illegible] with the faintest tinge of yellow, and in case 4 with a diffuse duskiness A glossy surface to the features of case 5 fused with the even pallor and immobility to simulate a thin wax mask The *buccal mucosa* was swollen greatly in case 6, slightly in case 4, and both had rather big *tongues* *Fat pads* were present above the clavicles of case 6 In case 5 the *skin* seemed a little thinner than normal and was flimsy and transparent over the shins Cutaneous atrophy was not evident in the others, even in case 7, who had an old woman's face but whose skin was elastic and compact on trunk and limbs Apart from the slightest roughness on the fore arms of cases 6 and 7 and on the forearms and shins of case 5, the skin surface was perfectly smooth Only case 4 had a faint diffuse *pigmentation*, probably her natural tint Deeply pigmented *erythema ab igne* covered the lower limbs of cases 4, 6, and 7 (see figure) The rarely come to operation or necropsy, so oppor- s for direct observation are uncommon; but tical considerations are much against his view. area of a roughly elliptical orifice, 1·5 by m., can hardly be greater than 1 sq. cm., and we een that to obtain a cardiac output of only 6 litres inute a pressure gradient across the valve in excess cm. of water is required. This would necessitate siderable rise in left-auricular and pulmonary s and capillary pressures, but catheterisation s of this type of case, with outputs at this level gher), have shown normal pulmonary pressures.[4]

partment of Cardiology,
al Infirmary, Manchester.

GEOFFREY WADE.

BUTAZOLIDINE

—Œdema is not uncommon during treatment with ylbutazone (butazolidine). and there is no need to for swelling of the ankles or face in order to detect f the patient is weighed before and during treatment, ll be found that there is an increase in weight of lb. within two or three days, and as much as lb. at the end of seven to ten days. When the ylbutazone is discontinued, the patient passes us amounts of urine and the weight returns to the nal.

eel that the action of this drug is analgesic rather specific, because pain recurs fairly frequently if njections are more than two to three days apart, t does, in fact, relieve pain in other conditions. For nple. I have observed dramatic relief on two to three sions in severe dysmenorrhœa which had not nded to antispasmodic treatment.

ndon, W.1.

WILLIAM W. FOX.

PINK DISEASE

R,—We were interested in Dr. Vulliamy's [5] suggestion an increase in circulating adrenaline and noradren- might be responsible for the vascular disorder in disease, because we have ourselves been investi- ng this possibility following a suggestion made to us Prof. J. H. Burn in November, 1951.

e have made some preliminary observations on the ary excretion of noradrenaline in normal children and hildren with pink disease; and one of us (G. P. B.) also made studies on adults with proven phæochromo- oma. In each case a 24-hour collection of urine was ained. Noradrenaline was adsorbed on aluminium droxide, and subsequently assayed by intravenous ction into a cat.[6]

he urinary excretion of noradrenaline in 9 convales- t children, whose ages ranged from 3 months to 10 rs, lay between 10 µg. and 27 µg. per 24 hours. In hours the child aged 3 months excreted 18 µg.; and hildren aged 20 months and 2 years excreted 12 µg. 14 µg. 3 adults with proven phæochromocytoma reted 180 µg., 300 µg., and 3700 µg.

o far we have made estimations on only 2 children h Pink disease. Both were classical and fully estab- ed examples of the syndrome, showing prominent rovascular signs—that is to say, hypertension, tachy- dia, sweating, and cold pink puffy hands and feet. affected child excreted 16 µg., and the other 21 µg., adrenaline in 24 hours. These figures lie well within normal range, and contrast sharply with the levels have found in urines from adults with phæochromo- oma. The excretion of noradrenaline fluctuates widely m day to day, and therefore a small average change in retion would be difficult to detect.

he scanty figures that we have so far obtained do support the suggestion that noradrenaline output is greatly increased in pink disease. This does not in any way invalidate the use of 'Priscol' in treatment. Further work is in progress.

Departments of Pædiatrics
and Biochemistry,
Radcliffe Infirmary, Oxford.

GEORGE P. BURN
CHRISTOPHER OUNSTED
VICTORIA SMALLPEICE.

CHRONIC OTITIS MEDIA

SIR,—Mr. Layton (Jan. 10) seeks to revive the old idea that the acellular mastoid process is due to sclerotic obliteration of the air cells in a once "normal" pneumatised process. The cases he cites do not support this view: they show merely that inflammation may inhibit further pneumatisation. X-ray examination of the mastoid was practised long before twenty-four years ago when "the first mastoid X-ray picture was taken at the North Eastern Hospital," and since then has been a common procedure. Where is the evidence that a normally pneumatised mastoid (say in a child of 5) ever becomes an acellular or so-called "sclerotic" process? Since hundreds of patients have been radiographed without such a finding we must reject the theory.

Bristol.

E. WATSON-WILLIAMS.

LIGATION OF THE POPLITEAL VEIN

SIR,—Mr. Goligher (Jan. 10) states that the facts recorded in my paper (Jan. 3) do not warrant the conclusion that popliteal ligation is of any value. To refute this conclusion he considers one group only of the recorded cases (those with ulcers) and fails to remark that all of the second group (7 legs), where the patients complained of aching, swelling, &c., of the legs, were relieved of their symptoms.

To return to the group he does consider, he simply states that 7 of the 11 patients showed no sign of recurrence and takes no note of the fact, clearly shown in the paper, that of the cases which failed (5 of 13 legs) 3 should not have been operated upon (in 1 the femoral and popliteal veins were occluded, in 2 there was an arterial deficiency) and were a failure of judgment, not of method; 1 patient refused to wait for a graft but was relieved of her pain and swelling; and 1 ulcer broke down after 2 years. Therefore of the 10 cases which were suitable 8 were successful, 1 partially so despite incomplete treatment, and 1 failed.

Mr. Goligher also "considers that the results are not very different from what might be obtained after bed rest and grafting alone." This, of course, may be so, but such a statement would bear more weight if backed by figures; and it is of interest to note that of 5 cases treated by grafting alone in the Massachusetts General Hospital [1] none remained healed, while of 13 treated by excision of the ulcer and grafting 10 broke down.

The second half of Mr. Goligher's letter concerns the results of superficial femoral vein ligation. He states that "the principle of this operation and that of ligation of the popliteal vein are the same, and the results should presumably be also similar." It might as well be said that because the principle of ligation of the superficial femoral artery and of the popliteal artery are the same, the results should also be similar. Bauer [2] has given the reasons for ligation of the popliteal vein in preference to the superficial femoral; and it is worth noting that Linton [3] has given up ligation of the superficial femoral vein, although he was one of its chief advocates,[1] because of a 30% rate of failure—the same percentage failure as that of Glasser.[4]

I would suggest, then, that Mr. Goligher's failures after superficial femoral vein ligation should not lead him to condemn out of hand ligation of the popliteal vein.

General Infirmary,
Leeds.

H. D. MOORE.

1. Linton, R. R., Hardy, I. B. *Surgery*, 1948, 24, 452.
2. Bauer, G. *J. int. Chir.* 1948, 8, 937.
3. Linton, R. R. *Angiologia*, 1952, 3, 439.
4. Glasser, S. T. *Surg. Gynec. Obstet.* 1948, 89, 541.

Vade, G. M.D. thesis, University of Manchester, 1952.
Vulliamy, D. G. *Lancet*, 1952, ii, 1248.
Von Euler, V. S., Hellner, S. *Acta physiol. scand.* 1951, 22, 161.

Blood-sugar levels were all estimated by Dr W H R Auld, using the Nelson method He made the *insulin tolerance tests* with a third of the standard intravenous dose in all but case 4, who showed insulin resistance to the full dose

Apart from states of collapse, the levels of *plasma-chlorides, serum-sodium,* and *serum-potassium* were within normal ranges A *fractional test-meal* showed a histamine-fast achlorhydria in case 2, small amounts of free acid after histamine in cases 6 and 7, hypochlorhydria in cases 3 and 5, and normal acidity in case 4 *Hæmoglobin* levels were mildly to moderately depressed (see table) *Stool benzidine* reactions were negative *Peripheral blood smears,* examined in the department of medicine of the University of Aberdeen, showed no macrocytosis Abnormalities in the *chest radiograms* have been mentioned The *pituitary fossa* was radiologically normal in all

DISCUSSION

The nature of the pituitary lesion is not known in 2 cases in case 7, who has tuberculosis of the lungs and skin, the symptoms came on gradually after an easy confinement, which may have been followed by puerperal sepsis, and in case 2 the onset was insidious after the menopause Case 1 had a craniopharyngioma, and in cases 3–6 the illness began abruptly after severe obstetric shock Case 6 recollects pallor and weakness after her first delivery, and recovery of well-being after the second, and it is tempting to postulate a temporary cure of pituitary insufficiency by the second pregnancy (Sheehan and Murdoch 1939) Histological proof of a pituitary lesion was obtained in case 1 In each of the other cases there is reasonable clinical evidence of the presence of a lesion, and only cases 2 and 4 do not satisfy the strict demands for the laboratory diagnosis made by Anderson (1950). low B M R, insulin sensitivity, and hypoglycæmia unresponsiveness, negligible urinary excretion of 17-ketosteroids, and a positive "water test" A Kepler index of over 30 in case 2 can hardly outweigh the rest of the evidence in favour of the diagnosis, case 4 showed some resistance to injected insulin, and part II of the Kepler test yielded a marginal result, but it seems certain that she has an incomplete form of the syndrome, because the symptoms date clearly from appalling obstetric shock, after which she lost her body hair

Clinical recognition of pituitary insufficiency was easy, except perhaps in the postmenopausal case, where some of the symptoms and signs might have been attributed to ageing Nevertheless (apart from infantilism and interference with vision in case 1) the illness *did not conform* to a constant design, and the various pituitary activities were not equally affected, for example, spontaneous hypoglycæmia was calamitous in cases 1 and 2, and moderately severe in case 7, but in the remainder it was absent It seemed, too, that the way in which the patients were altered by the disorder depended not a little on their native mould and temperament Yet 4 of them, including the unconscious dwarf, were left with such a remarkable resemblance to each other that one might have recognised their pituitary insufficiency at a glance These were cases 1, 2, 5, and 6 with the milky skins and puffy faces The first impression of myxœdema was heightened when the eyebrows were sparse, and the correct but incomplete diagnosis of thyroid insufficiency had been made long before in cases 2, 5, and 6 However, these 3 were set apart from the primary myxœdemas by qualities of their own, probably not greatly affected by previous thyroid treatment Patients with severe primary myxœdema, however dulled, often wear a self reliant robustness to match the coarseness of their skin and features, and A Lyall (personal communication) has often been impressed by their dry sense of humour But here the whiteness of the skin was in keeping with the helplessness of case 2 and the sadness and withdrawal of cases 5 and 6, one was aware of an uncanny [illegible] almost as if their hold on life was precarious, one [illegible] worried about these people

The fragility of cases 3 and 7 was less unearthly because it was in harmony with their thin delicate features Case 7 had an old face, but the skin of her body was even and well formed Case 4 was closer in appearance (and in response to injected insulin) to the primary myxœdemas She was dull, almost unconcerned and her features were heavy, but much of all this was inborn, as were the thick lips and faint duskiness of the skin There was an unexpected feebleness about her big frame

The main findings in cases 2–7 are in close keeping with the account of Sheehan and Summers (1949), who selected for review only those patients who were proved to have gross destructive lesions of the anterior lobe of the pituitary A few minor points of disagreement with these workers may be explained by incompleteness of the pituitary lesions Sheehan and Summers (1949) emphasise the lack of localised cutaneous pigmentation, but the erythema ab igne on the legs of cases 4, 6, and 7 was of a deep brownish-black tint (see figure), and case 2 showed dark staining at the site of old varicose dermatitis, the breast areolæ of cases 2 and 4 were deeply pigmented, and they were of a light fawn colour in the remainder—only the dwarf could be said to have had no areolar pigmentation Sheehan and Summers (1949) always found a lack of the normal capillary flush in the exposed skin, very atrophic breast parenchyma, and advanced atrophy of the vagina and external genitalia Case 6, however, had a red nose and red cheeks, and flushed deeply in response to vasodilator substances, there seemed, on palpation, to be abundant breast parenchyma in cases 2 and 7, and vaginal stenosis was absent in cases 3–6 despite superinvolution of the uterus

The *erythrocyte sedimentation rate* (Westergren) was increased in cases 2–7 (see table) Case 4 had chronic cholecystitis, and case 7 old fibroid pulmonary tuberculosis, but in the remainder the increase was not explained

Teeth —In case 1 an excellent set of teeth had not been marred by lack of pituitary hormones There was no clear evidence that the pituitary lesion had led to loss of teeth in the other cases, and this is in keeping with the opinion of Sheehan and Summers (1949)

Myxœdematous swellings have been described in the faces of cases 1, 2, 5, and 6, and were seen in the form of pads above the clavicles in case 6, and in swelling of the oral mucosa and of the tongue in cases 4 and 6 The texture of the skin may have been influenced by previous thyroid treatment in cases 2, 4, 5, and 6 The speech of cases 4 and 5 suggested myxœdema

Arterial disease —There is a high incidence of the effects of arterial disease cases 3, 5, 6, and 7 had angina pectoris, and case 3 has had a myocardial infarction and cases 3 and 6 complain of intermittent claudication in the calves The angina pectoris of case [illegible] was greatly aggravated whenever thyroid extract was prescribed

Adrenal cortical insufficiency —Case 7 had much asthenia and was observed in three attacks of collapse simulating addisonian crises One of these was precipitated by the diarrhœa which followed an aperient, and another by thrombophlebitis The arterial hypotension of cases 1 and 2, when they were first seen in coma, may have been due to concomitant adrenal cortical insufficiency, but blood-pressures were quickly restored by treatment The selective sparing of some pituitary functions is seen again in the lack of any tendency to adrenal crises in cases 3, 4, 5, and 6, and it is of interest in this connection that cases 4 and 5 had taken thyroid extract for long periods, because thyroid has been held responsible for the development of acute adrenal insufficiency in several patients (Cook et al 1951) operation or any line of treatment which ignores this extensive incompetence is not likely to be uniformly sful in healing leg ulcers. Mr. Cockett and Mr. Elgan agree that their follow-up is short, allowing of no e conclusions about the efficiency of their operation, venture to suggest that its basic premise is untenable.

constant finding in phlebograms of ulcerated legs, of column of unsupported blood in the deep veins due to most total absence of valves, led Bauer and others to igate the effect of ligature of the popliteal or superficial But as Mr. Goligher has pointed out (Jan. 10), the s of this operation are equivocal. This is not surprising the column of blood is not a static phenomenon, and a ng valve will hardly be improved if a complete block aced across it. The deep veins are the main channels which blood returns to the heart from the lower limbs, he swelling which follows the operation is ample witness e further rise in venous pressure caused by it. Rest bandaging are even more constantly required than ever.

seems an inescapable conclusion that a reduction enous pressure (and hence healing of the ulcer) can be brought about by restoration of the valvular on in the muscle pump. (In animals an attempt been made to insert acrylic-resin valves, or grafts healthy vein with valve.) Such a restoration can be cted by the simple manœuvre of firm bandaging n toes to knee. Its very simplicity is regarded as ject by a few, but it does in fact appear to provide rm of valvular action within the deep veins. Originally consistently advocated by Mr. Dickson Wright,[1] it y far the most successful form of treatment yet ised, even in the presence of enormous ulcers. It bably acts in this way:

he successive turns of the bandage apply a slightly ying pressure along the leg. Although the surgeon tries ut the bandage on evenly, he never can achieve theoretical ality of pressure throughout, as the faint ridges on the skin icate when the bandage is removed. This "even" pressure uces the average calibre of the vein and the slight variations lude the deep vein at intervals along its length, the rage pressure applied being very little greater than the stolic pressure in that vein. In systole the muscle pump ces blood both up and down the limb through the occluded ments, but mainly upwards, as the resistance is greater tally. In diastole once more, the various points of lusion due to the turns of bandaging prevent regurgitation wnwards of the blood forced upwards during systole.

This valvular action is imperfect but hydrostatically ost effective. The muscle pump has been repaired d venous pressure falls. Inevitably the ulcer heals.

Hampstead General
Hospital, N.W.3.

GERARD KRAFFT.

SIR,—I should like to join in congratulating Mr. ckett and Mr. Elgan Jones on their work on the ankle blow-out syndrome," which is clearly of ndamental importance both in the ætiology and eatment of certain leg ulcers.

The following quotation from John Hilton[2] seems an teresting prelude to the careful anatomical investigaons of Cockett and Elgan Jones:

"Why is it that varicose ulcers occur so frequently at e inner and lower part of the leg? It might be said that ey occur because the blood in the veins of the lower tremities has to run up-hill, and gravitation interferes very uch with the return of the blood; the valves get broken own, and the whole pressure is retrograde, if we may so term , and so these ulcers arise. If that were the sole reason, lcers should occur by preference on the feet or on the toes, ecause these are more remote from the general circulation an the ordinary site of ulcers from varicose veins. Hence, I spect that this cannot be the explanation. The explanation as always—at least for some time past—appeared to me to e this: The superficial and deep veins of the leg freely ommunicate with each other in the neighbourhood of the nkle-joint. The first two inches above that point is the spot here the greatest stress is laid upon these superficial veins; below that point they freely communicate, and if the blood cannot return by the superficial veins, it can do so by the deep veins, or vice versa; but when you reach the point above the inner malleolus (where that brown patch of skin so often occurs in old persons) it is otherwise, and that appears to me to be the reason why ulcers from varicose veins occur so frequently about that neighbourhood."

Leeds.

S. T. ANNING.

COLORIMETRIC ESTIMATION OF POLYVINYLPYRROLIDONE BY IODINE

SIR,—Recent experimental work has enabled us to increase the sensitivity of the colorimetric method for estimating polyvinylpyrrolidone (P.V.P.) described by Thrower and Campbell.[1] The reaction has now been shown to involve free iodine and not the I_3^- ion as previously stated, and consequently, with solutions of iodine in aqueous potassium iodide, the intensity of colour developed depends on the concentration of free iodine, which is governed by the equilibrium

$$I_2 + I^- \rightleftharpoons I_3^-.$$

It is not possible to increase the sensitivity by the use of alcoholic solutions of iodine, in which all the iodine is present in an un-ionised form, since ethyl alcohol interferes with the colour reaction. The behaviour of this coloured complex between iodine and P.V.P. is very similar to that with starch. Thus the colour of the complex is completely discharged by sodium thiosulphate, sodium arsenite, or a strong base. On warming, the colour of the complex disappears but it reappears on cooling.

The observations described here were made at 500 mμ with a Unicam SP 500 spectrophotometer and cells of optical path length 1 cm., but similar results have been obtained with an Eel colorimeter (Ilford 603 filter). The optical densities are measured against an aqueous solution of identical iodine and potassium-iodide concentrations without any P.V.P. All concentrations referred to below are the actual concentrations in the solution being measured.

At constant potassium iodide and iodine concentrations the relationship between optical density and P.V.P. concentration is not a straight line but may approximate to this over a useful range of P.V.P. concentrations at low potassium-iodide and high iodine concentrations. Typical sensitivities in these straight line regions are given in the accompanying table (I, II, III). In addition the maximum sensitivity obtained under conditions similar to those described by Thrower and Campbell[1] are given (IV).

VARIATION OF SENSITIVITY WITH COMPOSITION OF REAGENT

—	Iodine conc. normality	Potassium iodide conc. normality	Sensitivity P.V.P. conc. (mg. per ml.) to give an optical density of 0·05	Useful range of P.V.P. conc. (mg. per ml.)	—
I	$5{\cdot}0 \times 10^{-4}$	$1{\cdot}0 \times 10^{-3}$	0·005	0–0·02	Poor straight line
II	$1{\cdot}0 \times 10^{-3}$	$2{\cdot}0 \times 10^{-3}$	0·0035	0–0·04*	Good straight line
III	$5{\cdot}0 \times 10^{-3}$	$25{\cdot}0 \times 10^{-3}$	0·0022	0–0·03*	Good straight line
IV	$1{\cdot}0 \times 10^{-3}$	150×10^{-3}	0·0175	0–0·425*	No straight line

* The useful range is limited by the inaccuracy of measurement above an optical density of about 0·7.

A further increase in sensitivity by increasing the iodine concentration is impracticable since the blank absorbs too much light. It is found that, with the most sensitive conditions, a considerable time (1–2 hours) is required for the maximum colour to develop, so that it is convenient to sacrifice some sensitivity for greater speed.

These results have suggested the following method, which is about five times more sensitive than that pre-

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1. Wright, A. D. *Lancet*, 1931, i, 457.
2. Hilton, J. *Ibid*, 1861, ii, 245.

1. Thrower, W. R., Campbell, H. *Lancet*, 1951, i, 1096.

Walker rat carcinoma 256 as well as a depressive influence on the myeloid series both in the rat and in man at a much lower dose than most other members of the series

Table I shows the relation between dose and inhibition of the growth of the Walker carcinoma for all members of the series from $n = 2$ to $n = 10$, here + indicates that the weight of tumour tissue in the treated groups (each of 10 rats) was 10% or less than that of the controls after two or three weeks' growth, the drug being administered in a single intraperitoneal dose twenty-four hours after implantation The activity was greatest with $n = 4$ and $n = 5$, and diminished towards either end of the series

TABLE I—ACTION OF MEMBERS OF THE SERIES ON GROWTH OF WALKER RAT CARCINOMA 256
(Each experiment based upon 10 rats)

Dose (mg per rat of average weight 200 g)	n								
	2	3	4	5	6	7	8	9	10
2	−	−	+	+	+	−	−	−	−
5	−	−			+	+	+	−	−
10	−	+						+	−

Table II, which is taken from the report of an investigation of the effects of this series on the blood by Elson and Timmis summarises briefly the main depressant action on circulating neutrophils in rats This action having been clearly established both in man and in rats, a clinical trial of 1 4-dimethanesulphonyloxybutane, which had already been started, was concentrated on cases of chronic myeloid leukæmia, with results which are described in the accompanying paper by Dr D A G Galton At the same time comparison of myleran with X rays (Elson 1951) and with the reported effects of the nitrogen mustards shows that, unlike these agents, it does not appreciably depress lymphocyte formation at a dose which causes a 50% or more decrease in the number of neutrophils

TABLE II—ACTION OF MEMBERS OF THE SERIES ON CIRCULATING NEUTROPHILS IN RATS

n	Dose (D) (mg per kg of body-weight)	Decrease (%) in no of neutrophils from normal 5–12 days after injection (F)	$\frac{F}{D}$
2	200	0	0
3	40	50	1 3
4	8	70	8 8
5	12	85	7 1
6	40	60	1 5
7	60	40	0 7
8	80	50	0 6
9	100	40	0 4
10	300	0	0

The relatively selective qualities shown by myleran are perhaps reflected in the lack of side effects which is one of its desirable features in clinical use

During clinical trials at the Royal Cancer Hospital and other centres, the code number GT 41 has been used to denote this compound

All these investigations were supported by grants to the Chester Beatty Research Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U S Public Health Service

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MYLERAN IN CHRONIC MYELOID LEUKÆMIA

RESULTS OF TREATMENT

D A G GALTON
M A , M B Camb
HON CLINICAL ASSISTANT, ROYAL CANCER HOSPITAL, LON

THIS paper reports the results of two years' t of 'Myleran' (1 4-dimethanesulphonyloxybutane) chronic myeloid leukæmia The rationale for the us this substance is explained in the accompanying pa by Prof A Haddow and Mr G M Timmis

DOSAGE AND ANCILLARY TREATMENT

Myleran was given orally in 2 mg tablets Two d schedules were used (1) *courses of 4–10 mg d* lasting 4–16 weeks during which 200–500 mg was giv and (2) one or more short courses in which 100–150 m was given in 1–6 days *Attempts at maintenance thera* with 4–6 mg daily for 1–12 months were made in se cases A modification of the first schedule is now favou in which daily doses of 4 mg are given as long hæmatological improvement continues

Most of the patients were treated in hospital for t first few weeks, but, when repeated small does myleran are used, treatment in hospital is often unnec sary, provided that weekly blood-counts are d Symptomatic treatment was given as required, but o two patients (cases 5 and 9) received blood transfu

Illustrative Case-records

Seven cases of acute leukæmia (five myeloid, c lymphoblastic, and one monocytic) did not respond myleran and are omitted from this report

Of the nineteen patients with chronic myeloid le kæmia seven had not received any previous treatme and twelve had been treated previously by other metho

NO PREVIOUS TREATMENT

Five patients (cases 5, 14, and 17–19) were referred trial of myleran They would otherwise have recei radiotherapy Two other patients (cases 7 and 9) wou have been given treatment other than radiotherapy ev if myleran had not been available, because the leukæm was considered too acute in case 7 and because of t hæmorrhagic state in case 9

Case 5 —A married woman, aged 71, was admitted Feb 15, 1951, with *3 weeks' history of pain of sudden on* over the left lower ribs

On examination she was thin, with pale mucosæ, and grossly enlarged firm spleen, over the upper part of wh friction was palpable and audible The soft edge of the liv was felt at the level of the umbilicus A capillary fragil test (Hess) was positive A blood count on Feb 16 show Hb 10 7 g per 100 ml , white cells 91,400 per c mm. (*neutr* phils 66,265 per c mm , immature myeloid cells* 15,538 p c mm)

Treatment and progress—The patient was given myler 10 mg daily on Feb 17 and 18, and 20 mg daily from Feb to March 4, 1951, to the total of 300 mg in 16 days H spleen and liver regressed rapidly, and her pain ceased S was discharged on Feb 20, 1951, but from March 22 to April 1951, she had repeated severe epistaxis, and multiple purpu spots appeared on her limbs Her Hb decreased rapidly 7 5 g per 100 ml , but the lowest recorded platelet count w 100,000 per c mm, on March 21, 1951 She was readmitt on March 22, 1951, and received a transfusion of six pints fresh blood *No further hæmorrhage took place after April* 1951 From then until she was last seen on Oct 16, 1952, sl has remained extremely fit Her spleen has been only ju palpable on inspiration since October, 1951, and *no immatu* leucocytes have been seen in blood films since April 1, 195 On Oct 16, 1952, her Hb was 17 5 g per 100 ml , and l idence of pulmonary tuberculosis, and the disease was tensive. Another soldier with a rudimentary 1st thoracic o had pulmonary tuberculosis.

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* The immature cell count is [illegible] cyte myel
cyte premyelocyte and [illegible] rom t
differential count of at

lley (quoted by Purves and Wedin[3]) mentioned an ation between unilateral cervical rib and scoliosis, but not find an example in my series.

one case of synostosis there was a minimal tuberculous in the lung, and in another a big echinococcus cyst of orresponding lung; both these findings were clearly dental.

ere were also 24 (0·13%) azygos-vein lobes in this group, he true figure is no doubt considerably higher, for an os lobe may be invisible on the miniature film. No iation was noted between this anomaly and costo-bral malformations, though Jalet[4] described 6 cases. of the 24 soldiers had tuberculosis of the azygos lobe sure.

aens. C. P. STAVROPOULOS.

E MEDICAL SERVICES IN THE KOREAN WAR

R,—Your article last week on this subject will, in ral, have given satisfaction to all interested in war ery.

was, however, disturbing to note that, while the Forces had ample supplies of fresh blood for trans-on, the Commonwealth Forces were relying mainly lasma. It was the opinion of almost all who worked he forward areas in the Western Desert, Sicily, Italy, North-west Europe that in the treatment of battle alties plasma was good but whole blood was very h better. It is stated that the terrain in Korea is lar to that of Tunisia. At the battles of Mareth and idaville the number of bottles of blood used per 100 alties outnumbered that of plasma by more than to one.[5]

he difficulties of supply of blood in forward areas are siderable; but it is not easy to understand why at was thought desirable, and moreover possible, in 3 does not hold good today.

ove. REX BINNING.

MORE FOOD

SIR,—"Your 1947 Correspondent" when he says "I d you so." (Dec. 13, 1952) is, of course, right in pressing more home food production. But surely he is wrong in cognate arguments? Firstly we cannot forgo any rt of our exports: on the contrary we need more ports to pay for our raw materials, our consumer goods, d our armaments. We need more exports and more me-produced foods. Secondly there can be no panacea nply by allowing the "scale of rewards to the farmer go on swinging up and up."

Many factors are involved in increased food production improved farming skill, dissemination of scientific owledge, improved soil fertility, increased scientific owledge, attraction of skilled farmers back to the hill rms, and cultivation of unused acres. All these cannot achieved simply by higher rewards. Industry has own that monetary reward alone is not a sufficient centive for human endeavour, and it is difficult to agine any reward that would attract a farmer to work arginal land when he can till fertile land instead. The pital outlay needed to convert marginal land into roductive farms requires large-scale investment: only ith the aid of something in the nature of a Home evelopment Corporation could any private individual ontemplate taking over.

It is a fact that many farmers could fairly easily nprove their output and so their profits by the application of scientific methods already practised by the more fficient farmers, yet they will not. Extra profit is not ffective in their case. Similarly, money alone will not attract farmers to the hills; they require the amenities of a civilised life as well.

On the other hand, I agree with your correspondent that farmers should be treated as a special and even privileged class. It is true that many people and political parties are not willing to allow anybody more than a "fair" reward; but would anyone grudge the coal-miner special rewards for doing a difficult and dangerous job that is so essential yet no-one else will do? Under conditions of national emergency we willingly treat our special categories on a privileged basis; and, in regard to food, we are in a world emergency.

We are moving into a period when the world food shortage will soon begin to affect us. At present two-thirds of the world are starving, including countries which export food to us. What will happen when the countries not only eat the food that they now export but even compete with us in the world market for available food?

There is no single solution to this problem. We must develop the underfed countries to help them to feed themselves; we must develop the unused territories; and we must grow more food at home. There is no single method of increasing food production at home; every practical proposal must be followed up—whether it is utilisation of leaf protein, fertilisation of the sea, development of marginal lands, increasing soil fertility, or really collecting all waste food to feed pigs and poultry.

There is an aspect of food prices of special interest to medical men and nutritionists. How can we persuade people to drink more milk and eat more eggs if the prices are high? They prefer to spend their money on films and cigarettes. Are subsidies, or is education, the answer? Or something else? I do not know; but at least I have indicated that your correspondent's panacea of more profit simply cannot work.

London, W.13. A. E. BENDER.

PARONYCHIA

SIR,—Mr. Lowden, whose paper you published last week, seems to have obtained some very good results in this infection, by combining systemic penicillin with locally applied chloramphenicol. This is interesting in view of the reported antagonism between these two antibiotics.[1] The series treated by Mr. Lowden with penicillin alone seems somewhat small for comparison, and no details of dosage are given. It would be interesting to know whether the bacteria isolated in this series were sensitive to penicillin and chloramphenicol together.

On theoretical grounds it might be more desirable to use a local application containing penicillin and streptomycin (of which there is a convenient proprietary preparation), as these two antibiotics are synergistic. It is unlikely that streptomycin resistance would be evoked during the short time of treatment; and the preparation is probably cheaper than the equivalent chloramphenicol one.

In general practice over the past five years I have not encountered any case of paronychia which did not respond to systemic penicillin alone, administered by methods described elsewhere.[2,3] However, my cases are nearly all early ones, as compared with the more extensive cases described by Mr. Lowden in hospital practice. It is probable that many more cases are successfully treated in general practice than reach the hospital casualty department. It might be instructive to hear something of the results obtained by general practitioners in this and allied pyogenic conditions, with regard especially to the periods of disability.

Twickenham. DAVID WHEATLEY.

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myeloid cells 65,660) per c mm (myeloblasts 3%), and platelets 286,000 per c mm Iliac bone marrow was highly cellular, with the characteristic picture of chronic myeloid leukæmia A capillary fragility test was negative

Treatment and progress—Myleran 10 mg daily was given from Feb 2 to Feb 26, 1951 (total 250 mg in 25 days) and 4 mg daily from May 27, 1951, to April 8, 1952 The patient improved rapidly, became afebrile by Feb 27, 1951, and was fully ambulant by March 7, 1951 Her spleen regressed steadily during the next year and could not be felt after April 8, 1952. A blood count on Feb 12, 1952, showed Hb 12 9 g per 100 ml and white cells 12,500 (neutrophils 11,125, immature myeloid cells 125) per c mm (no myeloblasts or premyelocytes) Iliac bone marrow on March 13, 1951, showed much decreased cellularity, with great relative increase in numbers of erythropoietic elements Sternal marrow on Nov 6, 1951, was of normal cellularity, and the differential count was within normal limits She was in excellent health on May 21, 1952, but was readmitted on July 24 with 3 weeks' history of progressive weakness Her spleen was again grossly enlarged A blood count showed Hb 5 6 g per 100 ml and white cells 64,200 (neutrophils 14,024, immature myeloid cells 49,500) per c mm She died on Sept 19, without responding to further treatment with myleran

Case 11—*A married woman, aged 50, was admitted on* May 19, 1951, with gross swelling of the abdomen, weakness, dyspnœa on exertion, and attacks of spontaneous bruising of the limbs The symptoms had increased in severity since their onset in October, 1949, when chronic myeloid leukæmia was diagnosed Radiotherapy of the spleen was given, but treatment was interrupted because of purpura Several blood transfusions were given but no further radiotherapy

On examination the patient was thin and somewhat pale A fading bruise was present on her right shin, and her abdomen was grossly distended, her umbilicus being everted and stretched The lower edge of her enormous spleen was below the level of both inguinal ligaments and the symphysis pubis The right border was within 3 cm of the right anterior superior iliac spine Her liver was 10 cm below the right costal margin in the midclavicular line A capillary fragility test was negative A blood count on May 29, 1951, showed Hb 6 0 g per 100 ml and white cells 430,000 (neutrophils 199,950, immature myeloid cells 187,050) per c mm (myeloblasts 7%)

Progress and treatment—Myleran 20 mg daily was given from May 25 to May 29, 1951, 4 mg daily from May 30 to July 14, 50 mg daily on July 15 and 16, 25 mg on July 18, and 6 mg daily from July 19 to Aug 29 (total 661 mg in 96 days) Progress was rapid In 3 weeks the patient was free from symptoms, but her spleen, though no longer uncomfortable, was still very large She was fit and active 12 months later A blood count on July 3, 1951, showed Hb 12 4 g per 100 ml and white cells 16,400 (neutrophils 9348, immature myeloid cells 2706) per c mm (no myeloblasts) Splenic regression continued until Nov 30, 1951, when the lower border was 15 cm above the level of the symphysis pubis, and the right border 5 cm to the left of the midline A blood count on Jan 8, 1952, showed Hb 14 4 g per 100 ml and white cells 10,000 (neutrophils 5930, immature myeloid cells 1050) per c mm (no myeloblasts) On June 17, 1952, the patient was in excellent health, but her spleen was rather larger and her liver, which had been impalpable since 1951, was again felt She complained of tiredness and of bruising When she was seen on July 28, her spleen was grossly enlarged and a blood-count showed Hb 9 3 g per 100 ml and white cells 92,000 (neutrophils 42,000, immature myeloid cells 32,000) per c mm A second course of myleran was begun on Sept 29, 1952 The patient responded as before, and when she was last seen on Nov. 4, her spleen was smaller and a blood count showed Hb 13 8 g per 100 ml and white cells 16,600 (immature myeloid cells 4540) per c mm (no myeloblasts)

Thus ten of the nineteen patients were treated as "trial" cases with myleran instead of with X rays, and nine received myleran because radiotherapy was contra indicated or was deemed useless

Review of Results

The results are summarised in the accompanying table, but features of particular interest are considered here in more detail

Symptomatic Relief

The common symptoms were those referable to and to splenic enlargement with its complications perisplenitis and infarction Night sweats and rhagic symptoms were also common In the ten successfully treated patients symptoms were relieved and the patients returned to their normal activity or employment The initial symptomatic response, however, was also satisfactory in the seven patients who relapsed quickly, five of them within 2 months [illegible] of general symptoms sometimes took place abruptly and was evident before any significant increase in Hb (in cases 8 and 9 even while the Hb was decreasing) it was always associated with rapidly falling leucocyte counts when these had been quickly rising before treatment

Splenic Regression

Splenic regression was variable but never less than might have been expected after radiotherapy, and was sometimes better than it had been after radiotherapy previously given Even grossly enlarged spleens became impalpable, this was particularly striking in one patient (case 4), who had already had eleven courses of radiotherapy The spleen remained impalpable for 6–12 months after treatment in cases 4, 7, 14, 15, and 16 Splenic regression was rapid when large doses of myleran were used, but with repeated small doses it often continued slowly for several months.

Hæmatological Changes

Leucocytes—Myleran led to granulopenia in every case The onset was rapid (8 days) with large single doses (100–150 mg) but with repeated small doses was often delayed to 21 days after the first dose The leucocyte count fell steeply with the large doses to reach normal levels in about 4 weeks but with repeated small doses the count fell more gradually for as many months The lymphocytes were affected inconstantly and never significantly Immature myeloid cells were affected sooner and more drastically than were mature neutrophils and in eight cases disappeared altogether for several months, in *case 5 they have not returned 21 months after treatment*

Hæmoglobin—Of all the effects of myleran therapy, that with the greatest prognostic significance is the increase of Hb The average increase in the first 12 weeks was 5 g per 100 ml in the eleven patients whose remissions exceeded 5 months, but in the remainder it was less than 2 g per 100 ml The Hb before treatment was less than 6 5 g per 100 ml in four of the nine most successfully treated patients, and in them the gain in the first 12 weeks after treatment was 4–7 g per 100 ml In several cases the Hb continued to increase after 12 weeks, and the highest levels were reached in an average of 23 weeks (longest 38$^1/_2$ weeks in case 3, shortest 13$^1/_2$ weeks in case 14) The highest level varied from 12 2 g per 100 ml in case 3 to 17 5 g in case 5, but only one of the seven patients whose remissions lasted less than 5 months achieved 12 6 g Blood transfusion was required in only one (case 5) of the nine successfully treated patients, this was for a transient hæmorrhagic phase a month after treatment with large doses of myleran which induced thrombocytopenia

Reticulocytes—Regular changes in the reticulocyte count during treatment were noted in some cases in which reticulocyte levels were below 1% before treatment, the count rose to a peak (up to 17 2% in case 19) between the 3rd and 5th weeks and then fell to pre treatment levels

Bone marrow—Estimates of bone marrow cellularity that are based on aspiration films are unreliable, but gross changes observed repeatedly after treatment are probably significant Comparison of samples taken at the time of the lowest leucocyte count with those taken before treatment showed that the aspirates were markedly hypocellular, erythropoiesis was relatively more con

During the year there were 303,000 admissions to l, and 31,000 operations were performed. There was a epidemic of meningococcal meningitis with 57,000 Over 350,000 patients were treated for malaria, and ly 25,000 a blood film proved positive. In the Gezira d area some 17% of the population are infected with somiasis. There are 35 students in the Kitchener of Medicine. Over 38,000 routine bacteriological and ical tests were carried out.

e real achievements are set out so briefly and with so omment that only a reader experienced in tropical ne will grasp that the Sudanese people have the benefit nall but efficient and progressive medical service. For dinary reader the report lacks flesh and blood. In the today exciting battles are being fought against malaria, gococcal meningitis, schistosomiasis, tuberculosis, mal- ion, and maternal ignorance. Could not next year's describe some of the highlights of the campaigns in ige which all can understand? Some pictures would is to appreciate the work. The work is of interest aportance to us all today, when departments of African aments are liable to fall suddenly within the searchlight rld opinion. And proper judgments for future policies aly be formed if educated people, both in Africa and in orld outside, know something about African technical ems.'

ART FROM MENTAL HOSPITALS

r May an exhibition of amateur paintings organised by ociety for Education in Art included a large section ed to entries from mental hospitals; and a collection of ngs and sculptures by psychiatric patients is at present exhibited at the Geffrye Museum, Kingsland Road, on, and will remain on view until Feb. 1. Among the ures, a moving series of fourteen carvings depicting ay to the Cross were previously shown at the S.E.A. ition. These are the work of a young woman patient—fessional artist—at Netherne Hospital, Coulsdon. The ngs are from Leavesden Hospital, where art-therapy ns have been held weekly for nine months. Many of the ats whose work is shown are mental defectives with al ages from about nine years downwards (on scale I e Wechsler-Bellevue intelligence test); but the speech me of them was so poor that they could not be tested. ame as a surprise," according to a note in the catalogue, discover that many of these patients were capable of taneous activity. They really enjoyed the painting ons—the mere application of colour to paper had its t upon them." The note adds that much of their initial essness and uncertainty of conduct disappeared while were painting.

ae National Association for Mental Health have set up a ommittee which, during the past year, has been inquiring the position of art-therapy in mental hospitals, its aims functions, and the qualifications desirable in those who tise it. Doctors have long recognised that a patient's tings may reflect the progress of his illness remarkably ifully—sombre colouring and subjects giving place to ier tones and more cheerful themes, for instance, as he es out of a depression and regains his normal mood. Art nental hospitals has thus been regarded as contributing iagnosis, rather than as a form of therapy; yet it almost ainly has therapeutic value too. An interim memorandum ining some of the difficulties and complexities of the ject has been prepared and presented to the main com- tee of the association, but has not yet been made public.

CENTENARY IN BAVARIA

N the first half of the 19th century Bavarian doctors an to feel a need for greater cohesion and opportunity for ring experience. Accordingly, in 1833 twenty doctors up the Münich Medical Society. Several attempts publish regularly a Bavarian medical journal ended in are; but at the end of 1852 Dr. Alois Martin, probably ired by Hermann Oettinger, announced his intention of ading another such journal, and after some delay the first e appeared on Jan. 7, 1854, under the title *Aerztliches elligenzblatt: Organ für Bayerns staatliche und öffentliche lkunde*. Martin retired in 1869. In 1885 Bernhard Spatz k over the appointment, and in 1886 the title was changed *Münchener Medizinische Wochenschrift*. The change was nore than the title; for under Spatz's wise leadership the nal increased its scope and became known and read by ny beyond the range of Bavaria. In the jubilee issue of the journal (Jan. 2, 1953) G. B. Gruber recalls that in its time it has published much well-known original work. Between 1944 and 1950 publication was suspended; but, as Gruber shows, the circulation is rapidly climbing back towards the 1944 peak of 18,000. Dr. Hans Spatz, the son of Bernhard Spatz, now shares the editorship with Prof. Georg Landes.

JOURNAL OF EMBRYOLOGY AND EXPERIMENTAL MORPHOLOGY

AN editorial board has lately been at work preparing the way for a new quarterly journal, the *Journal of Embryology and Experimental Morphology*. The first issue is planned for the coming spring. The editorial board, a strong international team, has decided that the scope of the new journal shall include "work on embryogenesis, growth, and developmental processes in the older organism as well as studies on fœtal-maternal relationships." Most articles will be in English, though some in French and German will also be included. The editor is Mr. M. Abercrombie, M.A., reader in embryology in the University of London. Prof. J. Z. Young, F.R.S., is chairman of the editorial board, and Mr. D. R. Newth, PH.D., lecturer in the department of zoology, University College, London, is its secretary.

University of Cambridge

On Dec. 23 the following degrees were conferred by proxy:

M.B., B.Chir.—C. W. M. Adams, L. P. Balfour-Lynn, W. M. Beatley, M. H. Bennett, D. W. K. Bird, G. M. P. Boyes, D. A. P. Burton, W. H. Chapman, H. S. Chen, R. C. Curry, S. H. Dallas, Aileen B. Donnison, J. A. Fiddian, S. J. Fisher, D. B. Fox, Hanna French, A. M. B. Golding, R. K. Greenwood, J. M. S. Grieve, A. N. Griffith, H. F. Grundy, R. D. Hernaman-Johnson, M. D. Heyman, Vera M. C. B. P. Hollyhock, B. L. Hoskyns, B. S. Jay, H. E. Lichtenstein, I. S. Lister, Gillian G. Matthews, P. L. Maybury, R. L. Morgan, K. F. Morrice, T. M. O. Morris, M. T. O'Donnell, E. M. Orton, J. T. H. Pick, J. F. Preece, P. M. H. Rack, Frederic Reisceger, T. L. Ringrose, R. D. W. Romanis, W. A. G. Roper, C. S. Savage, T. L. Scully, E. P. Simkin, I. F. Smith, I. A. Stewart, G. D. Stones, L. J. Stretton, M. C. Thornton, D. S. Trouton, J. A. M. Tudor-Hart, Ruth M. Turner, A. E. Wagstaff, H. C. M. Walton, A. W. Warltier, P. A. Watt, Ian Weinbren, F. L. Whalley, W. G. Williams, J. O. Winter.

Dr. A. D. Gardner, F.R.C.P., regius professor of medicine in the University of Oxford, will deliver the Rede lecture in the Senate House, at 5 P.M., on Thursday, May 14. He will speak on the Proper Study of Mankind.

University of London

Prof. P. Mallet-Guy of the department of surgical pathology, University of Lyons, will deliver a lecture at St. Mary's Hospital Medical School, Paddington, W.2, at 5 P.M. on Thursday, March 5. He will speak in French on Les Opérations Sympathiques dans le Traitement des Pancréatites Chroniques Récidivantes.

University of Sheffield

On June 26 the honorary degree of D.SC. will be conferred on Sir Ernest Finch, formerly professor of surgery in the university.

Scottish Society of Anæsthetists

The annual meeting of this society will be held at Dunblane Hotel Hydro from the evening of Friday, April 24, until Sunday, April 26, under the presidency of Dr. W. M. Shearer. Dr. I. W. Magill will be a guest of the society.

Liverpool Medical Exhibition

On Monday, May 18, at 11.30 A.M., Dr. E. Noble Chamberlain will open this exhibition at St. George's Hall, Liverpool. Only doctors will be admitted, and the exhibition will be open daily from 11 A.M. to 6.30 P.M. until May 22.

Institute of Psychiatry, London

On Monday, Feb. 2, at 8 P.M., at this institute at the Maudsley Hospital, Denmark Hill, S.E.5, Prof. Konrad Lorenz (Max Planck Institute, Buldern, Westphalia), will deliver a lecture on Comparative Psychology and Psychiatry. On Feb. 6, at 3 P.M., Prof. H. C. Rümke (Utrecht) will give a lecture on the Clinical Significance of Obsessional Phenomena.

Conference on World Health

The United Nations Student Association is holding a conference on this subject on Saturday, Feb. 7, at 2.15 P.M., at 16, Queen Anne's Gate, London, S.W.1. The speakers will include Dr. Neville Goodman, Dr. Harold Balme, and Dr. C. H. Andrewes, F.R.S. Further particulars may be had from UNSA, 25, Charles Street, W.1.

during the terminal pancytopenic phase, was predominantly myeloblastic

Platelets —The platelet count fell somewhat in all the patients treated, especially in those who received the larger doses of myleran The fall continued longer than that of the granular leucocytes, and the lowest counts were recorded 13–21 weeks after the first dose of myleran Hæmorrhagic states necessitated blood-transfusion in cases 5 and 13

Resistance to Myleran

The leucocyte count fell in every patient treated with myleran for the first time In cases 6, 10, and 12 subsequently rising counts did not respond or were arrested for only a few days, although doses of myleran several times larger than were necessary to bring about the initial fall in leucocyte-count were given In cases 10 and 12 all the circulating granulocytes shared this rapidly acquired resistance to myleran, but in case 6 the mature neutrophils responded as they had at first, and the rising counts were made up largely of dwarf undifferentiated hyperchromatic blast-cells It is perhaps significant that these three patients received large doses initially

Side effects of Myleran

No patient complained of any symptom that could be attributed to myleran Three patients (cases 3, 11, and 14) developed diffuse brownish pigmentation of the face, forearms chest, and abdomen during treatment, this wore off during the next three months In case 1, when repeated blood-transfusions were given during the terminal phase, the more intense and widespread pigmentation characteristic of hæmosiderosis appeared Agranulocytosis is due to overdose, but thrombocytopenia may develop with therapeutic doses, particularly when large doses are used or when the platelet-count is much below 100,000 per c mm when treatment is begun Myleran therapy therefore requires constant hæmatological supervision Weekly estimations of hæmoglobin total and differential leucocyte counts, and platelet-counts are necessary during the critical phases of treatment, when rapid changes are taking place

Discussion

Radiotherapy is the best palliative treatment in chronic myeloid leukæmia that has stood the test of time It can induce repeated remissions for as long as 12 years, although most cases enter the resistant phases in less than half this time (Ledlie 1953) Its disadvantages are (1) that radiation sickness sometimes accompanies it, though much less often than formerly, (2) that splenic regression lessens with the later courses and the symptoms resulting from chronic splenomegaly are no longer relieved and may be further aggravated by perisplenitis caused by X rays, and (3) that treatment must be given at specially equipped centres In spite of these disadvantages no other palliative treatment has taken the place of radiotherapy, although several drugs are useful, especially in areas remote from radiotherapy centres, or when radiotherapy has lost its efficacy The best-known drugs are arsenite (as *Fowler's solution*), benzene, urethane, nitrogen mustard, and such recent modifications as 2-naphthyldi 2′ chloroethylamine and 2 4 6 tri-ethylene-imino-1 3 5-triazine Radioactive phosphorus should be regarded as a form of radiotherapy Drug-induced remissions are usually short lived, compared with those brought about by radiotherapy, and side-effects are often objectionable Radioactive phosphorus requires specialised equipment, must be handled by skilled personnel, and has no advantages over X rays 2 4 6 tri-ethylene imino-1 3 5 triazine has few side-effects, but its performance is inferior to that of radiotherapy (Karnofsky et al 1951, Paterson and Boland 1951, Silverberg and Dameshek 1952)

If a new palliative remedy is to compete successfully with radiotherapy it must be as efficacious and it must be safe, free from undesirable side effects, and easy administer If it is to take the place of other must improve on their performance in patients for radiotherapy is contra-indicated An essential feature radiotherapy is that it can induce remissions rep In considering the claims of myleran to a place in peutics, it is emphasised that little is yet known of its action on relapse following prolonged first remission

The severity of disease represented in this small ranges from that of the very chronic case, with few symptoms, which might have responded equally well any of the recognised treatments, to that of rapid advancing disease which had already responded poor to them Some patients were treated for the first time and others had already been treated, in some cases repeatedly, by other methods, to which they were becoming more or less refractory With this wide range of clinical types it is not surprising that the response to myleran varied accordingly, and that some patients were extremely sensitive to myleran and obtained dramatic and prolonged remissions, whereas others responded poorly and relapsed quickly It is therefore difficult to give more than a preliminary and tentative assessment of myleran Except in three cases the results were no worse than those which might have been expected with any other form of treatment, and in at least seven cases they were similar to the best of which any other method is capable Five of the nine patients who were regarded as unlikely to obtain any further benefit from radiotherapy nevertheless obtained useful, and in four cases outstandingly successful, remissions with myleran The three exceptions include cases 6 and 12, who acquired resistance to myleran, and case 13, whose bone marrow failed 4 months after treatment These three had all received large doses of myleran, which are consequently considered dangerous, although several of the most successfully treated patients tolerated these large doses without mishap (cases 3, 5, 7, 11, and 14)

Even if later experience fails to confirm the present impression that myleran is superior to other drugs in respect of the extent of splenic regression, the length of remissions, and the rapidity and completeness with which symptoms are relieved, myleran will still have the advantages of simplicity of administration, absence of side effects, and occasional effectiveness after other methods have had to be abandoned

Any benefit which patients with chronic myeloid leukæmia derive from myleran probably results solely from the removal of the ill effects of excessive myelopoiesis for it is unlikely that myleran's action depends on anything more specific than its ability to depress granulopoiesis In non-leukæmic people single doses of 2 mg per kg of body-weight depress the monocyte and neutrophil counts and sometimes the platelet count, but lymphocytes are irregularly and inconstantly affected In therapeutic doses myleran acts preferentially on myelopoiesis, but this apparent selectivity is only relative Large doses may have contributed to the terminal failure of erythropoiesis in cases 1, 3, 6, and 12 The non specificity of action of myleran is well shown by its failure to induce remission in acute leukæmia, chronic myeloid leukæmia in acute myeloblastic relapse, and myelofibrosis, where disturbed myelopoiesis is merely incidental to some more fundamental upset and is not a major cause of the symptoms

The preliminary results described here are nevertheless encouraging, and myleran clearly merits further trial in cases for which radiotherapy would ordinarily be given as well as in cases where radiotherapy is considered to hold out no chance of further palliation

Summary

1 4 Dimethanesulphonyloxybutane (myleran) was given orally to nineteen patients with chronic myeloid leukæmia In therapeutic doses myleran depressed

TUITARY INSUFFICIENCY IN WOMEN

A CLINICAL STUDY OF SEVEN CASES

L. A. WILSON
M.A., M.B. Aberd., M.R.C.P.
OR MEDICAL REGISTRAR, ABERDEEN ROYAL INFIRMARY

> "... that whiter skin of hers than snow,
> And smooth as monumental alabaster."—*Othello*.

E find sometimes that rare diseases become strangely mon after we have learnt how to recognise them ; , ever since Sheehan (1939) dealt so lucidly with the tetric lesions, it has been known that pituitary defects far from rare. Defective function of the anterior of the pituitary gland is now the subject of much arch, and it is not surprising that this is being sued in the laboratory more than at the bedside ; for ny excellent clinical descriptions, particularly that of ehan and Summers (1949), leave little for others to If something remains to be added, it is because uitary mischief varies so much in its extent and effects, l the portrayal of another 7 selected female cases y illustrate the manysidedness of the syndrome. I ve not attempted a general picture of pituitary ufficiency, because writings on this topic are volumi- us, and we are fortunate in having the comprehensive iews of Sheehan and Summers (1949), Farquharson 50), and Perkins and Rynearson (1952).

I have followed Perkins and Rynearson in preferring term "pituitary insufficiency," if only because it ls a little easier on the tongue than "hypopituitarism," anhypopituitarism," "hypoantuitarism," "anterior popituitarism," and "hypo-anterior-pituitarism." Simmonds's disease" is a well-worn term, but the unds of its meaning are ill-defined. This objection does t apply to "Sheehan's syndrome," which is used below mean pituitary insufficiency after obstetric shock.

Sheehan and Summers (1949) and Perkins and ynearson (1952) do not deal with dwarfism, but I have cluded a pituitary dwarf in this series to emphasise at cases of pituitary insufficiency with onset in childood need not differ in some important aspects from ases with onset in adult life.

THE PATIENTS

The patients have been observed in the past three and half years. According to the likely time of onset, the ituitary defects are classified as prepuberal (case 1), ostmenopausal (case 2), and postpartum (cases 3–7). ome general and laboratory data of cases 2–7 are given n the accompanying table ; case 1 is not included, ecause the patient was admitted in coma and few of hese data were obtained. Treatment and progress are ot discussed but are mentioned briefly when indispensable to the clinical description.

Prepuberal Lesion

Case 1.—A spinster, aged 39, whose first symptom was loss of the sight of the right eye at the age of 12 years, retained a juvenile appearance and stature, did not menstruate, and disliked cold. Examinations in other hospitals in 1936 and 1945 revealed right optic atrophy, left temporal visual field defect, and pituitary dwarfism ; and there were radiological signs of a pituitary tumour whose calcified capsule was seen to extend intracranially. She had been bright and intelligent, but after October, 1950, was often mentally deranged. On Oct. 20, 1951, she vomited and thereafter became confused and incontinent, and had cold sweats, and little nourishment seems to have been given while she was in this state.

On admission on Oct. 31, 1951, she was deeply unconscious, and her blood-pressure was unrecordable. She was small and somewhat plump, looking about 15 years old ; her face was puffy and remarkably pale ; her Hb was 82% (Haldane). Her skin was a little rough on her limbs but smooth elsewhere ; there was healed psoriasis of the elbows. Her scalp hair was profuse and dry, eyebrows scanty, axillæ hairless but greasy, pubic hair absent, and hairs on the vulva scanty and dark. There was no palpable breast tissue ; the nipples were tiny ; and the areolæ were tiny and devoid of pigment. Bilateral optic atrophy was present. The limbs were flaccid, becoming rigid in extension later that day, with extensor plantar reflexes. Tightly clenched jaws prevented close inspection of the teeth, but they appeared strong, white, even, and flawless except for a few metal fillings.

Blood was removed for sugar estimation, and intravenous dextrose was given. Ventriculograms done two hours later by Mr. W. Martin Nichols showed no ventricular shift or dilatation. Meanwhile we learnt that the blood-sugar on admission was 3 mg. per 100 ml. (Nelson method). The blood-sugar level and blood-pressure were promptly restored and maintained, and intensive treatment included the use of cortisone acetate, but the patient did not recover consciousness. She lay in a state resembling decerebrate rigidity, with fixed jaws and firm abdominal muscles, spastic extended limbs, and extensor plantar reflexes ; her arms were adducted and fully rotated inwards, and her hands were clenched ; and her feet became rigidly inverted. There were frequent tonic spasms, with arching of the back. Bronchopneumonia and purulent stomatitis appeared early, and it was astonishing that she did not die until thirty-one days after admission.

Necropsy findings (Dr. A. Wynn Williams).—There was a large cystic suprasellar craniopharyngioma, 3 cm. in diameter, associated with softening of the cerebral tissues for 3–4 mm. around its upper margin ; the sella had been destroyed and no normal pituitary tissue was found. There was considerable hypoplasia of the various organs and tissues, particularly the other endocrine glands and the genitalia. Bronchopneumonia and ulcers in mouth were found. The teeth were healthy.

The immediate clinical problem was to find out if the large pituitary tumour had caused unconsciousness from intracranial pressure effects ; but the ventriculograms did not show any internal hydrocephalus. Spontaneous hypoglycæmia was also considered, and its presence was confirmed by a blood-sugar level of 3 mg. per 100 ml. Since the subsequent necropsy findings did not indicate that the tumour had caused any significant pressure on the brain stem, it seems very likely that spontaneous hypoglycæmia was indeed responsible for the mental derangements of the previous year, and for the terminal coma with its peculiar neurological accompaniments. Unfortunately it was impossible to revive a patient whose blood and brain had been starved of glucose for some eleven days before treatment was started. Even so, it is worthy of note that this pituitary dwarf survived to the end of the fourth decade, and that she retained her juvenile appearance.

Postmenopausal Lesion

Case 2.—A married woman, aged 64, had been subject, since the age of 16, to epileptic fits preceded by bitemporal headache and vomiting. She had borne two children normally in 1910 and 1913, and each baby was at the breast for six months. Menstruation ceased in 1936, when she was 50. Strong, energetic, and quick-witted until 1940, she was then slowly afflicted by weakness, listlessness, depression, anorexia, and dread of cold. Her daughters described a shuffling gait, thinning eyebrows, and a pale swollen face, so different from her former sharp features and dimpled chin. She took thyroid extract irregularly and without benefit. She ate little during a head-cold in January, 1950, and was drowsy and muddled ; after this she was often confused in the afternoons or during the night. Her appetite failed and she lost flesh. She complained of severe pain and stiffness in the knees.

On admission on Oct. 2, 1950, she was weak, sluggish, miserable, muddled, and peevish. She was well nourished. Her skin was milky pale and exceedingly smooth, her face puffy and finely wrinkled. Her scalp hair was thinning a little but of good texture ; she had sparse eyebrows, scanty lower eyelashes, and only a few axillary and pubic hairs. Breasts, nipples, and areolæ appeared normal. Her abdominal muscles were firmly contracted. Knee movements caused pain and palpable grating. She had a slight dorsal kyphosis. The skin of her legs was pigmented from healed dermatitis associated with varicose veins. A few lens opacities and moderate retinal arteriosclerosis were discovered ; the visual fields were later found to be full. Radiography showed some left ventricular patient could have projected delusional ideas, exaggerated or prevaricated *An interview with the wife and an investigation* by the psychiatric social worker revealed that the essence of the wife's reports was true, though she tended to give highly coloured versions, and also that there was some basis for the patient's allegations, though these were much exaggerated.

Rarely it may happen that a fact and a delusional statement made by a patient agree by sheer accident This does not make the statement less delusional, for the psychiatrist, *in such a case, is concerned more with the manner* in which the patient arrives at his belief than with the belief itself For example, a paranoid patient asserts that he is persecuted by a person whom he has never met, and further imputes a certain bad trait to that person's character, it may well happen that the person in question does exhibit such a trait, but this does not make the accusation any the less delusional, since it was derived from paranoid thinking, not from factual observation.

Some of the delusional statements of a patient may be factually true—and a consequence of his abnormal behaviour A paranoid schizophrenic who behaves in an odd, eccentric manner will surely be remarked upon or pointed out, and this will confirm his original feelings that he was being watched Neighbours are not always patient with the divagations of a psychotic and may retaliate against his abuse or aggression—which is then quoted by him as proof of the neighbour's persecutory activities

Very rare indeed must be an instance where fate arranges so that delusions are neatly confirmed by reality An excellent example is given by Dostoievsky in *The Friend of the Family* Tatyana Ivanovna imagined that rich, elegant suitors were paying court to her

She was already on the borderline of a psychosis when, as Dostoievsky puts it, destiny played a last fatal jest at her expense'—she inherited immense wealth. And now indeed dozens of real suitors began to pay her ardent attentions, and the lady was too deluded to realise that it was her money they were really after Had she consulted a psychiatrist at this stage and told him that she was pestered by many men, he would hardly have been able to assess her complaint as delusional He might indeed have doubted the motivations of the suitors, but would have found it very difficult to prove or disprove whether they were driven by love (as the patient believed) or by cupidity (as was the fact)

A reality situation which plays into the hands of the psychotic's delusions need not, however, prevent his recovery In Pirandello's *Henry IV* the environment had been altered to conform with the psychotic's delusions; when the hero recovered his sanity, he turned the tables, and decided (because it suited him) to play up to the environment, and pretend to be insane Here a psychiatrist would have been hard put to it to disentangle pretence from delusion

Though the mere harbouring of a delusion does not matter, provided behaviour is not disturbed in a person leading a tolerable social life, yet it can be of vital importance to diagnose after a patient has been certified and detained in a mental hospital In certain paranoid states, where delusions are limited in relation to some one person or a particular situation, the patient can be a model of good behaviour in the hospital, and to make matters more difficult he may minimise or completely deny delusions he had previously expressed, in order to obtain his discharge

Case 2 —A married man aged 67 was admitted because he had made a suicidal attempt, and because he threatened to kill his wife (12 years younger), alleging that she was having an affair with a neighbour The evidence he gave of her alleged infidelity was circumstantial and unconvincing, but he managed to persuade a newly appointed house physician, who recorded He may be unduly jealous but it is not entirely certain that his suspicions have not been supported by fact" The patient was perfectly well behaved and soon made light of his delusions He was discharged, but had to be readmitted after only two months, having aga his wife's life intolerable by his threats and repeated d accusations Again he settled down as a model of in the hospital, enjoying the amenities of extended Subsequently he was discharged to the care of a br promising not to return to his wife

HELPFUL CRITERIA

The presence of other symptoms of mental illness example, depression, apathy, elation, or hallucinat *will support the likelihood that* the patient's sta are delusional, if these fit into a recognised c pattern. But difficulties arise in the type of ca other symptoms are absent, or so slightly beyond variation as not to be conclusive Careful, detail tioning may reveal that the "factual evidence" pr by the patient to substantiate the veracity of hi are too vague, wild, or bizarre for acceptance

Case 3 —A married man aged 64 was admitted after having threatened to kill his second wife, alleg had been unfaithful He had divorced his first wi infidelity and his second wife was nearly 25 years h so there was a suitable situation for an attitude of However, the type of evidence he produced was not con ing He said that he heard noises downstairs, and wh descended he found his wife alone but the back of h was covered with dog's hair He came to the co that she must have been lying on the floor on h *obviously for sexual purposes*

Fortunately we do not have to rely merely on feasibility of the patient's statements we can obtain some guidance by studying his manner of pre tation or his reactions to the alleged insults The pa patient over-protests his probity, innocence, or exhibits a self-righteous attitude, and readily be heated in forcibly insisting upon the justice of h arguments Generalisations such as "jealousy of o —tongues of other people make mischief—libel a slander," are often repeated, but somehow one ca track down specific incidents that could be investig and confirmed Allegations are accompanied by self-justifications as "I keep myself to myself—I like mind my own business and expect others to do the —I don't like gossip" Colourful, exaggerated phr may be used

Case 4.—A paranoid epileptic who had been disch to the care of her husband *ranted as follows* "My husb has been mean, cruel, brutal—he is a filthy beast an gluttonous skunk—eighteen years of my married life h been torture—I must have justice—I will show the w by God I will—he was let free whilst I had to suff because the solicitor and doctor wouldn't do their w properly—do you wonder why the country is in such a s and so on

In contrast I would quote a case where it was felt th the allegations were not delusional Here the pati was calm, able to reason, and could see both sides of th problem

Case 5 —A male outpatient aged 45 was referred f claustrophobia He found his clerical work in an o a great strain and sometimes he made errors in his accou for which he had been reprimanded He suspects, howev that an ambitious younger man had "fiddled" his accou with the result that he (the patient) was reduced in rank Th injury he believes was motivated because some time pr viously he had reported certain improprieties of that empl to the manager A verbatim report of part of the inter best illustrates how the rational mind works

Doctor Could you prove to the satisfaction of a co of law that this other person had played about with yo accounts?

Patient No It would be my word against his

Doctor Perhaps you did make the errors in ques yourself—as you admit you sometimes did

Patient I generally ferreted them out myself and th made the necessary corrections

Doctor But perhaps not all of them

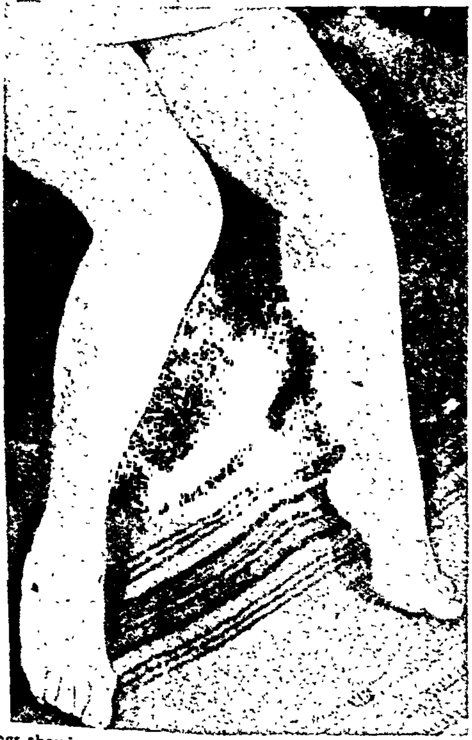
ls of case 4 were brittle ; those of cases 3, 5, 6, and 7 wed longitudinal ridging, and those of cases 5, 6, and howed terminal curving. The scalp *hair* was healthy, ring some thinness in case 7, dryness in cases 4 and 6, l early greying in cases 5, 6, and 7. Case 5 had normal ebrows, but those of the others were thinned, particu- ly in the outer halves. The lower eyelashes of cases 3 d 7 were scanty. Fine down could be seen on minute pection of face and limbs. Axillary and pubic hair re absent or nearly so. Although the *breast* contours emed normal, hardly any mammary tissue could be t in cases 3, 4, and 6, and very little in case 5 ; but se 7 had a good allowance of glandular breast substance. e breast areolæ were deeply pigmented in case 4 and ht brown in the rest. Case 4 had big, and the others all, nipples. On *vaginal examination* the body of the erus was not palpable and the cervix could barely be lt as a tiny nodule. The vagina was atrophied in case 7 t admitted two fingers in the others. Cases 3 and 4 d small internal *hæmorrhoids*, which had not produced mptoms. The *thyroid glands* were not palpable. ases 4, 5, and 7 showed a slight *dorsal kyphosis*. Early *inal arteriosclerosis* was recorded in cases 5 and 6. *utrition* was fair in case 7 and normal in case 3 ; and ses 4, 5, and 6 were fat.

There follows additional information about individual atients.

Case 3 had had angina pectoris for three years. Since coming der observation she has complained of intermittent claudi- tion in the calves and has had a myocardial infarction.

Case 4.—Tuberculous neck glands were dissected in 1940. had been prescribed regularly since 1947 ; epiness, cold intolerance, and Raynaud's he fingers, but did not restore energy and infected gall-bladder was removed recently.

Case 5.—In 1919 she had severe influenza. A retained piece f placenta was removed five days after the postpartum æmorrhage in 1926, and she was dangerously ill with puerperal septicæmia " for the next three months. She had wo further vaginal bleedings, both heavy, before the meno- ause in 1928. She took thyroid extract regularly after 1928 ; it " made life worth living " after the intense misery of the previous two years, and relieved intolerance of cold ; but it did not bring back strength. She had angina pectoris and intermittent claudication. There were systolic cardiac murmurs ; the popliteal and ankle pulses were absent. There were scars on the legs from ulcers in childhood.



Legs showing deeply pigmented erythema ab igne in case 6.

GENERAL DATA AND SOME LABORATORY INVESTIGATIONS IN CASES 2–7

Case no.		2	3	4	5	6	7
Age (yr.)		64	45	48	55	46	49
No. of children born ..		2	1	3	3	3	5
Duration of symptoms (yr.) .		10	10	11	23	21	21
Weight (lb.)		119	106	155	134½	148½	78
Height (in.)		62	61	64	62½	63	58
Blood-pressure (mm. Hg) ..		126/84	100/70	114/80	138/80	120/95	126/74
Hæmoglobin (%) (Haldane)		66	70	88	60	64	68
Basal metabolic rate (%) ..		−24	−45	−22	−15	−44	−38
Urinary 17-ketosteroids (mg. in 24 hr.)		0·91 and 2·3	1·16 and 1·16	1·30 and 0·84	0·77 and 0·54	0·71 and 1·24	0 and 0
Kepler	"Night" volume (ml.)	320	360	240	300	204	650
	Greatest "day" volume (ml.) ..	132	28	60	64	25	20
	Index	36·8	7·7	31·5	5·51	5	1·6
Insulin-tolerance test	Insulin sensitivity	+	+	0	+	+	+
	Hypoglycæmia unresponsiveness	+	+	0	+	+	+
Erythrocyte - sedimentation rate (Westergren) (mm. in first hr.)		14	20	15	28	39	14
Blood Wassermann reaction		Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Case 6.—Her memory is poor, but she thinks she bled heavily with each of her three confinements ; after the first she was pale and weak, but felt stronger after the second. Thyroid extract was prescribed about the time of onset of her angina pectoris a year before admission, but it so aggravated the cardiac pain that she became afraid of the drug and took it only rarely. X rays showed considerable expansion of the aortic arch. The blood-plasma was laden with fat. The skin flushed deeply in response to inhalations of amyl nitrite and injections of nicotinic acid.

Case 7.—She was ill for three weeks after her last delivery with a " poisoned stomach." She was pitifully feeble, complained grievously of cold, and whined if disturbed. Her face was little and wizened, her lower jaw small and receding, her palate low and flat ; and her tongue narrow, red, and pointed. Her hands were unusually small, and her arms short and thin. Despite her loss of weight she had a fair covering of subcutaneous fat. Both optic discs showed slight temporal pallor, of doubtful import ; the visual fields were full. A solitary nodule of lupus vulgaris was present on the nasal skin. The left hip was stiff, and the left leg short.

Radiography revealed old-standing fibroid tuberculosis of the upper zones of both lungs ; the left femoral head was flattened, apparently from old osteochondritis ; no calcification was seen in the adrenals.

On Dec. 5, 1951, a dose of laxative was followed by diarrhœa and profound circulatory collapse, with hypochloræmia and moderate hypoglycæmia. Later she had an attack of spontaneous hypoglycæmia ; and two other episodes of circulatory collapse occurred, one preceded by unexplained diarrhœa, the other by thrombophlebitis.

SPECIAL INVESTIGATIONS

Many special investigations were made, but only pertinent ones relating to cases 2–7 are mentioned. Some results are shown in the table.

Basal metabolic rates (B.M.R.) were estimated by Dr. A. Lyall or by Dr. W. Bowman by gas analysis of specimens collected in Douglas bags. Case 5 was taking thyroid 2 g. daily at the time ; case 2 may have taken thyroid extract until a week before the estimation ; case 4 had had none for four weeks.

Urinary 17-ketosteroids were assayed by Dr. W. Bowman, who used Callow's method in cases 2–6, and the M.R.C. standard method in case 7. Excretions were negligible.

Kepler test.—Part I was positive in all. In cases 2 and 4 part II was negative, but a repeat test in case 4 gave an index of 23.

Storage Temperatures

Samples were kept either at −79°C or at −20°C The lower temperature was maintained in a tank containing a mixture of solid carbon dioxide and alcohol, the tank itself being surrounded by large blocks of solid carbon dioxide within an insulated box Although an attempt was made to keep the alcohol bath continuously supplied with chipped carbon dioxide, in practice this was not always achieved, and the temperature of the alcohol was sometimes as high as −70°C for several hours at a time

A temperature of approximately −20°C was maintained in an ordinary deep-freeze cabinet, in which the temperature varied between approximately −17°C and −22°C

Percentage Hæmolysis

The percentage hæmolysis in a sample was calculated as follows

The hæmoglobin concentrations of the supernatant (Hb_s) and of the whole sample (Hb_W) were determined in a photoelectric colorimeter using an Ilford 625 filter Percentage hæmolysis was then expressed as

$$\frac{Hb_s \times \frac{100 - P\,C\,V}{100}}{Hb_W} \times 100,$$

P C V being the packed cell volume of the whole sample

RESULTS

Glycerol Concentration and Optimum Rate of Freezing

Using the 15% glycerol-saline solution described by Sloviter (1951), it was noted that for blood frozen to −79°C in bulk (500 ml) the mere process of freezing and thawing often resulted *in as much as 10–20%* hæmolysis On the other hand, small samples (2–5 ml) showed much less hæmolysis, and it was suspected that the more rapid freezing and thawing attainable with the small volumes of blood was responsible for the discrepancy

In attempting to find a means of diminishing the hæmolysis occurring during the freezing and thawing of large volumes of blood, the effect of a range of glycerol concentrations (2 5–30%) was investigated, using blood-glycerol mixtures sealed into capillary tubes of approximately 1 mm bore It was found that when freezing was rapid (about 3 seconds), hæmolysis occurred in all the glycerol concentrations used, however, the degree of lysis varied, amounting to only about 30% in glycerol concentrations of 8–10%, compared with almost 100% in glycerol concentrations of 15–30% For slower freezing (between 15 and 100 seconds), glycerol concentrations of 15–30% were optimal, and concentrations below 15% showed distinctly more hæmolysis It was concluded that hæmolysis during freezing and thawing was determined to some extent by the relation of glycerol concentration to the rate of freezing, and that higher glycerol concentrations (20–30%) would be more suitable for large quantities of blood.

Independent studies by Lovelock (1953) confirmed the desirability of using a higher concentration of glycerol for freezing to −79°C His work also suggested that lowering the final plasma concentration of sodium chloride from 0 15 *M* to 0 12 *M* would further enhance the value of using the higher glycerol concentration Accordingly, bottles containing 420 ml of blood, mixed with 120 ml of the standard acid citrate dextrose solution and stored at 4°C for not more than 7 days, were prepared for freezing by removing 240 ml of citrated plasma and replacing it by 200 ml of a mixture of 50% glycerol and 0 425% sodium chloride solution Such bottles were frozen to −79°C by one of two methods

(1) Plunging them directly into a CO_2 alcohol bath, when solidification was complete in 15–20 minutes

(2) Rotating the bottles in a CO_2 alcohol bath, using the mechanical roller device described by Mollison and Sloviter (1951), when solidification was complete in 8–10 minutes

As had been anticipated, hæmolysis was slight in all bottles, and did not in fact exceed 5% in any instance Evidently with large volumes of blood, containing relatively high concentrations of glycerol, rapid f unnecessary

Some bottles of blood frozen in this way and at −79°C showed less than 5% hæmolysis after 2

Rate of Hæmolysis of Red Cells Stored in Different Ve at −20°C (Test-tube experiments)

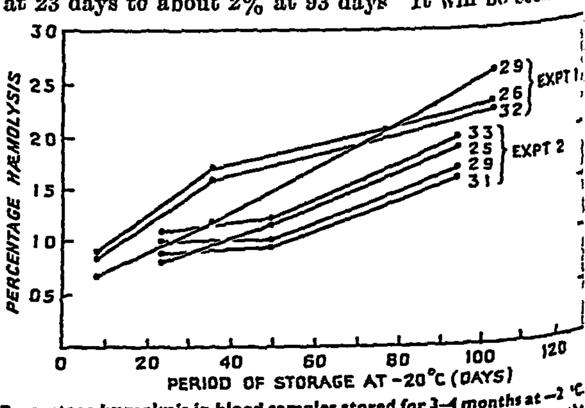
Since storage of large volumes of blood at −79 very costly, it seemed desirable to carry out la experiments at −20°C Lovelock (1953) suggested t glycerol protects red cells from damage at low tem tures by preventing the attainment of high intracel salt concentrations It seemed possible that the us mixture containing 30% glycerol in a hypotonic salt sol might permit satisfactory storage at temperatur high as −20°C Trials of such mixtures were in fact d appointing but, as described below, very sati fa results were obtained when sodium citrate was sub tit for sodium chloride

Glycerol-saline mixtures—Blood mixtures were p pared containing a final concentration of 30% glyc and concentrations of sodium chloride varying fr 0 5 to 1 0% After a week's storage there was l than 5% hæmolysis, but the rate of hæmolysis increa rapidly thereafter, and there was more than hæmolysis in all mixtures stored for more tha month Hæmolysis was least when the sodium chlor concentration was 0 75%

It will be noted that the amount of lysis observed in the experiments is greater than that previously reported b Mollison et al (1952) for blood mixed with glycerol sal This discrepancy is probably due to the fact that in th previous experiments blood drawn into acid citrate-dextro solution was used, and not all the supernatant plasma-citr was removed before adding the glycerol saline In the pre experiments, on the other hand, glycerol saline was added t packed red cells obtained from heparinised blood As we sh now show, the presence of citrate in blood glycerol mixtu stored at low temperatures greatly reduces hæmolysis.

Glycerol citrate mixtures—Blood mixtures were pr pared containing final concentrations of 20%, 25% ar 30% glycerol and concentrations of trisodium citra (dihydric) varying between 2 0% and 3 3% *The be* results were obtained with 30% glycerol and 3% tr sodium citrate, with this mixture there was about 2 *hæmolysis* after 3 months' storage, with *25%* glycer there was about 4 5% hæmolysis, and with 20 glycerol *about 6 5% hæmolysis* Small variations in th concentration of trisodium citrate had little effect, 2 5 and 3 3% being scarcely less effective than 2 9% or 3 1%

Some of these findings are shown in the accompanyin figure In experiment 1, in the mixtures contain between 2 6% and 3 2% trisodium citrate, hæmoly increased from about 1% *at 8 days to 2 5%* at 102 da in experiment 2, hæmolysis increased from about 1% at 23 days to about 2% at 93 days It will be seen tha



Percentage hæmolysis in blood samples stored for 3–4 months at −2 °C In all mixtures the final concentration of glycerol was 30%, the concentration of trisodium citrate is shown against each curve Blood from two donors was used (experiments 1 and 2)

Neurological complications of spontaneous hypoglycæmia.—This theme is too complex for detailed treatment here and I have limited myself to a few clinical observations. It has long been known that hypoglycæmia may be associated with neurological disorders which may persist long after the blood-sugar level has been restored to normal or to hyperglycæmic levels, and which may be irreversible. Their occurrence with insulin overdosage in diabetes mellitus, insulin shock therapy, and pancreatic hyperinsulinism is discussed by Baker (1939) and Fineberg and Altschul (1952). The records of cases 1 and 2 show that similar neurological complications may occur with the coma of pituitary insufficiency, and it is considered that the effects in these cases were due to spontaneous hypoglycæmia. While they lay in coma, both patients had tight jaws and abdominal muscles, intense spasticity of the limbs, tonic spasms, and extensor plantar reflexes; in case 1 the limbs were held in adduction and extension, in case 2 in adduction and flexion. Neither patient responded when the blood-sugar level was restored: case 1 remained in coma and died; case 2 remained unconscious for two days, despite continued treatment, and her complete recovery was preceded by several weeks' madness and signs of organic nervous disorder. The early diagnosis and treatment of spontaneous hypoglycæmia is of vital importance, and three points require emphasis:

(1) Both patients had been subject to recurring mental derangements for several months before unconsciousness, and case 2 was actually in hospital for some time, and had an insulin-tolerance test, before her peculiar mental state was connected with spontaneous hypoglycæmia.

(2) Coma was precipitated in case 2 by a urinary infection, a condition easily overlooked in a confused patient.

(3) In each case the psychic changes and the coma with its neurological accompaniments might have been ascribed to other causes—in case 1 to the intracranial extension of a large pituitary tumour, and in case 2, a woman of 64, to cerebral arteriosclerosis and cerebral thrombosis.

SUMMARY

Clinical findings in 7 women with pituitary insufficiency are presented: 1 was a pituitary dwarf with a craniopharyngioma, and 4 had Sheehan's syndrome. The nature of the lesion was uncertain in 2 patients, of whom one had postpartum and the other postmenopausal onset.

The clinical picture was not uniform, and there were minor disagreements with previous descriptions; the sparing of some pituitary functions and the effects of the syndrome on patients of different constitution are illustrated. Facial resemblance was striking in 4 cases.

Mental changes, coma, and neurological effects in 2 cases were thought to be due to spontaneous hypoglycæmia, and pitfalls in the diagnosis of this condition are discussed.

I wish to thank Dr. Ian Gordon for suggesting this study on his patients, and for his constant advice and encouragement throughout; Dr. A. Lyall for his generous personal help and for all the investigations done by his laboratory staff; Dr. W. Bowman and Dr. W. H. R. Auld for their personal conduct of special tests; Prof. J. S. Young and Dr. A. Wynn Williams for permission to publish the necropsy summary; Dr. C. D. Needham and Mr. W. Martin Nichols for valuable criticism; Mr. R. G. M. Drummond for the clinical photograph; and, not least, the nurses and many resident medical officers for much assistance.

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MYLERAN IN CHRONIC MYELOID LEUKÆMIA

CHEMICAL CONSTITUTION AND BIOLOGICAL ACTION

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In an endeavour to enhance the therapeutic efficacy of the nitrogen mustards, in which R = either CH_3 or CH_2CH_2Cl (fig. 1), Haddow et al. (1948) investigated a series of aromatic analogues, of which one member (fig. 2) was subjected to clinical trial and found to have limited usefulness when administered orally in cases of Hodgkin's disease, chronic lymphatic leukæmia, and polycythæmia vera. As an outcome of this work, a series of sulphonic-acid and other esters were synthesised by one of us (G. M. T.), on the assumption that the biological action of compounds of these types might resemble that of the nitrogen mustards because of a common ability to alkylate—i.e., to become linked to some body constituent (X) via the ethane group to form the structure indicated by fig. 3.

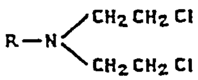

Fig. 1

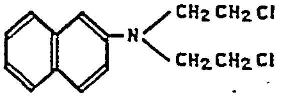

Fig. 2

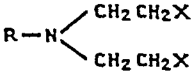

Fig. 3

Of the various types examined, only the sulphonic-acid esters proved active in inhibiting the growth of various tumours in animals, and of these the compound whose formula is given in fig. 4 was characterised by a striking activity combined with a relatively less toxic effect on the bone-marrow than that of the nitrogen mustards (Haddow and Timmis 1951).

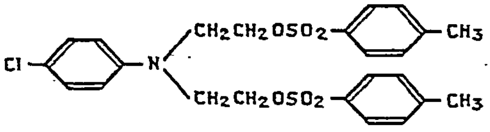

Fig. 4

This result encouraged a further search in the field of the sulphonic-acid esters, and the series of compounds represented by $CH_3SO_2O(CH_2)_nOSO_2CH_3$, in which n may be from 2 to 10, was selected (Timmis 1950) because the relation between chemical constitution and biological action—e.g., inhibition of tumour growth and of hæmopoiesis—could probably best be studied by using the simplest chemical structure possible. Since this structure consists only of the functional groups ($-OSO_2CH_3$) and a chain of CH_2 groups capable of modification by regular gradations, it was hoped that the influence of different numbers of CH_2 groups might here be better assessed than in cases where the structure is complicated, as in fig. 2, by other moieties which might add to the pharmacological complexities.

Various degrees of inhibition of tumour growth (table I) and of blood-cell formation (table II) were observed in the members of this series, and one member in particular, 'GT 41' or 'Myleran' (1 : 4-dimethanesulphonyloxybutane, $CH_3SO_2OCH_2CH_2CH_2CH_2OSO_2CH_3$), showed an intense inhibitory effect on the growth of the has already been shown that storage of red cells mixed with glycerol (final concentration 15%) and saline solution (0 9%) at −15°C† for 3 months has no effect upon the survival-time of the recovered cells (Mollison et al 1952) Experiments are in progress to discover whether cells stored in glycerol (30%) and citrate (3%) also survive normally after transfusion Provided that they do, the only remaining obstacle to the long storage of red cells will be the development of a convenient sterile process for the removal of glycerol

SUMMARY

Red cells mixed with a glycerol citrate solution to provide a final concentration of 30% glycerol and 3% trisodium citrate undergo only very slow hæmolysis when stored at −20°C After 3 months' storage, 98% of the cells remain unhæmolysed, and it seems probable that about 90% of the cells will still be intact at the end of a year Although this method of storage seems certain to be useful in laboratory work, its value in blood transfusion has yet to be proved

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REMOVAL OF GLYCEROL FROM PREVIOUSLY FROZEN RED CELLS

A MODIFIED METHOD

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Sloviter (1951) reported a method for the removal of 15% glycerol from red blood-cells, utilising dialysis through a semipermeable membrane against successively weaker concentrations of glycerol in saline solution This technique was applicable to 500 ml volumes of blood, but was extremely cumbersome and took 48 hours to complete Moreover, elaborate precautions were needed to ensure sterility Lovelock (1952) subsequently described a technique for the more rapid removal of 15% glycerol from red cells by exposing them to strongly hypertonic citrate solution The addition of citrate increases the osmotic pressure outside the red cells and causes water and glycerol to leave the cells, the mixture is then centrifuged, the citrate glycerol supernatant removed, and the cells resuspended in ten volumes of isotonic saline

It has been possible to adapt the citrate method to the higher concentrations of glycerol which are now being used for storage of blood in the frozen state (Chaplin and Mollison 1953) However, in order to process 500 ml of blood, it was necessary to centrifuge it five or six times, and the whole process took 5–6 hours Moreover, when the red cells from an entire bottle of blood are processed in this manner in a standard blood bottle, there is marked "sludging" of the shrunken cells during centrifuging Vigorous agitation is required to resuspend the "sludged" cells in saline solution, and this may be accompanied by considerable additional hæmolysis

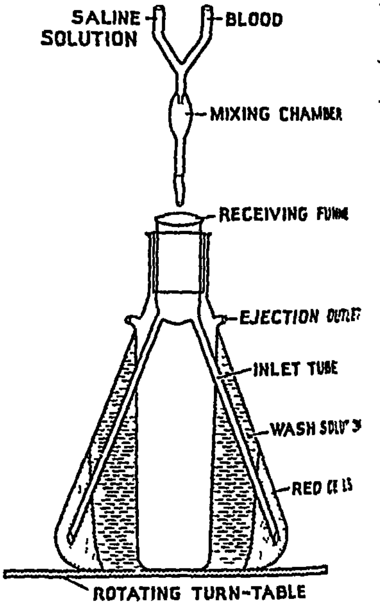
In order to shorten the time required for processing a complete bottle of blood, and to eliminate the hæmolysis associated with "sludging" of the shrunken cells, two main problems had to be overcome

(1) Separation of the cells from their suspending had to be accomplished with the least possible ce force, thereby diminishing the tendency to "sludg

(2) Large volumes of wash solution (up to 5 litre be used, but repeated centrifuging had to be avoided

THE "LONG TRAVERSE CENTRIFUGE" METHO

Buckley et al (1950) described the "long tr centrifuge" method for the continuous washing of cells to free them from their plasma The principle of this method is that the vessel in which the red cells are washed is rotating at a speed great enough to keep the cells at the periphery of the vessel the wash solution is introduced into the peripheral red-cell mass and creates sufficient turbulence to achieve efficient washing The wash solution, being of lower specific gravity than the cells, collects at the centre of the vessel and may be drawn off continuou



Apparatus for the continuous washing of red c

The advantages of applying the "long trav centrifuge" principle to the citrate method for glyc removal are

(1) It is possible to wash the cells while exposing them a centrifugal force of as little as 100 g (compared with 15 2000 g in the standard centrifuge)

(2) It is practicable to use large volumes of wash solut

(3) The suspending medium is removed by continu *dilution and displacement* by isotonic saline solution, t minimising osmotic shock to the shrunken cells

THE NEW APPARATUS AND ITS USE

An apparatus has been designed on this principle f use in the citrate method for glycerol removal As th apparatus is still in a preliminary form, its constructi and use will be described only in general terms Th washing unit consists of an upright conical flask, wi ejection outlets near the neck (see figure) A receiv funnel is fixed in the neck of the flask and from its b several inlet tubes run downwards and outwards to th bottom of the flask The flask is partially filled wi wash solution, and together with its receiving funnel, is rotated as a single unit on a turntable The wa solution takes up a position against the lateral walls the flask, the upper margin being determined by th position of the ejection outlets

To a blood mixture containing 30% glycerol, th necessary quantity of hypertonic citrate solution added This mixture is then allowed to drip into a sm chamber where it mixes with an equal volume of 0 8 saline solution From the base of the mixing chamb the blood flows into the rotating flask After all the blo has entered the flask, washing with 0 85% saline soluti continues until all the glycerol and citrate have be removed Wash solution is continuously ejected fro the outlets at the neck of the flask, and is collected in surrounding glass jacket equipped with suction

This apparatus has been used for fresh red cells i 30% glycerol, and it has been possible to recover 95%

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† Although it was previously reported that the storage temperature was −15°C the refrigerator used in the experiments referred to is now known to maintain a temperature closer to −20 C

‡ Senior assistant surgeon U S Public Health Service (Res)

e cells 13,700 per c.mm. (neutrophils 70%), no immature being seen.

ase 7.—A stevedore, aged 40, was admitted on March 29, ; with a year's history of night sweats and loss of weight a history of increasing breathlessness since November,), which compelled him to stop work. During the summer 950 his teeth were extracted and he bled excessively on n occasion. A blood-count at another hospital on March 8, 1, showed Hb 9·6 g. per 100 ml. and white cells 336,000 c.mm. (170,016 immature myeloid cells).

n examination he looked fit but was febrile, and his spleen s grossly enlarged. On March 30 his Hb was 6·3 g. per ml., and his white cells were 380,000 (neutrophils 146,300, mature myeloid cells 212,800) per c.mm. (myeloblasts %). In counting 200 white cells 9 nucleated erythrocytes re found. Sternal marrow was hypercellular, and 74% of nucleated cells were immature myeloid cells and 5·8% eloblasts.

Treatment and progress.—Myleran 20 mg. daily was given 5 days from March 31 and from April 9, 1951. Maintenance ses of 2–4 mg. were given from May 3 to July 26, 1951. tal 420 mg. in 118 days. The sweats and dyspnœa ceased thin a month, the patient's general condition improved pidly, he gained weight, and his spleen regressed. From ly 3, 1951, when he returned to work, his spleen was palpable until March 4, 1952, when it could be felt on spiration. By Sept. 2, 1952, the symptoms had returned, e spleen was grossly enlarged, the Hb was 7·3 g. per 0 ml., and the white cells numbered 100,000 (immature yeloid cells 48,000) per c.mm. Treatment with myleran mg. daily was begun, and by Oct. 14 the patient was ck at work, with his spleen regressing, Hb 11·4 g. per 0 ml., and white cells 37,000 (immature myeloid cells 10,000) r c.mm.

Sternal bone-marrow was aspirated on May 4 and Aug. 21, 951, and showed much-diminished cellularity, with a striking elative increase in erythropoietic elements and decrease of ore primitive myeloid cells. On April 1, 1952, marrow smears ontained hypercellular fragments, active megakaryocytes ere relatively numerous, and 3·6% of cells were myeloblasts.

PATIENTS PREVIOUSLY TREATED

Five patients (cases 6, 12, 13, 15, and 16) were referred pecially for trial of myleran.

Case 12.—A married woman, aged 61, was admitted on July 10, 1951, with a month's history of pain in the left flank and over the lower ribs and of lassitude. Chronic myeloid leukæmia had been diagnosed in September, 1947, and courses of radiotherapy to the spleen had been given in November, 1947, February, 1949, February, 1950, September, 1950, and January, 1951.

On examination her general condition was good, but she was febrile and her spleen was grossly enlarged and very firm. The edge of her liver was felt in the right lower abdominal quadrant. A capillary-fragility test was negative. On July 11, 1951, her Hb was 8·3 g. per 100 ml., and her white cells numbered 124,800 (neutrophils 32,947, immature myeloid cells 41,293) per c.mm. (myeloblasts 11·8%).

Treatment and progress.—Myleran 100 mg. was given on July 13 and 25 mg. on July 14, 1951. From July 15 to 28, 1951, 6 mg. daily was given and a further dose of 100 mg. on Aug. 14, 1951. Subsequent courses of 100–150 mg. in daily doses of 25 mg. were begun on Sept. 4, Sept. 18, and Oct. 17, 1951. She became afebrile, her spleen regressed considerably and did not enlarge again. The Hb level remained unchanged. On Sept. 3, 1951, multiple raised discrete pink nodules appeared in the skin of the chest, abdomen, and lumbar region; these increased slightly in size and number during treatment. Her condition deteriorated slowly, and she died on Dec. 17, 1951. Although the initial response was brisk, in the later phases of treatment large doses of myleran had little effect on the leucocyte-count, especially on the immature-cell count. On Aug. 1, 1951, a blood-count showed Hb 10·4 g. per 100 ml., and white cells 13,400 (neutrophils 9045, immature myeloid cells 804) per c.mm. (myeloblasts 1%). On Sept. 7, a blood-count showed Hb 8·5 g. per 100 ml. and white cells 20,000 (neutrophils 5400, immature myeloid cells 12,200) per c.mm. (myeloblasts 21%, many of which were dwarf forms).

Case 13.—A married woman, aged 47, was admitted on June 26, 1951, with a history of pain in the left side since April, 1951, and of excessive bruising after trivial injuries for a year. Chronic myeloid leukæmia had been diagnosed in May, and urethane had been given with little effect.

On examination the patient appeared fit, but her spleen reached the umbilicus. A capillary-fragility test was negative. On July 11, 1951, a blood-count showed Hb 11 g. per 100 ml., white cells 168,800 (neutrophils 124,300, immature myeloid forms 33,700) per c.mm. (myeloblasts 2%), reticulocytes less than 0·5%, and platelets 100,000 per c.mm. Sternal marrow was hypercellular, with 44% of immature myeloid cells; the myeloid-nucleated erythrocyte ratio was 22 : 1.

Treatment and progress.—Myleran 100 mg. was given on July 13, 1951, and 25 mg. next day, followed by 4 mg. daily until July 29. Total 185 mg. in 17 days. Further maintenance therapy (4–6 mg. daily) was given from Sept. 4 to Oct. 2, 1951. The spleen regressed until it was impalpable, and the pain was relieved. On July 23, 1951, sternal bone-marrow was less cellular than on July 12, with 22% of immature myeloid cells and a myeloid-nucleated erythrocyte ratio of 11 : 1. On Aug. 8, 1951, the Hb was 13·8 g. per 100 ml. and white cells numbered 5200 per c.mm., no immature forms being seen. The patient remained well although she bruised easily; but on Oct. 15, 1951, epistaxes and gum-bleeding began, and on Oct. 30, 1951, the platelet-count was 10,000 per c.mm. and Hb 8·2 g. per 100 ml. From then on repeated transfusions of fresh blood were given, but hæmorrhage continued and progressive leucopenia supervened. The iliac bone-marrow on Dec. 12, 1951, was hypoplastic and 84% of the nucleated cells were dwarf myeloblasts. She died on Jan. 7, 1952.

The remaining seven patients who had had other treatment were all treated with myleran because radiotherapy was contra-indicated or was considered unlikely to be of value.

Case 1.—A married woman, aged 37, was first seen on Oct. 5, 1948, with 6 months' history of lassitude, 3 months' history of painless abdominal enlargement, and recent dyspnœa on exertion. She looked ill and her spleen was grossly enlarged. A blood-count on Oct. 19, 1948, showed Hb 7·8 g. per 100 ml., white cells 357,800 (neutrophils 149,909, immature myeloid cells 180,689) per c.mm. (myeloblasts 4%, premyelocytes 9%), and platelets 220,000 per c.mm.

Treatment and progress.—2-Naphthyldi-2′-chloroethylamine was given to a total of 7 g. in 35 days, and radiotherapy to the spleen was given with good effect. Further radiotherapy was given in September, 1949, with equally good result. A third course in May and June, 1950, was followed by short-lived improvement, and splenic regression was less than after previous treatment. On Sept. 26, 1950, she complained of weakness and easy fatigue. Her spleen was grossly enlarged. On Oct. 10, 1950, a blood-count showed Hb 10·7 g. per 100 ml. and white cells 86,600 (neutrophils 33,774, immature myeloid cells 42,000) per c.mm.

Myleran 6 mg. daily was given from Sept. 26 to Oct. 9, and 8 mg. daily from Oct. 10 to Oct. 31, 1950. Total 258 mg. in 36 days. The patient's condition rapidly improved, and on Dec. 19, 1950, her spleen had receded 10 cm. medially and upwards, her Hb was 15·1 g. per 100 ml. (more than at any time since the onset of her illness), and her white cells numbered 26,400 (neutrophils 14,256, immature forms 7128) per c.mm. (premyelocytes 2%). She remained well for a time, but by Feb. 27, 1951, her spleen extended 9 cm. to the right of the midline and almost reached the symphysis pubis, her Hb was 12·9 g. per 100 ml., and her white cells numbered 65,800 (neutrophils 28,294, immature myeloid cells 30,597) per c.mm. (myeloblasts 0·5%, premyelocytes 6·0%). Further myleran given in March, 1951, was followed by a remission which lasted only 2 months, splenic regression being only slight. In May, 1951, radiotherapy of the spleen did not arrest enlargement of the spleen, and thereafter repeated blood-transfusions were required. She died on Oct. 6, 1951.

Case 4.—A married woman, aged 62, was admitted on Jan. 31, 1951, with a history of dyspnœa on slight effort, exhaustion, fainting attacks, and heavy sweats since October, 1950, and more recently of pain over the left lower ribs. She had received eleven courses of radiotherapy between January, 1944, and May, 1950.

On examination she was very pale and febrile. Her abdomen was greatly distended, her spleen almost filled the left side, and the edge of her liver was felt 15 cm. below the costal margin. A blood-count on Jan. 31, 1951, showed Hb 4·5 g. per 100 ml., white cells 134,000 (neutrophils 56,950, immature regard to the barbiturates, the evolution of thiopentone enabled the anæsthetist to obtain a depth of unconsciousness or anæsthesia which could not be obtained safely with longer-acting derivatives Similarly in the relaxant group greater flaccidity is obtainable with succinylcholine chloride than with any other agent, because of its evanescent qualities, succinylcholine chloride administered in a drip gives *safe continuous relaxation at any* desired level

The promise of greatly increased flexibility and safety in controlled hypotension induced by arfonad prompts us to report these preliminary trials

We were fortunate enough to obtain 1200 mg of arfonad, which was brought back from the U S A by one of us (I W M) Because this amount was small we have only been able to investigate the five cases here reported Our trial of this agent in a larger series of cases depends on obtaining further supplies of the drug

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STREPTOKINASE AND STREPTODORNASE IN THE TREATMENT OF SURGICAL INFECTIONS*

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STREPTOKINASE and streptodornase offer the surgeon a new biological approach to the treatment of infected wounds, for by helping to remove fibrin and pus they enhance healing

Tillett and Garner[29] observed that broth cultures of certain strains of hæmolytic streptococci caused the rapid lysis of fibrin clots of human blood The lytic factor was subsequently shown to consist of two ingredients, one was a fibrin-lysing system present in the euglobin fraction of the serum,[20] and the second a catalyst produced by the streptococcus[1] The activated fibrin-lysing system liquefied fibrin and inhibited conversion of fibrinogen to fibrin A human group-C strain of the β-hæmolytic streptococcus (H46A), which was found to be a potent producer of streptokinase, has since been used in the development of streptokinase and streptodornase[28]

Crude concentrates containing streptokinase were found to liquefy pus Sherry and his co workers[26] observed that the viscosity of purulent material was due to desoxyribonucleoprotein and desoxyribonucleic acid, a less viscid ribonucleoprotein was also present A distinct enzyme, desoxyribonuclease or streptodornase, causing liquefaction of desoxyribonucleoprotein, was also found to be elaborated extracellularly by the same streptococcus[7 26] Other enzymes have been discovered in the concentrates hyaluronidase,[9 10] a proteinase,[3] a ribonuclease,[7] and several nucleotidases and nucleosidases[5 22]

Sherry and Goeller[5 22] showed by paper chromatography and ultraviolet absorption spectra that streptodornase causes depolymerisation of desoxyribonucleoprotein and desoxyribonucleic acid into many fragments with the formation of nucleotides, nucleosides and finally purine and pyrimidine compounds Because number of products of digestion several enzymes seem to be present For its action streptod requires magnesium ion as a catalyst Streptod acts only on extracellular nucleoprotein and do attack living cells[23]

GENERAL PRINCIPLES

When introduced into a collection of thick pus, st dornase changes the coarse sediment to a thin In this process it hydrolyses desoxyribonucleic which clumps and thus inactivates leucocytes T removal of desoxyribonucleic acid causes a local in motile leucocytes and an increase in phagocyt

Streptokinase and streptodornase have been p many uses Because of the dual or perhaps mul *enzyme systems in the concentrates,* these liquefy and pus in diverse places Originally, streptokinase used to dissolve sanguineous coagulums in the ple cavity[21 27 28 30 31] The discovery of the accompan streptodornase[25] has greatly widened the field usefulness[8 24 25 32] Local application of streptok and streptodornase benefits all wounds containing and pus by lysing the substrates of these substan To be effective the enzymes must be kept in sust contact with the substrates, and this sometimes ca for much thought and ingenuity

Slough and foreign bodies must be manually rem from the wound since they are not susceptible to action of these enzymes *The mucoproteins,* incl mucins and mucopolysaccharides, and collagen likewise not hydrolysed[28] The blood supply to involved area must be good, and auxiliary meas to improve the local blood supply may be nece Streptokinase itself does not lyse fibrin, the fibrin lys system must be carried by the blood to the site of lesion Similarly, magnesium ions must be supplied catalysis by streptodornase

Treatment should be continuous, rather than int mittent Since the products of digestion are thought interfere with healing, they should be removed fa promptly

Streptokinase and streptodornase act at a pH 6–8[23] Their local irritative action produces exudation enough serum to act as an effective buffer, and no spe steps to change the pH before treatment are necessar

Tillett[28] feels that parts of the fibrin lysing system m be depleted locally for a short time after an injection streptokinase, particularly in hæmothorax, so th treatment should be given on alternate days to per reaccumulation of serum factor The pleura, howev responds to sanguineous irritation by a serous effu and it seems to us that treatment should be given dail since we believe that the fibrin lysing system is sufficientl replenished after twenty-four hours

The toxic effects from the local application of strep kinase and streptodornase are practically neglig Elevation of temperature, particularly when the enzym are applied to a closed space, is the commonest side effe Tillett[28] reports a very low incidence of allergic reactio but we have not seen any Hæmatological, hepatic, renal toxic reactions have not been observed[28] Pr thrombin-times do not deviate significantly from normal Hæmatomas and areas of ecchymosis do not result fr the local administration of the enzymes[11] Living tis is not affected

The results are usually so good that failures shou be carefully investigated Even though pus liquefi healing may be hindered by other factors

METHODS OF ADMINISTRATION

These compounds, as supplied in the U S A, have potency of about 100,000 units of streptokinase and 25,000 units of streptodornase per ampoule For th treatment of a sterile or infected hæmothorax or emp ous, and the leucopoietic elements showed relatively mature cells and fewer primitive forms. In case 4 rd sample, examined 9 months after the first dose yleran, appeared normal. In case 7 a third sample n 20 weeks after the first dose, when the neutrophil count had fallen to 450 per c.mm., showed that the marrow was still hypocellular; but a fourth sample, taken when the spleen became palpable a year after the original course of treatment, contained some densely cellular fragments. In case 13 a third sample, examined

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* Reviewed in the Veterans Administration and published with the approval of the chief medical director The statements and the conclusions do not necessarily reflect the opinion or policy of the Veterans Administration

CHRONIC MYELOID LEUKÆMIA TREATED WITH MYLERAN

	Age (yr.)	Sex	Previous treatment	General condition before myleran therapy	Splenic enlargement before myleran therapy	Splenic regression after myleran therapy	Hb (g. per 100 ml.) before myleran therapy	Hb increase (g. per 100 ml.) in first 12 weeks after myleran therapy	Length of remission following myleran therapy	Remarks
	40	F	Di-2-chloroethyl-2-naphthylamine; radiotherapy	Poor	Gross	Moderate	10·7	4	5 mos.; 2 mos. second course	Response to myleran better than that to previous course of radiotherapy, which had lost former efficacy
	58	F	Radiotherapy urethane; radioactive phosphorus	Poor	Gross	Slight	6·0	2	3 weeks	Myleran was given during acute terminal relapse; transient remissions only
	60	F	Radiotherapy	Poor	Gross	Slight	5·7	4	10 mos.	As in case 1
	62	F	Radiotherapy	Poor	Gross	Marked*	4·5	5	18 mos. no response to second course	Radiotherapy not given because of poor condition; excellent response to myleran
	71	F	None	Fair	Gross	Marked	10·7	4	21 mos.; remission continues	Excessive dosage of myleran; transient hæmorrhagic phase delayed increase in Hb; subsequent response excellent
	44	F	Radiotherapy	Fair	Moderate	Marked*	9·6	3	3 mos.; no response to subsequent treatment	Acute relapse supervened, perhaps precipitated by excessive doses of myleran
7	40	M	None	Fair	Gross	Marked*	6·3	8	18 mos.; responding to second course	Was considered too acute for radiotherapy; excellent response to myleran
8	60	F	Radiotherapy	Poor	Gross	Slight	12·7	Hb decreased	2 weeks	As in case 2
9	60	F	Transfusions only	Poor	None	..	6·4	Transfused	6 weeks	Radiotherapy to long bones not given, because of hæmorrhagic state; acute relapse followed transient response to myleran
10	47	M	Radiotherapy	Poor	Gross	Slight	6·3	4	6 weeks	Rapid relapse after radiotherapy; resistance to large doses of myleran followed initial clinical and hæmatological response
11	50	F	Radiotherapy	Poor	Gross	Marked	6·0	7	14 mos.; in remission 3 mos. after second course	Radiotherapy not given, because of bruising; excellent response to myleran
12	61	F	Radiotherapy	Fair	Gross	Moderate	8·3	0	2 mos.	Resistance to large doses of myleran followed brief remission
13	47	F	Urethane	Fair	Moderate	Marked*	11·0	3	4 mos.	Pancytopenia with myeloblastic marrow followed large doses of myleran
14	52	F	None	Fair	Moderate	Marked*	10·4	5	15 mos.; remission continues	Excellent response to myleran; generalised diffuse transient pigmentation during treatment
15	45	M	Radiotherapy; radioactive phosphorus	Fair (1st)	Moderate	Marked*	8·1	6	6 mos.	Second remission interrupted by severe infective hepatitis
				Fair (2nd course of myleran)	Slight	Marked*	9·3	4	6 mos. second remission	
16	40	F	Radioactive phosphorus	Fair	Moderate	Marked*	9·6	3	13 mos.; remission continues	Excellent response to myleran
17	69	M	None	Poor	Gross	Moderate	9·3	3	5 mos.	Initially good response to myleran not maintained
18	33	M	None	Fair	Gross	Proceeding	6·8	7	5 mos.; remission continues	Remission proceeding satisfactorily
19	47	M	Transfusions only	Poor	Gross	Proceeding	5·4	4	6 weeks; remission continues	Remission proceeding satisfactorily; decrease in Hb arrested by myleran; brisk increase preceded by reticulocyte peak 17·2%

* Spleen became impalpable.

Non-tuberculous Empyema

The response of non-tuberculous empyema to local application of streptokinase and streptodornase has paralleled that of hæmothorax. Treatment is guided by the temperature of the patient, the character of the aspirated fluid, and repeated radiographs of the chest. 12 cases have been treated, with excellent results.

Non-tuberculous bronchopleural fistula associated with other types of infection is not a contra-indication to treatment with the enzymes. 3 patients with such a lesion have been treated by us, with excellent results.

Resolving Pneumonia

Streptokinase and streptodornase may be applied intrabronchially for the treatment of slowly resolving pneumonia.[16] The pus is composed of fibrin, desoxyribonucleoprotein, living and dead leucocytes, and desquamated bronchial epithelium, and thus is susceptible to attack by the enzymes.

Ocular Infection

A severe ocular infection caused by *Pseudomonas aeruginosa* was successfully treated with combined polymyxin B and streptokinase and streptodornase therapy.[2] In addition to systemic administration of the antibiotic, local therapy consisted in irrigation at intervals of two hours alternately with a saline solution of polymyxin B and a saline solution of the enzymes.

Antro-oral Fistula

Streptokinase and streptodornase were used successfully in a left antro-oral fistula which had ensued after extraction of a tooth, and had been present for about five months.[15]

Numerous irrigations of the sinus had been done without effect. *Streptococcus viridans*, diphtheroids, neisseria, and *Hæmophilus hæmolyticus* were isolated from the pus. The enzymes were instilled into the fistula through a short length of 'Polythene' tubing, which had been introduced through the inferior meatus by trocar puncture. Treatment was given once daily for two days and then twice daily for twelve days. The result was excellent, with disappearance of sinus tenderness and headache, thinning and decrease of exudate, and reduction in the size of the fistula. Twelve days after this treatment was discontinued, a plastic closure of the fistula was done. Treatment with the enzymes was given for a further three days, starting on the day after operation. Final healing was complete.

Postoperative Prophylaxis

Streptokinase and streptodornase are valuable in many postoperative situations where the collection of blood and/or pus is feared. In these conditions the enzymes are administered through a catheter with a second catheter to provide air-vent suction, which is maintained by a Stedman pump. The following are illustrative case records.

ILLUSTRATIVE CASE RECORDS

Case A.—A 23 year old Negro had a large abscess in the right lobe of the liver. About 400 ml. of pus was evacuated through a small incision. Two no. 18 French urethral catheters were inserted into the abscess and the wound was packed open with nylon. Air-vent suction was provided by a Stedman pump. *Strep. anaerobius* and *Strep. fæcalis* were isolated from the pus. The patient was given aureomycin by mouth. Streptokinase and streptodornase were injected into the wound once daily from May 5 to 18, 1951. The catheters were clamped for about four hours after injection of the enzymes to permit digestion, and then suction was re-established. By May 13 the cavity held only about 15 ml. There was no hæmorrhage from the wound during the treatment with the enzymes. The wound was almost completely healed on June 5, when the patient left the hospital against advice.

Case B.—A 43 year old white man had chills, and fever up to about 102°-103° F, owing to an abscess in the left psoas area. On Aug. 7, 1951, the abscess was incised and a large amount of pus released. Two urethral catheters were placed into the depths of the wound. An unidentified gram-negative bacillus was isolated from the pus, and later *Bacterium aerogenes* was isolated. Clinically, however, this abscess was considered to be tuberculous. The right, and then the left, [illegible] were removed at later dates and were shown to be tub[illegible] The patient recieved procaine penicillin G in aqueous [illegible] sion, sulphapurazole, streptomycin, and *p*-aminosalic[illegible] at various times after operation. Streptokinase and [illegible] dornase were injected into the wound once daily from [illegible] to 28. The catheters were clamped for a period [illegible] hours to permit digestion, after which the suction was [illegible] lished. The exudate became thinner and decreased [illegible] in amount. The wound became clean, dry, and much [illegible] and by Aug. 18 it held only about 5 ml. The remainder [illegible] wound closed somewhat more slowly, but was heal[illegible] Sept. 17 when the patient was transferred for further [illegible] ment of his tuberculosis. Repeated radiographs of th[illegible] tebral column showed no evidence of disease. The [illegible] remained healed and the patient was discharged on [illegible] 1952.

Case C.—A 57 year old white man with diabetes [illegible] developed a large postoperative ventral hernia after [illegible] gastrectomy for a bleeding duodenal ulcer on June 2[illegible] The defect measured about 15 × 12 cm. When [illegible] orrhaphy was done on Sept. 18, 1951, the abdominal [illegible] had to be extensively mobilised. The lower portion of [illegible] fascial defect was closed without tension; in the [illegible] portion a piece of fascia lata was used as a patch. Hem[illegible] was as complete as possible; but, because such repair [illegible] commonly followed by collections of serosanguineous [illegible] no. 18 French urethral catheter was placed on each [illegible] the wound down to the deep fascia. 20 ml. of blood [illegible] aspirated from the wound in the next twenty-four [illegible] Streptokinase and streptodornase were injected [illegible] wound every six hours from Sept. 19 to 23. The ca[illegible] were clamped for four hours to permit digestion of th[illegible] after which suction was applied for two hours. Altog[illegible] about 650 ml. of serosanguineous fluid was aspirated fr[illegible] wound during the treatment with the enzymes. The w[illegible] healed uneventfully.

Case D.—A 65 year old white man had a combined [illegible] minoperineal resection done for carcinoma of the rectum [illegible] March 20, 1952. One no. 20 French urethral catheter [illegible] inserted on each side of the perineal wound down to the [illegible] of closure of the peritoneum. The perineal wound was cl[illegible] Streptokinase 74,000 units, and streptodornase 8500 un[illegible] 10 ml. of physiological saline, were injected through one of [illegible] catheters every eight hours. Digestion of the clot proce[illegible] for four hours, and then the suction was reapplied for [illegible] hours until the time for the next injection. This regime [illegible] continued from March 21 until April 7, after which the [illegible] were injected only once daily. About 250 ml. of serosangu[illegible] ous fluid was removed from the wound during the first f[illegible] eight hours and about 125 ml. in the next forty-eight h[illegible] On March 27 the colostomy clamp came off and the colost[illegible] stoma retracted to the deep layer of the fascia. This nece[illegible] tated an operation for the elevation of the stoma. Dehisce[illegible] of the abdominal wound occurred on April 4 and a second[illegible] closure was necessary. Despite the poor healing of th[illegible] abdominal wounds, the perineal wound healed rapidly. [illegible] March 31 the perineal cavity held about 30 ml., and [illegible] April 7 only about 15 ml. The catheters were removed [illegible] April 17. The perineal wound healed by first intention. [illegible] catheter tracts were almost healed on April 24 and [illegible] completely healed on May 1. All wounds were healed [illegible] May 10. The patient was discharged from hospital on May 1[illegible]

This instance shows that the enzymes do not advers[illegible] affect healing, and may even help it. The abdomin[illegible] wounds did not heal; but the perineal wound, wh[illegible] was treated with streptokinase and streptodornase healed well.

A similar method of treatment was used in a 25 year-o[illegible] Negro who had multiple gunshot wounds with a rect[illegible] perforation and an extensive retroperitoneal hæmatoma.

Surgical therapy included a colostomy, repair of the re[illegible] laceration, insertion of two urethral catheters well into th[illegible] retroperitoneal area, and placement of a rectal tube pe[illegible] the site of repair in the rectum. Streptokinase and strep[illegible] dornase were given through the catheters. Air-vent suct[illegible] was used to remove the products of digestion. An excell[illegible] result was obtained.

The streptokinase and streptodornase were supplied by th[illegible] Lederle Laboratories Division, American Cyanamid Compan[illegible]

References at foot of next column

poiesis without seriously affecting other hæmo- tic elements.

the patients responded initially to the treatment. nine relapsed within 6 months. Eight patients ained remissions of 21, 18, 18, 15, 14, 13, 10, and 6 ths.

e response in three patients who had received no ious treatment was comparable with the best results diotherapy. Five of nine patients for whom radio- apy was not advised obtained useful, and in four s outstandingly successful, remissions.

three patients the response to myleran compared vourably with what might have been expected of otherapy, but excessive dosage may have been ponsible by causing irreversible damage to the bone- row in one patient and by leading to drug resistance he other two.

hrombocytopenia is the only important side-effect is unlikely to be serious if large doses (more than mg.) are avoided, and if treatment is withheld when platelet-count is below 100,000 per c.mm.

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DIFFICULT DELUSIONS

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ONE of the more important criteria on which both doctor and lawyer rely when assessing a person alleged to be of unsound mind is the presence of delusions; and yet there are occasions when a decision as to whether a particular belief is delusional or not may prove difficult. Fortunately it is not solely on the presence of delusions that mental illness is most often decided; we diagnose, for example, a state of mania not merely because a person expresses delusions of grandeur, but because he is also euphoric, overactive, exhibits a flight of ideas. However, there are instances where delusions are almost the only symptoms in evidence—other disturbed features of the mind being at a minimum, as in various paranoid states—and then it becomes important to assess the nature of the supposed delusional statement. If a person says that he is made of glass or is King of Siberia, we need not investigate further; if he alleges that he is suffering from diabetes, we can make the appropriate physical investigations to settle the issue. But if the statement is within the bounds of possibility and cannot be decided by a simple examination—e.g., that the neighbours annoy him or that his wife is drunk and unfaithful—then careful questioning not only of the patient but also of relatives, friends, neighbours, or employers may be necessary. The opinion of the family doctor who knows the home and neighbourhood can be of great assistance in such cases. He may have witnessed a relevant scene or quarrel which will enable a judgment to be made with some confidence.

It might be thought, inasmuch as from the social point of view it is the outer behaviour of the person which matters rather that his inner beliefs, that an assessment of the latter is of no great practical importance, and indeed in many cases this is so. A man who is deluded that the earth is flat, or that he is a reincarnation of Tutankhamen, but who remains well behaved and continues to perform his usual social duties satisfactorily is not a case for treatment by the psychiatrist in practice. There are many eccentric paranoiacs in society whose most abnormal behaviour is no worse than preaching in Hyde Park. They are quite happy and are only seen by the psychiatrist who happens to take a stroll in the park. When, however, behaviour is affected in such manner as to disturb other members of society, an assessment of the alleged delusions becomes important: if the person is deluded, there is a mental illness which requires treatment; but if he is not, the abnormal behaviour may fall in the criminal category.

SOME DIFFICULTIES

A variety of difficulties may present themselves when attempting to decide whether a person's statement is delusional or not. Assessment may become a problem when:

(1) There is some basis of fact.
(2) A deluded psychotic utters a statement which seems far-fetched but could be true.
(3) Pseudologia, malingering, or lying is a probability.
(4) Delusion conforms with reality.
(5) A delusion is reinforced by the environment, which had reacted appropriately to a psychotic's odd appearance or behaviour.
(6) Reality plays into the hands of the delusions.
(7) Conduct is not disturbed and the patient is evasive.

Perhaps the most common instance is where there is some basis of fact, which is exaggerated, elaborated, or misinterpreted. The undue stressing of some items in a topic of conversation is such a common human trait that it can hardly be called pathological, and most of us have exhibited such artistry when recounting our favourite yarns. Misinterpretation is a distortion of a more serious nature. The delusional jealousy of Leontes in *The Winter's Tale* is based on a misinterpretation of Hermione's friendship for Polixenes, and this typifies a situation often seen in psychiatric practice.

Again, not all the statements made by an obviously psychotic patient are delusional; but when a number of beliefs seem to fit into a recognised syndrome there is the danger of classifying them all as delusional, though some may be statements of fact. A hypomaniacal patient claimed to know personally all the distinguished political leaders of Europe and also boasted that he was well versed in about a dozen languages—all of which was recorded as delusional. It turned out that the second claim was true. A coloured patient, suffering from dementia paralytica, was euphoric and expressed a number of grandiose delusions; he claimed that he was a king. Information received revealed that in fact he was king of an African tribe.

The patient may be confabulating with varying degrees of awareness, as in malingering or hysterical pseudologia. Evidence of possible motivation, such as a desire to avoid prison or service in the Forces, will put the psychiatrist on guard. Addicts can lie brazenly in an attempt to obtain the appropriate drug, or when excusing their disturbed conduct.

Case 1.—A married man was admitted on an urgency order, in which the wife recorded that he had threatened her life and that he was an alcoholic. When examined the patient was lucid, polite, and well behaved. He minimised his drinking and alleged that his wife also drank and had aggravated him. It was impossible to get at the truth amidst the many accusations and counter-accusations. The minutes) In the 4 cases the skin became shiny, and a punctate erythema appeared, followed by diffuse petechiæ

DISCUSSION

The use of phenylbutazone in rheumatoid arthritis, as seen from our 34 cases, seems to increase mobility and muscle power, and reduces pain to a significant degree, and the first two effects appear to depend on the relief of pain In 6 patients joint swellings diminished, possibly because joint mobility increased, on the other hand, joint swellings increased in 2 patients, and an effusion into a knee-joint developed during treatment The changes in E S R were inconclusive, and there were no significant changes in white cell counts Thorn's test and 17 ketosteroid estimations, which were carried out in 8 rheumatoid patients having phenylbutazone, showed no changes similar to those known to occur with adrenocorticotropic hormone The analgesic effect, as seen in rheumatoid arthritis and osteo-arthritis, seems to be phenylbutazone's major quality

On these experiences we consider that phenylbutazone has a place in the management of chronic joint disease in which the outstanding feature is pain, for it seems to relieve pain more readily than the usual aspirin and codeine mixtures we have used in the past

Toxic effects appeared in 22 out of the 50 patients, and were often quite severe The careful selection and constant supervision of patients who receive th are therefore very necessary

In the selection of patients, we consider that history of peptic ulceration, or the presence of tension, chronic bronchitis and emphysema, or heart-disease with a past episode of failure are al contra-indications because cardiac failure may salt and water retention

SUMMARY

34 patients with rheumatoid arthritis and 1 osteo-arthritis had courses of oral or intram phenylbutazone (butazolidine)

The clinical effects and toxic manifestations hav discussed

It is thought that phenylbutazone is prim potent analgesic in joint disease, but its indiscr use is not without danger

We would like to thank Dr Francis Bach and Dr Ellman, under whose care these patients were trea their interest in this study Our thanks are also Messrs Geigy, and particularly to Mr N Peter A.R I C, who provided the early supplies of phenylbu

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New Inventions

MALTBY'S SUTURE-HOLDER FOR FULL-THICKNESS SKIN GRAFTING

THE instrument described here was designed by Mr John T Maltby, my senior theatre orderly at St James's Hospital, Leeds It is an adaptation of Prof T P Kilner's ligature-holder which is attached to his Shadwell gag used for repair of the palate

In any operation where it is necessary to leave many of the sutures long, the ends are apt to become tangled in an exasperating manner unless secured and held out of the way For instance, when a full-thickness skin graft is sutured in position, it is usual to leave alternate stitches long, so that at the end of the operation they can be tied over sponge rubber to fix this securely over the graft After the stitches have been inserted, it is a great advantage to anchor each suture in a wire spring (fig 1) so that the strings radiate from the wound like the spokes of a wheel from the hub (figs 2 and 3) A strong but malleable wire, curved in an ellipse, acts as a framework for the wire spring, being malleable, it can be adapted to fit the irregular contours of the face The framework is fixed to the operation sheets with towel-clips inserted through loops on each side of the ring When all the stitches have been inserted and the sponge applied, two of the sutures, diagonally opposite to each other, are released from the wire spring and over the sponge

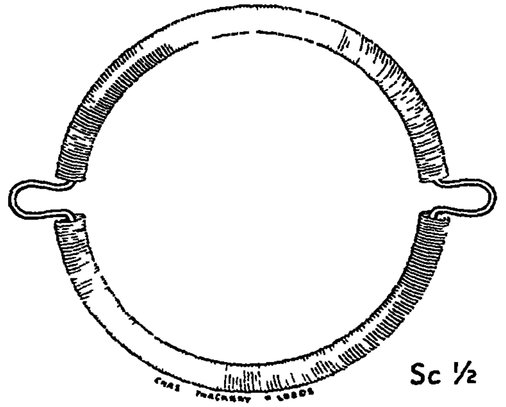

Fig 1—Maltby's suture-holder for full thickness skin grafting

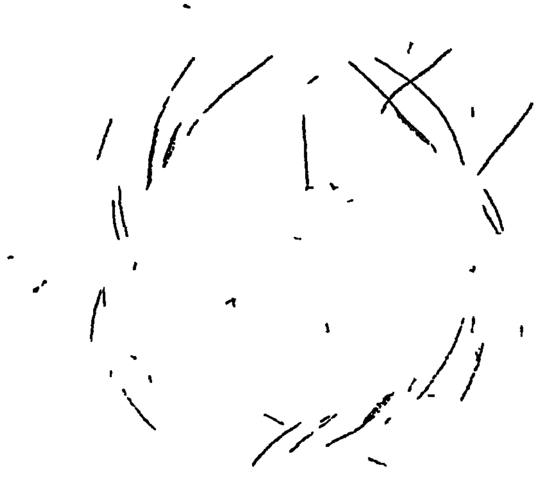

Fig 2—Ligature holder in position The full thickness skin gra been sutured into the defect, some of the sutures have bee long so that they can be tied over the sponge which is used to f graft in position The long ends of the sutures are held o the way in the spring of the suture-holder Towel clips, ins through rings in the suture-holder are fixing it to the ope towel

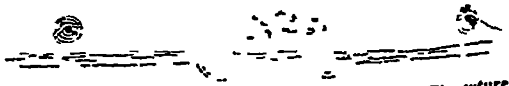

Fig 3—A cross section of full thickness skin graft. The sutures been left long and are held out of the way in the spring ligature car The sponge, over which the ligatures will be tied later, is lying the graft.

This little gadget ensures an orderly procedure obviates the chaos which is so likely to develop if or twenty sutures are left long and to their own dev

The instrument is made in two sizes—4 in and 5 diameter—by Messrs Chas F Thackray Ltd, Park St Leeds 1

MICHAEL C OLDFIELD
Leeds M B E, M A, D.M, M CH Oxfd, F.R C

ient : That is possible. But there was animosity st me—and I cannot blame them—after I had exposed nproprieties I have mentioned.

this case no useful purpose could have been served ending the psychiatric social worker to investigate. in other cases help may be obtained by a visit to the e of employment or home of the patient.

ise 6.—A woman, single, aged 27, was referred because iad complained that her workmates accused her of stealing of being pregnant. On examination she was found to be tally defective (intelligence quotient 63%) and poor at aining herself. She was the type of person who would nade a butt by others, and her sister felt sure that it was leg-pulling" by the other employees. It was of import- to assess the exact nature of the patient's beliefs, as hizoparanoid reaction was a possibility. The psychiatric al worker was asked to visit the place of employment after lengthy interviews with the manager and several loyees came to the firm conclusion that the patient was ressing delusional ideas.

t will be helpful to question relatives, friends, and ghbours. Indeed, in a difficult case, one cannot seek many sources of information. It must be admitted, vever, that on occasion a multiplicity of informants prove confusing for a variety of reasons, and careful ting out will be required. Sometimes there are family ds (e.g., a sister will support the patient's unjustified gations against his wife). Sometimes there is a *folie nmuniquée* involving the patient and several members his family. The opinions of neighbours are often verted through local gossip or their own specific nplexes. An informant may have personal reasons denying truthful statements made by a patient if h reflect badly on himself. If, for instance, the patient tes (truthfully) that the domineering or cruel attitude a relative has harmed him, such relative is not likely admit this, especially if other relatives have implied t this was a cause of the patient's breakdown. On other hand, confirmation by a relative of a patient's gation is not necessarily foolproof—very often the ative is merely repeating a communicated allegation. is obvious that the greatest tact and diplomacy is quired when questioning informants, and their reaction ist be carefully watched. But with the greatest care ere will be the occasional case where one feels that thing less than living in the home of the patient can cide a certain item; in one such case the family ctor exclaimed, in the face of accusations and counter- cusations between husband and wife, "Where the truth s, Heaven knows!" The following case illustrates w the reactions of an informant help in assessing the lue of the patient's beliefs.

Case 7.—A married woman who suffered from a depressive iction blamed many years of marital disharmony for this, d related details of her husband's misbehaviour. When questioned him, he became very irritable, and refused to swer, merely saying, "She should not have discussed r intimate married life. I will certainly not do so." I inted out that without his coöperation I could not decide iether the patient's allegations were truth, lies, or delusions, it he still refused to discuss the problem. I naturally me to the conclusion that the patient's statements had a od basis of truth.

SUMMARY

It is sometimes difficult to evaluate the possible elusional nature of a patient's statements if one con- ders the bare content, which may not obviously disagree ith a reality situation. Criteria which can help are the anner of presentation by the patient and informants, ieir reactions to questioning, and the evidence afforded y the family doctor, social workers, and psychiatric ocial worker.

I am indebted to Mrs. A. Smith, the psychiatric social orker, to Mrs. K. Wade, the social worker, and to many eneral practitioners for their help in unravelling a mélange f truth, exaggeration, distortion, prevarication, and delusion i difficult cases.

IMPROVED STORAGE OF RED CELLS AT -20°C

H. CHAPLIN, JUN.*
M.D. Columbia

P. L. MOLLISON
M.D. Camb., M.R.C.P.

From the Medical Research Council Blood Transfusion Research Unit, Postgraduate Medical School of London

FOLLOWING the observation of Polge, Smith, and Parkes (1949) that glycerol would protect spermatozoa against the effects of low temperatures, Smith (1950) showed that red cells could be similarly protected. Subsequent work on the storage of red cells in the frozen state was reviewed by Mollison, Sloviter, and Chaplin (1952), who described the results of experiments in which red cells were stored at −15°C or −79°C for long periods and then used for transfusion. In these experiments a concentrated suspension of red cells was mixed with an equal volume of a glycerol-saline solution before freezing. It was found that red cells recovered after storage had virtually unimpaired viability. However, the proportion of cells lost during freezing, storage, thawing, and dialysis was considerable, only about 50% of the red cells being recovered after storage for 6 months at −79°C or after 1 month at −15°C. It was emphasised that before storage of red cells in the frozen state could be of practical value in transfusion work, the proportion of red cells recovered after storage would have to be increased and a simple method of removing glycerol devised.

The present paper demonstrates that very low rates of hæmolysis can be achieved by a simple modification of the original method, and that with this modification satisfactory storage is possible at −20°C. Thus any laboratory can now store red cells for at least a year in an ordinary deep-freeze cabinet. This should be particularly valuable to blood-grouping laboratories since storage in the frozen state does not appear to affect the serological reactions of red cells (unpublished observations).

To establish the value of the new method in transfusion practice it must be shown that red cells stored in this way survive normally after transfusion. Experiments are in progress to discover whether this is so.

METHODS

Blood-glycerol Mixtures

One volume of glycerol-saline (or glycerol-citrate) solution was added to one volume of packed red cells, obtained either from fresh heparinised blood or from blood mixed with acid citrate-dextrose solution and previously stored at 4°C for 1–3 days. Hæmolysis could be minimised by first warming the glycerol and red cells at least to room-temperature, and then adding the glycerol to the red cells relatively slowly while agitating the mixture.

The concentration of sodium chloride or of sodium citrate in the various mixtures mentioned below is the concentration (weight/volume) in the glycerol-saline or glycerol-citrate solution which was added to the packed red cells. However, glycerol concentrations have been calculated on the assumption that glycerol diffuses freely into a volume equivalent to 60% of the red-cell mass. The specific gravity of the glycerol was taken as 1·24, since the preparation used was known to contain only 97% glycerol. Thus if one volume of undiluted glycerol plus one volume of 6% trisodium citrate solution were added to two volumes of packed red cells, the citrate concentration would be given as 3% and the glycerol concentration (*w/v*) as:

$$\frac{\text{Weight of glycerol}}{\text{Volume of glycerol-citrate mixture} \div 60\,\%\text{ of volume of red cells}} = \frac{1{\cdot}24}{2 \div \frac{(60\times 2)}{100}} \times 100 = 40\,\%.$$

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[*] Senior assistant surgeon, U.S. Public Health Service (Res.).

and carping in criticism "Dr Singer's comments are querulous and niggling" and are described "as talk of the kind one expects to hear in club corners" Mr Ivins bases his essay on a study of the original woodcuts, and of books and articles dealing with Vesalius He concludes that the illustrations were drawn by John Stephen of Calcar without help from Vesalius, who merely wrote a commentary on them. Stephen therefore is the hero of *De Fabrica*

This essay will arouse vigorous discussion among historians, who will find the book of great interest even if parts are infuriating

Visceral Circulation

A Ciba Foundation Symposium Editor G E W WOLSTENHOLME, O B E, M B, assisted by M. P CAMERON, M A, and J S FREEMAN, M B London · J & A Churchill. 1952 Pp 278 30*s*

IN the recent symposium on the visceral circulation, held in London by the Ciba Foundation, 49 guests took part, comprising anatomists, physiologists, biologists, biophysicists, biochemists, pharmacologists, and clinicians in medicine, surgery, and anæsthetics This admirable book of the proceedings contains summaries of papers presented by each of the 25 speakers, and of the discussions which followed There are contributions on visceral vascular structure, vascular patterns in the alimentary canal, vascular architecture of the kidney, the laws of physics and the flow in blood-vessels, sympathin production and excretion, visceral blood-vessels as pain perceptors, afferent paths of cardiovascular reflexes, aortic and coronary flow, determinants in hepatic hæmodynamics, vasoconstriction and vasodilatation in the normal and failing circulation, physiological changes during fainting, and many other subjects of topical and permanent interest

The Knee and Related Structures

Injuries—Deformities—Diseases—Disabilities PHILIP LEWIN, M D, F A C S, professor of bone and joint surgery, Northwestern University Medical School London Henry Kimpton 1952 Pp 914 120*s*

IT is difficult to see to just which section of British medicine this massive book will prove attractive As a monument to the industry of the author it is comparable to his previous volume on the foot, any subject with any conceivable connection with the knee has been included It is too vast a book for the student, while insufficiently eclectic and perhaps too "popular" in style to be likely to appeal to orthopædic surgeons in this country But it has at least collected an immense amount of material under one cover One cannot but admire the hard work that has gone into this volume, but the result remains very indigestible

Lumbar Disc Lesions

Pathogenesis and Treatment of Low Back Pain and Sciatica J R ARMSTRONG, M D, M CH, F R C S, orthopædic surgeon to the Metropolitan, Lambeth, and Manor House Hospitals Edinburgh E & S Livingstone 1952 Pp 228 42*s*

Mr Armstrong's extensive experience of lumbar disc surgery qualifies him to write a more engaging clinical account of the subject than he offers us here The style is somewhat dry and didactic, and, though diagrams and arguments about lumbar mechanics abound, case-histories and radiographs would have been more refreshing It is not made clear that senescence and degeneration of the discs is a universal and indeed normal process, nuclear pathology is emphasised at the expense of annulus lesions, and nothing is said on the newer developments in discography and the electron-microscope study of ground structure In the clinical section Mr Armstrong underestimates, we think, the value of the plaster-jacket, which, efficiently applied and renewed as necessary, makes bed rest or other fixation unnecessary for the great majority of acute cases Manipulation, epidural analgesia, and the local anæsthesia of sites of referred tenderness are all decried, on largely theoretical grounds, though experience shows that, used judiciously, they may greatly ease those patients, often decrepit or elderly, who are unfit for plaster or laminectomy and who would be rotted by bed rest Lest these criticisms seem ungrateful, we should add the important fact that the book succeeds in presenting every fact relevant to diagnosis, differential diagnosis, and treatment of lumbar disc lesions, including the indications for operation and the technique of laminectomy and spinal fusion.

Intracranial Aneurysms

WALLACE B HAMBY, M D, *professor of neurosurgery*, University of Buffalo School of Medicine and Dentistry, Buffalo General Hospital Springfield, Ill: Charles C Thomas Oxford Blackwell Scientific Publications 1952 Pp 564 £5 2*s* 6*d*

INTEREST in intracranial aneurysms has much increased during the past ten years with the development of percutaneous angiography and more radical surgical methods of treatment A monograph on the subject was needed, and this book, besides giving a clear account of the clinical syndromes caused by intracranial aneurysms in various situations and the possible methods of treatment, also describes arteriovenous malformations The style is informative rather than inspiring, and the text is broken by a series of case-histories The clinical and pathological illustrations are good, but the definition of the angiograms varies greatly and in some it is difficult to see the vessels clearly There is a useful bibliography

Human Milk

Yield, Proximate Principles and Inorganic Constituents S D MORRISON, B SC, Institute of Physiology, Glasgow University Farnham Royal Commonwealth Agricultural Bureaux 1952 Pp 91 10*s* 6*d*

IN this book is collected much of the information in the literature on the yield and chemical composition of human milk Besides the three major constituents and related compounds (nitrogenous—mainly protein materials, lipids, and carbohydrates), it deals only with minerals No consideration was given to the vitamin content because this aspect of the subject has recently been comprehensively covered by Kon and Mawson (Medical Research Council Special Report Series no 2 1950) Mr Morrison not only brings together many interesting data from papers published in a wide variety of journals, some of them not readily available, but presents them critically, sometimes recalculating statistics so as to make comparison easier He is often on less sure ground when he theorises, as he does here and there on the biochemistry of milk formation

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Forensic Medicine (2nd ed London Edward Arnold 1952 Pp 344 21*s*)—Dr Keith Simpson's textbook, as attractive and lucid as his lectures, is now brought into line with the last year or two's forensic progress It is encouraging to see that the chapter on war gases has given way to one on poisonous plants and fungi The new chapter usefully sums up their lethal properties, and it will be all the more welcome now that the trifling monograph on this subject by a Baker Street toxicologist is out of print

Muscle Relaxation as an Aid to Psychotherapy (London Actinic Press 1952 Pp 65 5*s* 6*d*)—This little book is written primarily for physiotherapists, to enable them to give effective relaxation exercises to certain types of psychiatric patients The author, Dr Gerald Garmany of the Westminster Hospital, points out that the use of relaxation in psychiatry is limited, and that it cannot by itself effect cure in cases of muscular tension due primarily to emotional disturbances By abolishing tension and in teaching the anxious patient how to relax properly, the techniques described may, however, bring about a better all round adjustment to the stresses of life The ways in which emotional disturbance can affect bodily functions and muscle tension are clearly described, the James Lange theory and the work of Jacobson are discussed, and the part that bodily feelings play in emotional states is not overstressed The need for coöperation and a working knowledge of the technique used by the other partner in the joint enterprise of psychotherapist and physiotherapist is constantly borne in mind There is a chapter on *indications* for the treatment and its difficulties, and another on the types of concurrent psychotherapy The book is very well written, concise without being dry, and authoritative without being dogmatic rates of hæmolysis remained approximately constant these periods. If hæmolysis continued at the rates n in the figure there would be only 7% lysis at the of a year.

n an experiment in which disodium citrate (mono- ric) was substituted for trisodium citrate, mixtures aining 2·4% and 2·6% showed just over 1% hæmo- s at 23 days and slightly less than 2% hæmolysis at days. These results are not significantly different n those obtained with trisodium citrate. It was noted, ever, that when disodium citrate mixtures were added red cells, considerable lysis resulted unless some itional plasma was left with the packed red cells.

n another experiment red cells from blood mixed with d citrate-dextrose solution were used instead of cells m heparinised blood: the rates of hæmolysis were entially the same.

n a further experiment the effect of storing cells shed free from plasma was investigated. 12 ml. of ked red cells were washed three times with 15 ml. of ine solution, and then mixed with 12 ml. of a mixture ntaining 2·9% trisodium citrate and sufficient glycerol give a final concentration of 30%. As a control, 12 ml. unwashed packed red cells were mixed with the same cerol-citrate solution. After 93 days' storage the xture containing the washed cells showed 1·4% molysis, whereas the control showed 2·4%. Little phasis can be placed on such small differences, but it at least be concluded that washed cells do not molyse any more rapidly than unwashed cells under se conditions.

fect of Repeated Freezing and Thawing at −20°C and 79°C

Blood mixtures containing 30% glycerol and 3% sodium citrate were divided into four bottles, two ing stored at −20°C and two at −79°C. One bottle each pair was thawed weekly for sampling, and the cond was stored without interruption until the end of e experiment. In the bottle which was repeatedly awed and refrozen to −79°C, hæmolysis increased rogressively and amounted to 28% after 6 weeks, hereas the bottle kept continuously frozen showed only % hæmolysis at that time. On the other hand, of the air stored at −20°C, the repeatedly thawed bottle owed less than 4% hæmolysis after 6 weeks, compared ith 2% hæmolysis in the control. Thus, repeated freezing nd thawing causes very little hæmolysis when the orage temperature is −20°C, but considerable hæmo- sis when the temperature is −79°C.

ractical Procedures

The following method is recommended for the storage f small blood samples (up to 5 ml. of packed cells). repare packed cells by centrifuging heparinised or itrated blood for 30 minutes at 3000 revolutions per ninute, and removing almost all the supernatant plasma. Now add to the volume of packed cells an equal volume of glycerol-citrate mixture, prepared by mixing 4 volumes of glycerol with 6 volumes of 5% trisodium citrate solution. Add the glycerol-citrate mixture in stages, agitating the ube continuously. Then place the tube in an ordinary deep-reeze cabinet at about −20°C. As noted above, the same ube of blood can be repeatedly frozen to −20°C and hawed without much increase in hæmolysis. However, t is often convenient to divide the mixture between everal small tubes before freezing, so that a small quantity can be thawed out at a time.

For the recovery of the red cells, prepare three solutions containing respectively 16%, 8%, and 4% of glycerol (w/v) in 3% trisodium citrate. Thaw the tube of blood by placing it in tepid water; then transfer the blood to a 1 oz. bottle ("universal container") and fill it to the top with the 16% glycerol solution. Mix well and centrifuge at 3000 r.p.m. for 5 minutes. Replace the supernatant with the 8% glycerol solution, then with the 4% solution, and finally with 1% saline solution. With this method red cells can be recovered in 1 hour with very little lysis.

When larger amounts of blood are to be stored for transfusion, the procedure is essentially the same. The red cells are packed by centrifuging the whole bottle. The bottle is then provided with an air outlet by passing a short needle through the rubber diaphragm of the bottle. The supernatant plasma is now removed through a long sterile needle plunged through the rubber diaphragm. Sterile glycerol-citrate mixture is then run in through a short length of rubber tubing with a wide-bore needle at each end. It is convenient to autoclave about 220 ml. of glycerol-citrate solution in an ordinary blood bottle, and to run this by gravity into the bottle containing the red cells. The bottle containing the glycerol-citrate solution must be provided with a long sterile needle as an air-inlet. The bottle containing the red cells is rotated while the glycerol-citrate mixture is run in, the whole procedure taking about 10 minutes. The bottle can then be frozen. (It is recommended that, before freezing, a sample of the mixture should be taken through the rubber diaphragm using a sterile needle and syringe; this sample may be cultured at room-temperature and at 37°C, adding 1 ml. of the blood-glycerol mixture to 50 ml. of nutrient broth.)

To prepare the red cells for transfusion, a method based on that described by Lovelock (1952) has been tried. The modified method consists in replacing the supernatant with 12–15% citrate solution and washing the red cells four or five times with saline solution to obtain a clear supernatant. With the ordinary large bottle centrifuge the process takes 5–6 hours. Moreover after the addition of hypertonic citrate there is gross "sludging" of the red cells and this leads to considerable additional hæmolysis. The method described above for small samples should give better results, but it also is too time-consuming to be convenient for large volumes of blood. These difficulties should be overcome by the further development of the continuous washing device described by Chaplin and Veall (1953).

DISCUSSION

It is of considerable interest that red cells can be frozen to −79°C and stored at that temperature with much less lysis if the final glycerol concentration is raised from 15 to 30%. However, the interest of this observation has been eclipsed by the discovery that if a citrate-glycerol rather than a saline-glycerol solution is used, red cells can be satisfactorily stored at −20°C. Disodium citrate appears to be as effective as trisodium citrate, but since most of the experiments have been made with the trisodium salt and since this salt is more readily available, it has been specified in the procedures recommended here. Although the reason for the superiority of sodium citrate over sodium chloride is not fully understood, it is presumably related to the fact that citrate does not penetrate the red cells.

The fact that when red cells are mixed with an appropriate glycerol-citrate solution and stored at −20°C a high proportion (probably more than 90%) can be recovered after a year is of considerable importance. It means that any laboratory equipped with an ordinary deep-freeze cabinet can keep samples of red cells for long periods at a negligible cost. This should be of particular value to blood-grouping laboratories.

The high cost of maintaining bottles of blood at −79°C can be illustrated by an example: in this laboratory an insulated box holding about thirty bottles of blood required more than £120 worth of carbon dioxide in a year, a cost of £4 per bottle per year. This is probably 80 times the cost of storing a bottle of blood at −20°C for a year.

The time has come to consider whether this method of storage would be useful to transfusion-services. It

Since first impressions are often lasting, the council are anxious that our hospitals should display themselves favourably from the start The patient (who is often low-spirited when he arrives at hospital) needs a friendly greeting, and the council attach particular importance to the personality of the person receiving him They suggest that a lay receptionist *of the right type is often suitable*, but it does not much matter who does the work provided she is kind, smiling, and sensible Then, the patient should be shown the way to the ward or department he is seeking, or should find the route well posted with signs, and he (and his visitors) should be allowed the use of lifts for surely the patient is more important than his dinner or his washing, and at least as important as the senior consultant, of whose very existence he is, after all, the cause Incidentally it is not the consultant, as a rule, who wishes to enjoy amenities denied to the sick he is merely a victim of the hospital practice (deriving from a very different age) of deifying the doctor according to a set of unwritten laws In some hospitals one of these laws, the council point out, decrees that neither bite nor sup shall pass a patient's lips while a doctor is in the ward, and many a meal is thus delayed while patients chafe and rumble The council rightly believe that few members of the medical staff would wish to see the rule maintained, and suggest that it should be abolished In hospital, as on sea-voyages, meals acquire a significance quite out of proportion to their intrinsic merit they are the only counterpoint to a dull tune, and should keep strict time

The council note how little thought is nowadays given to noise in hospitals (though it was, of course, a matter to which Miss NIGHTINGALE gave a good deal) They suggest that every hospital should analyse causes of noise, with the help of patients and staff, and find means of removing them One modern source of noise is the loudspeaker, and there is no excuse for it when earphones and pillow-phones can so easily replace it Trolley wheels are another, but there are silent wheels on the market Short visiting periods should be allowed daily whenever possible, with one or two longer periods for the convenience of those who come from a distance When the patient leaves hospital the family doctor takes over, and he ought to be properly and quickly informed of the stage his patient's illness has now reached Too often he has to wait weeks for information which, in the patient's interests, he ought to have at once Would such slipshod methods be tolerated if the patient were being transferred from one department to another within the hospital?

The many other recommendations made in this memorandum for the patient's well-being or comfort cannot be enumerated here, but it is worth noting that the council have not asked for a large outlay of anything much beyond kindness, forbearance, and good manners "We see no reason," they say, "why financial stringency should prevent the carrying out of the greater part of our recommendations" Where funds are needed voluntary societies will often be willing to help, and every hospital should think of forming its own group of "friends" How much such friends can accomplish we have only recently told [2]

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[2] *Lancet* Jan 24, 1953, p 191

Blood Hazards in Industry

MENTION of industrial hazards usually conjures up pictures of whirling unguarded belts, crushed hands or diseases like "hatters' shakes" and cancer of the bladder in aniline workers The modern industrial hazard is more insidious but just as dangerous, and *many of these hazards affect the blood* In the second Ernestine Henry lecture to the Royal College of Physicians, Prof R E LANE [1] reviewed these blood hazards and criticised methods of assessing and preventing them

Industrial poisons can affect either circulating blood or blood formation in the bone-marrow; in the peripheral blood they may act on the hæmoglobin by changing it to forms like methæmoglobin which are valueless for the transport of oxygen, or they may actually hæmolyse red cells Thus arsine gives rise to hæmolysis, aniline to methæmoglobin and also some hæmolysis, and benzene and ionising radiations to failure of hæmopoiesis Of the hæmoglobin changes, the best known is the formation of carboxyhæmoglobin by exposure to carbon monoxide Methæmoglobinæmia, often accompanied by some sulphæmoglobin and methæmalbumin in the blood, gives rise to cyanosis, and in industry it is usually caused by organic nitro or amino compounds Professor LANE points out that many such substances are used in industry while new ones are constantly being introduced, they are especially dangerous because they can be absorbed through the skin and through the respiratory tract Arsine, the worst hæmolytic poison is a not uncommon industrial hazard, LOCKET et al have collected reports of such poisoning from several industries, including electroplating and the smelting, refining, and galvanising of metals The most familiar industrial hæmolytic poison is lead, which is used extensively Work by RIMINGTON [3] and by Professor LANE and his co-workers [4] has shown that lead also interferes considerably with hæmopoiesis by impairing hæmoglobin formation Aplastic anæmia became a prominent industrial hazard in the first world war since it is liable to follow exposure to trinitrotoluene Benzol, which is also known to cause aplastic anæmia, is widely used as a solvent, and Professor LANE mentions the production of rubber cement and of quick-drying inks, and the leather industry, as providing conditions in which exposure cannot be easily controlled With benzol it is the continual daily exposure that is dangerous, and the safe limit of 35 parts per million proposed by the International Labour Office may not, in these circumstances, give protection.

The hazard most in the public eye at present is that due to ionising radiations It is not only workers *in atomic plants that are exposed*, powerful X rays and radium are used to detect flaws in metals, radium paint is still used for luminising, and the X ray plant in the shoe shop can be a source of danger to the assistants who operate it

Most of these industrial hazards are now fully understood, and much has been done to protect workers, indeed Professor LANE thinks that few ells using this method of washing. In the pre- ary trials, "sludging" has been absent or slight, it can almost certainly be entirely eliminated by r regulation of the rate of inflow of blood relative e rate of rotation of the flask. The volume of blood h can be successfully washed by this technique will etermined largely by the size of the conical flask. sk of one litre capacity has been found adequate for processing of one pint of blood in about $2^1/_2$ hours.

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vestigations are now in progress to determine the num speed of rotation and optimum rate of inflow. application of this method to blood that has been ed for a long time is also being studied. The washing aratus is being modified in an effort to permit sterile essing of the blood.

SUMMARY

he principle of the "long traverse centrifuge" has n applied to the removal of glycerol from blood- erol mixtures.

n apparatus based on this principle has proved a essful means of removing glycerol in preliminary ls on fresh blood.

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CONTROLLED HYPOTENSION BY A THIOPHANIUM DERIVATIVE

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HE method of producing deliberate hypotension during esthesia by the injection of pentamethonium or xamethonium bromide has now been in use at this spital for four years (Organe 1950). Various workers ve presented detailed reports of the technique (Davison 50, Enderby 1950). Following our own ended experience certain limitations d disadvantages of these drugs have ome apparent.

1. In order to ensure an adequate fall in od-pressure and to provide a really dry erative field it is advisable to give one large tial dose of the hypotensive drug. Repeated aller injections are less effective; it seems at the patient becomes increasingly resistant subsequent doses. In subjects who are sitive to these agents the large initial dose ay lead to prolonged and excessive depres- on of the blood-pressure.

2. Very young subjects and thyrotoxic tients are resistant to the effects of penta- ethonium bromide. Either the fall in blood- essure is inadequate, or the duration of the potension is very brief. As noted above, peated doses do not solve this problem; tisfactory hypotension cannot be obtained such subjects by increasing the dosage.

3. Although induced hypotension can be ded by injections of pressor agents, this oes not indicate a direct physiological versal. True recovery is complete only after e, occasionally tardy, elimination of the ypotensive drug.

In 1949 Randall et al. described a new anglionic blocking agent. This compound d-3, 4-(1′, 3′-dibenzyl-2′-ketoimidazo- do)-1, 2-trimethylene thiophanium *d*-camphor-sulphonate; it is known by the code number Ro 2-2222 or the trade name 'Arfonad.'

Sarnoff et al. (1952) have used this drug to produce graded reduction of arterial pressure in the treatment of acute pulmonary œdema. A single intravenous injection of 0·2 mg. per kg. body-weight produced a prompt and brief depressor response lasting about three minutes. Tachyphylaxis did not occur when repeated doses were given. The drug was therefore administered in a continuous intravenous drip. Different degrees of reduction in the arterial pressure were obtained according to the rate at which the drug was administered. Cessation of the infusion was followed by prompt recovery of the arterial pressure. Nicholson et al. (1952) have reported on the intravenous administration of arfonad during surgical anæsthesia.

RESULTS

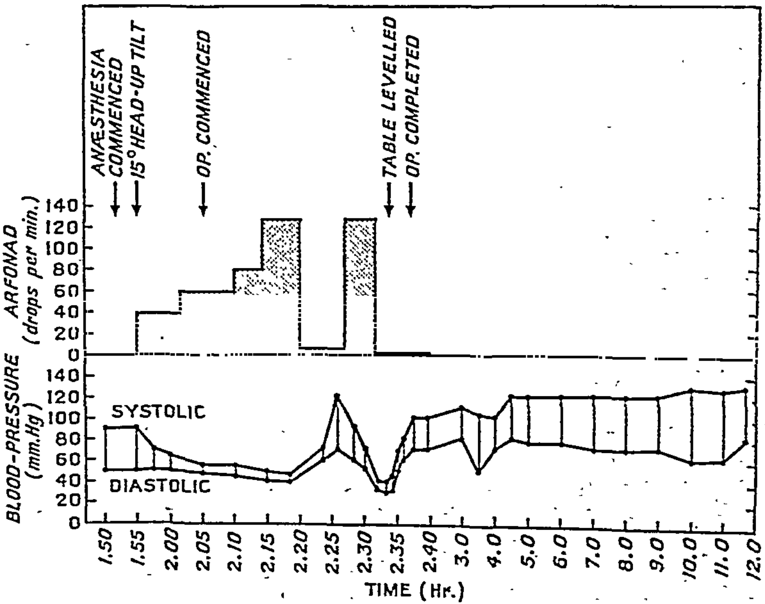
Recently we obtained a small supply of arfonad; and we have given this in intravenous drips to produce controlled hypotension during anæsthesia in 5 cases, as follows: (1) stellectomy, (2) radical mastectomy, (3) laminectomy, (4) thyroidectomy, and (5) mastoidectomy.

The drip solution contains 1·0 mg. of arfonad per ml. The drug is given at the rate of approximately 3 mg. per minute. As shown from the observations in case 1 (see figure) the blood-pressure level is readily controllable by varying the rate of drip. After the drip was stopped recovery was rapid, and the blood-pressure remained very stable during several hours' postoperative observation. In every case highly satisfactory results were obtained. No undesirable side-effects or complications have been observed.

DISCUSSION

So far our results lead us to believe that in arfonad we have an agent suitable for the production of hypotension in a manner that is readily controlled and which overcomes the disadvantages of the methonium compounds. Should these early hopes be confirmed, arfonad will probably supplant other agents for producing controlled hypotension.

Elsewhere close parallels can be seen in the evolution of safer and more efficient techniques by the introduction of agents which are rapidly eliminated. Thus, with



Arterial blood-pressure in case 1 during and after intravenous drip containing arfonad (1 mg. per ml.), with the drip calibrated at 15 drops per ml. Anæsthetic: *thiopentone* 0·5 g.; succinylcholine chloride ('Scoline') 100 mg.; endotracheal intubation with nitrous oxide/oxygen and a trace of trichlorethylene.

gangrene necessitates resection of the bowel—in the past decade it has fallen from over 80 to 23 5% Resection has been most successful when completed by an anastomosis between the ileum and the transverse colon Ileoascending-colon anastomosis has invariably proved fatal There seems to be no particular advantage in the Mikulicz type of two-stage exteriorisation procedure, which should be reserved for patients in a very poor condition Concomitant appendicectomy is advised by LAWRENCE and ULFELDER but condemned by WANSBROUGH and CRAM, who had 2 deaths after leakage from the stump of the appendix In any case this procedure does not prevent an enterocolic recurrence More than forty years ago, at St Mary's Hospital, London, STANSFIELD COLLIER carried out the following routine

> Under anæsthesia, and on the operating-table, through a small catheter inserted into the anus normal saline was allowed to flow in from a height of 2 ft A small incision was made in the right iliac fossa With the aid of one finger in the abdomen the reduction of the intussusception was assisted Reduction might be complete, and always the ileocæcal junction was pulled out of the abdomen and inspected to see if this was so

This combined procedure may be the best There is less shock than if distension alone is relied on, the operator makes certain that it has been effective, and it can be carried out through a small incision. If resection should prove necessary it is a simple matter to enlarge the incision These children always have very mobile colons, which can be easily drawn out of an incision in the iliac fossa

Clinical statistics on the efficacy of any particular form of treatment are seldom very reliable Until we know far more of vital processes and can control them, these *problems are not really susceptible of* exact mathematical analysis Hence the surgeon must, on the evidence before him, decide for himself what course he shall pursue

Annotations

RADIOLOGY IN HÆMATEMESIS

IN this country radiological examination is used almost routinely in the diagnosis of perforation or obstruction of the gastro-intestinal tract Its use to define the source of bleeding from the upper part of the tract, in the acute stage, is much less favoured The reasons for this wariness are broadly two Firstly, one of the accepted principles of hæmostasis is to avoid all unnecessary movement, and it has been thought that the transport and disturbance of the patient that are necessary for a reasonably good barium series may provoke or prolong the bleeding that menaces the patient's life Secondly, in many centres the treatment of hæmatemesis or melæna is still usually expectant and supportive, and thus the exact cause is, for the moment, of secondary importance In recent years, however, improvements in supportive, anæsthetic, and surgical techniques have led to a move towards radical treatment in cases of hæmatemesis thought to be "bad risks" The mortality in elderly patients with chronic peptic ulceration who have had severe or recurrent hæmorrhage is high Avery Jones[1] for example, reported a mortality of over 20% in patients over 70 years of age, compared with one of 2% in patients under 45 years It is in this group of patients with continuing or recurrent bleeding that radiology may help, provided that the examination does not impose too great a risk Such an examination may, in the first place, discover cases that are unsuitable for any emergency surgical procedure, by demonstrating œsophageal varicosities, a large hiatus hernia, or extensive malignant disease of the stomach or upper small bowel More positively, it may reveal the site of a resectable lesion, such as a duodenal or gastric ulcer or a simple tumour

As early as 1937, Hampton[2] described what he regarded as a safe method of demonstrating radiographically bleeding duodenal ulcers, in selected cases Zamcheck et al[3] have now described a study on the safety and reliability of radiological diagnosis in 123 patients, ranging in age from 13 to 88 years, in whom a barium series was carried out soon after massive bleeding from the upper gastro intestinal tract This series included 93 patients who were examined less than three days after admission to hospital, at least 50 of these had a hæmoglobin level under 27%, and all required transfusions In the first 52 cases examined elaborate precautions were taken in handling the patients, both during transport from the ward to the radiological department and during the examination itself, but, in the light of this experience,[4] the more elaborate precautions were discontinued. Preparation for examination consisted in blood transfusion until the hæmoglobin level was 28% or higher, and starvation for twelve hours Examination was postponed when there had been gross hæmatemesis or fluid melæna earlier in the day, when shock was obviously present, or when the patient could not cooperate The result was unsatisfactory in 4 cases, in only 3 was the patient not examined in the erect position, but the routine technique was modified in about two-thirds of the total In 98 cases the initial radiological diagnosis was later confirmed in 25 this initial diagnosis was incorrect or no satisfactory diagnosis was reached After examination 10 patients showed evidence of further slight bleeding, 12 more had severe bleeding, but 8 of these were bleeding at the time of examination Of the 12 who bled severely after examination, 6 were operated on with 2 deaths, the remaining 6 were treated medically, and 2 died

Zamcheck et al believe that there is no evidence for or against a connection between radiological examination and subsequent hæmorrhage, but they feel that the investigation need not be hazardous They are perhaps influenced by the fact, stated by them, that half of the patients admitted to their hospital with massive gastro-intestinal hæmorrhage are chronic alcoholics In their experience hepatic cirrhosis is a common cause, and œsophageal varices were found in 5 cases Gastritis figures rather prominently in their diagnostic summaries —5 times as a single diagnosis, 35 times in multiple diagnoses—and they comment that this, *too*, may be associated with the high prevalence of chronic alcoholism in their cases During the period of their first 52 examinations they saw 12 further patients with severe hæmatemesis who were too ill to be examined radiologically these comprised 3 who were immediately treated surgically after œsophageal varices had been excluded, 6 with hepatic cirrhosis who died without recovering enough to be examined, and 3 without cirrhosis who died within twenty-four hours despite repeated transfusions

Zamcheck and his associates have stated a good case for more liberal use of radiology for early diagnosis in cases of hæmatemesis or melæna There is always a hard core of such cases in which nothing right can be done, and radiology may perhaps help *to reduce* this group the contents of one ampoule are dissolved in 20 ml. sterile isotonic sodium chloride solution, and injected the pleural cavity through an intercostal catheter, which the fine end at other times drains under water. Digestion is then allowed to proceed for about eight s, after which the products of digestion are removed during the next sixteen hours by applying suction of cm. of water by a Stedman pump. Large partly digested particles can be washed from the pleural cavity with physiological saline just before the next dose of streptokinase and streptodornase is given.

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For infections of soft tissues a similar solution of the enzymes may be used. The wound is filled with the solution and then covered with 'Nylon' gauze. If the wound is deep, catheters are placed into its depths, a piece of nylon invaginated into the area over the catheters, and the area packed with ordinary gauze. The enzyme is then injected through the catheters. Applications are repeated once or more times daily according to the severity of the infection.

'Lubafax,'† a water-soluble base, has proved a useful vehicle for streptokinase and streptodornase in the treatment of superficial infections. 300,000 units of streptokinase, 75,000 units of streptodornase, and 0·5 g. of crystalline aureomycin are dissolved in 5 ml. of physiological saline solution; and 30 ml. of lubafax is added. The suspension retains its potency for about one week when stored in a refrigerator.

The effects of the enzymes in the treatment of osteomyelitis are improved by the use of a 1 : 1000 aqueous solution of benzalkonium chloride as a solvent, instead of physiological saline solution. Another addition to the chemical treatment of osteomyelitis is a 1% solution of acetic acid in glycerin. Dilute acetic acid dissolves collagen; and glycerin lowers surface tension and aids penetration by acetic acid.

For the treatment of osteomyelitis we suggest a round-the-clock schedule. At 8 A.M. 4 ml. of a 1% solution of acetic acid in glycerin is injected into the wound through the catheter. At 12 noon the wound is irrigated with physiological saline solution. Immediately afterwards and again at 4 P.M., 8 P.M., midnight, and 4 A.M. 4 ml. of the solution of streptokinase, streptodornase, and aureomycin in aqueous benzalkonium chloride is injected into the wound. At 8 A.M. next day the wound is washed with physiological saline solution, and the cycle is repeated. The acetic acid may be used more frequently if necessary; in which case it is substituted for one of the applications of streptokinase and streptodornase.

VARIOUS USES

The causative organism of the infection does not affect the action of the enzymes. Infections due to all of the bacteria commonly found in surgical infections and those due to the gas-forming anaerobes, the tubercle bacillus, *Blastomyces dermatitidis*, actinomyces, and *Histoplasma capsulatum* have been treated successfully.

The micro-organism isolated from the wound will determine the choice of chemotherapeutic or antibiotic agent to be given systemically. Aureomycin may be used topically, since sensitivity to this is rare. The sulphonamide compounds and penicillin should not be used topically, because of the high incidence of induced sensitivity.

Of 85 cases of wounds and infections treated with streptokinase and streptodornase, excellent results were obtained in 80.[11] Of the 5 failures 3 were in cases where gangrene was so far advanced, and the blood-supply so poor, that the action of streptokinase and streptodornase was inhibited. 1 failure was in a case of osteomyelitis where infection in a bone-flap of the skull could not be controlled and it had to be removed; removal of the bone resulted in prompt healing. The 1 failure among the soft-tissue infections was in a patient with severe infection in an advanced carcinoma of the head and neck.

Osteomyelitis

Excellent results were obtained in 30 out of 44 instances of pyogenic osteomyelitis.[13] Of the failures 7 were in patients with gangrene of the lower extremity, which is a definite contra-indication to the use of streptokinase and streptodornase. The 27 cases with a good vascular system included 7 failures. In all of these 27 cases the general condition of the soft tissues improved, but the underlying disease did not heal. When most of a long bone is involved with osteomyelitis, not all the infected bone can be removed, because of the need to retain continuity; and the inability to saucerise to healthy bone then prevents a good result from treatment with streptokinase and streptodornase. In another case similar caution in debridement about a joint led to failure. 2 further cases were classed as failures arising from the patients' lack of care of the area after their discharge from the hospital.

Tuberculosis of Bone

Excellent results were also obtained in 13 out of 15 patients ill with tuberculosis of bone. This group included 8 patients with tuberculosis of the vertebral column; in the 2 failures the local condition of the wound improved but the patients died of progressive systemic tuberculosis.

Pilonidal Cysts with Abscess

Abscesses in pilonidal cysts have also responded well. In 16 such cases the enzymes were applied locally for a period before incision and drainage. These patients, who had to be retained in the hospital until healing was complete, were discharged after an average of 33·7 days. This figure contrasts sharply with the 60–90 days usually lost by such patients in hospitals of the U.S. Armed Forces during the late war. (The number of man-days lost in the U.S. Army during the war from pilonidal cyst and its complications has been estimated at about 3,470,000.[4])

Hæmothorax

Streptokinase and streptodornase are extremely useful in the treatment of hæmothorax, since the fundamental need in the treatment of this complication is the removal from the pleural cavity of clotted blood, fibrin, and cellular debris to permit prompt re-expansion of the lung. Treatment should be started as soon as bleeding is controlled. 12 patients have been treated with excellent results.[17] In 11 of these cases the date of onset was known; and treatment was started, on average, slightly more than eight days after injury; in 3, however, the interval was well above the average, and in 1 of these it was as long as twenty-six days. Radiological evidence of slight pleural thickening or a small amount of pleural fluid was found in each case at the time of discharge, but such residua usually disappeared in the succeeding months. This method is applicable to battle casualties. The operation is simple and can be done with few instruments in a forward area. It does not preclude air evacuation.

Tuberculous Abscess

Many surgeons are reluctant to drain tuberculous abscesses because they fear secondary infection. In 19 cases, however, where streptokinase and streptodornase were applied, no secondary infection ensued.[18] These cases included 4 of tuberculous empyema, 5 of tuberculous lymphadenitis, and 10 of tuberculosis of bone, joint, or tendon. In 16 of these cases, the tuberculous infection was controlled and all wounds and sinuses healed. The remaining 3 patients had advanced and progressive tuberculosis; in each there was local improvement, but the systemic tuberculosis led to death.

Tuberculous empyema with bronchopleural fistula has to be treated with care, since thinning of the pus may promote spread of the infection.

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† Manufactured by Burroughs Wellcome & Co. Inc.

a combination of the effect on the blood-vessels and the direct action on the nerve cells [2] Meigs and Hughes add that severe cases may also show abnormal respiratory signs, such as dullness, râles, and rhonchi, and skin lesions ranging from circumscribed erythema to ulceration and dry gangrene, commonly at pressure sites The heart may also be damaged, probably because its rate of working and its need for oxygen are great [2] The degree of permanent residual damage in any organ is directly related to the duration of unconsciousness, further emphasising the necessity for speedy treatment

CEREBRAL SWELLING

Two patients may have apparently identical cerebral tumours, and yet in one there is only a local neurological disturbance while in the other intracranial pressure is high and there may be signs of a tentorial pressure cone Atkinson,[4] discussing this problem, considers that the contrast may be due to differences in cerebral swelling in the two cases He uses the term to mean any increase in brain volume, however small, and prefers to confine the term "cerebral oedema" to a condition where there is an increase of fluid in the interstitial tissues of the brain The volume of the brain varies to some extent under physiological conditions—for example, during respiration At the end of inspiration the brain seems to recede from a dural defect, and at the end of expiration it swells towards the defect, and, as O'Connell[5] emphasised in 1943, this respiratory variation is probably an important factor in the normal circulation of the cerebrospinal fluid There is also pulsation of the exposed brain with each heart beat, and this small alteration in cerebral volume is increased when the systemic arterial pressure rises In animals a greater proportion of carbon dioxide in the inspired air, and to a lesser degree a reduction in the oxygen content, will also cause an increase in cerebral volume[6], and a similar effect can be seen in a brain exposed at operation if there is a temporary failure of oxygen-supply Atkinson says that obstruction of cerebral veins near the superior sagittal sinus in man results in cerebral swelling in the area normally drained by these veins, and he bases this opinion on the swelling visible in the adjacent gyri when a vein is occluded during craniotomy On the other hand, Beck and Russell[7] were unable to demonstrate cerebral oedema in experimental animals after division of cerebral veins near the sagittal sinus

Atkinson's thesis is that these mechanisms are of importance in the production of brain swelling in a patient with a cerebral tumour cerebral veins may become occluded, with swelling of the adjacent gyri, and arterial occlusion may develop, leading to damage to the capillary endothelium in the infarcted area, pooling of blood, and transudation of fluid through the capillary walls The brain swelling produced in these ways may in turn lead to tentorial and other pressure cones, and these in themselves may further increase the cerebral swelling When part of the temporal lobes herniate through the tentorial opening the cisterna ambiens may be occluded, obstructing the free circulation of the cerebrospinal fluid and disturbing the normal equilibrium between the cerebral venous blood and the cerebrospinal fluid When this happens, anything which suddenly raises the intrathoracic pressure, such as an attack of coughing, may cause serious cerebral venous congestion with further brain swelling, and Atkinson considers that this is an important cause of serious tentorial coning Herniation through the tentorial opening or the foramen magnum may also cause occlusion of branches of the basilar artery, supplying the brain stem, or the posterior cerebral arteries, supplying the occipital lobes, and effects may again add to the cerebral swelling

Atkinson makes out a good case for the importance of brain swelling in the manifestations of intracranial tumours and for the vicious cycle which may result once swelling has started, but he leaves us still wondering why gross swelling may develop in association with only one of two apparently identical tumours

"VISCO-ELASTICITY" OF LUNG

EVERYONE who has seen a rubber balloon or a tin of treacle knows in a general way what is meant by the terms "elasticity" and "viscosity" it is when we attempt to measure these properties that we run into trouble Nor is there much disagreement about their importance in the living body Even those of us who could not look a poise in the face are aware that blood is thicker than water, and that the viscosity of the blood-stream is thought to have a physiological as well as a rheological significance As for elasticity, like Macaulay's schoolboy we all know the distribution of elastic fibres in the body, and, perhaps rashly, assume that they confer elasticity on the tissues with which they are associated Some of our illusions are, however, being undermined The "spring" ligament, whose very name begs the question, springs no more, for it has been shown to consist only of white fibrous tissue with no elastic fibres[1] On the other hand, the auricle and the nose continue to return to their original shape so long as they are not subjected to excessive violence, and the *ligamentum nuchæ* can be stretched to 140% of its length and return to its former dimensions

We are accustomed to cite the lung as an elastic organ, when it is no longer sucked outwards by the negative pressure in the pleural sac it recoils inwards and collapses This collapse takes place in life when the intrapleural pressure is raised, or, as McIlroy[2] has shown, after death, a considerable volume of air is expelled from the chest in the first two or three hours after death When, however, we attempt to relate this "elastic" behaviour of the lung to the physical law propounded by Hooke—to which, as McIlroy points out, no known material conforms—we find that the lungs behave as a "visco-elastic" system rather than a purely elastic one In a viscous system the response to a force depends on the time for which the force is applied, while in an elastic system the response depends on the magnitude of the force, systems giving intermediate results are called visco elastic The visco elastic behaviour of the lung has been established for dead material by McIlroy and Christie,[3] who measured spirometrically the response of the lung to variations in the pressure within a lung plethysmograph On occasion there was a time lag of several minutes before equilibrium at a given pressure was reached, and a predictable response was obtained only when small pressures were applied repeatedly, as in ordinary respiration The lung is thus not a purely elastic organ, a viscous factor is present Because of the time taken to reach equilibrium, the volume of the tidal air in simulated respiration varies inversely with the rate of this respiration McIlroy and Christie have used the relation of the tidal air at 3 "respirations" per minute to the tidal air at 15 "respirations" per minute as an index of the viscous resistance of the lung This index, they found, increased with the age of the patient from whom the lung was derived, and they suggest that what is usually called "loss of pulmonary elasticity" is really an increase in lung viscosity In ten emphysematous lungs the viscous resistance was increased, and it was shown that this was not due to any significant bronchial obstruction

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ENYLBUTAZONE (BUTAZOLIDINE) IN THE TREATMENT OF CHRONIC ARTHRITIS

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E introduction of phenylbutazone (butazolidine) e management of rheumatoid arthritis (Currie 1952) been followed by discussions of its "antirheumatic" ts and its toxicity (Hart and Johnson 1952, on et al. 1952, Crowther and Elgood 1952). This r describes our experience in the first 50 cases of nic joint disorder treated with phenylbutazone in hospital.

any of these patients were attending the routine cs of the rheumatism unit, and detailed laboratory stigations were not always possible.

he duration of treatment with phenylbutazone ged from four months to a few days, and some patients ived a total dose of as much as 73 g. The daily was varied according to the response of the patient, never exceeded 1 g. per day. Oral preparations have become available during the last five months, and re this, daily intramuscular injections were used.

RESULTS OF TREATMENT

umatoid Arthritis

henylbutazone was given to 34 patients with imatoid arthritis.

bjective results.—Objective results of treatment were ssed in terms of

) Grip (mm. Hg.).
) Range of movement (in degrees).
3) Swelling of joints (circumference in mm.).

20 patients (59%) there was objective improvement, luding reduction of joint size in 6 but in 12 (36%) improvement could be demonstrated by these ndards. The other 2 patients became worse and e swelling of their joints increased.

Subjective results.—19 patients (56%) considered themselves improved, and 4 of them were in fact able to walk again; 2 (5%) thought that they were worse; 5 (15%) noticed no change in their condition; and 8 (24%) became free from pain, 2 of them were able to discard a calliper and crutches respectively.

Effects on erythrocyte-sedimentation rate.—Changes of less than 5 mm. were ignored. In 9 patients (31%) the E.S.R. (Westergren) fell; in 11 (38%) there was no significant change; and in 9 (31%) it rose.

Ankylosing Spondylitis

In the 3 patients with this disease who were treated, subjective and objective improvement occurred in 1, and there were no changes in the other 2. The E.S.R. rose in 2 and remained unchanged in the other.

Osteo-arthritis

The 11 patients with this disease were treated in the same way as those with rheumatoid arthritis. Objectively, 7 patients improved, as judged by increase in power and range of movements. The other 4 patients remained unchanged. Subjectively, 8 patients experienced relief from pain, and of these, 5 became free of pain altogether, including 1 patient who was also suffering from Paget's disease.

Other Conditions

A patient with spondylolisthesis, who was severely disabled by low back pain, was sufficiently relieved to return to work.; and another with tendonitis of the shoulder, had less pain and more movement.

SIDE-EFFECTS

Side-effects developed during treatment in 22 (44%) of the 50 patients. The side-effects encountered were:

Abscess at site of injection	3
Gastro-intestinal symptoms	6
Reactivation of peptic ulcer	2
Melæna	2
Salt and water retention with œdema ..	8
Rashes	5

The abscesses were sterile and required incision. Healing was delayed for three months in one instance.

The patients who had gastro-intestinal symptoms included 4 who were having phenylbutazone by mouth. One patient was able to continue treatment when the dose was reduced from 1 to 0·6 g. daily, and the other 3 were relieved by Mist. Mag. Trisil. Co. *B.P.C.* However, in 2 patients treatment had to be stopped. In 2 patients with histories of peptic ulcer, there were recurrences—in one case fourteen years after the original episode.

A patient who had been having oral phenylbutazone for two weeks, and another who had had 17 g. by injection over seventeen days, became rapidly anæmic and dyspnœic, and developed cardiac failure. Their Hb levels dropped from 92 to 69% and from 102 to 52% respectively. These patients subsequently had massive melæna, but without appreciable gastro-intestinal upset. Hæmorrhagic effects had not been encountered before and coagulation-times and platelet-counts were not measured.

In 3 patients who showed evidence of salt and water retention, there was a significant fall in urinary chloride output in the early stages of the development of œdema. In 2 patients œdema was controlled with mersalyl, and in one case treatment was continued with both mersalyl and phenylbutazone for twelve weeks in view of the considerable clinical improvement.

Of 5 patients who developed rashes, 4 were first affected in the second week of treatment and 1 in the fourth week. The way in which the drug was given seemed to be of no significance. The prodromal symptom in each case was severe pruritis, which was followed in one instance by a pyrexia of 103°F. A severe facial urticaria and a morbilliform rash appeared in 1 patient. After these eruptions faded, they were followed by a petechial rash and the development of splenomegaly. The clotting-time was prolonged to 7 minutes (normal 4–5

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Public Health

DECEMBER FOG IN LONDON AND THE EMERGENCY BED SERVICE

G F Abercrombie
M D Camb
CHAIRMAN, EMERGENCY BED SERVICE COMMITTEE,
KING EDWARD'S HOSPITAL FUND FOR LONDON

In the first half of December, 1952, a violent and untimely "epidemic" smote the people of London, and applications to the Emergency Bed Service (E B S) for the admission of general acute cases far exceeded all previous records In what follows, E B S admissions only are considered, there must have been a great number of direct admissions of which the E B S has no knowledge

Fig 1 shows day by day the applications for this month of December (7992 applications, 6852 [85 73%] admitted) compared with those for the previous August (2946 applications, 2815 [95 53%] admitted) Plotted thus, the graphs are too erratic to be of use in predicting how many requests the service is likely to receive in the immediate future, but if, instead, a "moving" weekly total is calculated and charted, the more extreme irregularities disappear and the general trend becomes discernible Fig 2 shows the moving weekly totals each winter from 1949 to December, 1952 Each point on these tracings shows the total applications received during the previous seven days for example, the weekly total up to Nov 30, 1952, was 1313, and next day 243 applications were received, adding these and subtracting the 220 received on Nov 24, the moving weekly total for Dec 1 is 1336

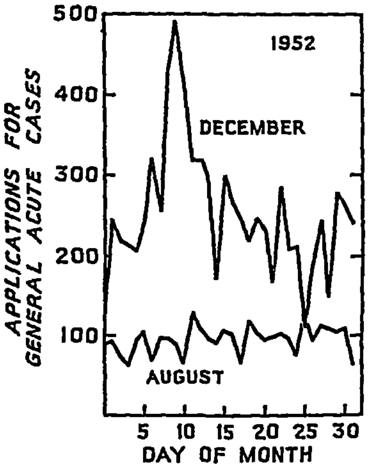

Fig 1—Totals of daily applications for admission of general acute cases in August, 1952, and in December, 1952

The annual rhythm is now fairly clear After a quiet summer the line begins to move upwards as winter approaches, there is usually (though not in 1951) a characteristic fall just at Christmas, and then the line rises steeply to its peak in early January, after which it declines more or less steadily to reach the summer levels in April

WARNING SYSTEM

After January, 1951, when 7064 applications were received and only 65 5% of patients were admitted, the service evolved a warning system which is now on trial When the percentage of admissions to applications, calculated on the moving weekly totals, falls below 85%, a "white" warning is sent to the appropriate hospital authorities This is a precautionary signal, saying in effect "E B S is hard pressed and may be in serious difficulty in the next day or two" If the percentage falls below 80% a "yellow" warning is issued, and if below 75% a "red" warning These are urgent calls for help and mean "The situation is serious, the resources of E B S are rapidly being exhausted, and for one patient in five—or four—no bed can be found" On receipt of these warnings, regional-board hospitals take prearranged action to provide more accommodation by slowing down admissions from the waiting list putting up extra beds, and so on Teaching hospitals also informed and cooperate as far as possible

THE FIRST YELLOW WARNING

In 1952, owing to the prevalence of cold weather early November the work of the service rose st throughout that month with the result that on D 243 general acute applications were received in the normal 130 or so This rise continued until D when the fog settled on London, and the numb

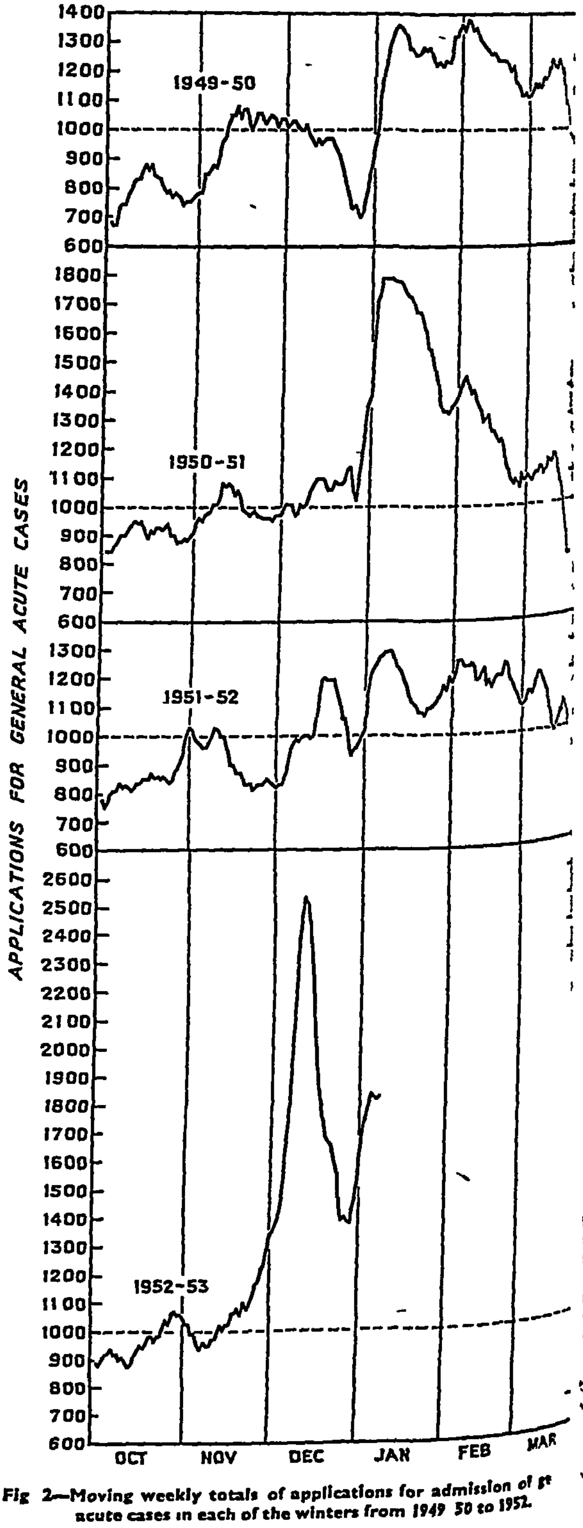

Fig 2—Moving weekly totals of applications for admission of ge acute cases in each of the winters from 1949 50 to 1952

Reviews of Books

al Radiology of the Ear, Nose, and Throat

RIC SAMUEL, M.D., F.R.C.S., F.F.R., D.M.R.E., late hon. adiologist, Middlesex Hospital, London. London: I. K. Lewis. 1952. Pp. 339. 70*s*.

TIL the appearance of this book there had been no cation in this country wholly devoted to the logy of the ear, nose, and throat. Dr. Samuel has ght together the best recent writings on the subject, 1 have hitherto not been easy of reference, and he lso kept the anatomical and clinical aspects well to ore. For each region there are chapters on the logical techniques employed, and on the develop- and anatomy of the structures. These are followed hapters on the normal and abnormal radiological arances and the clinical features connected with . This arrangement has resulted in some repetition, ially of anatomical material. The style, moreover, t easy and there are some errors which would not escaped more careful editing. The illustrations numerous but their quality is varied. On the r hand, the full references, and the indexing, both uthors and subjects, suffice in themselves to make ook valuable.

land's Forceps

E. PARRY JONES, M.B., M.R.C.O.G., consultant obstetrician and gynæcologist, St. Asaph General and Maternity Hospitals. London: Butterworth. 1952. Pp. 212. 35*s*.

OUT half this book concerns forceps in general: the inder describes the Kielland instrument, its design nanufacture, the indications for its use, the technique plication, the dangers, and the results that may be cted. Mr. Parry Jones has used the instrument on ccasions, and from careful personal observation and l review of the literature he gives a detailed and useful unt of the place he thinks the instrument should hold iodern obstetric practice. There is a translation in ppendix of the original article by Christian Kielland hich his forceps and his special method of insertion described. The book is beautifully illustrated and ly read; it will certainly revive interest in an obstetric eps which has never achieved the popularity in this ntry which it holds in Scandinavia. The instrument ers considerably from the more usual forceps, and iy useful and important technical details are described Mr. Parry Jones, which will undoubtedly help others ise the instrument with judgment and skill. On the er hand, some of the statistical tables and many of illustrations (especially of other types of forceps and hose who have designed them) might have been left . They make the book much more costly than it d have been.

icer Cytology of the Uterus

J. ERNEST AYRE, M.D., director, Dade County Cancer Institute, Miami, Florida. New York: Grune & Stratton. London: J. & A. Churchill. 1952. Pp. 407. 105*s*.

To the few in this country who practise cytological gnosis of uterine carcinoma by smears this new book ll be of interest. It is an atlas of 362 figures accom- nied by full, though often discursive, descriptive gends, and a text of some 53 pages interspersed with ges of figures. Based on 150,000 preparations—vaginal iears, cervical cell smears, and cervical cell scrapings—om over 22,000 women, the work is a cytomorphological udy chiefly of epidermoid carcinoma of the cervix. tological findings in cancer of other sites in the female nital tract, in certain benign conditions, and in normal iears are also given. Such topics as the organisation the service, the technique of taking and preparing ecimens, and the method of reporting on smears are cluded.

There is much in "gynecytology" and in this book iich is disputable and open to serious criticism. urticularly is this true of what Dr. Ayre calls "nearo- rcinoma" ("the precancer cell complex": "incom- etely developed carcinoma cells"), which lies at the art of the problem and on which the chief value of iear diagnosis depends. To quote the author, "when adequate scientific data are available to prove the specific character of the anaplastic precancer cell of the cervix, a significant advance in knowledge of carcinogenesis will have been achieved." Adequate scientific data have yet to be provided.

Congenital Dysplasia of the Hip Joint and Sequelæ

VERNON L. HART, M.D., F.A.C.S., assistant professor of surgery, University of Minnesota. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1952. Pp. 187. 36*s*.

IN this small book Dr. Hart makes an appeal for the earlier recognition and treatment of the dysplastic hip-joint; the pleasant style and beautiful production make it well worth reading. Although few cases of frank congenital dislocation escape skilled orthopædic care in this country nowadays, there is still a vast amount of avoidable disability in the form of subluxation and osteoarthritis secondary to lesser degrees of unrecognised dysplasia. Because simple abduction treatment in the infant can prevent all this, early recognition is of cardinal importance; and Dr. Hart clearly describes the separate clinical and radiographic signs, all minor in themselves but adding up to a convincing total picture, which must be looked for.

Comparative Biochemistry of the Carotenoids

T. W. GOODWIN, D.SC., F.R.I.C., senior lecturer in the department of biochemistry, University of Liverpool. London: Chapman & Hall. 1952. Pp. 356. 50*s*.

THE carotenoid pigments are widely distributed in plants and animals, and are sometimes present in micro-organisms. Except when they are concealed by other pigments, such as chlorophyll, their intense yellow colour always makes their presence obvious. Research on their physiological importance has resulted in prolific studies of the function of carotene as provitamin A, but little else has been clearly established. We have no adequate explanation, for example, of the tendency of carotenoids to be concentrated in the reproductive organs of animals and plants.

In writing this comprehensive account of the distribution of carotenoids in all forms of living tissues, Dr. Goodwin has not only worked hard to collect information, but has spent much time in constructive thinking. Information from a wide field has been cleverly condensed, often into tables. The two main parts of the book deal with carotenoids in plants and animals, and attention is focused on current theories which give hopes of explaining their biological functions and on possible lines of future research. Though the book as a whole has been written primarily for biologists and biochemists, parts of it are of considerable medical interest—especially those on the distribution of carotenoids in the tissues and blood in health and disease, and on the factors controlling the conversion of carotene to vitamin A.

Three Vesalian Essays

SAMUEL W. LAMBERT, WILLY WIEGAND, and WILLIAM IVINS, jun. New York: Macmillan. 1952. Pp. 128. $6.00.

MOST of the wood blocks used to illustrate the original editions of Vesalius's *De Fabrica* and *Epitome* were found in 1932, in the library of the University of Munich; unfortunately they perished during the late war. In connection with their discovery these three important essays were written.

Dr. Lambert describes and reproduces the drawings used for the initial letters of the first two editions of *De Fabrica*. These show anatomical and surgical subjects in which the acting parts are taken by young children, a conceit which heightens their artistic merit. Dr. Wiegand, of Munich, gives an account of the discovery and history of the blocks, and also some interesting points about the title page of *De Fabrica* and the continuous landscape which forms the background to the twelve muscle men in that book. The charm of the book vanishes with the third essay, by an art-expert who admits he has no knowledge of anatomy or Latin. Smooth reading is lost by the inclusion in the text of bibliographic details and lengthy bracketed material which should have been printed as footnotes. In the main the essay is a sustained attack, not always in good taste, on the Vesalian writings of Dr. Charles Singer—which are described as careless, lacking in exactness,

TABLE II—AGE DISTRIBUTION OF RESPIRATORY DISORDERS

Age	0–4	5–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	Over 80
No of patients	—	3	—	1	—	2	8	13	12	4

Digestive Disorders

6 patients were seen during this period with sudden attacks of vomiting This came on at the peak of the fog, and it was not accompanied by other digestive disturbance, such as abdominal pain or bowel alterations Presumably the cause was gastric irritation produced by swallowing fog

Respiratory Disorders

It was here that the fog produced its most serious effects 43 patients, with varying degrees of illness, were seen with signs of involvement of the lower respiratory tract They very often gave a history of previous chest trouble in 37 of these patients there was a history of either recurrent productive winter coughs and dyspnœa—i e, chronic bronchitis—asthma, bronchiectasis, or one of the forms of pulmonary fibrosis In this practice there are 105 people with these chest troubles, and 37 of them were affected

The *age distribution* is shown in table II, which shows how the elderly suffered most

The *sex-distribution* showed a 2 1 preponderance of men, there being 29 men and 14 women in this group

The majority of the illnesses had a fairly sudden onset on the third or fourth day of the fog This latent period has been noted during other fogs, and it may be due to the fact that by the third or fourth day the concentration of atmospheric contaminants reaches a certain threshold level, or it may simply be that it takes this period for the respiratory defences to be overcome The symptoms and signs seemed to arise from a combination of

(1) Mucosal irritation (cough and sputum)

(2) Bronchial obstruction (dyspnœa, cyanosis, and loud rhonchi during both inspiration and expiration)

(3) Infection (fever and general constitutional upset—probably a secondary factor superimposed on the local irritation)

(4) Cardiac failure (evident in many of the more elderly patients)

On clinical assessment, 16 patients were severely ill, with considerable distress, and in some danger, the other 27 had only a moderate degree of dyspnœa and general disturbance Quite a number of these were able to remain up and about in their homes, and some even went out to work

The severe cases were medical emergencies with paroxysmal dyspnœa, accompanied by an irritating and distressing cough and blackish mucopurulent sputum Cyanosis was obvious in some patients, and in all of them the pulse-rate was around 120, the respirations were between 35 and 40 per minute, and the temperature varied from 100° to 104°F

There were loud rhonchi all over both sides of the chest in both phases of respiration Râles were noted in some cases, especially after a few days' illness In no case were signs of clinical consolidation detected The picture was therefore one of severe asthma, if asthma is taken to mean a condition of dyspnœa produced by bronchial obstruction, but these patients did not respond to the usual antispasmodics

It was impracticable to carry out any radiological or pathological investigations there was so little time and so much work

Most patients improved slowly and it took four to nine days for the symptoms and signs to clear up This course was not influenced in any obvious way by the treatment adopted This was directed to controlling the infection by using antibiotics—procaine pen the first instance and chloramphenicol if there wa improvement after four days—and to attempt relieve the bronchial obstruction with antispa such as adrenaline, ephedrine, isoprenaline, and a phylline, whose effects were at the most very short The less severely ill were not treated with antib but with simple hot saline expectorants, combined antispasmodics It was not possible to use oxy these cases

Of this group of 43 patients, 2 died and 1 was adm to hospital A man, aged 66, with a past hist pulmonary fibrosis which had caused great dis for some three years, died within four hours of onset of symptoms An old lady of 76, who had a severe pneumonia four years previously, which left her prone to winter coughs and dyspnœa die the eighth day of illness from cardiac failure The pat admitted to hospital was an elderly man, who was ill to be nursed at home by his even older wife

CONCLUSION

These observations agree with the analysis the effects of the November fog of 1948[1] effects of a fog, in association with cold weather, principally on the respiratory and gastric mucosa Irritative symptoms, such as cough, nasal discharge and vomiting, are the primary results, but in ch respiratory invalids secondary infection and complications often appear in the lungs and bron The most severe cases are found in the elderly, being rare under the age of 45. It is remarkable that although there are quite a number of asthmatic children in this practice none of them was affected, in fact, th *was less illness than usual in children during this* The same observation was made during the influe epidemic of 1950–1951, when there was wide illness in adults but less than usual in children

Influenza

Last week reports of widespread influenza on Continent and in the United States were quickly follow by news of large numbers of cases in this count especially in the south of England There is so no evidence that the disease is taking a severe and recovery from the acute symptoms within 48 h seems usual In some patients the respiratory sympt have been followed (not accompanied) by gastro intestin disturbance Early laboratory evidence suggests an A-prime virus is responsible

The latest figures from the 160 great towns of En and Wales show 72 deaths from influenza in the ended Jan 17, compared with 51 in the preceding There were 76 deaths from influenza in the great in the corresponding fortnight of 1952 Deaths pneumonia showed no significant increase up to Jan Notifications of pneumonia (primary or influen in England and Wales numbered 1204 in the week Jan 17, compared with 1107 in the preceding week 869 in the corresponding week of 1952

These figures give no indication of the rapid spread mild influenza that is taking place One doctor on outskirts of London reports that Monday, Jan. was his heaviest day in 15 years of general prac On Jan 27 the Emergency Bed Service issued a " warning to hospitals This warning is given when service finds that London hospitals can take less t 75% of the cases referred to the service for adm Regional boards have asked their hospitals to resp to this warning by bringing into action plans for restr ing the admission of non-urgent cases and for fre as many beds as possible

On the Continent epidemics are reported in Fra and Germany (where the U S zone is particular affected) An influenza vaccine has been distrib for the inoculation of American troops in Europe

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[1] Logan, W P D *Lancet*, 1949, i, 78

THE LANCET

LONDON: SATURDAY, JAN. 31, 1953

The Patient in His Hospital

> "It is difficult for those who are familiar with hospital life to realise just how incomprehensible and alarming hospital routine appears to the outsider."

ifficult indeed; for as we cross the hospital threshold ır rhinencephalon responds to the familiar odour of lish and medicaments with a host of pleasing sociations: here we have enjoyed work and comnionship in wonderfully stimulating surroundings. or the patient it is otherwise. If he has been to ospital before it was in a mood of anxiety, either ild or severe, and possibly he suffered discomfort or ain: such memories colour his emotions at a second isit. If he has never before been to hospital his npressions are coloured by both anxiety and fear of ne unknown. The Central Health Services Council, n the memorandum[1] from which the above quotation s taken, warn all who work in hospitals of the danger f thinking of patients as "cases," and identifying hem as—for instance—"the duodenal in the first ed on the left." The atmosphere in hospitals which are for people, they say, is profoundly different from he atmosphere in hospitals which deal with cases: nd they add that here the general hospitals have something to learn from the mental hospitals, in which "there is no mistaking the atmosphere of genuine interest and sense of community which greets the patient and which helps him towards recovery."

A patient should be able to count on the help and friendship of his hospital: and especially since it is nowadays his hospital indeed. He has, for instance, a perfect right to ask questions and expect courteous replies; and, in fact, as the council point out, he will respond much more readily to sensible explanations and requests for help than to instructions delivered in an autocratic spirit. In hospital today the patient often encounters a string of specialists, each examining some aspect of his bodily function—and each engrossed with his own specialty. The story of the expert who put a needle into a vein, and only noticed when the blood failed to flow that the patient had no further need of his services, is possibly an invention; but undoubtedly doctors do, from time to time, arrive at a bedside bearing alarming equipment, and set about their humane purposes without so much as a "good morning," let alone a "by your leave." This is not what they would wish to befall their young children or their old mothers, or possibly even their wives (though doctors' wives are notoriously equal to anything); and they would certainly not lie down under such treatment themselves.

Akin to such ill-manners is the practice, still strangely prevalent, of discussing the patient's more alarming symptoms, across his bed, with a class of students, or of withdrawing to a short distance and saying in a penetrating whisper: "Of course we can't say when the next catastrophe will come: it may be in six years—or six days." The patient naturally wants to learn what to expect, but not through unwilling eavesdropping, or in terms which nibble at his self-confidence—or even devour it altogether in a single ill-considered mouthful. The council note (as we have often done) that there is a widespread feeling among patients and their relatives "that they do not receive enough information either about the nature and probable course of their illnesses or about its implications for their family and business affairs." Their questions should be answered kindly and clearly, and the council hold that they should have access to the medical staff in order to put them: each patient, indeed, should be told whom to consult and when. At visiting times the ward-sister or her deputy should be available—and on view—to answer visitors' questions and to have a word with those who have come long distances. Telephone inquiries, too, should normally be answered by the sister or her deputy; and the character of her reply, as the council are careful to point out, can do much to make or mar happy relations with the relatives. They wish to impress not only on doctors but on all who work in hospitals that good relations cannot be regarded as a natural growth. "They require cultivation, and will only be attained if everybody who comes into contact with the patient, from the consultant to the charwoman, regards it as part of his or her job to produce them."

Consideration, and understanding, of the patient's point of view should operate even before he is admitted. As soon as his name is put on a waiting-list he should be sent a letter giving him any information he and his relatives need while he is waiting for a bed. A second message, telling him the bed is vacant, should also be sent in a letter, for a postcard bearing the name of the hospital may betray the nature of his complaint to others. Many hospitals nowadays give the newly admitted patient a brochure describing the work of the hospital and the part it plays in the life of the community, and reminding him that he is going to be looked after by people with a tradition of service behind them. It also tells him what amenities are provided: the library, the newspaper round, the services of a hairdresser, the telephone facilities, the arrangements about smoking, the visiting days. The names of visiting chaplains, and the times of services of the different denominations, are also given; and it may be worth mentioning here a point not mentioned in the memorandum: old people, and people in chronic wards, are often much helped by the visits of ministers of their religion, yet because long-stay hospitals are often large, the minister (who usually has a parish or other appointment to serve) cannot possibly visit them as often as he and they would like. There is a good case in such large hospitals for the appointment of whole-time chaplains.

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[1] The Reception and Welfare of In-Patients in Hospitals. London: H.M. Stationery Office. 1953. Pp. 24. 9d.

General practitioners who are interested in this type of teaching are asked to notify the secretary of the college, as soon as possible, as to the ways in which they are willing to help in these teaching schemes

Postgraduate Instruction —The college will encourage and help practitioners to accept postgraduate instruction

This will need close coöperation with the British Postgraduate Medical Federation of the University of London, whose director has put aside a room for this purpose at his headquarters (2, Gordon Square, London, W C 1) It has been suggested that the college's regional faculties shall, in a similar way, work in close liaison with the postgraduate deans and directors of the eighteen other universities—Aberdeen, Belfast, Birmingham, Bristol, Cambridge, Cardiff, Cork, Dublin, Durham, Edinburgh, Galway, Glasgow, Leeds, Liverpool, Manchester, Oxford, St Andrews, and Sheffield

This postgraduate instruction can be of several kinds—attendance at hospital outpatient departments or at medical society meetings, lectures, half-day courses, weekend courses, 5½ day courses (from Monday to Saturday), and courses lasting a fortnight or longer For the last four of these courses, most National Health Service practitioners are allowed grants paid by the Ministry of Health (fees, subsistence and travelling allowances), and for the last two, payment of a locum tenens may also be approved

Practitioners are asked to notify the secretary of any suggestions they may care to make about this postgraduate instruction—where and when they think it can most conveniently take place in different districts, and what are the subjects in which they feel they most want help

Research in General Practice —The encouragement of accurate observation, investigation, and recording of results by general practitioners is to be an important part of the work of the college

The research committee of the college wishes to establish a register of members and associates of the college who are interested in the possibilities of research work in their practices It is hoped that this register will provide means of introducing to one another practitioners who share common research interests, to enable them to pool and exchange their ideas and information

A panel of experienced practitioners, and workers in other fields of medicine and science, is being formed to advise and help not only groups of doctors but also individuals who may wish to carry out research work by themselves in their own practices A number of investigations will be initiated by the college itself, and study groups are to be set up throughout the British Isles Methods of collection of this material by practitioners will vary, and will be designed to throw as little strain as possible on the routine work of each day Cards and flimsies suitable for these investigations, and which will fit the N H S envelopes, may be printed.

In order to explore the possibilities of coördinating research by large groups of general practitioners, it has been suggested that an " Investigation of the Year for General Practitioners " might be undertaken Suggestions are invited about the possible nature and scope of such an investigation

Members and associates are invited to apply to the secretary if they would like their names to be placed on the research register Applicants are asked to state any particular research interests they may have, and whether they would be willing to participate in group-studies

All suggestions made to the college on these subjects are to be carefully considered and analysed , and a report upon them will be published later The deans of many medical schools, the director of the British Postgraduate Medical Federation of the University of London, the postgraduate deans and directors of other universities, the Medical Research Council, and many university research departments have expressed their interest in these proposals, and have agreed to advise and to help in their possible development

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[1] Correspondence should be addressed to the Secretary, the College of General Practitioners, 14, Black Friars Lane, Queen Victoria Street, London, E C 4

Points of View

DAILY PAPER PANTHEON

A NEW FANTASIA OF THE UNCONSCIOU

ALAN McGLASHAN
M C, B A Camb, M R C S, D P M
PSYCHOTHERAPIST TO THE WEST END HOSPITAL AN
ST GEORGE'S HOSPITAL, LONDON

MILLIONS of adults read the comic strips in the papers Those who do not are amused, baffled exasperated by those who do Unhappily addicts either dumb (in both senses) or evasive, and there seem able to give valid reasons for their semi secret It is a minor sociological mystery, inviting minor

Even a first glance shows something interesting strips for adults, an offshoot from children's comic are not homogeneous they fall into two main One is simply a tabloid version of the every thriller The other, distinguished always by an of the miraculous or magical, has an attraction compulsive, altogether different

Examples of this second kind occur everywhere, strangely, by far the clearest were to be found till in a single newspaper, the *Daily Mirror*, where no than four of the six comic strips unmistakeably to it—three of them on one page

CONTEMPORARY MYTHS

Garth and Jane, Jimpy and Captain Reilly Ffo it possible that someone on the staff of the *Daily* chose these grotesques with full understanding of he was doing ? It is wildly unlikely Yet beyond and the even less likely explanation of pure cha there lies only one other possibility—that they chosen by the uncannily accurate processes of un scious selection, operating at the deepest level of human psyche If this were so, they would be *to exert a curiously compulsive power, overriding* ra repudiation, on the minds of multitudes Which precisely what they do

For these figures are no casual products of the ima tion Faintly through all their exploits, vulgar puerile as these usually are, sounds an echo of some unimaginably archaic the adventure cycles of the gods Kerenyi, latest among many, has shown with probability that such adventure cycles are the themes of human mental activity as far back as it ca traced They recur endlessly in the likeliest and unlikely places, the noblest and most degenerate forms

Consider *Garth*, that beefy and bewildered giant, suffering, virtuous, strong, faced by a never ending of heroic tasks Is there not more than an echo here Hercules and his labours, much-enduring far travel Ulysses, blinded Samson, Noah, Gilgamesh and be all these the timeless image of the heroic principle in aided magically by Heaven in reward of faith and val

As for the often excruciating *Jane*, beautiful virginal, constantly wooed but never wed above —far, far above—does there not float, as on vau ceilings of Venetian palaces, a company of bright figu Hainuwele the moon-maiden, irresistible Helen, Ap dite from the wine-dark sea, flower gathering Perseph and the countless images of Kore the maiden god La Belle Dame sans Merci, the unpossessable yet e nally nubile she, whose golden promises invest with brief splendour the too credulous heart of man not *Jane* in Fritzy the dachshund even poss appropriate animal attribute, as Diana has her ho and Cynthia her hare ?

In *Captain Reilly-Ffoull* the echoing image is at o more immediate and more remote His life of sham gusto, full of shady triumphs and richly earned hu dustrial workers are exposed to as great a hazard the nurse who is looking after a patient who is being eated by radium. A great deal of work is naturally eing done on the best method of supervising workers xposed to radiation, so that they can be removed rom exposure before irreversible damage is done to heir bone-marrow; and this work is not made easier y the fact that the ill effects are liable to appear ong after the exposure. At first efforts were directed o carrying out frequent blood-counts, especially white-cell counts, on all workers, even if the exposure was only slight. It is now clear that normal variation s so wide that such counts are not helpful; nor are outine six-monthly counts really effective. The present view seems to be that where the total internal and external radiation does not exceed 10% of the maximum permissible level, routine blood examinations are unlikely to help; better protection may come from the wearing of a "film badge" which measures the exposure of the whole body to radiation. For workers exposed to higher levels of radiation the total and differential white-cell counts seem likely to give the most satisfactory protection.

There have also been moves to improve the protection of lead workers. Lane[5] has faith in the punctate-basophil count, provided it is done under standard conditions. The possibility of using the coproporphyrin excretion in the urine as an early index of lead intoxication has been explored, but Lane's experience is that this varies too much from case to case for a "danger level" to be agreed on; he prefers the direct estimation of lead excretion in the urine.

Examination of the blood is necessary for the control of many industrial hazards. The larger concerns have their own hæmatological laboratories; but smaller businesses cannot afford the expense, and the responsibility then falls on the local factory doctor, who may or may not have access to a hospital laboratory for prophylactic blood-counts. Professor Lane emphasises that blood-counts have their limitations and that they are only one method of finding out whether toxic substances are causing damage, so that too much reliance should not be placed on them alone; this applies especially to single counts at long intervals. Potentially dangerous compounds are being increasingly used in industry, and the industrial medical officer has to be constantly vigilant. It would, of course, be better to investigate the effects of potentially dangerous substances before they are brought into general use than after they have been found to poison industrial workers.

Intussusception

The resolution of biological problems is seldom easy; for very few of the multifarious activities of living cells are fully understood. As it is impossible to devise a test with only one variable, crucial experiments are almost unknown. If this is so when experimenting on single cells, how much more true it is in clinical work, where the observer is dealing with a whole organism and is not free to vary conditions at will. It is hardly surprising that, despite careful observation, there are continuing doubts as to the relative merits of surgery and medicine in duodenal ulcer and in Graves's disease, and of surgery and radiation in malignant disease. We do not even know whether it is better to apply heat or cold to inflammatory processes.

Such thoughts are provoked by three papers on the diagnosis and treatment of intussusception.[1–3] Intussusception is a mechanical disorder that is influenced by vital reactions. The inconstancy of the symptoms bears witness to the variability of the primary biological material. Thus Lawrence and Ulfelder,[1] who report 53 cases, say it is disturbing to find that there was no history of pain in 5 of the 6 younger patients with gangrenous bowel, nor in 3 babies with non-gangrenous acute intussusception. In adults there was always a history of pain, and the disease developed much more slowly—in more than half over a period of 9 days or more. Vomiting was noted in nearly all the children but in only half the adults. In half the children and in nearly all the adults there was no bleeding from the bowel. On the other hand, Wansbrough and Cram[2] found bleeding in 85% of 575 cases. Lawrence and Ulfelder detected a palpable mass in half the children but in only a third of the adults, whereas Wansbrough and Cram found a mass in 84%. Neither pair of workers mention a characteristic feature in acute intussusception—namely, that the mass disappears between the attacks of pain, when the bowel wall is relaxed, and reappears when a peristaltic wave causes it to harden. Lawrence and Ulfelder remark that between attacks the children appeared well, whereas the adults "reflected more truly the abdominal disease." These two workers noted resistance of the abdominal wall in the absence of a mass in two-thirds of their patients, adults and children. But in babies it is the very relaxed abdomen between the spasms of pain that often obscures the diagnosis. Lawrence and Ulfelder found in one-third of the patients a definite suggestion of intussusception by a simple abdominal radiograph which showed absence of cæcal gas, often with an associated soft-tissue mass; dilated loops of bowel were seen only late in the disease. A barium enema proved a valuable diagnostic aid.

Both groups of workers warmly advocate operative treatment; whereas Nelson,[3] of Sydney, and Lindberg and Morales,[4] of Sweden, extol conservative methods. Nelson uses for reduction hydrostatic pressure of 3 ft. of saline solution under complete anæsthetic muscular relaxation; success is indicated by uniform distension of the abdomen. Of 102 intussusceptions in patients under two years of age, 43 were completely reduced by this method. By the Scandinavian method a radio-opaque enema is given and the intussusception reduced under screen examination. This was done successfully in 18 consecutive cases. With surgical treatment the mortality has been much reduced in recent years, partly through the aid of chemotherapy. Lawrence and Ulfelder had no deaths in 28 cases of non-gangrenous intussusception treated by simple reduction. Wansbrough and Cram report a mortality of 5·2% in 575 cases, including those requiring resection. The reduction in mortality has been most striking in cases where brought before the Courts previously because of the expense of litigation

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[5] Lane, R. E. *Brit. J. industr. med.* 1949, 6, 125.

[1] Lawrence, G. H., Ulfelder, H. *New Engl. J. Med.* 1952, 247, 499.

[2] Wansbrough, R. M., Cram, R. W. *Canad. med. Ass. J.* 1952, 67, 307.

[3] Nelson, T. Y. *Med. J. Aust.* 1949, i, 825. See *Lancet*, 1949, ii, 246.

[4] Lindberg, G., Morales, O. *Amer. J. Dis. Child.* 1949, 77, 303. See *Lancet*, 1949, ii, 246.

He agreed with Lord Merthyr that probably the right way to tackle this problem was at the start, and not when it was halfway down the hill He did not underestimate the importance of attempting conciliation in suitable cases, and he was sure that the marriage guidance councils were doing valuable work On these grounds it might well be argued that not only ought the cuts to be restored but that a good deal more money ought to be given to the marriage guidance councils But the amount of aid which the State could give depended on the economic circumstances of the time Again, if marriage guidance councils were to do any good they must be voluntary services He did not believe that they would receive the same public confidence if they were in any way a State organisation But if they were to remain voluntary services there must obviously be a limit to the amount of financial aid which they could receive from the State Thirdly, marriage guidance was still in its infancy, and the methods of counselling and attempting reconciliation were still to a great extent experimental The Marriage Guidance training board were inquiring into the selection and training of counsellors Their findings would be helpful in assessing the progress so far made The Harris Committee, which had recommended that Government grants should be made to these councils, had suggested that the grants should be for an experimental period of five years That period ended in the financial year 1953–54 Present arrangements would have to be reviewed next year, and he assured the House that full weight would be given to what had been said in that debate about the importance and value of the councils' work

QUESTION TIME

Hospital Block Grants

Mr **Peter Roberts** asked the Minister of Health whether he would consider the possibility of allowing hospitals to run their block grants over a spread of five years, in the same way as universities were financed —Mr **Iain Macleod** replied. The annual amount involved would be for Great Britain some £280 million I think that, apart from other considerations, a sum of this magnitude must be examined each year by the Government and by Parliament

Atmospheric Pollution

Replying to a question, Mr **Macleod** said that there were 15,114 deaths registered in Greater London in the five weeks ended Jan 3, 1953, compared with 9125 in the corresponding period a year earlier Figures for the country as a whole were not yet available, but there were 34,764 deaths registered in the 124 great towns in the five weeks ended Jan 3, 1953, compared with 25,821 in the corresponding period a year earlier The only relevant figures of hospital admissions available were of those arranged by the Emergency Bed Service in Greater London these were 6852 in December, 1952, and 4300 in December, 1951 While a large part of the increases in Greater London could be attributed to fog, the trend of the figures for deaths did not suggest that the fog caused any substantial increase in the rest of the country

Lieut Colonel **Marcus Lipton** asked the Minister what representation his department had on the Atmosphere Pollution Research Committee, and whether he had notified the committee that 4703 persons died in the Greater London area during the week ending Dec 13, 1952, as compared with 1852 during the corresponding week of 1951, a large part of which increase he had attributed to the fog —Mr **Macleod** replied My department is not represented on the committee, but I have confirmed that the committee are aware of the figures quoted

Lieut-Colonel **Lipton** Will the Minister see, as a matter of urgent priority, as the fog in December, with its man made atmospheric filth, killed thousands of people in the London area, that his department is represented on this committee and will take the most vigorous steps in association with the departments concerned, to reduce this appalling and unnecessary loss of life, which in the light of the figures that he has mentioned—6000 more deaths in five weeks in London—is on the scale of mass extermination ?—Mr **Macleod** My department has been looking into this matter as a problem of the very greatest urgency, as I agree it is, but this committee is mainly a scientific body concerned with causes, whereas, for obvious reasons, I am far more concerned with effects I think that the method that we are adopting—there is a between this committee and the M R C —is a better

Mr **P J Noel-Baker** Will the Minister give consideration to the granting of a subsidy to the Smoke Abatement So —Mr **Macleod** I will look into that suggestion.

Butazolidine in Rheumatism

Mr **Edward Evans** asked the Minister if he would statement on the claims made in respect of the drug 'Butazolidine' as a cure for rheumatic ailments including rheumatoid arthritis —Miss **P M Hornsby-Smith** replied The of this substance is still under investigation in this Current evidence suggests that in view of the possibility undesirable toxic side effects it should not be taken under medical direction

Mr **Evans** Is it not in the highest degree undesirable cruel that the lay press should spread among the public most extravagant claims causing false hopes in regard cure of this disease ? Is it not possible to call the attention of the press to the need for caution in the publication of statements until some authoritative announcement has made ?—Miss **Hornsby-Smith** I agree whole heartedly it is most undesirable that hopes should be raised with to drugs which are not yet wholly proven

Prescriptions at Child-welfare Clinics

Mr **Gerald Williams** asked the Minister if he arrange for doctors at child welfare clinics to give prescriptions which could be exchanged for medicine under National Health Service —Miss **Hornsby Smith** replied It is for the family doctor to issue any necessary prescription The clinics exist to give advice and not medical treatment There would be a very real danger if patients were able treatment in the clinics when they might also get treatment from their own doctors That would only create and might be dangerous

Capital Expenditure on Hospitals

Mr **Wilfred Fienburgh** asked the Minister what was estimated capital expenditure on hospitals in 1950-51 England and Wales compared with the capital expenditure 1937–38 after allowing for changes in the price level Mr **Macleod** replied About £9 million compared about £17 million

Bone-conduction Hearing-aids

Replying to a question Mr **Macleod** said that hundreds of bone conduction aids had been supplied patients taking part in clinical trials The bulk supply on order should begin to reach distribution centres within next few weeks, and he hoped there would be enough to most, if not all, of the expected demand for about England and Wales

Anthrax

Replying to a question, Sir **Thomas Dugdale**, Minister Agriculture, said there were 382 and 730 cases of anthrax involving cattle in 1951 and 1952 respectively Anthrax this country was mainly caused by the use in feeding and fertilisers of contaminated imported materials It seldom practicable to identify the particular ingredient responsible, but there was little doubt that imported products, such as bone meal, were a fairly common source infection As a first step the Ministry of Agriculture now discussing with the appropriate trade associations measures to reduce the risk from this source Until the discussions had been concluded, he would be reluctant take any action which might substantially reduce the quantity of feeding stuffs and fertilisers available in this country An effective vaccine against anthrax had been used number of years under the supervision of the Ministry veterinary staff, but only for animals known to be exposed particular risk of infection During 1952, vaccine sufficient to vaccinate about 13,000 cattle or twice as many pigs issued The vaccine had now been made available generally to veterinary surgeons for use at their discretion, but it too early to say to what extent its use would increase the new arrangements Generally, the vaccine had good results

Antibiotics for Livestock

Sir **Ian Fraser** asked the Minister of Health if he amend the Penicillin Act, 1947, to provide that antibiotics might be used for the treatment and feeding of livestock especially pigs —Miss **Hornsby Smith** replied The Government propose to introduce a Bill on this subject shortly

TOXICITY OF STREPTOMYCIN AND P.A.S.

THE treatment of tuberculosis calls for administration potent substances for long periods; and it is thus pecially important to know the smallest effective daily se of these agents. With streptomycin it has been und that 1 g. daily can replace the 3 g. that used be given; and thereby the incidence of toxic reactions s been much reduced. Similarly intermittent dosage streptomycin has proved effective against the less ute types of the disease or after daily administration s reduced toxæmia. Fewer injections are an advantage, so, to the nursing staff, for the risk of a nurse developing in sensitivity to streptomycin depends partly on the umber of injections she gives. This cutaneous sensitivity, hen it develops, is persistent; and those affected may ven have to abandon tuberculosis work. In patients, ith the reduced dosage and the purer forms that are ow marketed, streptomycin causes comparatively few rious complications; even vertigo seems to be much ss common. Dihydrostreptomycin, it is true, occasionlly gives rise to deafness; a survey by the research ommittee of the British Tuberculosis Association[1] suggests that such disasters will be rare if the daily dose does ot exceed 1 g., but perhaps on the whole dihydrotreptomycin is best avoided except as a local application or tuberculous empyema, where it seems to act more ffectively than streptomycin,[2] though even here a ourse should not exceed 20 g.

In general we can now feel easier about administering treptomycin; but increasing experience has done othing to allay anxiety about the risks with its usual artner—*p*-aminosalicylic acid. Originally its only rawbacks were thought to be alimentary disturbance and the unpleasant taste of the drug; but now they are nown to be many. Some of the most serious reactions are due to the development of drug hypersensitivity. Pyrexia, skin rashes (including exfoliative dermatitis), and liver damage have been reported increasingly often; and associated effects include hypopotassæmia, hypoprothrombinæmia, eosinophilia, cardiac arrhythmia, myxœdema, anuria, mental confusion, glandular enlargement, and splenomegaly.[3] Nor is this all; for hypersensitivity, when it occurs, may not be to P.A.S. alone but also to other substances which contain a phenol group with an amino radical in the para position—for example, certain sulphonamides, picric acid, and even hair dye.[4] The allergy may be still more general; for P.A.S.-sensitive patients have reacted adversely to the subsequent administration of streptomycin and penicillin. Clearly this drug, though relatively innocuous to many, produces profound disturbance in some. The nature of this disturbance is by no means clear, but there is much evidence that the endocrine system is intimately involved; in particular there are indications that the pituitary, the thyroid, and the suprarenal are affected, and it is also significant that A.C.T.H. will overcome the allergy due to P.A.S.[5]

Pugh et al.[6] have lately described 7 cases of psychosis with onset during treatment with sodium P.A.S. They suggest that this complication was due primarily to salicylate stimulation of the pituitary gland. The tuberculous infection, they believe, created the original non-specific stressor, the additional stressor being sodium-P.A.S. stimulation of the pituitary with consequent hypercorticoidism and associated mental confusion. When the phase of pituitary stimulation was followed by pituitary exhaustion and hypocorticoidism, a paranoid reaction ensued. In each case other conditioning factors were present—for instance, sustained resentment and hysteria before the tuberculous illness, an unhappy love affair in a patient with an over-dependent personality, and long-continued domestic worry—but, according to Pugh et al., the common additional stressor factor, with one possible exception, was sodium P.A.S. According to these workers, the tubercle bacillus thrives in an environment characterised by depressed thyroid activity, a relatively active adrenal, and an actively functioning gonad; they further suggest that, in addition to its recognised bacteriostatic effect, P.A.S. may owe some of its therapeutic success to its ability to correct hormonal imbalance in tuberculous patients.

Even if the explanation by Pugh et al. is not wholly correct, their work seems to point the way to more direct hormonal treatment of tuberculous disease. Already success is claimed for A.C.T.H. (given in association with streptomycin and P.A.S.), not only in overcoming hypersensitivity due to chemotherapeutic agents but also in other cases where lesions have not responded to more orthodox measures. We may be on the verge of an era when chemotherapy will be supplemented by hormonal therapy.

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1. Maher-Loughnan, G. P. *Tubercle*, 1952, 33, 342.
2. Ståhle, I. *Amer. Rev. Tuberc.* 1952, 66, 271, 285.
3. Mann, B. *Tubercle*, 1953, 34, 23.
4. Jeffrey, B., Borrie, P., Macdonald, N. *Brit. med. J.* 1952, ii, 647.
5. Houghton, L. E. See *Tubercle*, 1952, 33, 381.
6. Pugh, D. L., Edwards, G. F., McLaren, R. G., Jones, E. R. *Ibid*, p. 369.

CARBON MONOXIDE POISONING

CARBON monoxide, the commonest suicidal and accidental poison, has two possible modes of action. The better-known one is its displacement of oxygen, and its alteration of the oxyhæmoglobin dissociation curve. Less well known, and said to occur only with high concentrations of the gas, is its interference with the cytochrome-oxidase system in any tissue. The affinity of carbon monoxide for hæmoglobin is more than 200 times that of oxygen, so that a concentration of carbon monoxide $^1/_{200}$ of that of oxygen in inspired air would eventually reduce the oxygen-carrying power of the hæmoglobin by 50%; and such a mixture would be dangerous if breathed for long. Like simple oxygen lack, the effects of carbon monoxide on respiration are slight until the subject is on the verge of collapse, so that he may not realise he is in danger until it is too late. Haldane[1] noticed no remarkable symptoms when his blood was one-third saturated with carbon monoxide.

Accidental poisoning usually arises from partial combustion of fuel or leakage of coal gas or exhaust gas; and leakage of carbon monoxide in aircraft can be particularly serious. Experienced pilots know that one of the earliest signs is loss of brightness perception and of fine coördination of the ocular muscles.[2] With slow cumulative poisoning, the effects include weak and aching limbs, an increased pulse-rate, frontal headache, and nausea. If enough carbon monoxide has been inhaled to cause collapse, a number of after-effects may develop; and Meigs and Hughes[3] have lately analysed the different effects of mild, moderate, and severe poisoning in an attempt to find which signs are of prognostic value. They confirmed the observation that mental relapse after apparent recovery is of serious significance. In severe poisoning the commonest findings were abnormalities of the nervous system, lungs, and skin, excessive sweating, a palpable liver, pyrexia, a tendency to bleed, a high white-cell count, and albuminuria. In the human central nervous system oxygen lack seems to damage the globus pallidus most readily.[2] Clinical and experimental evidence has not yet identified the exact function of the globus, though it is known to be concerned in the smooth and coördinated movement of voluntary muscles: hence, perhaps, the frequency of spasticity and tremor in carbon monoxide poisoning. Cerebral cortical damage and profound demyelination are also seen at necropsy, and they are probably due to

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1. Haldane, J. S. *J. Physiol.* 1895, 18, 430.
2. Lilienthal, J. L. *Pharmacol. Rev.* 1950, 2, 324.
3. Meigs, J. W., Hughes, J. P. W. *Amer. J. industr. Hyg.* 1952, 6, 344.

Letters to the Editor

POLIOMYELITIS

SIR,—Your leading article of Jan 10 is surely unfortunate In it long-tried orthopædic principles are rejected, although no new information is produced in favour of such rejection, and in addition there are a number of confusing contradictions

Thus we read, without any evidence being adduced in support of this reversal of established principles, that "in the care of muscles and joints no rigid splinting, plaster casts, or orthopædic frames should be applied even in the acute stage", instead, "passive movements and maintenance of a neutral position by simple means, such as sandbags, footboards, and pillows are the best remedies" It is also stated that "trick movements should not be discouraged" although four lines above is the recommendation that "the *patient should* be spending most of the day exercising the weak muscles and not the strong" During the period of active treatment trick movements offend not only, as you say, the "well-trained" physiotherapist but also anyone familar with the consequences of early subordination of the weakest to the strongest muscles—which subordination is unavoidable in performing trick movements

You give as fact that deliberately induced fatigue does not harm the paretic muscles and that immediate active vigorous exercise to the point of fatigue will give maximal muscle recovery in a matter of weeks rather than months or years, adducing the testimony of Mead[1] (in fact wrongly) and Ritchie Russell[2] *in support of your views* and saying that Ritchie Russell has failed to confirm that deliberately induced fatigue harms the muscle But if we are to judge from the chart which Ritchie Russell uses to illustrate this statement in his book *Poliomyelitis* we are forced to the opposite conclusion We see that the greatest progress made by the patient took place in the first three weeks, when only "ordinary physiotherapy" was given, and that during the subsequent three weeks, when contractions to the point of fatigue were performed hourly for twelve hours every day, there was no progress at all, when, however, the frequency of these repeated fatiguing exercises was reduced to only *four days in every seven improvement re started, though* not at the rate of the first three weeks One might add that we are accustomed to expect more of treatment than that claimed here—namely, that it "does no harm" In fact a more extensive investigation was carried out by Green[3] on two hundred patients divided into three groups He showed that the most constant improvement was obtained by the group of patients kept most at rest, the least by those having most exercise, and an intermediate result by the intermediate group This corresponds better with our knowledge of training of normal muscle in the laboratory and in athletics

It is not my purpose, however, to discuss here the merits or failings of different methods used to improve muscle power, but only to object to the way in which problems still under investigation are presented in your leader as solved Above all, one must deplore the way in which the subject is presented, an example is the statement that "even the severely paralysed should be walking or in a wheeled chair and ready to go home 5–8 *months from onset*" *In such a variable disease as* poliomyelitis the claim that a particular method of rehabilitation will give such rapid recovery as to allow even severely paralysed cases to be discharged from hospital within eight months of their attack may bring transient discredit to centres where some patients are, because of the particular severity and distribution of their paralysis, still struggling after more tha months to overcome their disabilities sufficiently to hospital Some of these patients will need re surgery—e g, tendon transplants and arthrod obtain the maximum use of the muscles which rem them Such a programme cannot possibly be s into the prescribed eight months

Further, I am convinced that if you atter prevent deformity by the methods you advise, a "alternate active movement and rest in the position," the results will not be dissimilar to tho such men as Robert Jones, Vittorio Putti, and Ridlon found thirty or forty years ago before it wa last recognised that a case of paralytic polio presented an orthopædic problem from the beg *It is surely only because in some countries* o Continent orthopædic treatment of poliomyelit not begin until deformity is established that man from abroad are now attending British orth hospitals It would seem paradoxical, to say the that when some of these Continental countr diligently starting to follow the British lead we revert to conditions which prevailed before the ti Robert Jones

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Oxford

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[1] Mead S *J Amer med Ass* 1950, 144 458
[2] Ritchie Russell W *Poliomyelitis* London 1952
[3] Green W *Amer J Dis Child* 1952 83 4

KWASHIORKOR

SIR,—*In your leading article of Nov* 29 you co on Kahn's request that the term "Kwashiorkor" be restricted to cases with pigmentary change note that "he seems to be in error (with C Williams)" But if you will refer to your is Nov 16, 1935, when the word kwashiorkor was printed,[1] you will see that there was no reference to literal interpretation of the word, nor was re described as necessary to, though it might be prese the condition It may well be that, as MacPherson s it applies rather to the mystique of the disease and to pigmentation

In your first paragraph you refer to the difficult comparing the disease as it appears to different ob in different countries I have now been able to see of this disease in the Gold Coast, Uganda, Ke Tanganyika, India, Ceylon, Malaya, Thailand, Bu Indonesia, Egypt, and Jamaica—though I have no course been able to make anything like detailed stud It seems to me that there is similarity, although there many degrees of it As you point out, there are as m variations as there are different possibilities in die patterns and accompanying infections and infestatio not to mention individual variations In a country Uganda, where the diet is remarkably standardi ed, disease is much more uniform than in a country Jamaica where there is a much larger variety of po bilities This disease varies greatly in appearan according to the various stages of its development

In recent years the enormous extent of the proble of child nutrition has begun to be recognised Th have been great advances in the investigation of t pathology of nutritional diseases, but little has b done towards their prevention

In England, and in the developed countries in gene the child health services have produced great impro ments The "underdeveloped" countries are tendi concentrate all their efforts on hospitals and dis control programmes These do not of themselves af the standard of living and of education of the pe who are most in need of help *The major cau* mortality and morbidity are not malaria, smallpox, cholera, nor are they surgical conditions They mainly malnutrition, worms, skin diseases, and ga enteritis, which are in fact due to dirt and ignora is work relates only to dead lungs under artificial itions, and in the living body other factors might into play. Nevertheless, these experiments have a iderable interest in relation to respiratory physiology pathology: and, perhaps more important, they rate once again the difficulty of applying simple ical concepts and measurements to biological erial. In any biological system so many influences ract with each other that it is often almost impossible eparate the effect of one of them for study. To call lungs elastic, however satisfactory in everyday versation, is clearly an over-simplification; and such -simplifications can be dangerous.

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[1] Williams C D *Lancet* 1935, ii 1151

TECHNIQUES OF VIRUS TYPING

HE merits of different animal sera in typing strains nfluenza virus have long been disputed. Workers in tralia, Holland, and this country have used mainly et sera; while in the U.S.A. rabbit, fowl, and ister sera have been preferred. With ferrets and isters the serum is taken after the animals have been cted with influenza virus, whereas the other sera obtained after immunisation. The argument has more than academic since epidemiological deducs based on results with ferret sera could not have made with, for example, fowl sera. Hitherto the ute has been mainly emotional with each laboratory ly to swear by its own results. Now Sampaio [1] has le a direct comparison between the different sera. chose four strains of influenza virus; one was a ntly isolated A-prime strain, and the others were, logically speaking, a brother, a first cousin, and a y-second cousin. With all the sera tested the distant tive was easily spotted; but the fine distinctions ween the near relations were detected with ferret l hamster sera only. Sampaio's work would appear settle the argument—though if hard facts were to le all arguments this would become a quieter and ler world.

ABSORBABLE GLOVE POWDER

SOME years ago it became clear that contamination of operation field by talcum powder from the surgeon's ves might give rise to serious after-effects.[2] In women clean" appendicectomy was occasionally followed by rility, owing to the reaction of the fallopian tubes to c granules picked up from the peritoneal cavity. perimentally talc applied to the peritoneum gave rise intraperitoneal adhesions and granulomata. Spilling talc glove powder in more superficial wounds also ve rise to non-healing granulomata. These findings l surgeons to wash their gloves in a sterile solution er putting them on, and to discard at once a glove with y defect that might allow powder to escape.

Since this danger was brought to light there has been a stained search for an absorbable substitute for talc a glove lubricant; and corn starch has been widely ed.[3] Lee and his colleagues [4] at Cincinnati suggest at the feeling of security with such powders has sulted in some carelessness on the part of surgeons. eing convinced that they now have a "fool-proof" owder, they no longer observe the precautions they ice did against wound and peritoneal contamination. this lack of caution justified? Lee and his co-workers ave carried out a series of experiments, similar to those hich proved the dangers of talc. From these they onclude that under ideal conditions starch powder is bsorbed without ill effect. Nevertheless, until it is bsorbed it is a foreign body and produces a foreign-body eaction in the tissues. The intensity, duration, and eversibility of this reaction is influenced by many ariables. Complete dispersal of the powder into individual granules is essential, and can be assured by admixture of the starch with either 2% magnesium oxide or 3% magnesium carbonate; the tissues tolerate these two dispersal agents equally well. "Tanning" of the starch with epichlorohydrin renders the starch granules resistant to autoclaving, but does not affect either the tissue tolerance or the absorbability of the starch as long as it is well dispersed in fine particles. "Clumps" of powder imbedded in tissue will produce more reaction and will be absorbed more slowly. The experiments by Lee et al. included heavy dusting of the bowel surfaces of animals with the starch powder; and even with such gross contamination the reaction was relatively slight. Infection of the operation area would, however, greatly increase the foreign body reaction, and might produce unabsorbable adhesions.

The conclusion is therefore that sterilisable starch approaches the ideal as a glove lubricant; that it must be combined with a suitable dispersal agent; and that the surgeon should adopt the simple precautions of washing his gloves just before approaching the operation field and of avoiding spilling deposits of powder through defects in the fingertips of his gloves.

ENZYMES AND TRACHEOTOMY

IT is not easy to maintain a clear airway in patients who have respiratory paralysis due to poliomyelitis or who are unconscious during the treatment of meningitis and head injuries. Repeated aspiration of the pharynx and postural drainage are usually effective for the first day or two, but small quantities of material from the pharynx inevitably find their way into the trachea. So long as the antibiotics are fully effective this is of no clinical significance; but when resistant organisms replace the normal flora of the nose and throat, infection spreads into the trachea.

Tracheotomy will prevent this complication, but it will not relieve it once the tracheal infection is established. The trachea and bronchi then become filled with exudate, and, unless free drainage is provided, death results from a combination of asphyxia and bronchopneumonia. The exudate is mucoid at first, becoming purulent and then mucoid again as the infection subsides. After tracheotomy it tends to dry into tenacious masses and crusts because it is exposed to air unmoistened by passage through nose and throat. Crusting can probably be prevented by providing a fine mist of water or saline for the patient to breathe, but the exudate is still sufficiently viscid to reduce the airway.

Enzymes will liquefy the exudate, and encouraging clinical results have been reported [1]; but they must be chosen carefully, for enzyme action is highly specific. Three constituents can be responsible for the viscidity of a tracheal or bronchial exudate: (*a*) a fibrous gel of mucoprotein during the early and the late stages of an infection; (*b*) fibres of deoxyribonucleoprotein when the infection is fully established and the exudate purulent; and (*c*) fibrin, which is particularly prominent in diphtheria. Simple cytochemical tests are available for the identification of these constituents; the enzyme should be selected accordingly and administered as an aerosol. A satisfactory fibrinolysin is available commercially, but pure deoxyribonuclease and specific mucinases are not. Crystalline deoxyribonuclease from ox pancreas is very effective in liquefying purulent exudates,[2] but the streptococcal nuclease accompanying streptokinase is rarely sufficiently concentrated for this purpose. Lyophilised crystalline trypsin acts rapidly on mucus in solution,[3] but only slowly on mucoprotein gel. Until more specific and pure mucinases and deoxyribonucleases become available commercially, lyophilised crystalline trypsin is probably the best enzyme to use.

Sampaio, A. A. C. *Bull. World Hlth Org.* 1952, 6, 467.
. See *Lancet*, 1947, ii, 430.
. See Graham, J. D. P., Jenkins, M. E. *Ibid.* 1952, i, 590.
. Lee, C. M. jun., Collins, W. T., Largen, T. L. *Surg. Gynec. Obstet.* 1952, 95, 725.

1. Steigman, A. J., Scott, C. H. *J. Amer. med. Ass.* 1952, 150, 1403.
2. Armstrong, J. B., White, J. C. *Lancet*, 1950, ii, 739.
3. Limber, C. R., Reiser, H. G., Roettig, L. C., Curtis, G. M. *J. Amer. med. Ass.* 1952, 149, 816.

faculty might wish to make from time to time The faculty has therefore appointed a committee composed of

Sir Harold Graham Hodgson, Middlesex Hospital (chairman), Dr Hugh Davies, National Hospital for Nervous Diseases, Prof A S Johnstone, Leeds General Infirmary, Dr J W McLaren, St Thomas's Hospital, Dr P H Whitaker, Liverpool United Hospitals, the president and hon secretary ex officio

This committee will study at regular intervals the problems arising out of the units system referred to them by the Ministry

In the light of experience, the faculty will doubtless have sufficient information to enable it to advise the Ministry on the desirability of retaining the scheme with appropriate modifications or replacing it by a more satisfactory scheme

Faculty of Radiologists,
45, Lincoln's Inn Fields,
London W C 2

PETER KERLEY
President
ROHAN WILLIAMS
Hon secretary

A HARLEQUIN COLOUR CHANGE IN THE NEWBORN

SIR,—We have been interested, since the publication of our article on this subject,[1] to receive letters from twelve mothers in various parts of this country, and one in the United States, describing the same colour change in their own babies, most of whom appear to have been normal mature infants That the condition is no new one is confirmed by the fact that one of the babies in question is now 52 years old and herself the mother of a healthy family

We have also heard from a man who is affected by what appears to be the same colour change at times, particularly during severe exertion in a hot climate

Children's Department,
Royal Victoria Infirmary,
Newcastle upon Tyne

G A NELIGAN
L B STRANG

LEG ULCERS

SIR,—The articles in your issue of Jan 3, concerning the stubborn gravitational ulcers around the malleoli, will not I think help us forward very far One is written to support Bauer's contention that ligature of the popliteal vein is a help, but too many have been disappointed with it The second method, of Mr Cockett and Mr Elgan Jones, attempts to do the same thing at a lower level, and this unfortunately involves an incision into the devitalised tissues of the ulcer-bearing area *This incision makes my flesh creep, for I remember* the struggles I have had with ulceration in this area in the scars that have followed operations on veins, injection necroses, excisions of indurated skin treated by Thiersch and even pedicle grafts, and Corlette's Λ shaped incision to stop pain These ulcers in surgical scars seem to be far more stubborn than those in the scars of previous ulcers The tissues of the lower part of the leg from marrow to skin are affected by the high venous pressure, and excisions of skin cannot reach healthy tissues, *so I feel strongly that the golden rule* of no incisions or excisions in this area must not be broken

I do not think that the inveteracy of recurrence of deep venous incompetency is fully realised A study of the excellent phlebograms in Cockett and Jones's paper shows vast venous pools left behind after dealing with the important perforating arteries, and these are bound to cause mischief later

The best explanation of all the phenomena of ulceration of the *leg is provided by* Morgan's theory that the high pressure in the veins opens the skin shunts and capillary circulation fails This explains why some ulcers recur immediately after healing and others may stay healed for years before recurring in exactly same form as previously The high venous p there all the time, but it does not always cause capillary circulation of the skin to fail and there is unknown conducive factor which comes into play

I still feel that the best way to treat these ulcers with elastic adhesive bandage and pads, co operation on the veins to those of the saphenous sy The troubles from deep incompetency are met by of various kinds to prevent œdema and recurrence

London, W 1 A DICKSON WRIGHT

PARTIAL THORACIC STOMACH IN CHILDH

SIR,—I was interested in the article by Dr Car his colleagues[1] on partial thoracic stomach in child Now that so much interest is being taken in this dis all pædiatricians will agree that it is relatively co At the same time I am struck by the larger numb infants with an apparently typical history of this dis who respond most dramatically to the upright po only In these infants a barium swallow shows n appearances, and in particular a normal angle of e of the œsophagus into the stomach with no re the head-down position

I would be most interested to hear if other have found the same, and if so what they regard a ætiology of these symptoms Is the vomiting in cases functional or is it due to a sliding hiatus he If the latter, one would have thought that the an entry might not be normal Should the *term* " cardia," which has now largely fallen into disrepute used to cover these cases?

Plymouth HUGH JOLLY

MITRAL STENOSIS

SIR,—Your annotation on mitral stenosis (Jan 1 deals with only certain aspects of controversial iss

Anatomical and physiological studies by my coll and myself[2] have demonstrated a good correla between the type and severity of symptoms on the o hand, and the severity of the mitral stenosis and pulmo vascular disease on the other Our evidence favour view that progressive valvular stenosis and progres clinical incapacity usually go together We do n concur with Brock that the stenotic mitral valve is al always the same size Mild and moderate stenos observed at necropsy or operation, was usually associ with mild to moderate symptoms We do agree, howev that major symptoms do not result until the valve 20% of normal, or 1 cm in area

While there are admittedly errors in its applicat the hydraulic formula for calculating mitral valve s defines the relationship between heart rate, blood fl and blood-pressure at the valve Variations in b state during cardiac catheterisation may well alter a or all of these factors, but their relation to one anot cannot be changed as this depends on the valve ar Errors in assessing clinical status by physiolog measurements can be avoided if this fixed relationship appreciated

A word of caution is necessary about apical systo murmurs These may be caused by tricuspid as well a mitral incompetence, and mitral incompetence ma exist without a murmur Furthermore, the massive l atrium is more often a sign of mitral incompetence th of stenosis[3], when it is present with mitral steno may well be the *result* rather than the cause of a relativ benign prolonged course Finally, tricuspid insufficie is associated with a " benign " course only in so far

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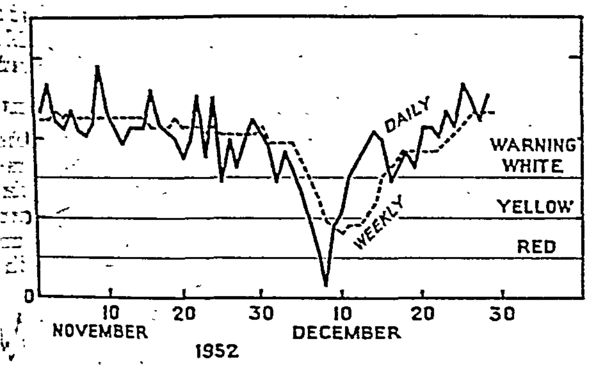
[1] *Lancet*, 1952, ii, 1005

[1] Carré, I J, Astley R Smellie, J M *Lancet* 1952, ii 115

[2] Gorlin R, Gorlin S G *Amer Heart J* 1951 41, 1 Gorlin, R Haynes, F W, Goodale, W T Sawyer C G, Dow J W Dexter L *Ibid*, p 30 Lewis, B M, Gorlin R Hou H E J, Haynes F W Dexter L *Ibid*, 1952 43, 2 *Ibid* p

[3] Gorlin, R Lewis B M, Haynes F W Dexter, L *Ibid* p



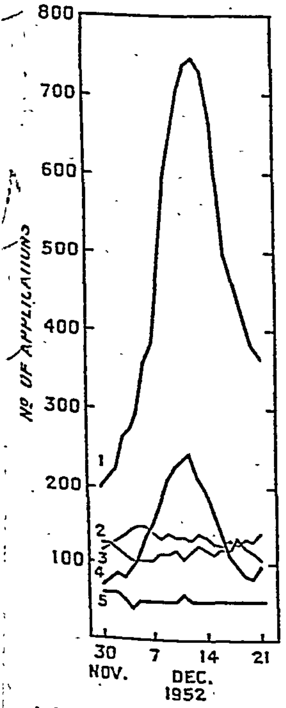
—Percentage of patients admitted to hospital in November and December, 1952, (a) daily and (b) by moving weekly totals.

ications rose very rapidly, reaching an unprecedented : on Dec. 9, when 492 were received. Applications inued in abnormally high but diminishing numbers l the 13th, after which a fairly stable state was hed (fig. 1).

a Dec. 1 the admission-rate was 88·5%, and in spite ncreasing pressure it was kept above 85% until lay, the 7th, when it fell to 84·9%; a "white" ning was issued at 11 A.M. next day (fig. 3). On sday, the 9th, the rate was 79·9%, and the "yellow" ning was issued. The response was such that, despite high total of applications, the admission-rate fell a further 1·5%. The "yellow" warning was cancelled on the 15th, and the "white" on the 17th.

Prior to these warnings the admission-rate had been maintained above 85% by the action of the regional medical admission officers, who freely used the power to refer any given case to the group medical referee for immediate admission. This must have been a very severe burden on the regional-board hospitals.

It is interesting to note that, whereas on Jan. 1, 1951, at the height of the influenza epidemic, 293 applications were received by the E.B.S. and 185 cases were admitted, on Dec. 9, 1952, at the height of the fog "plague," 492 applications were received and 390 cases were admitted. The highest weekly total of admissions previously recorded was 1169 on Jan. 2, 1951; but in the week ended Dec. 13, 1952, 2019 cases were admitted.



: 4—Weekly totals of applications n December, 1952, by types of lisease. (1) Respiratory disorders. (4) Cardiac disorders. (3) Other acute medical disorders. (2) Acute surgical disorders. (5) Cerebral hæmorrhage.

TYPE OF ILLNESS

The increase in sickness was due almost ntirely to respiratory disease, which was nearly quadrupled (fig. 4). The rise in heart-disease to about three mes the normal numbers, though less spectacular, should ot be overlooked. As in the winter of 1951–52,[1] the increase in sickness was almost exclusively confined to the over-45 and under-5 age-groups.

CONCLUSION

The warning system appears to be satisfactory, and the magnificent response by the hospitals undoubtedly saved the day.

EFFECTS OF A SEVERE FOG ON A GENERAL PRACTICE

JOHN FRY
M.B. Lond., F.R.C.S.
GENERAL PRACTITIONER, BECKENHAM, KENT

THIS is a report on the effects of a severe fog on a general practice of 4500 patients in the south-eastern outskirts of London. The fog reduced visibility at times to nil, and persisted for five days from Dec. 5 to 9, 1952. It was preceded and accompanied by intense cold; illness was widespread, and there was an increase in the number of deaths. In the week ending Dec. 13 there were 4703 deaths in Greater London, compared with 1852 in the corresponding week of 1951; and during the same week the Emergency Bed Service dealt with 2007 hospital admissions, compared with 917 in 1951.

VOLUME OF WORK

There was a remarkable increase in the work of the practice during the period of the fog and the following two weeks. This was largely accounted for by the increased number of visits that were necessary. The normal average number of weekly visits for this time of year is 75; during the week of the fog the number rose to 125. The number of attendances in the surgery did not vary from the anticipated average, which is 250 consultations per week.

TYPE OF WORK

There was a considerable increase in the prevalence of two conditions—namely, the upper respiratory tract affections and the respiratory disorders. The former included all coughs and colds with no abnormal chest signs and with relatively little constitutional upset; "respiratory disorders" means all conditions with symptoms referrable to the lungs and where abnormal signs were detected.

Table I shows clearly this rise during the period of the fog compared with the number of attendances for the preceding three weeks. Of course, these figures give no idea of the total number of people affected by the fog, for very many did not seek medical advice.

Upper Respiratory Tract Affections

Between Dec. 1 and 22 201 people sought medical advice for symptoms referrable to the upper respiratory tract. The chief complaint was a very irritating cough, with little sputum; what sputum there was was black or grey mucoid material. Nasal discharge and sore throat were the other prominent symptoms. All ages were affected, but there was a high proportion of patients in the 40–50 age-group. No abnormal signs were detected in the chests of these patients.

TABLE I—ATTENDANCES FOR UPPER RESPIRATORY TRACT AFFECTIONS AND FOR RESPIRATORY DISORDERS

Week	Nov. 10–16	Nov. 17–23	Nov. 24–30	Dec. 1–7	Dec. 8–14	Dec. 15–21
No. of attendances for upper respiratory tract affections ..	36	48	47	68	94	75
No. of attendances for respiratory disorders	19	29	30	51	93	62

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1. See Abercrombie, G. F. *Lancet*, 1951, ii, 1175.

welfare service for children provided in temporary premises such as church halls Fortunately this decision has, I understand, been reversed

The extracts in last week's issue from the report by the medical officer of health for Glasgow is a welcome warning, indeed Dr George and his colleagues stress the need to maintain the welfare centre distinct from the doctor's surgery

Dr Tabbush in his stimulating letter last week misses a very important point—the time factor With many general practitioners it is the lack of time which makes it impossible for them to give satisfactory preventive and supervisory medical care Linked with the higher capitation fee which he suggests for children under 5 there should be a reduction in the list of the doctor wishing to work in clinics, this would then give the general practitioner the right to work in a local-authority clinic if he wished The same principle could be applied to those wishing to undertake obstetrics

By the courtesy of the medical officer of health I have at present the opportunity of seeing some of my antenatal patients at the local welfare centre with the midwife present and the health visitor available if required, and I find this a great advantage I should welcome the same opportunity to work in a child-welfare clinic, but would have great difficulty in finding time unless I curtailed my general-practice work

Let us hope that the useful analysis, by Dr George and his colleagues, of child-welfare clinic work will be followed by a similar analysis of the work of the school medical clinics

Many of the problems we are attempting to solve today without health centres will be more easily dealt with when we have them, meanwhile let us ensure that the concrete buildings of the local authority clinics are not swept away, whatever sweeping changes may take place within their walls

Birmingham M BARROW

AUGMENTED RESPIRATION

SIR,—There are two points in the article by Dr Donald and Dr Lord (Jan 3) on which I would like to take issue with them

In the first place the persistent failure of less ingenious methods raises doubts as to whether artificial respiration, however effected, can modify the physical state of the atelectatic lung in the newborn, beyond just overdistending the alveolar ducts [1] [2] Some hold that the cause of the atelectasis in many cases is alveolar cohesion from delayed absorption and progressive desiccation of normally aspired amniotic fluid, and if this supposition is correct the value of enforced respiration in increasing oxygenation might be offset by its action in accelerating this process The view of Dr Donald and Dr Lord that the atelectasis at autopsy in their cases is unrelated to the antemortem state cannot be accepted, for in similar cases there is often persistent aeration of the upper and right middle lobes after death

Secondly I would question that clinical spirometry, as described, is of value as a diagnostic aid The authors do not state how they calibrated their apparatus or what the margin of error was with varying speeds and tidal volumes with and without leaks Furthermore in my own experience the range of minute volume in newborn infants, both normal and with respiratory distress, is so considerable, especially if crying periods are included, that it is valueless to accept and compare readings unless they have been obtained under well standardised basal conditions

Department of Obstetrics,
Harvard University,
Boston Massachusetts

DONOUGH O'BRIEN

HOSPITAL COSTS

SIR,—Consideration is now being given to the proposals of the Nuffield Trust and the King's The general idea seems to be that comparison mental costs in different hospitals may lead to and, as regards money, this may be true

But I believe that comparison must be betw things which are generally equal and differ only or two significant factors In the kind of (mental deficiency) in which I am interested, any functional units, whether departments or ward differ in as many as seven important aspects wh directly affect cost True conclusions are unlik such variable conditions

A particular fallacy is the assumption that is equal in the two units under comparison The of a unit, or the happiness of the patients or or the progress of the patients, or the satisfactio to their relatives, cannot be measured, and the unit is not necessarily as good as the more exp any of these respects The opposite is also tr more expensive is not necessarily better than the

These imponderables cannot be given money and, from the medical and nursing point of view cannot be the only criterion of economy in essentially a human activity Doctors must alw apprehensive lest the proposed costing system lead imposition of false standards in the care and tr of patients

The report of the King's Fund shows some aw of this point of view but does not really m difficulty

St Albans, Herts NOEL H M B

ANTRODUODENECTOMY AND X-RAY IRRADIATION FOR DUODENAL ULCER

SIR,—Mr Grayton Brown and his colleagues to treat duodenal ulcer by X-ray irradiation al September, 1949, following the lead of Walter P and his colleagues of Chicago [3]

The other references given in the article do not one to the work of Dr Anthony Bassler, of New City, who forty or more years ago treated peptic by X-ray irradiation Dr Martin Rehfuss extensively to Dr Bassler's work [4] [5] in his book *Diseases of the Stomach* (1927) In June, 1951, B spoke before the American Therapeutic Society X-ray therapy in peptic ulcer [6]

Incidentally, mention might be made here of Benjamin Brodie's vagotomised dogs, in 1814, 140 years ago, it was found that vagotomy was follo by a prompt decrease of acid gastric juice [7]

Camden,
New Jersey, U S A

HYMAN I GOLDST

GONORRHŒA IN ANCIENT ROME

SIR,—I am obliged to Dr Geiringer for his letter this subject (Jan 17) He has given three citations, f the Bible, from Celsus, and from Juvenal I do not any reference to gonorrhœa in the Biblical ch dealing with the sanitary precautions and purifica connected with septic discharges, seminal emi and the menstrual flux, nor in Celsus's description paraphimosis, ulcers, growths and gangrene of the p and although tradition takes the same view Dr Geiringer, I believe it is wrong The supp

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1 Day R Goodfellow A M, Apgar, V, Beck, G J *Pediatrics* 1952 10 593
2 Potter E L Pathology of the Fetus and the Newborn Chicago and London 1952 p 250

1 See *Lancet*, 1952 ii 1067
2 Brown G Scott R K, Holman W P, Wood, I J E S, Weiden, S Davis, P *Ibid* p 1145
3 Ricketts W E, Palmer W L, Kirsner, J B, Hamm *Gastroenterology* 1949 11, 789
4 Bassler A *Medical Times N Y* 1909, 27, 259
5 Bassler, A Diseases of the Stomach and Upper Alime Tract 1910, p 672
6 *Rev Gastroent* 1952 19, 967
7 Goldstein, H. I *Ibid*, 1949, 16, 85

Special Articles

CONSULTATION AND CONTROL

THE MINISTRY'S ASSURANCES

Jan. 6 the members of the Joint Consultants Com- ee met Sir John Hawton and other officers of the stry of Health.

r Russell Brain, chairman of the committee, said the profession was extremely disturbed by recent its which seemed to point to an unwillingness on the of the Ministry to consult the Joint Committee or to keep it informed on matters in which it was lly interested, and on which its advice would be of greatest help to the Ministry. There also appeared e a growing belief on the part of the Ministry that the pital and consultant services should, and could, be rolled in detail from the centre.

eferring to the recent circular letter to boards of ernors of teaching hospitals, concerning medical blishments, Sir Russell reminded the Ministry that undertaking had been given that the results of the ical staffing survey undertaken by inspecting teams ld be discussed with the Joint Committee in general as before any decisions were taken. Although the ter was one which profoundly affected consultants, undertaking had not been fulfilled. On the contrary communication to boards of governors had been owed—again without the knowledge of the Joint mittee—by the recent circular to hospital boards and [illegible]: a 5% reduction in certain categories [illegible], [illegible]ezing the establishment of medical f and prohibiting any expansion except with the sent of the Minister. While medical staffs were luded from the 5% reduction, an examination of the ommendations of the inspecting teams revealed that ut into effect they would achieve almost exactly a reduction in the consultant establishment of teaching pitals. If the inspecting teams' recommendations olved a similar reduction in the case of regional rd hospitals it would mean the termination of the tracts of some 300 part-time consultants. It was e that the matter had not gone beyond the stage of ommendations; nevertheless it was difficult to avoid assumption that the recommendations indicated the nistry's intentions. Moreover, the Ministry's instruc- ns on economy in staffing made no distinction between spitals which were economically planned and those ich were not, and Sir Russell wondered what could be re discouraging to a conscientious hospital authority. e Ministry's attention was also drawn to the damaging ect of the recent instructions on the problem of sorbing the surplus of senior registrars.

Sir Russell Brain pointed out that further evidence of reased centralisation was to be found in the recent structions for statistical recording of the work of thological and radiodiagnostic departments. The easures suggested were open to serious criticism, and ere was a very real danger of over-standardisation. part from the fact that these instructions involved an borate recording system which would require addi- onal clerical assistance, they implied a belief that the ork of these departments could be assessed in terms of atistics and ignored the human element of its value the community.

He reminded the Ministry that the Joint Committee ad repeatedly urged the need for consultation with the rofession at all levels in the service. The committee, ad consultants generally, were very willing to help the inistry, but could not do so unless they felt that they ad the Ministry's confidence. Unfortunately, on a umber of occasions the committee had been placed in n invidious position. It had either had to explain to the profession that it had no prior knowledge of the Ministry's intentions in a particular matter, or to remain silent and appear to consent to something it felt it should criticise.

In reply, Sir John Hawton said that, although he readily admitted that there had been occasional failures on the part of the Ministry to consult the Joint Committee, these were lapses in performance rather than in intention. The Ministry from the outset of the service had always been anxious to consult with all the bodies concerned with hospital policy. They had no wish to depart from this position.

Dealing with the communication to boards of governors on medical staffing, Sir John agreed that it would have been better if the Joint Committee had been consulted, but the failure to do so was an error, and not an intentional one. He wished however to correct any mistaken impressions on the matter. The proposals that had been sent to the teaching hospitals were simply those of the inspecting teams. They were not the conclusions reached by the Ministry itself, nor was there any intention on the part of the Ministry to impose them on the boards. It was open to each hospital, and particularly to its medical staff committee, to look freely at them and interpret them in the light of their local knowledge. The Ministry was only too anxious to have the views of the hospitals themselves.

Referring to Sir Russell Brain's comment on a possible reduction of medical staff arising out of the staffing survey, Sir John said that similarity with the 5% reduction called for in the other grades of hospital staff was purely coincidental. There was no intention of imposing a 5% cut on medical staffs, and the Ministry had at the moment reached no conclusions.

Regarding other lapses in consultation, he hoped that the committee would appreciate that on occasion it was necessary for the department to announce an important item of Government policy without prior consultation with the profession, but fortunately this would be a rare occurrence and did not affect the general position. He added that there was no desire for increasing centralisation, and if centralisation had increased since the service began it was due not to any desire for it for its own sake but to the need for an over-all control of hospital expenditure, for which the Minister was responsible to Parliament.

Sir John Hawton stated that the Ministry was in full agreement with the Joint Committee on the need for effective consultation. He did not think this need could be formalised; it was rather a matter of the two sides keeping in close touch with one another. He gave an assurance that the Ministry, for its part, would do all in its power to provide effective consultation with the Joint Committee on all matters affecting consultants in the hospital service. The Joint Committee need be in no doubt as to the Ministry's recognition of the committee as the body speaking for consultants and members of hospital staffs, and of its very real desire to coöperate with the Ministry for the good of the service.

COLLEGE OF GENERAL PRACTITIONERS

The new college has issued a statement on some aspects of its work, inviting suggestions and help from practitioners.

Teaching of General Practice.—One of the objects of the college is to assist in the training of final-year students (and those newly qualified) in the principles and technique of general practice. It is already in touch with many medical schools that have started schemes by which young men and women get their first introduction to general practice by attending the surgeries, rounds, or lectures of general practitioners of experience; and information is being collected about these methods.

committee was able to advise the industry as to which *oils were relatively safe and which were unsafe*

The Local Government Act of 1929 gave further scope to Dr Veitch Clark's administrative ability This Act transferred to the city the functions of the former board of guardians In consequence, the public-health service was expanded to include a general hospital and pathological service, district medical and public vaccination services, and the work of infant life protection Dr Veitch Clark tackled vigorously the reorganisation of the former poor-law infirmaries, which speedily became active and first-class general hospitals The number of beds under his care rose from 1000 to 8000, and he gladly accepted the consequent administrative responsibility for a proper visiting consultant service, and for recording hospital statistics The Act also required the local authority to consult with representatives of the voluntary hospitals to avoid wastage of beds in municipal hospitals and shortage in others The success of the consultations led Dr Veitch Clark to propose that a permanent body should be set up, and in 1935 the Joint Hospitals Advisory Board was formed

He also welcomed the passing of the Housing Act, 1930, and his slum-clearance campaign, which removed from the city several bad areas of slum houses, was only interrupted by the outbreak of war in 1939 He was a man of strong character, and by example he inspired his staff to keenness and efficiency His readiness at all times to help and encourage his junior colleagues won their respect and affection

He served as president of the Society of Medical Officers of Health for the year 1934–35 and he was appointed honorary physician to the King in 1941 The following year he retired from his official duties, but only to continue to work as a senior hospital officer of the Ministry of Health Later he settled in the border country and made his home at Peebles

His wife died some years ago, but he is survived by a son and a daughter

THOMAS SHIRLEY HELE

O B E, M A, M D Camb, F R C P, D P H

Dr Hele, a former vice-chancellor of the University of Cambridge and master of Emmanuel College, died on Jan 23 at the age of 71

He was born at Carlisle and educated at Carlisle Grammar School and Sedbergh Though he came of Devon stock he appreciated the kindly severity of his northern upbringing, and he often recalled with affection and respect the rigours of his schooldays In 1899 he went up to Emmanuel College, Cambridge, where he took firsts in both parts of the natural sciences tripos, and in 1903 he took his London B SC with honours in physiology Meanwhile, with a Shuter scholarship, he had entered St Bartholomew's Hospital, where he qualified in 1906, taking his M B Camb the following year With a B M A research studentship he worked with Archibald Garrod on diseases of metabolism, and in 1909 he published a paper on cystinuria in the *Journal of Physiology* While still undecided whether to choose a career in clinical medicine or in research he took the D P H, and he also held house-appointments at Barts and at the Royal Infirmary Bristol Thus when in 1911, his college offered him a fellowship and he finally decided to choose research he approached his work in the laboratory with a wide experience of bedside and preventive medicine

His work at Cambridge was interrupted by the 1914-18 war when he served with the R A M C in Salonika Here his public-health experience proved valuable, and he used to describe his war-time post as that of professor of nuisances In 1919 he returned to his more formal academic activities at Cambridge, and in 1921 he was appointed university lecturer in biochemistry and in 1922 tutor of his college The burden of these administrative posts deflected him from research work he had begun with Gowland Hopkins Later he added to them the secretaryship of the faculty board of medicine and membership of the General Medical Council In 1935 he was appointed master of his college, and from 1943 to 1945 he served as vice-chancellor of the university In 1940 he was elected F R C P

Although Dr Hele filled high academic offices for many years he was no lover of formal occasions He could bear with a modicum of traditional cer
but he was sensitive to the slightest suggestion of
Not the least valuable quality he brought to
was his accessibility Every undergraduate kn
whenever he approached Dr Hele he could
a sympathetic hearing and good advice, but
talent for helping a man to reach a decision was
by his firmness in refusing to make another's
for him He liked to affect a general nescience
details of business on hand, but discussion
revealed that he had a firm grip of the matter
kindliness and simplicity, however, were at once
and they were unchanging

Dr Hele married in 1914 Audrey Muriel, d
of Mr John Hill, who died in 1941 His second
Audrey Louise, widow of Mr F M Davis, surviv
with two daughters of his first marriage One of
Dr Mary Hele, is a member of the staff of the
Research Council

MONTAGUE HENRY KNAPP

M R C S

Surgeon Captain Knapp, who died on Oct 13,
age of 84, played a big part in obtaining recog
and employment as trained male nurses for men of
sick-berth branch on their retirement from the
Navy after twelve or twenty years' service It
largely due to his efforts that the Nursing Act
reopened the list—closed in 1925—to Naval p
then qualified to register as State-registered nurs
Act also provided that sick-berth ratings with
qualifications were to be recognised as "Service-
male nurses," and could call themselves "nurse
practise as such, although not registered as S R

The son of Lieut Colonel Charles B Knapp, he recei
medical education at Queen's College, Cork, and St
Hospital, London, where he qualified in 1892 Two year
he joined the Royal Naval Medical Service Before he
in 1921 he had held such varied appointments as
officer in the training ships *Lion* and *St Vincent*, and
medical officer at the R N. Hospital School at Greenw
a plague camp at Bombay, and at Admiralty recruiting
quarters *He held the Order of Liakat of Turkey* and
knight of the Order of St John After his retirem
honorary appointments included the directorship of
Naval medicine section of the Imperial War Museum, the
manship of the Lord Chancellor's Pensions Appeal Tri
and the vice presidency of the Medico Legal Society
his main interest, of course, remained the R N Sick
Staffs Associations, and for many years he was the
chairman of the executive committee of the central
of the associations

J F H writes "It was Surgeon Captain Knapp's
tention that men of the sick berth staff who by tra
service, experience, and examination had attained the ra
sick berth petty officer should automatically qualify
admission to the State Register of Nurses He long reg
having been unable to ensure this deserved right for
officers of the sick berth branch, and he felt strongly
the want of timeous senior official support, and the agree
with the other Services and acceptance of the lower level
'Service trained male nurse' for fully and partly tra
Naval nursing personnel alike But many who served d
the late war, and became recognised as 'Service trained
nurses,' were with this status enabled to attain Regi
status the long way For most of us that might seem ach
ment enough in the higher octave of life, but it never sat
Surgeon Captain Knapp"

Births, Marriages, and Deaths

BIRTHS

CRAIG—On Jan 23, at the Bristol Maternity Hospital to
Jean Craig (née Simpson), wife of Dr R A Craig—a son.

HEATHFIELD—On Jan 13, at Chigwell, to Dorothy, wife of
K W G Heathfield, M R.C.P—a daughter (Angela)

PORRITT—On Jan 19 at 31, Queen's Gate, London, to Kay,
of Sir Arthur Porritt, K C M G—a son

MARRIAGES

LOVIBOND—CAREW JONES—On Dec 12, in London John L
Lovibond T D M D M R.C P, to Mary Carew Jones

rouses in us secret sympathies; for here is the ade, the lame god, our shadow self, the dark and knowledged side of brindled human nature. Here od so close to us that even the shallowest modern still ; his bold licentious whispers, yet so remote in origin without experience of him Man would not be Man.

der than all these are the dim unfocusable forms that ng "like pageantry of mist on an autumnal stream" nd the enigmatic figure of young *Jimpy*. These dim es are indeed the early gods, older far than "the ht static hierarchy of Olympus," older perhaps than e itself. They reach back, these primal figures, to e fluid ever-changing changeless archetypes that m and glow in the depths of the archaic psyche. edibly, *Daily Mirror* Jimpy is of their company. nally childlike, vague of parentage, he displays startling fidelity the weakness and insignificance bined with mysterious power possessed by the dawn- ge of god in the human mind. At one point in the e an adult character says to him, "Is it true, then, must always remain a boy?" It would be hard to se a clearer modern evocation of the Puer Æternus. ss, indeed, Barrie's sentimental and emasculate ion is adduced.

erhaps the key to the whole mystery of the comic 's compulsive force lies in this Jimpian paradox of kness and smallness combined with magical, boundless er. For paradox itself, that disquieting insult to ived opinion, is usually a pointer to the heart of gs. The approaches to wisdom are paved with kly paradox; hard going for bare rational feet.

Smaller than small, yet bigger than big." In these arently senseless words are expressed the earliest epts of the divine in the history of the human mind: Little Copper Man, for instance, of the Finnish *evala*, "no bigger than a thumb and no higher than x-hoof," who yet could fell the giant oak tree that ered the sun and moon with its branches; or *ayana*, the little Hindu boy asleep in the nyagrodha , in whose belly lay "the whole world with its lands cities, with the Ganges and the other rivers and the ." In widely differing cultures the same paradoxical kness-and-strength is visualised: in David with sling, Hercules strangling serpents in his cradle, Eros ed with fatal arrows, and—little Jimpy, deferential dults but gifted with his magic powers.

THE RETURN OF THE GODS

here is, of course, something both offensive and rageous in these parallels of the sublime with the enerate-ridiculous. The association is lunatic and the ional mind recoils from it at first in repulsion and gust. The rational mind should calm itself. There ve been in myth and legend many such divine *boule- sements*: as of Jove, lord of an antique heaven, indling down to bottle-nosed Father Christmas among kitchen pots and pans—though later, it is true, omoted to reindeers and a fur coat. That these cheap d paltry images in the corner of a popular newspaper ould have spiritual significance is painful to contem- ate. And yet, if accepted, it emerges as but one more istration of a phenomenon to which, perhaps the iverse is subject: *enantiodromia*, the incessant inevit- le turning of all things into their opposites. Heraclitus, Jung points out, was first of European minds to press this concept philosophically, but its parentage far more ancient. The *tegitu*, Chinese symbol of guessed age, conveys the same concept with incom- rable wholeness and precision. A white fish with a seed blackness at its centre curves into a black fish with a ed of whiteness, to form a perfect circle; each fish anges eternally into its opposite. What was important rried within itself the seed of its own destruction, and slowly emptied of meaning; what was derided carried orgotten truth, and leads to a new valuation.

Seen by this light, the values we now neglect, the stone which the builders have rejected, should be looked for in some such unexpected corner of daily life. It is a measure of our neglect that these values are forced to put on so mean a mask in order to re-enter human consciousness. The comic strip by its pathos and infantilism, by the derision it arouses, by its astonishing universality of appeal and crude vitality, fulfills the historic conditions for "the return of the repressed." The comic strip is in fact a ludicrous but valid symptom of our disease. For in one form and another "the return of the repressed" is precisely what is making the present century rock and quiver with premonitions of eruption.

Unpalatable though it may be to modern taste, the truth is that we cannot live without the early gods. It was said of Nature that even if you throw her out with a pitchfork she nevertheless comes back. So do the gods. If cast out in the forms of Man's profoundest apprehensions of them—if Christ and Buddha and Mithra, if Ashtaroth and Pan, are disowned—they nevertheless come back. However meanly and unrecognisably, they come back to the human heart whose inevictable tenants they are. And "there all smothered up in shade" they sit, radiating that strange compelling power which is Man's unconscious tribute to the Unknowable. In the comic strip may lie concealed the indestructible germ of natural religion.

Parliament

Grants to Marriage Guidance Organisations

In the House of Lords on Jan. 21, Lord MERTHYR, chairman of the National Marriage Guidance Council, deplored the drastic reduction in Treasury assistance to these organisations. The figures for divorce had now settled down from the peak reached in 1947 to a steady 30,000 a year, which was four times the figure for 1939. He believed that for every divorce case there was on the average a little more than one child involved. And this took no account of unhappy marriages which did not result in divorce. In his view delinquency could be unerringly traced back to broken homes and unhappy marriages. To say that it might prove cheaper to tackle delinquency early might be a platitude, but it was none the less true.

Marriage guidance, he continued, was a new thing, and the Treasury grants had been largely spent on the training of marriage guidance counsellors who gave their services without pay. A year ago these grants were suddenly cut by half and this had dislocated the work. Lord Merthyr estimated that under the scheme for legal aid some £1,200,000 a year was spent on matrimonial cases, yet grants for marriage guidance had been cut from £12,000 to £6000 a year. So we are spending two hundred times as much helping people to get divorce as on trying to guide them away from it.

Lord LLOYD, who replied to the debate, said though marriages were made in Heaven they had to be lived on earth Housing difficulties today led to many broken marriages. But even so we must ask ourselves whether the institution of marriage was still anchored by an effective public opinion. If it was not, how was that effective public opinion to be built up again? We would deceive ourselves if we imagined that this terrible problem could be overcome merely by an expansion of marriage guidance councils; something more was needed. But he agreed that the Government, and everyone else, should do everything possible to arrest this lamentable trend.

On the face of it, he admitted, it was unfortunate that as a nation we should spend so much money helping people to break up their marriages, and so little trying to stop them getting divorced. But if the principle of legal aid was accepted we could not say "you may have aid for this kind of case, but not for that." He hoped that in time the amount spent on matrimonial cases would be reduced. The present spate of divorce, he believed, was largely due to an accumulation of marriages which were already broken but which had not been order to meet them Dr Palmer evidently feels that psychiatrists are shaky in their grasp of symbols and meaning, for he proposes that they should receive a training in philosophy, "so that the intended meaning of terms used by them shall be stipulated, and the esotericism and the ambiguities of syntax so characteristic of their specialty shall be reduced to a *minimum* Only by so doing can the discussions of psychiatrists become communicable and discussable" While many will approve his aim, not all will agree that a course in philosophy is the only—or indeed the best—way of learning to use language without ambiguity

FILM OF THE BLOOD-FLUKE

IN the *Human Blood fluke* the staff of the Wellcome Research Institution has produced a colour film of the first quality This is in two sections the first deals with the life history of the human schistosomes in general, and the second with methods used in chemotherapy The film, which runs for about 40 minutes, has the advantage of having been taken by a great expert in colour photography and also of being provided with a sound track from which emanates an admirably clear, concise, and intelligible running commentary This demonstrates clearly how well suited a film of this nature is to students and research-workers alike Brigadier J S K Boyd, F R S, who introduced the film when it was shown in London on Jan 22, paid tribute to O D Standen, the director, Miss Florence Anthony, the producer, and Douglas Fisher, the photographer

The scheme which this film illustrates was commenced six years ago in an endeavour to infect water snails in the laboratory with blood flukes and eventually to produce active therapeutic agents and efficient molluscacides This entailed devising many novel techniques, both in rearing and maintaining colonies of freshwater snails in the laboratory, and in infecting laboratory animals with the schistosomes The film ranges over every aspect of this subject The species of schistosome selected was *Schistosoma mansoni*, which can readily be maintained in white mice, though golden hamsters and macaque monkeys are also very susceptible A survey made of the two other species of human schistosomes is also given, and there are pictures of their eggs and their snail hosts, as well as maps of their respective geographical distributions, from which it appears that about a hundred million people in the world are infected with schistosomes of one kind or another There are scenes showing absence of sanitation and the background of schistosomiasis in the Nile Valley, and the propaganda methods which have been devised to combat it The life history of the parasite in the human body is illustrated by actual photographs and by diagrams Egg deposition in the mesenteric veins by the female fluke, and the by passing of some ova which are then swept back past her head to be deposited in the liver, are excellently shown There are pictures of the live adult schistosomes moving up and down the blood vessels Then comes the deposition of the egg and the hatching of the miracidia, which dart around like some miniature meteors, and, more miraculous still, the miracidial bombardment of the antennæ of the snail which frantically attempts, by waving them about, to ward off their ferocious onslaughts, and finally development within the snail's liver (shown diagrammatically) and the clandestine and dramatic escape of the cercariæ in showering shoals from the snail host into the surrounding water Their free life lasts only 48 hours, but the pictures show that they make the most of it Next there is the dramatic penetration of the cercariæ through the skin and the shedding, in most instances, of the tail, invasion of lymphatic vessels, and ultimate arrival in the left subclavian vein and right side of the heart The journey is once more traced to the portal vein, where the schistosomulæ become mature and recommence the cycle Fæces of infected white mice produce the best crop of miracidia when subjected to special concentration techniques which have been elaborated The snails are infected in special glass jars, allotting 15 miracidia to each mollusc *Australorbis glabratus* the South American species, is the most susceptible snail and thrives best in self contained and balanced aquaria They flourish on a specially compounded food which is made of gel, eggshells, milk powder, 'Bemax,' and calcium algenate Some 150 cercariæ are applied to each mouse, and the adult worms become mature in 50 days

The chemotherapy section is most instructive and illustrates a new squash technique by which adult flukes may be demonstrated and studied in the liver itself This is most important since it has been shown, with inadequate therapy by 'Nilodin' or the antimonials, that many flukes escape unscathed into the liver If not sufficiently damaged by the drug they soon recover there, illustrating the mechanism of relapse By these means it has been shown that the antimonial drugs are three times more active than nilodin The first specific effect of an antischistosome drug is seen on the female worm, which immediately relaxes her hold on the vessel wall and is swept back into the blood stream while her more robust mate hangs on for some time longer before going to his grave

Small wonder that enthusiasms are raised in parasitologists and clinicians alike by a beautiful practical demonstration such as this

FOOD AND THE CARDIOVASCULAR SYSTEM

THE American Heart Association includes among its many useful publications a booklet on diets,[1] which first sets out some principles for patients with heart disease or hypertension, and then gets down to business, describing in detail (and with recipes) diets for reducing, and low sodium diets An appendix gives the sodium content of common foods (including public water supplies) The principles are well set out, and of course apply universally, but the diets, unfortunately refer to American rather than British tables Still heartening for those who are overweight to find th ordinary intake might very well qualify, in Americ reducing diet for not everybody expects to get much more in a day than a pint of milk, 5–7 oz 3 or more servings of vegetables, three slices of bread, teaspoonfuls of butter, and four servings of fruit

But if we may be better placed than Americans for reducing we encounter far more obstacles than they do when attempting a diet severely restricted in sodium For them, such things as low sodium breads, salt free canned and frozen vegetables unsalted butter and cooking fats, and low sodium milk are to be had, it seems, for the asking The British hypertensive pursuing such rare game would probably starve before he had bagged his first breakfast Nevertheless, this is a highly informative booklet, full of facts and hints, most of which can be interpreted to apply in a general way to British feeding customs, and it is designed for the use of doctors as well as patients

MORE X-RAY FILM

Messrs Ilford Ltd announce the completion of new plants for the coating of X ray film and the manufacture of film base They say that the output of these plants will end the shortage of X-ray film in this country All X ray film base has hitherto been imported, largely from the United States, and its manufacture in large quantities at home will mean a considerable saving of dollars The film base is being made in a plant owned jointly by Ilford Ltd and BX Plastics Ltd

AN ITALIAN TOUR

AT the end of May last year 130 members of the International Hospital Federation visited hospitals and other medical institutions in the region of Milan, Bologna, Rome, and Genoa A report of this study tour has now been published, and copies may be had from Captain J E Stone, the secretary of the federation, 10, Old Jewry, London E C 2

University of Cambridge

The Nuffield Foundation has made a grant to the university of £8650 spread over five years, in support of work in experimental embryology under the direction of Prof J D Boy in the department of anatomy

University of Birmingham

On Dec 19 the following degrees were conferred

Ch M—M J Roper Hall

M B Ch B—Monica A Axson A G Clews Anthea M S Con Sylvia J Darke J A H Davies G F Devey, John Edging J E Evans, C R B Hooper, T H Howells R C B [illegible] A C Pelides A G Pitchford, E C Raybould, M B Skirro Jack Wassell

Faculty of Radiologists

At a recent examination for the fellowship the follow were successful

P M Davies, J D Dow, I R Dow I P G Hou[illegible] Boulay C J Hodson J F K Hutton, G M Sinclair C G Whiteside (radiodiagnosis), Robert Gibb and C L L (radiotherapy)

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[1] Food for Your Heart a manual for patient and phy The American Heart Association 44 East 23 Street York, 10, N Y 1952 Pp 48

In England Now

unning Commentary by Peripatetic Correspondents

IOSE who question the value of notifying infectious se have never squatted in general practice. To e of us who have, the half a crown for each notifica- represents a good return on 1½d. postage. There of course, a few finer points worth noticing. not make the common mistake of forgetting pneu- ia, which is surprisingly common if you only look it. And what about whooping-cough? It is notori- y difficult to diagnose, so who can blame you if you ake an ordinary catarrhal infection for it? Then, n, I found that I was seeing many cases of d. and v., ch I presumed were due to food-poisoning (notifiable). s I am now satisfied was an error, as the sanitary ector pointed out. He said that the M.O.H., worried the rising incidence of food-poisoning, was insisting each case be investigated and specimens sent to the The S.I. suggested, rather diffidently, that these s were really due to Sonne dysentery. I agreed him that they were certainly cases of dysentery ifiable). The M.O.H. is satisfied that his prompt on put an end to a disturbing increase in food- oning.

carlet fever has been a big disappointment. Taking rôle as a health educator seriously, I always pointed to the parents that the diagnosis had no serious ificance, the illness being only an ordinary sore at with spots. This proved difficult to reconcile the appearance at the house of a fumigating van harge of the sanitary inspector, who proceeded to up the sickroom and to carry on in a most alarming ner. In a phone conversation, the health depart- it agreed with my view that this procedure was eless, but I was assured that, as his field of activity now so restricted, the M.O.H. insisted on it being tinued until the Minister says it is to stop. Since n, unfortunately, I have had no cases of scarlet er, but only sore throats with spots.

* * *

One of our colleagues on rare occasions travels to ndon to attend meetings, when he usually has a blame- s and uneventful midday meal at B.M.A. House. Last ek, however, he took his wife with him, and, one ng leading insensibly to another, he found himself ring lunch in one of these Temples of Fashion which est the broader streets of the Metropolis. He was half y through his chicken-and-ham patties (our colleague not a clinician, and cannot afford to aim high), when observed that his wife's eyes had narrowed, and, ning lethargically round, his gaze encountered that an exotic raven-haired beauty, liberally besparkled, d in full off-the-shoulder evening dress. The beauty ecuted a couple of brisk pirouettes, and, taking the unce of her skirt in one hand, swished it smartly at r colleague. After which she smiled radiantly and thdrew, leaving a large central scotoma in our col- gue's visual fields. Nothing in his previous experiences B.M.A. House had prepared him for such a pheno- enon, and he spent the rest of the meal in an uneasy ate. At intervals he fancied he heard a rustle of taffeta hind him and whipped round at great danger to life d limb only to find the waitress regarding him stolidly. uring his steamed fruit pudding he several times felt e hot breath of further exotic beauties on the back of s neck, but investigation disclosed no basis for this nsation, and he left the restaurant without any ditional manifestations being vouchsafed.

Nevertheless, the experience has left its mark upon m, and even while sitting in our own canteen he has a ndency to twitch violently and scrutinise the space mediately behind him. He expresses himself as issatisfied with rural life.

* * *

My practitioner friend, fuming after an altercation with patient who did not carry out his instructions, declares at things are not as they used to be. Wistfully recalling e good old days when patients were patients, he related ow, soon after he took over his present practice, he was alled to attend a lady with a fibrositis. For this he successfully, or fortunately, prescribed. On his next visit he said that she could now leave her bed. After a shocked silence he was coldly told that the patient had been bedridden for several years. Swallowing his pride my friend re-examined her but was unable to find a cause for such a grave drawback. Finally he elicited the following history:

> Seven years previously she had had severe chest pain with a high fever. My friend's predecessor had diagnosed a "congestion of the lungs." The patient, a hard-working housewife with a large family, had refused to go to bed. The doctor without further ado called the husband and eldest daughter. He told them that the patient was seriously ill. She must go to bed and stay there until he returned. On her feet she might collapse and die, and if she arose prematurely the results might be grave. Unfortunately he forgot to return.

With difficulty my friend persuaded the family that the patient could now safely rise, and later that she could even get out. On her first walk she found a housing scheme had been built in the green fields in front of her house.

* * *

Thoughts on the Archers: a problem family—always in some trouble or other—masochistically provoked, no doubt.

Dan Archer—constant undercurrent of pessimism barely concealed by forced conviviality—E.C.T. for him. Mrs. P.—flat monotonous voice—obviously Parkinsonian—try a dash of belladonna. Phil Archer—dithering about from one girl to another—Don Juan complex—analysis the only hope—he'll never save £2000 with that outlay—still, can't be helped. Better send Grace Fairbrother along too—must be lots of unhealthy fantasy there, the way she carried on when her stepmother became pregnant. Walter Gabriel—obvious inadequate psychopath—brisk course of rehabilitation at a neurosis centre followed by fortnightly supportive O.P. interviews—threaten leucotomy if he turns awkward. Spot of 'Antabuse' for Reggie Trentham. Marriage Guidance Council for Jack and Peggy. A good P.S.W. for Mary Jones. A bucket of 'Benzedrine' for the rest.

Let's see now—nine consultations at 5 guineas a go—45 guineas—bill to the Director-General at the end of the month—that should pay for my wireless licence for a few years to come.

* * *

An interesting point in diagnostic parasitology was raised on a recent visit to the farm. I had been scratching the biggest sow's ear for some time before I noticed the reason for her obvious enjoyment, and withdrew my hand quickly. My youngest brother noticed me abstractedly scratching my wrist some time later and asked if I were being bitten. We had a look, and a minute form of life went scurrying down the back of my hand from where it had been cowering under my wrist-watch. "A louse or tick or something," I said with the vagueness of a medical practitioner in the presence of his family. "That was a tick," said my youngest brother with assurance, and waited just the right length of time before adding "it came out of your watch."

* * *

THE REWARD OF VIRTUE

How patiently I strove to gain
Your confidence, but all in vain,
You peevish little pest.
How thoroughly (although you fought)
Examined, as I knew I ought,
Your little wriggling chest.

How reassuringly addressed
Your anxious parents, little pest,
And curbed their foolish fears;
Resisted the desire to smack,
Patted your father on the back,
And dried your mother's tears.

And having done my level best
For you and yours, you little pest,
I edged towards the door,
Only to hear your mother say;
"The nasty man is going away,
So don't cry any more."

Diary of the Week

FEB 1 TO 7

Monday, 2nd

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill S E 5
8 P M Prof Konrad Lorenz (Buldern, Westphalia) Comparative Psychology and Psychiatry

Tuesday, 3rd

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields W C 2
5 P M Dr A A G Lewis Control of the Excretion of Water by the Human Kidney (Arris and Gale lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Prof E J King PH D Silicosis and Asbestosis

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street, W C 2
5 30 P M Dr W R Bett Preparation and Writing of Papers for the Medical Journals

WEST END HOSPITAL FOR NERVOUS DISEASES, 10, Marylebone Lane W 1
5 30 P M Dr C Worster Drought Neurological demonstration

MANCHESTER MEDICAL SOCIETY
1 30 P M (University of Manchester) Dr G W Corner (Washington) Benjamin Franklin Consults the Doctors

Wednesday, 4th

ROYAL COLLEGE OF SURGEONS
5 P M Mr C J Longland Collateral Arterial Circulation in the Limb (Arris and Gale lecture)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
5 P M *Section of History of Medicine* Mr T G Wilson Benjamin Guy Babington (1791–1866) Dr David Nabarro Hitherto Unrecorded Facts in Connection with the *Discovery and Mode of Transmission of the Trypanosome* of African Sleeping sickness (1903)
5 P M *Section of Surgery* Dr J B Wyman, Mr Robert Cox Dr J Gillies Hypotension during Anæsthesia

INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Blood and Bone marrow in Dermatology

INSTITUTE OF UROLOGY, St Paul's Hospital, Endell Street W C 2
1 30 P M Mr F R Kilpatrick Tuberculosis of the Renal Tract

MIDLAND MEDICAL SOCIETY
8 15 P M (Birmingham Medical Institute, 154, Great Charles Street) Prof J M Smellie Chronic Diarrhœa in Children

MANCHESTER MEDICAL SOCIETY
1 30 P M chester) *Section of Medicine* Dr A S Scott Dr S Oleesky Clinic and A C T H

ROYAL COLLEGE OF SURGEONS OF EDINBURGH, 18, Nicolson Street, Edinburgh, 8
3 30 P M Mr S H Harrison Reconstructive Surgery of the Hand

MEDICO CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (Royal College of Surgeons of Edinburgh) Prof D M Dunlop, Mr K Paterson Brown Thymectomy in Myasthenia Gravis

Thursday, 5th

ROYAL COLLEGE OF SURGEONS
5 30 P M Prof Geoffrey Hadfield Co carcinogenesis

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine) Prof Matthew Stewart Pulmonary Asbestosis

ROYAL SOCIETY OF MEDICINE
8 P M *Sections of Neurology, Orthopædics, and Pædiatrics* Dr R M Norman, Dr P Sandifer Mr E S Evans, Dr J P M Tizard Infantile Cerebral Palsies

INSTITUTE OF CHILD HEALTH The Hospital for Sick Children Great Ormond Street W C 1
5 P M Mr T T Stamm Postural Disorders of School Age

ST GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, S W 1
5 P M Dr Denis Williams Neurological demonstration

ST JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY Lisle Street, W C 2
5 P M Dr E Prunty Dr E Bywaters, Dr G B Dowling Cortisone in Therapy of Skin Diseases

WEST LONDON MEDICO CHIRURGICAL SOCIETY
7 30 P M (South Kensington Hotel, 41, Queen's Gate Terrace, S W 7) Prof A M Boyd Management of Thrombophlebitis of the Lower Extremities and its Complications

MANCHESTER MEDICAL SOCIETY
8 P M *Section of Anæsthetics* Dr R G Gordon Jones Epidural Anæsthesia Dr P D Kelsall Anæsthesia for Bronchoscopy Dr J P Payne Arteriotomy in Neurosurgery

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee) Dr P I McKinley Statistical Concepts in Medicine and Public Health

Friday, 6th

UNIVERSITY COLLEGE Gower Street W C 1
5 30 P M Prof F Bergel PH D Chemical Aspects of Normal Growth (Last of three lectures)

ROYAL SOCIETY OF MEDICINE
10 30 A M *Section of Otology* Squadron Leader J H King, Miss M R Dix (with Dr J D Hood), Mr R S Dadson Hearing Tests and their Shortcomings
2 30 P M *Section of Laryngology* Mr R S Lewis, Mr A J Durden Smith, Dr G L Picolotto Management of Cervical Metastases from Laryngeal Carcinoma

INSTITUTE OF DERMATOLOGY
5 30 P M Dr S C Gold Contact Allergy

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square W C 1
5 P M Prof E Bay (Heidelberg) Dynamic Factors in Normal and Pathological Visual Perception

INSTITUTE OF PSYCHIATRY
3 P M *Prof H C Rümke (Utrecht) Clinical Significance of* Obsessional Phenomena

Saturday, 7th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W C 1
11 30 A M Prof D F Leman (Ghent) Some Problems Facing the Endoscopist

MIDLAND TUBERCULOSIS SOCIETY
3 P M (Chest Clinic, 151, Great Charles Street, Birmingham, 3) Dr J G Scadding Chronic Lung Disease with Diffuse Nodular or Reticular Radiographic Shadows

Appointments

BLANEY, P J, M B Belf, M R C P physician, St Kevin's Hospital Dublin
COCHRANE DYET MARY, M B Glasg asst M O Monmouthshire
CROLL, JEAN, M B Aberd asst M O (maternity and child welfare and school medical inspection
DOUGLAS, MARY, M B Glasg County Council (Southgate, Wood Potters Bar area)
GLENDINNING, DAVID M B Glasg, D P H, D P M consultant psychiatrist Rauceby *Hospital, Sleaford Lincolnshire*
HALL G F M, M D Brist, consultant pathologist, Nottingham General Hospital
HIBBERT, I J, M D Glasg, F R F P S asst physician (geriatrics) Norwich and East Norfolk area
JAMES, BRENDA M B Lond, D C H pædiatric registrar, Southmead Hospital Bristol
JAYES, P H, M B Lond, F R C S asst plastic surgeon, St Bartholomew's Hospital London
McKEE, KATHLEEN, M D Belf, D P H, D C H asst M O, Belfast
MACRAE, NANCY, M B Lpool, D I H asst M O, Hertfordshire
MAHON JAMES, M D Dubl physician, St Kevin's Hospital, Dublin
O CONNOR, M J A, M CH N U I, D P H D L O asst E N T surgeon, Jervis Street Hospital, Dublin
ROSS, F G M M B Dubl, F F R, D M R D consultant radiologist, united Bristol hospitals
ROSS, W M, M B Durh, D M R T consultant radiotherapist (asst), Newcastle upon Tyne regional cancer service
STEVENSON JANET, M R C S, D I H asst M O, Hertfordshire
TAGGART, J McA M B Belf, D I H, D P A senior M O Belfast
TURNER G M A, M B Edin medical registrar, Newmarket General Hospital
WATERS, CECILY, M D Lond, D P H asst M O, Monmouthshire

Factory Doctors

FAITH, C N, M D Lond, D I H Hampstead district, London
McCLURE, C R M R C S Paddington district, London
McINTYRE, WILLIAM, L R C I Jura Argyllshire

Liverpool Regional Hospital Board

BLEWITT, BASIL, M D Belf D T M whole time *consultant* pathologist, Newsham General Hospital and Mill Road Hospital
FRANCIS, I, B A, M B whole time asst anæsthetist North Liverpool area
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BRUCHER JOHANNA, B A, M B Camb asst chest physician (S H M O), Rhymney and Sirhowy Valleys H M C
MACKINNON, DONALD M D Lond consultant pathologist Merthyr and Aberdare H M C
PORCHER H I H, M D Lond D P M asst psychiatrist (S H M O), Morgannwg Hospital, Bridgend

West Riding of Yorkshire County Council

BARNES, ROY, M R C S asst M O (Wombwell division)
BUCKLEY, GWENDOLEN, M B Durh senior asst M O (Ship division)
BURRELL, P S R, M B Leeds, D P H senior asst M O (I gate division)
BURTON MARGARET, B A Lond, L M S S A, L M (Doncaster division)
GISBOURNE MARGARET M B asst M O (Brighouse
HAISTE DIANA M B Leeds asst M O (Castleford
MITCHELL HELEN M B Leeds senior asst division)
PULLAN MARY, M B Leeds asst M O (Harrogate
SHAW ETHEL, M B N U I asst M O (Colne Valley di
SMITH JEAN, M B St And, D I H senior asst M O *division)*
TAYLOR CECILIA, M B Leeds, D C H asst M O division)
WALL, DOROTHY, B A Oxfd, M R C S asst M O (Shipley division)

Dr GEORGE DUNCAN has not accepted the post of asst M O H for Burton upon Trent (*Lancet*, Jan 17, 1953 p 152) ost of the "underdeveloped" countries, the child h services are rudimentary, and in many places are ineffective because they have developed on established patterns—patterns unsuited to local needs and itions.

ke for example the maternity services. There has much concentration on building maternity hospitals on training midwives. Yet the antenatal work is slight and perfunctory and the postnatal work existent. But the main causes of maternal and infant ology are malnutrition, overwork, anæmia, and ated pregnancies in the mother. It is quite impossible any of these conditions to be affected simply by iding expert assistance at parturition.

hild health services should be established only after observation of the needs and resources of the le. They should then be built up in close coöperation the hospitals and in such a way as to make the test possible use of any available personnel.

small proportion of the money now being spent on tific work should be devoted to social observation experiment. I am convinced that it would not be before the revolutions in motherhood and in agriure that you mention could be within our vision—copic vision though it may be.

his is not idle fancy. I have seen the beginning of k in various countries that has actually changed the of the people towards better nutrition and living litions. But such experiments have been starved for ls and for personnel. They have never been provided the possibilities of development and expansion, of tinuity, and of publicity that would have established r value.

these days when the terrors of over-population are oming a real menace, surely we can persuade some of authorities to use the only really possible and effective ence—adequate care of the children automatically lts in smaller families and economy of resources.

ontpelier, Jamaica. CICELY D. WILLIAMS.

PRIMARY TUBERCULOSIS OF THE SKIN

IR.—The article by Dr. Miller (Jan. 3) is most stimuing and thought-provoking. We suspect that it has ened up a field that must call for serious consideration, l it is to be regretted that each case in Dr. Miller's portant series is not described in detail.

The dermatologist is familiar with the primary complex the skin presenting as a hard chancre and soon sociated with regional lymph-node enlargement. Later ere appear lupus nodules in the primary lesion and seation in the lymph-nodes. While it is probably true at other forms of cutaneous tuberculosis are not rmally associated with regional caseating adenitis, the rmatologist would not have regarded such adenitis th caseation as pathognomonic of a primary infection ly. It may well be that he must revise his ideas; but, taneous lesions apart, caseating tuberculous lymphodes are surely common enough apart from primary sions. The point is important, for the suspicion of a imary infection must set in train investigations and eatment of rather elaborate patterns demanded by the imary phase of infectivity.

In a series of 800 patients with tuberculosis of the skin en in the dermatological department at Leeds in the ast twenty-five years, there have been only 18 with a rimary tuberculous complex of the skin. This has led the feeling that the condition is uncommon; but from r. Miller's paper it is clear that patients with primary fections of skin or mucosa may present themselves to variety of departments so that the over-all picture is ot appreciated.

In our simplicity we should have questioned—on the cant evidence in the paper—the validity of regarding he 10 cases with a history of trauma as true primary infections. Other factors would clearly predispose to adenitis, and infection of a wound with tubercle bacilli would favour their passage to the lymph-nodes. Yet the negative Mantoux reaction on admission of the patient who had sustained a head wound in a road accident would favour Dr. Miller's thesis. He will nevertheless appreciate the desire of those interested to have further details of all these 10 cases.

The occurrence of a primary lesion on the skin and in the lung, as in case 2 in Dr. Miller's series, is most interesting. It would seem probable that, as in syphilis, while this is sometimes observed it is likely to be uncommon. The discovery of evidence of a lesion in the lung would generally exclude the probability of a lesion in the skin being a primary complex. The findings in the lungs in the other traumatic cases would be of interest.

The splash of lupus nodules in the site of a primary tuberculous chancre has invariably been seen with our patients; but this feature may follow ordinary chronic warty tuberculosis in the butcher and others, or the ulcerative pyogenic type of lesion that sometimes arises from this mode of infection.

JOHN T. INGRAM
Leeds. STEPHEN T. ANNING.

EVALUATION OF RADIOLOGICAL SERVICES

SIR,—The expansion of radiological services since the end of the war has been in the region of 200% over the whole country and it shows no sign of diminishing. Practically every new advance in medicine and surgery demands increased effort and increased output from radiological departments with a corresponding increase in costs. Since a financial limit has of necessity been applied to the National Health Service, it is essential that the funds available for radiological examinations should be used to maximum advantage in the interests of efficiency and economy. It may not be generally appreciated that in many instances the cost of a patient's X-ray investigations may be greater than the combined cost of the whole of his treatment.

It is known by radiologists that the usual methods of assessing the work done in X-ray departments are unreliable and of no comparative statistical value, and there is general agreement on the need for a more reliable system.

The Nuffield Provincial Hospitals Trust, in collaboration with a number of radiologists, carried out an experiment in what is now called the unit system of recording. The authors of this report emphasise that the experiment was not conducted "over a sufficiently long period to demonstrate the usefulness of their suggestions."

The Faculty of Radiologists, whose help at one period was sought by the Nuffield Trust, had, in the early days of this experiment, realised the difficulties which would arise in applying on a national scale the results of a localised survey.

The faculty is aware of the danger in any such system of wrong inferences being drawn as to the quality of the work done in a radiological department. It has, however, been assured by the Ministry of Health that this is not a matter of controlling the way in which medical work is done but only of recording its amount in a form which makes some allowance for the varying complexity of different examinations. There is no intention of seeking uniformity, which in any case is impossible; but study by individual departments of their own problems as compared with others in the light of these statistics might enable them to raise their own standards of efficiency, while at the same time decreasing costs.

Following publication of the memorandum RHB(52) 130, the Ministry of Health informed the faculty that it was recognised that the unit values might be found to need alteration in the light of experience and would be glad to receive any observations on them which the remaining acid-secreting cells, and the recurrence-rate in Visick's series was nil (Pulvertaft 1952) Though this operation, in skilled hands, may carry a mortality of no more than 4% and gives a high degree of protection against relapse, it is on occasion attended by undesirable side effects described in detail by many writers (Wells and Welbourn 1951, Braun and Stammers 1951, Adlersberg and Hammerschlag 1947)

The tendency to lose weight shown by patients who have had such high resections has been previously mentioned (Johnson 1948), and it was observed that the degree of weight loss appears to be proportional to the amount of stomach removed The "dumping" syndrome, too, is commoner and more severe when radical resection has been used, and we have found its incidence to be correlated with inability to eat more than a very small meal and with complaints of regurgitation of bile

It must be recognised that gastrectomy, without deliberate division of the vagi or their gastric branches inevitably destroys a large part of the vagal supply to other organs, a fact too often ignored by those who have inveighed against vagotomy

Several of our colleagues who use high gastrectomy regularly for all kinds of peptic ulcer have encouraged us to follow their patients along with, and by the same methods as, our own These together with those of our own high gastrectomies which fell into the beginning of the total period under review, before we had both adopted our present policy, amount to 241 cases

We have not explored the mortality in this particular group (there were no deaths among our own few cases), but from a separate study of over 3000 post-war gastrectomies, varying greatly in the proportion resected, we have ascertained that the average mortality has been 4%, being higher where high gastrectomy was routinely used and lower where conservative resection was the rule

MODERATE PARTIAL GASTRECTOMY WITH OR WITHOUT VAGOTOMY

Data about the spontaneous secretion of acid at night, collected from some 400 patients, show that, though duodenal ulcers and some juxtapyloric ulcers are associated with interdigestive hypersecretion of acid, most gastric-ulcer patients have levels of secretion below the average for normal people

Though anastomotic ulcer has been an occasional sequel to gastrectomy for duodenal ulcer, for combined ulcers, and sometimes for prepyloric ulcers it has seldom, if ever, followed even hemigastrectomy when performed for other gastric ulcers Moreover, the investigation into jejunal ulcer conducted by the Association of Surgeons (1935) showed that the patients who developed anastomotic ulcers were the ones with unusually high acidity of their gastric contents We therefore contend that high or subtotal resection is unnecessary for hyposecreting patients, such as most of those with gastric ulcers Not only is a moderate two-thirds resection sufficient for the cure and control of their disease but also it is possibly less dangerous to life and gives better symptomatic results We have found the Billroth I anastomosis most satisfactory in gastric-ulcer patients

Both we and others have found that vagotomy is a successful operation for the cure of anastomotic ulcer, and we therefore judged it likely to prevent them We have therefore felt justified in returning to moderate gastrectomy in hypersecreting patients as well, with the addition of vagus resection to prevent the recurrences otherwise to be expected in a proportion of these cases after a two thirds resection

An investigation by the American Gastroenterological Association into the results of some 2600 operations for peptic ulcer (Jordan 1951) showed that addition of vagotomy to ordinary high gastrectomy was not harmful whereas 91 6% of those who underwent gastrectomy alone survived and were satisfied with the result, in case of gastrectomy plus vagotomy the figure was 94 Since the recurrence rate was negligible with rad gastrectomy alone, it was thought that nothing m was to be gained by the addition of vagotomy We, the other hand, hoped that, by adding vagotomy to moderate gastric resection, we should achieve ulcer cu as dependable as those won by high gastrectomy, a at the same time we should have results as symp matically satisfactory as those which go with m conservative resection

For several years we have been applying a policy peptic ulcer which has implied the use, in nearly all ulcer cases, of either (*a*) two-thirds gastrectomy alone, (*b*) similar moderate gastric resection plus division of t vagi or their gastric branches The results of th operations performed during the five years end December, 1951, are described below

METHOD OF SELECTION

The spontaneous interdigestive secretion rate of ac is determined for each patient by continuous gas suction during twelve night hours The volume of ju in litres multiplied by the titratable free hydrochlo acid in clinical units gives the number of milliequivalen of hydrochloric acid produced in the whole night W have chosen the arbitrary figure of 20 m eq as the le of secretion above which the addition of vagotomy gastrectomy is indicated (Johnson 1951) However, often happens in practice that tubes become blocked aspiration is incomplete for some other reason A hi level of acidity (over 45 clinical units of free hydrochlo acid or over 65 units of total acid) in the bulked juice also adequate evidence of nocturnal hypersecretion, ev though the volume of juice aspirated has not been ve great

Following this rule we have employed moderate part gastrectomy alone for 90% of our patients with gastr ulcers and for 52% of those with duodenal ulcers, wi the addition of vagal resection in most of the other The choice of operations is shown in greater detail in th accompanying tables

Patients with carcinoma in ulcere, benign or malignan tumours, and pyloric stenosis with long since heale ulcers are excluded from consideration, the last name because they were often considered amenable to gastro enterostomy under any policy Patients with anastomoti ulcers after earlier gastro enterostomy were included fo we dealt with them by vagotomy alone or moderat gastrectomy with or without vagotomy, in accordanc with our principles in the "policy" series There was a similar proportion of such patients in the high gastrectomy series

Recurrence of symptoms after earlier gastrectomy is a different problem and could not be included, for the initial operation was sometimes a high resection not able to be modified to bring it into line with our policy, moreover, we are not seeking to show that the addition of vagotomy to very radical gastrectomy can do much to improve its results or to alleviate its occasional ill effects The results of vagotomy used for anastomotic ulcer after earlier gastrectomy will therefore be dealt with separately Patients who had emergency operations for massive hæmorrhage or for perforation could not be assessed in the usual way and submitted to the operation selected accordingly They, too, are therefore left for consideration elsewhere

MORTALITY

The operations used in applying the above policy have had few serious complications, and the mortality has compared favourably with that in any series of subtotal gastrectomies published

Of the 526 patients operated on under the policy during the period under review, 486 had gastrectomies illy arises as right ventricular failure supervenes roxysmal pulmonary symptoms wane. It signifies, er, that the disease process has advanced and now es pulmonary arterioles and myocardium as well ral valve.

homas's Hospital,
ondon, S.E.1.

RICHARD GORLIN.

All who have experience of mitral valvotomy agree nitral incompetence can be present when a systolic ur is absent or insignificant, and the Swedish rs on whose article we were commenting recognise A hypothesis of progressive narrowing of the mitral supported by Dr. Gorlin and by Dr. Wade (Jan. vould be satisfying; but Brock's experience gives for thought. Surgical widening of the mitral-valve ng does not always give the relief we should expect severity of symptoms depended entirely on the e of valvular obstruction. Furthermore, resting ares in the pulmonary artery may apparently be y normal in the presence of disabling symptoms.[5]

. L.

PARONYCHIA

—In his interesting paper (Jan. 17), Mr. Lowden ions circulatory inadequacy as a possible antagonistic r to satisfactory results.

aile reviewing rather over a thousand cases of finger ion[6] I followed up this point. I had expected to as Mr. Lowden suggests, that in the cold vasorictive winter months finger infections would be common and would do less well than during the ner months. I therefore worked out the incidence ises during each fortnight over a period of three , and also the average healing-time of cases during fortnight. I found that, while the differences in ence were not significant, cases were most numerous ine and July and fewest in October and November; s at other times of the year were intermediate. iously, other factors are involved; but these results ld not seem to suggest that winter weather increases incidence of finger infections. The average healing- was found to remain remarkably constant through- all months of the year. It seems, therefore, that e cold no doubt slows down the inflammatory onse, it also slows down the rate at which bacteria ide the tissues.

is noteworthy that in the majority of cases in our es where gangrene developed the patient was diabetic.

anmore, Middlesex.

B. VICTOR JONES.

ERFORATION OF DUODENAL ULCER AFTER BARIUM MEAL

IR,—In your issue of Dec. 27 Dr. de Fonseka cribed a case of acute perforation of a duodenal er immediately after a barium meal. I observed a ular case in 1947.[7]

> uring X-ray examination of the stomach a duodenal er perforated. The radiographs showed an ulcer in ompartment form" in the anterior wall of the duodenal b with a small perforation and a tiny streamlet of barium the outer surface of the bulb. The patient was operated within 3 hours (Dr. Suren). Only a small amount of barium s found in the immediate vicinity of the perforation, ich was closed. The patient made an uneventful recovery.

This case is interesting because of the extreme rarity radiographic records of the course of a perforation. ill more important is the fact that this ulcer showed e "compartment form" with a relatively long and narrow canal leading from the mucosal surface to a small cavity immediately beneath and in the thickened serosa of the duodenal bulb. Professor Deelman,[8] who has repeatedly described this type of ulcer, emphasises that it is only seen in duodenal ulcers of short duration, and is found especially in specimens removed during operations for acute perforation. The danger of perforation in duodenal ulcers of this type is again illustrated by our case, and we learned from it to be extremely careful about patients who show this type of ulcer radiographically.

Department of Medicine.
Charitas Hospital,
Roosendaal, Holland.

C. L. H. MAJOOR.

CHILD-WELFARE CLINICS

SIR,—Medical officers working in public-health departments will welcome the account (Jan. 10) of the investigation by Dr. George and his colleagues. It is right that the usefulness of local authorities' work should be questioned from time to time in the light of experience since 1948.

I should like to comment on some of the points raised. It is suggested that the advisory work at infant-welfare centres can be done just as well by health visitors as by medical officers. This of course is true. Indeed, it is often done better by the health visitor because she has an intimate knowledge of the home. This leaves the routine examinations and treatment. Local-authority medical officers commonly feel that their hands are tied when they wish to treat a child at an infant-welfare centre. Lack of therapeutic agents limits the amount of treatment they can give. Moreover, they feel under an obligation to refer the child to the general practitioner.

Dr. George and his colleagues have emphasised that preventive and curative services should not be divorced. A generation of general practitioners is arising who, by training and outlook, are equipped to educate, advise, and treat patients. By all means let them take over the work at infant-welfare centres. There are, however, some difficulties. Practising at the local-authority clinic, they would be consulted by mothers whose children were registered with one of a number of practitioners in the neighbourhood. What treatment other than that already being given could they prescribe for children not on their own lists? With health centres and an extension of group practice, this difficulty would not arise; but these ideals are still unrealised.

An alternative is the loaning of health visitors to practitioners to help them conduct their own infant-welfare centres at their surgeries. Some general practitioners are already setting aside one or two afternoons a week when they see babies and toddlers only. The drawback to this suggestion is that it leaves out proprietary foods—the reason for half the attendances at infant-welfare centres!

What is clear is the need for bold experiment along various lines, and for realisation that the closer integration of general-practitioner and local-authority services will benefit the children.

Smethwick, Staffs.

JOHN S. OWEN
Senior Assistant Medical Officer of Health.

SIR,—The discussion in your columns on the future of the local-authority child-welfare clinics and the clinic medical officers has arisen at a time when these clinics may be regarded as an extravagance by local authorities who are seeking to curb their expenditure; in fact, the Birmingham City Council about six months ago were not going to provide new welfare centres on the new housing estates because there was a prevailing opinion that the work carried out at the centres with regard to maternity could be done by the general practitioners and a limited

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Wade, G., Werkö, L., Eliasch, H., Gidlund, A., Lagerlöf, H. *Quart. J. Med.* 1952, 21, 361.
Bayliss, R. I. S., Etheridge, M. J., Hyman, A. L. *Lancet*, 1950, ii, 889.
Scott, J. C., Jones, B. V. *J. Bone Jt Surg.* 1952, 34B, 4.
Schulte, N. J., Majoor, C. L. H., Suren, Th. J. J. *Ned. Tijdschr. Geneesk.* 1948, 92, 3940.

[8] Deelman, H. T. *Ibid*, 1938, 82, 1190; 1942, 86, 1040, 1821; 1947, 91, 1769, 2234.

are given in the tables, but their significance to the patients is best assessed by considering the categories into which the patients placed themselves in answering the last question noted above

In the radical gastrectomy group 89% of the patients followed put themselves in one of the top two categories (cured and normal, or greatly improved) 8% were a little better and considered the operation worth while, and 2% did not feel any better for it at all Of the patients in this group 33% had gained weight up to or above their preoperative level and had been altogether free from any gastro intestinal or related symptom

TABLE III—AGE-DISTRIBUTION

Age group (yr)	Radical gastrectomy		Policy group	
20–29	5%	Under 50 58%	7.5%	Under 50 58%
30–39	21%		15.5%	
40–49	32%		35%	
50–59	23%	Over 50 42%	28%	Over 50 42%
60–69	14%		12%	
70 or more	5%		2%	

In the "policy" group 95% of patients selected one of the top two categories, 4% considered themselves a little better, and 1% were no better at all Of these patients, 52% had gained weight and been completely symptom free

It is clear that both approaches have achieved a high order of success Though the age and sex distribution and length of follow-up were similar in the two groups, it is, of course, impossible to know whether they were strictly comparable as regards "curability" But the claim that our policy has been vindicated is based less on these appearances of slightly superior results than on the fact that they have been won at so low a cost in lives Our preference for moderate gastric resection may be one of the factors which has helped us to achieve this low mortality

Comparison of the results of each operation used within the selection policy as regards success in preventing recurrence and curing ulcer disease would not be valid, for each was used for a different purpose However, it is interesting to compare the incidence of side effects These are enumerated in table II, and it is seen that the addition of vagotomy to moderate partial gastrectomy has made no significant difference to the incidence of any symptom except possibly "wind" pain, though when high gastrectomy is used this symptom is more frequent still Compared with two thirds gastrectomy or limited resection plus vagotomy high gastrectomy is seen to carry a greater risk of "dumping," bilious regurgitation, and weight loss Diarrhœa was so unexpected a sequel to vagotomy alone that its occurrence received much publicity in the early days of that operation In our experience it was often noted during the first few weeks after vagotomy alone, and 3 of the 108 patients submitted to this operation were still having intermittent diarrhœa three months and later after operation It is therefore interesting to observe that only 3 patients complained of this symptom out of the 246 followed after vagotomy plus gastric resection and that there were also 3 among the 241 submitted to low gastrectomy without deliberate vagotomy, and 10 among the 222 who had high gastrectomies

The last question put to the patients in the questionnaire was "If you were to go back to before your operation, but knowing what you now know about the effects it would have on you, would you again choose to undergo it?" 99.6% of our patients replied "Yes," and though asked not to do so, a great many wrote in such things as "most definitely," "A thousand times yes," or "Yes, but twenty years sooner"

DISCUSSION

Division of both vagi or of the whole of their gast branches has proved efficient in controlling excess interdigestive acid secretion However, when th manœuvre has been used alone in duodenal ulcer patien the symptomatic results have been marred by the effec of scarring and gastric retention Because vagotomy h not proved to be a surgical *mend all, its omission fro* the surgeon's repertoire has been suggested, but in o view this would be equivalent to throwing a spann away because it cannot do the work of the who tool-kit

We are *in full agreement with Ogilvie (1952)* when urges that no further use should be made of vagotom alone in the treatment of duodenal and gastric ulcer but we cannot endorse his statements that the vagi nerves are divided for gastric pain, that hormonal jui is unaffected, and that nervous secretion is harmless

In 1915 Sippy drew attention to the excessive continuo interdigestive or "resting" acid secretion characteristic *patients with duodenal or anastomotic ulcers now consider* to be mainly neurogenic He regarded this as the mo *dangerous element of gastric activity*

It has been repeatedly shown that vagotomy reduces th resting secretion by some 80% (Dragstedt 1945, Moore et a 1947, Orr and Johnson 1947) It also diminishes by som 70% the acid response to test meals and histamine injectio (Stein and Meyer 1948 Farmer et al 1951, Johnson 1950)

It has not been with any idea of interrupting pain pathway that we have used vagotomy Indeed, pain conduction fro the ulcerated area has been shown to be unimpaired b division of the vagi (Foerster 1927, Moore et al 1947, Johnso 1947)

Ogilvie cites division of branches of the vagi as on *of the criteria of a satisfactory gastrectomy*, though h divides them only to give greater mobility to the gastri remnant In our opinion routine high division of th vagi or of their gastric branches in all gastrectomies, without regard to the patient's pattern of secretion, ma be harmful in those whose stomachs are already hypotoni and hyposecreting Moreover, we believe with Butler and Capper (1951), that every effort should be made to preserve the natural supports of the stomach, even though this may make the operation slightly mor difficult

It has been suggested that patients who have had vagotomy plus pylorectomy are reduced to complete and permanent achlorhydria, and that this might increase the dangers of infection and of the supervention of carcinoma *From many hundreds of secretion investi*gations we conclude that there is no significant difference between the effects on gastric secretion of two thirds

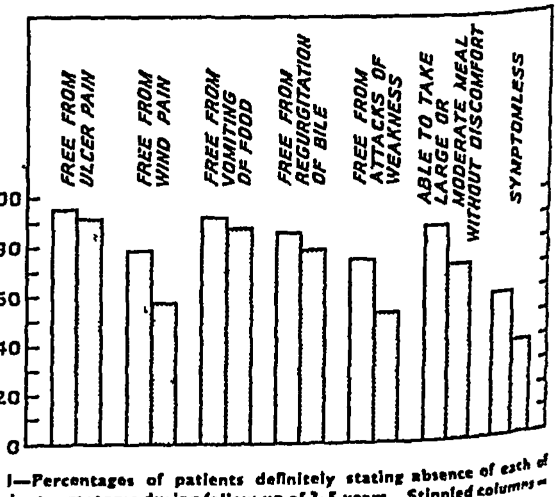

Fig 1—Percentages of patients definitely stating absence of each of various symptoms during follow up of 3–5 years Stippled columns = policy group Hatched columns = radical gastrectomy group

ce in Juvenal rests either upon a misprint or bad text.

Podice levi
Cæduntur *tumidæ* medico ridente mariscæ

ot *humidæ* (II, 12 and 13). "Cæduntur humidæ" ot scan.

But as he cuts the piles,
So smooth is all below, the surgeon smiles.

ne rest, there is that long list of authors, again it citation, coming this time from a certain raux. The only one of the authors mentioned whom I now have any anxiety is Martial. ich *are* those epigrams that describe a contagious itis?

ngton. H. St.H. Vertue.

BOVINE TUBERCULOSIS AND HUMAN TUBERCULOSIS

,—I do not wish to use Mr. Pitcher discourteously must answer his letter (Jan. 24) quite bluntly. cked only two items of Mr. Pitcher's data—the n of differences and the figures for Glasgow. simple check disclosed 4 errors—2 mistakes in action and both the notification-rates grossly . The result of this check is not, as Mr. Pitcher s, to strengthen his argument, but to call in question ccuracy of the remaining data which I have not ed. I think it is not unfair to say categorically on this showing Mr. Pitcher's numerical data ot be accepted as reliable premises for any argument. munity to tuberculosis can be produced by certain of *living* mycobacterium. Dead organisms or rial products have never been shown to produce unity. The only evidence for the presence of an nising substance in heat-treated tuberculous milk . Pitcher's inference of its existence from data which been proved unreliable.

ds. D. B. Bradshaw
Deputy Medical Officer of Health.

PRACTICAL PENICILLIN

R,—Mr. Cohen's article last week must not, I think, llowed to pass without comment. I will not linger nis ingenuous suggestion that general practitioners not yet acquainted with aqueous procaine penicillin. having myself treated very many more than his cases (of which 35 were apparently not followed I must disagree with him on several points.

n the first place, whilst he has shown that a single ction of 1,500,000 units of aqueous procaine penicillin ml. will produce significant blood-levels for about e days, there is little doubt that a daily injection of .000 units will produce a higher average level. Since entially serious infections, such as those of the d, breast, or middle ear, should be seen daily for the few days, there is no difficulty in a daily injection. the second place, the indiscriminate use of penicillin all minor sepsis is bad medicine, because less sensitive anisms may in this way become penicillin-resistant: applies especially to staphylococcal infections skin, such as boils and furuncles; and these in any e usually respond not much better to penicillin than simple local treatment. In the third place, Mr. Cohen kes no mention of bacteriology, and the type of ecting organism determines to a large extent the ount of penicillin required. For example, streptocal tonsillitis is cured rapidly with one or two injections 500,000 units, whereas carbuncles usually require ger doses over several days. Fourthly, I cannot agree h his generalisations on otitis media. Acute ear ections respond nearly always extremely well to nicillin; but ears which have been discharging for nths, presumably having become secondarily infected, on the whole respond poorly. Fifthly, the graphs illustrating percentage rates of cure are not comparable, since cases seen at hospital are obviously selected ones as compared with those seen in the surgery.

On one point I agree with Mr. Cohen: it is important to keep patients away from hospital outpatient departments—but for the patients' sake rather than the departments'.

Shrewsbury. John C. Ryle.

THE VASOMOTOR DISTURBANCE IN PINK DISEASE

Sir,—In his paper on the vasomotor disturbance in pink disease,[1] Dr. Vulliamy repeats the fallacy of Lewis and Landis[2] that there is no structural narrowing of small arteries or arterioles if their strong contraction can be released to full dilatation. Such dilatation shows only that elasticity has been retained, and not necessarily that structural narrowing, such as that in acrocyanosis,[3] is absent. A simple mathematical treatment[4] shows that narrowing, even though considerable when the vessel is fully contracted, will be negligible when it is well expanded.

Warwick. Edward S. Stern.

Obituary

ROBERT VEITCH CLARK

M.A., M.B., B.Sc. Edin., D.P.H.

Dr. Veitch Clark, who died on Jan. 20 at the age of 76, was in charge of Manchester's public-health services for twenty strenuous and progressive years, and had previously won a high reputation at Croydon.

He qualified at Edinburgh in 1901, having already obtained the M.A. in 1896, and the B.SC. in 1900. After holding resident hospital appointments he became lecturer in physiology in the University of Leeds. Here he developed a strong belief, to which he always held, in the importance of scientific laboratory work in the prevention as well as the cure of disease. His interest in preventive medicine led him to take the diploma in public health at Oxford in 1907, and he returned to Leeds as assistant medical officer of health and lecturer in public health. He remained there until he was appointed medical officer of health for Croydon in 1913. His promotion to the post of medical officer for health of Manchester came in 1922.

[Schmidt, Manchester

In Manchester he at once turned his attention and energies to the many public-health problems of a large industrial town. In 1924 he was appointed honorary secretary of the Manchester and District Regional Smoke Abatement Committee, a voluntary association of official representatives of local authorities in South-east Lancashire which acts in an advisory capacity in controlling smoke nuisance. In the same year, in accordance with recommendations of the Ministry of Health, the Manchester Committee on Cancer was formed. The first move was the formation of a provisional committee, and Dr. Veitch Clark was appointed the first chairman. He held this position until he retired. The committee conducted propaganda, experimental research, treatment, aftercare, and follow-up of patients, and statistical recording of cases. Particular attention was paid to mule-spinners' cancer and to experimental research on the carcinogenic properties of the lubricating oils used in the cotton-spinning industry. Seven years later the

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1. Vulliamy, D. G. *Lancet*, 1952, ii, 1248.
2. Lewis, T., Landis, E. M. *Heart*, 1930, 15, 151.
3. Stern, E. S. *Brit. J. Derm.* 1937, 49, 100.
4. Stern, E. S. *J. ment. Sci.* 1937, 83, 408.

from one of the early Rochdale cases and had been passed twice on the chorioallantois of chick embryos The smallpox strain had been passed 8 times since its isolation from a case of variola major in 1946 The vaccinia strain was recovered from the vaccination "take" on a young adult (Lister Institute lymph) and had been passed 8 times on the chorio allantois The cowpox strain was isolated in 1937 from lesions on the hands of a cowman and had been passed on 20–30 rabbits and 16 times on eggs

Complement fixation Tests

To sera in doubling dilutions from 1/5 upwards were added 3 M H D (minimum hæmolytic dose) of complement and an equal volume of antigen (0 2 ml) These mixtures were left in the refrigerator overnight, and next morning 0 4 ml of sensitised sheep red cells was added to each tube The tubes were placed in a water bath for thirty minutes and then allowed to stand for a further two hours at room-temperature before the results were read The titre was taken as the initial dilution of serum in the last tube to show less than 50% hæmolysis Antigens used were clear saline extracts of chorio-allantoic membranes of chick embryos which had been harvested three days after being infected with alastrim, variola, vaccinia, or cowpox virus These antigens were titrated beforehand against dilutions of rabbit immune sera, that dilution of antigen was chosen which was the highest to give maximum fixation with 1/10 to 1/80 dilutions of immune rabbit serum With egg membrane antigens the optimal antigen dilution was usually 1/15 to 1/25

Antihæmagglutinin Tests

The hæmagglutinin for these titrations was prepared only from vaccinia infected egg membranes Extracts from membranes infected with the other three viruses gave irregularly low titres of hæmagglutinin when tested against susceptible fowl red cells and were not used The blood cells from a number of fowls were tested and those birds whose red cells were found suitable were selected as blood donors for routine work Blood from a wing vein was taken into citrate The cells were washed three times and suspended in buffered saline to give a 1% suspension for the tests, 1% inactivated normal rabbit serum being added as a stabilising agent Saline extracts of vaccinia infected chorioallantois were titrated against fowl cells to find the minimum hæmagglutinating dose, and four times this amount in a volume of 0 25 ml was used in testing the sera from alastrim patients Doubling dilutions of serum from 1/10 upwards were mixed with 4 hæmagglutinating doses of antigen in a series of tubes These were placed in a water bath at 37°C for one hour, 1% suspension of fowl cells was then added The tubes were shaken after twenty minutes at 37°C and then kept for another hour at 37°C They were left for one hour at room temperature before the results were read The titre of the serum was taken as the highest dilution which prevented all but a trace (±) of agglutination of the red cells

TABLE I—ANTIBODY TITRATIONS ON 21 SERA FROM 19 ALASTRIM PATIENTS

Case no	Days after onset	Complement fixation titre[1]*	Antihæm-agglutinin titre[2]*	Per cent neutralisation[3]
1	2	neg 1/5	neg 1/10	46
2	3			88
3	6	"		18
4	9		80	94
5	10	20	160	87
6	10	5	160	85
7	11	5	40	81
8	11	10	80	91
9	12	40	160	91
10	14	10	80	96
11	15	40	80	93
12	16	10	80	97
13	17	40	320	92
14(a)	18	20	160	96
15	20	10	160	98
14(b)	21	20	80	N T
16	22	20	320	97
14(c)	31	10	80	97
17	36	40	160	97
18	37	5	80	97
19	43	10	80	96

*Figures in these columns are reciprocals of titres

1 Egg antigen used
2 Vaccinial hæmagglutinin
3 Tested against alastrim virus

N T =not tested

Neutralisation Tests

The technique used has been described by McCarthy and Downie (1948) The virus suspensions had been prepared from infected egg membranes and partially purified by differential centrifugation The virus preparations were titrated by inoculating tenfold dilutions on the chorioallantois of groups of fertile hen eggs which had been incubated for twelve days After three days' further incubation the eggs were opened and the number of lesions present on the membranes noted For tests with the sera, that virus dilution was chosen which would give between 50 and 200 lesions on the chorioallantois All the sera were tested against alastrim virus A 1 in 2 dilution of serum was mixed with an equal volume of the selected dilution of virus and after forty minutes at room-temperature each mixture was inoculated on 5 or 6 eggs Three days later the membranes were examined and lesions counted The percentage neutralisation was obtained from the average number of lesions per membrane as compared with the average number of lesions resulting from the inoculation of the same amount of virus mixed with normal sera from non-vaccinated individuals One serum was also tested by this technique in dilutions against each of the four viruses

TABLE II—COMPLEMENT FIXATION TESTS

Serum from case no	Days of illness	Complement fixation titres* against antigens of			
		Alastrim	Variola	Vaccinia	Cowpox
2	5	—	—	—	—
3	6	—	—	—	—
4	9	—	—	—	—
5	10	20	40	20	20
7	11	10	40	10	20
8	11	10	20	10	20
9	12	20	40	40	N T
10	14	10	20	10	N T
11	15	40	40	40	N T
12	16	10	20	10	20
13	17	40	40	40	40
16	22	10	20	10	40
18	37	10	5	5	N T

*Expressed as reciprocals
N T =not tested
— =negative at 1/5 serum dilution

RESULTS

Results Obtained by Three Methods of Detecting Antibody

The results of the tests on 21 sera are shown in table I It should be noted that the complement fixing titres shown were obtained against alastrim antigen and that the neutralising titres were measured against alastrim virus For the determination of antihæmagglutinin a vaccinia antigen was used for the reason given under "methods" It has been shown (Chu 1948) that the complement-fixing antigen and the hæmagglutinin of vaccinia are different and that neutralising antibody is not the same as that concerned with complement fixation It is therefore not surprising that there is not complete correlation of the results of the three tests with individual sera The results, however, show that from the tenth day of illness all sera were positive to each of the tests The neutralisation test using only a single dilution of serum (1/2) does not give very accurate quantitative results Such assessment of neutralising antibody can be better made by testing dilutions of the serum against a constant amount of virus (see table IV) Estimations of this kind on all the sera would have required a larger number of eggs than could readily be handled in our laboratory

Time of Appearance of Antibody

By the complement-fixation technique antibody was not found in the four sera obtained before the tenth day of illness (table I) Antihæmagglutinins were found in the serum taken on the ninth day but not in the three taken earlier The neutralisation test, however, gave a positive result with the serum taken on the fifth day and those taken from the ninth day onwards From fairly extensive experience of this type of test we have found that more than 50% neutralisation is significant, while less than this

Notes and News

W.H.O. FINANCES

executive board of the World Health Organisation has iscussing in Geneva the financial difficulties due to in the funds provided by the United Nations Technical nce Board for part of the Organisation's work. These which had been fixed at $10 million for 1953, may be l to $5 million. The chairman of the executive board. Jafar, said that no sharp distinction could be drawn n W.H.O.'s regular programme (financed by the regular udget of nearly $9 million) and its Technical Assistance mme for Economic Development. Social develop- economic progress, and health improvement were rable, and to abandon or postpone projects already in ion, or even well advanced, would, in Dr. Jafar's do incalculable harm to the whole W.H.O. programme. cussion, a reduction in the administrative machinery I.O. was urged; and some members felt that continuity ng-term planning were needed to allow the Technical ance Board to forecast more accurately the funds it have at its disposal. Mr. David Owen, executive nan of the Technical Assistance Board, said that many ments had not yet fulfilled their 1952 pledges to bute to his board's funds—hence the cuts that had been ary in all parts of its programme. But he hoped that end the gap between the sum expected and the amount ed would not be as great as was feared.

RESEARCH PRIZES

some time past the South West Metropolitan Regional tal Board, like some of the other boards,[1] has had a ch committee which supports investigations with the at its disposal. The board has now gone a step further by ig prizes to encourage "minor items of clinical research." year nine prizes of £100 each will be offered—three for ltants and senior hospital medical officers, three for registrars and registrars, and three for house-officers. noney for this purpose will come from regional research , which are supplied from the Central Endowment ; and the board has apparently taken this step because lises that members of its staff may hesitate to apply lvance for grants to aid work that is not of major rtance.

spital management committees have power to organise own research funds; and Dr. Avery Jones[1,2] has pointed that these funds can foster "small growing-points of ledge in the regional hospitals." The South West opolitan Board, it seems, is pursuing the same objective different way.

ROCKEFELLER GRANTS

E Rockefeller Foundation has made a grant of £10,000 niversity College, London, for the continuation of studies the selection and training of medical students. The will be done in the anatomy department by Miss M. L. ison, PH.D., under the direction of Prof. J. Z. Young. The foundation has supported preliminary work during last five years, and some of the results have been published ur columns.[3] One outcome of the earlier work[4] has been development of free group discussions as a technique to plement the usual methods of teaching in the lecture- atre, the dissecting-room, and the practical class. The n aim of these discussions is to help to develop skill in rate and comprehensive observation, the precise use of guage, and the weighing of evidence. They are conducted way designed to encourage the students to become aware he preconceived ideas which determine how they approach blems, and to examine their usefulness. The discussions recorded on tape, and students can listen to them again l to those of other groups. It is thus possible to get a ter understanding of some of the difficulties of thinking arly which crop up in all groups. The teachers' contribu- ns to the discussion can be studied and their effectiveness essed. With the coöperation of a psychologist, it is ned later to make some objective assessment of the results this teaching method. The discussions lead to the free change of ideas, and a broadening of the students' experience of other people. The students get practice in expressing their own ideas quickly and clearly, in understanding other people's, in giving and accepting criticism, and, in general, in handling the "human," as well as the scientific, side of a doctor's job.

The foundation has also made grants to Prof. W. I. B. BEVERIDGE towards his coming visit to the United States, during part of which he will be visiting professor in the department of bacteriology at Ohio State University; to Dr. ANDREW TOPPING, dean of the London School of Hygiene and Tropical Medicine, for the purpose of observing teaching methods and the practice of public-health administration in the United States and Canada; to Dr. ALEXANDER MAIR, of the University of St. Andrews, for observing teaching methods in public health in the United States and Canada; to the University of Oxford for the purchase of apparatus and supplies for neurophysiological research by Dr. E. M. VAUGHAN WILLIAMS, of the department of pharmacology; and to the University of Manchester for the purchase of laboratory equipment for the use of Dr. S. W. STANBURY in the department of medicine.

PHILOSOPHIC APPROACH TO PSYCHIATRY

Dr. Harold Palmer,[1] faced with the scientist's duty of integrating his concepts and the psychiatrist's duty of coping with his patients, finds himself hampered by the lack of a common language—let alone a common outlook—among the many disciplines with which his specialty has commerce. At one point he encounters neurologists engaged in describing and measuring anatomical and physiological mechanisms, at another psycho-analysts concentrating on mental events, at another behaviourists who have agreed to leave mental events entirely out of their calculations, and at another those who have concepts which they relate to the term "soul." In such awkward company channels of communication are apt to run sluggishly, and Dr. Palmer is quite right to try to open them up: though non-philosophic readers may wish he had done it without the use of terms from yet another discipline, and one notoriously difficult for beginners.

Some proleptic basic assumptions, he suggests, are necessary to the theory and practice of psychiatry (and it is surely an interesting illustration of our semantic entanglements that "proleptic" no longer has anything—except its root—in common with "epileptic"). He assumes, then, for practical purposes, that there is life, and that one aspect of living human beings is connoted adequately by the term "mind"; there are also awareness, experience, knowledge, memory, and introspection. Moreover human beings are either awake (conscious) or asleep; and conscious human beings are "'experiencers' and constitute the 'subject' in a total biological field whose 'objects' are determined in part by their biological relevance and in part by the subject's attention." He thinks of the subject as composed of "the 'self' and its subsystems," and he holds the self to possess a bodily and a mental aspect. Selves communicate by means of symbols, and symbols possess meaning for minds. "Mind is the name we employ to signify both the territory in which we operate with symbols as symbols, and the faculty whereby these operations take place." He also assumes that human minds resemble one another, and that men with the same racial, social, temporal, linguistic, and educational background will tend to collect a similar meaning from any given set of symbols.

Psychiatry, then, concerns itself with "selves"; and mental disorder, whatever its cause, is associated with dislocation of a "self" and a "self-image." A science of "selves," he suggests, is "the only philosophically unassailable discipline within which the psychiatrist can manipulate his terms without offences against logic." It allows him to establish a framework of reference for data from studies of the anatomy, physiology, and pathology of human tissue, studies of the behaviour of institutions, groups, and societies, and studies relating to the notion of "soul" and the notion of purpose (for which Freudian psycho-analysis, being too narrowly mechanistic and deterministic, does not, he thinks, make sufficient allowance).

He suggests that any contribution which the psychiatrist brings to the understanding of human nature is in the order of that made by the novelist, dramatist, or practical man, rather than that made by the scientist. This does not hold, however, when the psychiatrist is engaged in treatment; for then he is invested with special responsibility, and is accountable at law for his acts.

Faced with so many claims on his capacity, a man may well begin to look critically at the training he has received in

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Jones, F. A. *Lancet*, 1951, i, 961.
Jones, F. A. *Ibid*, 1952, i, 922.
Johnson, M. L. *Ibid*, 1949, ii, 529; *Ibid*, 1952, ii, 876.
Aitken, J. L., Johnson, M. L. *Ibid*, p. 409.
Johnson, M. L. *Ibid*, 1950, ii, 313.

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[1] The Philosophy of Psychiatry. By HAROLD PALMER, M.D. New York: Philosophical Library, 1952. Pp. 70. $2·75.

ously Although the test for antibody by complement-fixation and antihæmagglutinin estimation may be negative in the first week of illness, other more reliable diagnostic methods give positive results at this time The detection of virus in skin lesions by egg-culture techniques, or of virus antigen by complement fixation, are always to be preferred in the early stages of the illness In recently vaccinated patients they are the only reliable laboratory methods at all stages of illness The antibody in the serum of alastrim patients was no more specific than that in the sera of artificially immunised animals, it reacted practically to the same titre with the viruses of alastrim, variola, vaccinia, and cowpox The isolation of virus from the patient provides the only laboratory method of distinguishing smallpox and alastrim from generalised vaccinia, the distinction between smallpox and alastrim still rests on clinical and epidemiological considerations

SUMMARY

21 sera from 19 alastrim patients who had not previously been vaccinated were examined for antibody by complement fixation, hæmagglutination, and neutralisation techniques The neutralisation techniques using the pock-counting method on the chorioallantois of chick embryos was the most reliable, and the antihæmagglutination method was rather more sensitive than the complement fixation test

All three methods gave positive results on sera taken on the tenth day or later

The sera fixed complement equally well with antigens prepared from egg membranes infected with the viruses of alastrim, variola, vaccinia, and cowpox In neutralisation tests also, the sera were equally active against the four viruses.

We are indebted to Dr J Innes, medical officer of health of Rochdale County Borough, for information about the patients from whom blood was collected

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THE METHOD OF ADMINISTERING DICOUMAROL

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IN the administration of dicoumarol care must be taken to avoid hæmorrhage on the one hand and ineffective treatment on the other

The incidence of hæmorrhage in some published series has been so great that dicoumarol has been discredited as dangerous Hæmorrhage has usually been observed in 5% or 6% of hospital patients, two thirds of the hæmorrhages being mild and a third severe (Allen et al 1947, Allen 1948, Nichol 1950, and others) Some of the hæmorrhages have been fatal (Duff and Shull 1949, Nichol 1950, and others) In prolonged treatment of ambulant outpatients the incidence of hæmorrhage has been still greater, up to 15% (Olwin 1949)

One reason why hæmorrhage occurs so often is that there is still considerable disagreement about how to determine the requisite dosage

Two main methods of administering dicoumarol are used at present (1) intermittent dosage, and (2) daily maintenance dosage

Intermittent dosage consists in giving relatively large doses of dicoumarol at intervals of up to 10-12 days How frequently the doses must be given depends on the individual patient's response to dicoumarol Each single dose should be large enough to reduce the prothrombin value to the therapeutic range and keep it there for several days The next dose is given when the prothrombin value has again increased above a certain level As the effect of even a large dose of dicoumarol is seen only after a certain time lag, the effect of each new dose will usually be delayed in relation to the often rapidly increasing prothrombin value Hence the prothrombin values are likely to vary widely, the greatest variations being observed in those patients who metabolise dicoumarol rapidly and therefore require large and frequent doses This method is especially used in the U S A, and has recently been enthusiastically recommended by Shapiro and Weiner (1951) who hold that the danger of overdosage, through accumulation of dicoumarol in the body, is least when this method is used They also claim that *intermittent dosage makes it easier to maintain* a stable and effective concentration I do not agree with this opinion, for reasons discussed below

Maintenance dosage aims at keeping the prothrombin value most nearly constant in the optimal therapeutic range by *giving daily doses in amounts varying according* to the patient's tolerance for dicoumarol This method is most commonly used and I regard it as the only practicable one when treatment of the ambulant patient has to continue for a long time It has, however, proved difficult in practice

This is evident from the many different dosage schedules published *Greatly varying initial doses have been given* In continuing treatment, most physicians have decided the particular day's *maintenance dose according* to the prothrombin value (given in seconds, percentages, or prothrombin index) which has been determined the same morning Some authors have divided the prothrombin scale schematically into intervals and recommend definite *doses for each interval* the lower the prothrombin value the smaller the dose Usually, in schedules outlined no consideration is given to whether the prothrombin value is tending to rise or to fall In other words, the dosage is determined *only from the day's prothrombin value* without regard to previous days' values As a guide for other workers dosage schedules like these have little value Dosage schedules based on the prothrombin time (in seconds) or on the prothrombin indices are valueless unless one uses not only the same method but also the same type of thromboplastin as the originator The relation between a given prothrombin time (or prothrombin index) and the prothrombin value, expressed *as a percentage of normal*, depends not only on the activity of the thromboplastin but also on the type of thromboplastin used (*Owren* 1947, 1949)

The varying nomenclature and methods and the many different dosage schedules have created uncertainty about the administration of dicoumarol Those seeking information can easily become confused and may overlook the important basic point of the treatment I propose to state here the most important principles of dicoumarol treatment and *to describe* a rational maintenance dosage originally introduced in Norway by P A Owren

To assure the rational administration *of dicoumarol* three conditions are necessary

(1) An exact and quick method of estimating prothrombin and a laboratory with the necessary equipment and a staff familiar with the method

(2) The physician who determines the dosage must have theoretical knowledge and preferably also practical experience *of the effect of dicoumarol on man*

(3) Quick and dependable contact between laboratory, administering physician, and patient

Royal College of Physicians of London

Dr. W. R. S. Doll will deliver the Milroy lectures on Tuesday and Thursday, Feb. 10 and 12, at the college, Pall Mall East, S.W.1, at 5 P.M. He will speak on Bronchial Carcinoma—Incidence and Ætiology.

Royal Society of Medicine

Mr. Philip Wade has been appointed librarian of this society. Mr. Wade has been sub-librarian for the past three years.

North of England Obstetrical and Gynæcological Society

The following officers have been elected for 1953: president, Mr. D. Currie; hon. treasurer, Dr. C. H. Walsh; hon. general secretary, Mr. H. Agar; hon. reporting secretary, Mr. S. Bender.

Chadwick Public Lecture

Dr. George Decharneux (Liège) will deliver a lecture at the Royal Society of Tropical Medicine and Hygiene, 26, Portland Place, London, W.1, on Tuesday, Feb. 24, at 2.30 P.M. His subject is to be Industrial Medicine and Hygiene in Belgium.

Course in Tropical Hygiene for Laymen

The annual course in tropical hygiene for laymen will be held by the Ross Institute this year from Monday, July 20, to Friday, July 24. Further particulars may be had from the institute at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

International Hæmatology Congress

The fourth European Congress of Hæmatology will be held in Amsterdam from Sept. 8 to 12. The English speakers will include Dr. J. V. Dacie, Dr. J. F. Ackroyd, and Dr. C. C. Ungley. The main subjects chosen for discussion are: Immuno-hæmatology, Erythropoiesis and Hæmoglobin Metabolism, Acute Leukæmias, Lymph-gland Puncture, Thrombocyties, and the Physiology and Pathology of Coagulation. Further particulars may be had from Dr. M. C. Verloop, secretary of the congress, Maliesingel 15, Utrecht, Holland.

Chronic Rheumatic Diseases

A weekend course on these diseases will be held at the rheumatism unit of St. Stephen's Hospital, Fulham Road, London, S.W.10, on March 21 and 22. Dr. Peter Bishop will give the opening lecture on the Endocrine Aspects of the Chronic Rheumatic Diseases, and other speakers will include: Dr. Francis Bach, Dr. Grace Batten, Dr. Raymond Daley, Dr. Phillip Ellman, Mr. H. E. Harding, Dr. F. Dudley Hart, Dr. J. H. Jacobs, Dr. J. A. Purser, Dr. F. Sargent, and Dr. G. Signy. Further particulars may be had from the secretary of the Fellowship of Postgraduate Medicine, 1, Wimpole Street, W.1.

Royal Sanitary Institute's Congress

The institute will hold its health congress this year at Hastings from April 28 to May 1, under the presidency of Lord Eustace Percy. The speakers will include Dr. J. F. Warin and Dr. R. Scott (section of preventive medicine); Dr. B. E. Schlesinger, Dr. F. J. W. Miller, Dr. Maurice Woods, Dr. Dorothy Egan, and Dr. Mary Hellier (section of maternal and child health); Dr. Charles Wilcocks and Dr. D. Khatri (section of tropical hygiene); and Dr. Andrew Meiklejohn, Dr. C. O. S. Blyth Brooke, and Dr. J. G. Billington (section of occupational health). Copies of the programme of the congress can be had from the secretary of the institute, 90, Buckingham Palace Road, London, S.W.1.

Registration of British Medical Graduates in Victoria, Australia

Now that the full provisions of the Medical Act, 1950, of Great Britain have come into operation, an amendment of the Victorian law is necessary to restore reciprocity of registration. As Victorian law is now framed the necessity for Victorian graduates in medicine to produce the further evidence of experience when seeking registration by the General Medical Council of Great Britain and Ireland makes it impossible for the Medical Board of Victoria legally to recognise qualifications in medicine gained in Great Britain and Ireland. The Victorian government are considering the necessary amendment, but meanwhile the Medical Board of Victoria intends refusing applications for registration, in the

Association of Whole-time Salaried Specialists

The annual general meeting of this association will be h at the Royal College of Surgeons, Lincoln's Inn Fiel London, W.C.2, on Friday, Feb. 20, at 4.30 P.M. The ann dinner will take place the same evening at the college. F particulars may be had from the secretary of the associati 45, Lincoln's Inn Fields, W.C.2.

Assistant Medical Officers' Claim

At a meeting of committee C of the Medical Whit Council on Jan. 22, the staff side put forward the claim an adjustment in the remuneration of assistant medi officers. Agreement was not reached, and the staff si requested that the matter should go to arbitration. T management side agreed to this course.

An Indian Chest Institute

The Vallabhbhai Patel Chest Institute at New Delhi w opened on Jan. 12 by the Indian health minister. T institute has grown out of the chest department of De University, and the World Health Organisation has recogni the department as a training centre for its fellows fr the south-east Asia region.

Poisons Rules

The Home Office draws attention to the Poisons (no. Rules 1952,[1] which came into operation on Jan. 1. Th rules make good the omission from the first schedule to Poisons Rules 1952[2] of dinitronaphthols, dinitrophenols, a dinitrothymols.

Lady Tata Trust

The trustees of this fund invite applications from inve gators of any nationality, working in any country in which is possible to make payments, for grants, scholarships, fellowships for research on diseases of the blood, with spec reference to leukæmia. In view of the affinity betwe leukæmia and other forms of neoplastic disease, candida who wish to undertake research on any aspect of malign disease which may throw incidental light on the rela problem of leukæmia will be eligible.

Grants are made for research expenses or to provide scientific technical assistants for senior workers. Scholarships (at the rate £600 per annum) are awarded for the personal remuneration workers carrying out approved research under suitable directi In addition, the trustees may award one or more fellowships (£1 p.a.) to workers with considerable research experience. Furt particulars may be had from the secretary of the scientific advis committee, c/o Medical Research Council, 38, Old Queen Str London, S.W.1. Applications must be submitted before March 1953.

Administrative Costs of Executive Councils

The Minister of Health has informed executive councils England and Wales of the cost per head of population of administrative expenses of each council in the year 1951– Among 49 English county and combined county and coun borough executive councils the cost per head was highest the Scilly Isles (2s. 10d.) and Westmorland and the Soke Peterborough (each 1s. 9d.), and lowest in Gloucester city a county, Berkshire, and the East Riding of Yorkshire (ea 10d.); among these councils the average cost per head w 1s. 2d. Among 74 English county-borough executive counc the cost per head ranged from 2s. 2d. in Chester to 11d. Coventry and Huddersfield; the average cost among th councils was 1s. 4d. Among 12 Welsh county and co bined county and county-borough executive councils cost per head ranged from 2s. 2d. in Cardigan to 10d. Glamorgan, with an average of 1s. 6d.; and among 3 Wel county-borough executive councils the cost per head w 1s. 5d. for Cardiff, 1s. 4d. for Swansea, and 1s. 6d. for Merth

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EMERGENCY BED SERVICE.—In the week ended last Mond applications for general acute cases numbered 2191. The proporti admitted was 73·48%. A red warning was issued last Tuesd

DR. WILLIAM PICKLES, of Aysgarth, is sailing on Feb. 26 for So Africa, where he has been invited by the University of Cape To to give a series of lectures. He will be away 10 weeks.

The photographs of the new Central Public Health Laboratory Colindale (*Lancet*, Jan. 24, 1953, p. 190) should have been attribut to Cecil Walden, Ltd.

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1. Poisons (no. 2) Rules 1952 (S.I. 1952 no. 2268). H.M. Station Office. 2d.

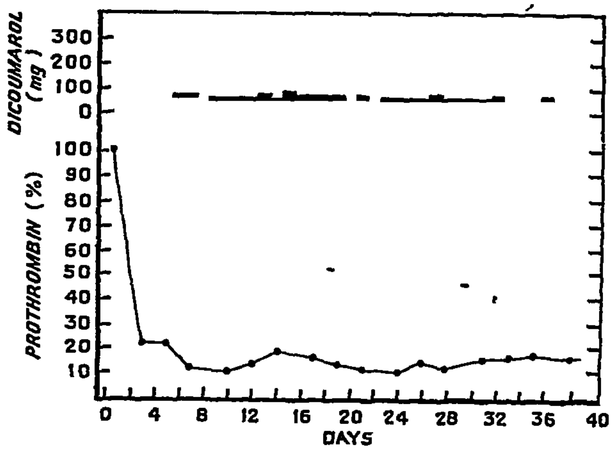

Fig 2—Adjustment of dosage of dicoumarol according to effect on prothrombin in a man, aged 73, with coronary thrombosis and moderately resistant to dicoumarol

previous doses of dicoumarol that we see on the curve because of the prolonged cumulative effect of dicoumarol What we aim at with the dosage is to reduce the prothrombin value as quickly as possible to the therapeutic range, which seems to lie between 10% and 30% The next step is to learn the patient's tolerance towards dicoumarol—in other words, to establish the daily maintenance dose needed to keep the prothrombin value as nearly constant as possible in the therapeutic range Experience shows that the daily maintenance dose can vary from about 20 mg to about 150 mg We can obtain the first impression of the patient's requirement of dicoumarol by studying the effect of the initial dose after two or three days, as already mentioned If the prothrombin value diminishes rapidly and extensively it indicates that the patient is relatively sensitive If the effect is slow and weak, one can count on the patient being resistant As one continues the dosage, the curve will constantly show the effect of the doses which have already been given The practical method of determining the dosage can be most easily understood from illustrative cases in which the adjustments of the dosage were based on fluctuations in the curves

Fig 2 shows the progress of the treatment of a moderately resistant patient The prothrombin value fell evenly to the therapeutic range and the correct maintenance dosage was quickly reached

Figs 3 and 4 are from two patients, one moderately sensitive and the other very sensitive The prothrombin values of both fell rapidly to the therapeutic range In the first patient (fig 3) the dose was therefore omitted on the fourth day, and during the rest of the course the prothrombin value was kept in the therapeutic range with daily doses varying between 37 mg and 50 mg In the second patient (fig 4) the prothrombin value fell (in spite of small doses on the third, fourth, and fifth days) to 6%, but climbed above 10% when dicoumarol was withheld for a couple of days After small doses of 37–50 mg daily for five days the prothrombin value again fell (to 3%) and it remained too low for eight days in spite of intravenous vitamin K No complications were observed

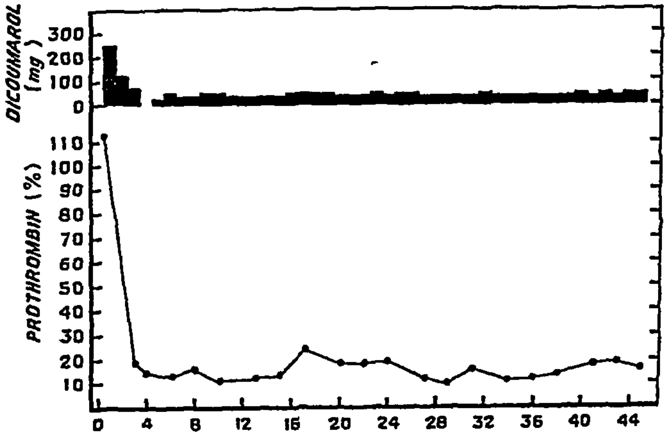

Fig 3—Adjustment of dosage of dicoumarol according to effect on prothrombin in woman, aged 66, with thrombosis of a femoral vein and moderately sensitive to dicoumarol

Fig 5 shows the course in a very resistant patient With the usual initial doses, the prothrombin value had decreased very little at the end of the first three days During the next ten days very large doses, 125–200 mg, were given daily, and the prothrombin value fell relatively slowly to the therapeutic range, taking about a fortnight to get below 20% As the prothrombin value continued to fall, the dosage was reduced moderately for a few days But even that reduction caused the prothrombin value to climb to 45%, so the dosage was increased again

Fig 6 shows the secondary rise of the prothrombin value which often takes place after the effect of the initial dose has ceased, when the subsequent dosage has been reduced too much Increased dosage on the sixth day brought the prothrombin value down to the therapeutic range, where it was kept fairly constant by continued slight adjustment of the dosage

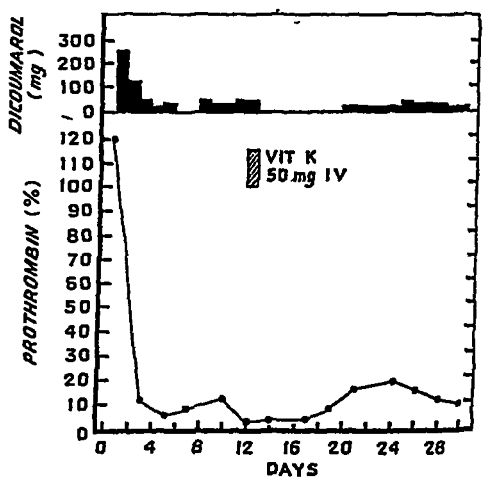

Fig 4—Adjustment of dosage of dicoumarol according to effect on prothrombin in a man, aged 75, with coronary thrombosis and very sensitive to dicoumarol

Fig 7 illustrates another phase A patient with myocardial infarction, who was at first moderately sensitive to dicoumarol had his prothrombin value kept down to about 10% with 50 mg of dicoumarol daily Thereafter his resistance to dicoumarol increased, and the maintenance dosage had to be more than doubled to produce the same effect At the time when small doses were sufficient to keep the prothrombin value down this patient was in a state of shock When he started to recover and his general condition improved, his resistance increased Such an increase of resistance is common in heart patients, especially those with myocardial infarction when their condition improves

Fig 8 shows how doses of dicoumarol should not be given The doses from day to day vary too much This is a very common mistake which is easily made when the dosage is based only on the current prothrombin value and not on the shape of the curve

It is clear from figs 2–8 that the dosage of dicoumarol must be based on the previous shape of the prothrombin curve A rise or a fall in the curve must at once be met by an increase or a decrease of the dosage The closer one approaches the ideal maintenance dosage for the patient, the smaller will be the variation in doses from day to day

A SURGICAL POLICY FOR PEPTIC ULCER

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The mortality of gastrectomy has fallen so satis- ctorily in recent years that this operation is no longer nned because of the risk it entails. Moreover, more d more physicians are recognising that only surgery n alter the course of the lifelong disorder from which ptic ulcers arise. At the same time, the great increase the number of gastrectomies, and particularly the ndency to make them subtotal, has caused concern out these patients' capacity to maintain health and ficiency on the diet obtainable in Britain today.

The aim of surgery must always be to discover and ctise the least interference that will adequately trol disease, imposing the smallest possible cost in e, function, and tissue. It was with this in mind that e set out, seven years ago, to ascertain whether the fer and less drastic operation of vagotomy might rove sufficient for the cure of peptic ulcer, and five ears have passed since we published our earliest xperience with it (Orr and Johnson 1947).

We remarked then that vagal resection might be ooked on as a reconnaissance in force in the war against eptic ulcer. Little is lost, we added, if on occasion it ails, for we still have at our disposal the full-scale attack y gastrectomy. A lasting success by vagotomy is a riumph of physiological strategy. A failure following gastrectomy, however, is an irretrievable reverse in which much has been sacrificed without hope of withdrawal.

By the time we next reported our results (Orr and Johnson 1949), though ground had been won and valuable information gained, we had been forced to resort to more comprehensive operations for most of our patients. The conclusion had become inescapable that, for permanent symptomatic relief, correction of the deformity and obstruction caused by scarring is at least s important as healing of the ulcer. We therefore ged that, for all ulcers which had become large and lous or had penetrated into adjacent organs, or where ajor hæmorrhage had taken place, gastrectomy should used, with or without the addition of vagal resection. Though, like most others, we abandoned vagotomy ne as a treatment for duodenal ulcer, we continued he follow-up on the patients who had been submitted to this operation, and we are thus able to analyse the results from four to seven years after.

LONG-TERM RESULTS OF VAGOTOMY ALONE

[illegible] original 108 patients submitted to vagotomy [illegible]duodenal ulcer in 1946–48 60% have received [illegible] and have declared themselves greatly [illegible] or since, 33% having been without even the [illegible] symptoms. However, 25% have had to [illegible]further surgery, either to relieve stenosis and [illegible] or to remove a recurrent ulcer, before a [illegible] achieved, 3 of the new ulcers being gastric ones. A further 15%, though they have not relapsed to the extent of requiring another operation, are only partially relieved of symptoms and have to have intermittent medical care. (81% of the original 108 patients now have *good* results, and the mortality has been nil.) In his survey of 736 patients submitted to vagotomy alone by many different surgeons, Pollock (1952) reported 44% of them as having unsatisfactory results and found evidence of ulcer relapse in 9·4%.

It was reported by St. John and Flood (1939), and many others have published similar figures, that after the successful medical cure of peptic ulcer 65% of patients have recurrent ulcers within two years. All our patients had long histories and recalcitrant symptoms and perhaps, on the average, had relatively advanced lesions. Hence it certainly cannot be said that vagotomy made little difference to their hitherto downhill progress, and there can be no doubt that the operation substantially alters the course of ulcer disease. Moreover, though 40% of patients *did not have sustained symptomatic relief* after this safe and modest manœuvre, only a few of those reoperated on had ulcers, most of them showing only *gross scarring and deformity* as the cause of their continued symptoms.

In the treatment of anastomotic ulcer following gastrectomy, there is still *an important place* for vagotomy; for a second gastric resection is a relatively dangerous undertaking. Moreover, a second gastrectomy has too often been followed by further ulcer recurrence. Again, for jejunal ulcer after earlier gastro-enterostomy, vagotomy is sometimes the wisest choice when the patient, as is so often the case, is a poor surgical risk.

Even in the absence of obstruction, vagal resection usually causes retention of food in the stomach; and though this contributes to the cure of duodenal ulcer, it may give rise to untoward symptoms. Fortunately this retention does not occur when a well-designed drainage operation has been added to vagotomy.

VAGOTOMY PLUS GASTRO-ENTEROSTOMY

Neither vagotomy nor gastro-enterostomy alone can be depended on to cure and control ulcer disease with sufficient regularity; but, when the two operations are done together, the results are said to have been excellent. Crile and his colleagues (1952) have used this combination well over 400 times for duodenal ulcer, and report only 6% recurrences and less than ½% deaths. This is surely preferable to less than 1% recurrences but 4% deaths, such as may be expected with radical gastrectomy.

We have used vagotomy in 12 cases of anastomotic ulcer after earlier gastro-enterostomy, and in 2 of our early patients who had had vagotomy alone gastro-enterostomy was added later. In 26 cases of duodenal ulcer we have used vagotomy and gastro-enterostomy together. Such small numbers can give no very weighty support to Crile's claims, but the results have been very satisfactory, and we are bound to keep an open mind about this operation. Pollock (1952) has collected and followed up 462 cases after vagotomy and gastro-enterostomy by a number of different surgeons and has found only 8% of clinical failures among them.

It has so far been our policy to reserve vagotomy and gastro-enterostomy for a few patients in whom, because of obesity and emphysema, for example, gastrectomy might have been unduly difficult and hazardous.

SUBTOTAL GASTRIC RESECTION

A radical gastrectomy is the operation perhaps most widely favoured in Britain at present and we have used it extensively ourselves.

Visick (1948) defined subtotal gastrectomy as one which removes the first part of the duodenum, the pylorus, the whole of the lesser curvature, and the greater curve up to, but not including, the *uppermost* of the short gastric vessels. Done in this way gastrectomy leaves a very small gastric pouch indeed, with few tional doses of only 2–4 mg a day, the same result would be *obtained* The figure proves, better than words, the dependability and exactness of Owren's *method* of prothrombin estimation when done by trained personnel

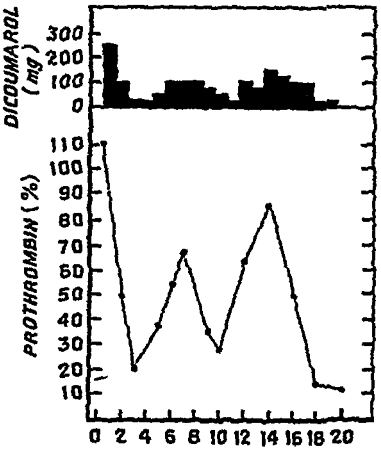

Fig 8—Wrong way of adjusting dosage of dicoumarol—on current prothrombin value instead of previous shape of prothrombin *curve*—in a man, aged 69, with phlebitis

The long interval between each estimation of the prothrombin value makes it necessary to be very cautious One rarely has to make any great change in dosage because of the patient's tolerance having increased or decreased, but it will sometimes be desirable or necessary to have an extra estimation made, especially if the prothrombin value has decreased too much As a rule one estimation a week will even then be sufficient

The adjustment of dosage in ambulant outpatients with infrequent estimations of the prothrombin value is much more a matter of experience than in the treatment of inpatients It can only be learnt by trial and error It is essential to have a diagram with a constant scale for showing the variations in prothrombin values in relation to time intervals, so as to assess the effect of a change in dosage It is also of the utmost importance to make sure that patients really take the dose prescribed for them even the most intelligent patient can be forgetful I have therefore made it a rule that each patient receives a written dosage schedule, covering each day of the period between two estimations of prothrombin After taking each day's dose the patient is required to cross off the dose If he forgets to take his daily dose, the fact will be shown on his schedule and will be noticed Unfortunate consequences can then be avoided By taking these precautions effective treatment can be given to nearly all ambulant patients without incurring any risk

Experience has further shown that it is difficult to achieve a stable maintenance dosage and an even prothrombin curve in heart-failure This is probably caused by variations in the degree of congestion in the liver, involving variations in the synthesis of prothrombin, and leading to fluctuations in tolerance of dicoumarol

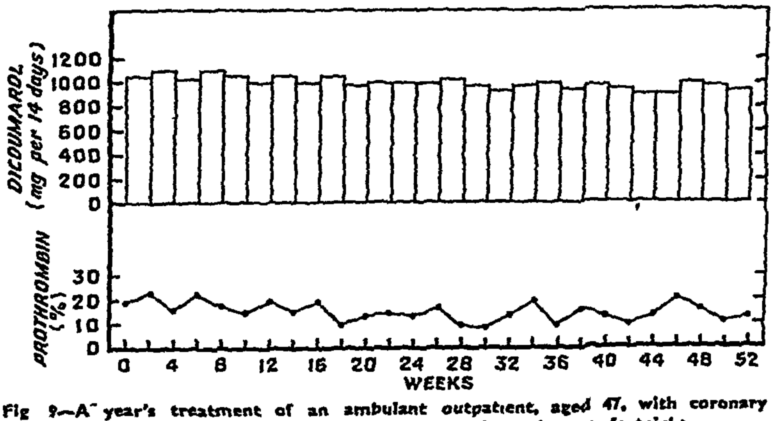

Fig 9—A year's treatment of an ambulant *outpatient*, aged 47, with coronary thrombosis the prothrombin value being estimated every fortnight

It is a good rule to make patients aware of the dan of hæmorrhages, and to advise them to report to th physician immediately if they should observe hæmatu epistaxis, blood in the stools, or ecchymoses in the s and mucosæ without traumatic cause

The *only* complication of any importance fr dicoumarol treatment is hæmorrhage, and it is r when one uses a dependable method for the estin tion of prothrombin and administers the dicouma according to the above-mentioned principles In hospital treatment of 522 patients in Oslo Munic Hospital not a single serious hæmorrhage was observ Slight hæmorrhages, such as hæmaturia, epista bleeding hæmorrhoids, and streaks of blood in the sputu all of short duration, were seen in 8 patients In one these patients (bleeding hæmorrhoids) the hæmorrh was thought serious enough to need a blood-transfusi particularly as the patient had recently had coron thrombosis In the 7 other cases it was sufficient to g vitamin K intravenously and to withhold dicoumarol fo while Among 107 ambulant patients treated for perio varying between one and twenty-six months no serio hæmorrhage was observed One patient had an epista which required tamponage Another, a man aged 70, h a muscular hæmatoma in the right thigh after a long wa In the epistaxis case the prothrombin value had remain low (8–9%) for a fortnight before the hæmorrhage to place In the hæmatoma case the prothrombin val was 15%, and possibly a slight traumatic episo was partly responsible Both patients have sin continued to receive dicoumarol treatment witho complication

Vomiting can sometimes be a hindrance in admin tering the initial dose, particularly where patients fe nauseated and vomit before receiving treatment, as often the case in coronary thrombosis In such instanc it is advisable not to administer the whole initial do (10 tablets) at once but to give it in smaller portio during the day.

From what has been said above it is evident that o cannot schematically specify a universal dosage dicoumarol, even where patients have the same pr thrombin value The dicoumarol dosage must vary fro one patient to another according to the shape of t prothrombin curve The only dosage which can universal is the initial dosage, by which is meant t first and second days' doses The advantage of this h been stated above but is worth repeating it takes som time from the administration of the initial dose unt full therapeutic effect is achieved The longest time required in resistant patients, in whom the given initi doses are too small to decrease the prothrombin val to the therapeutic range Continued heavy doses duri the following days may be necessary (see fig 5) Despi this, a substantial number of days can often pass befo one achieves full therapeutic effect Out regard to sensitive patients it would inadvisable to increase the size of the initi dosage much beyond that mentioned abov In all cases where one wishes to obtain th quickest possible effect one ought to beg treatment with heparin and dicoumar together The heparin treatment mu then be continued until the prothromb value has reached the therapeutic range

The indications and contra indication of dicoumarol treatment in differen thrombo embolic *conditions* will not b discussed here They have been extensivel treated by other workers (for referenc see Marple and Wright 1950), nor ar the results of treatment in differen thrombo embolic conditions considere here

36 of them with vagotomy added), 26 had vagotomy us gastro-enterostomy, 2 had short-circuits for stenosis ter earlier vagotomy, and 12 had vagotomy alone for nastomotic ulcers after earlier gastro-enterostomy.

There were 6 postoperative deaths, a mortality of 1% for the policy as a whole or 1·2% for the 486 astrectomies. The causes of death were: coronary rombosis; burst abdomen followed by general eritonitis; uræmia in an elderly man with prostatic bstruction; septic thrombophlebitis starting in a vein sed for blood-transfusion; general peritonitis developing fter discharge from hospital after an apparently neventful convalescence; and suppurative cholecystitis a patient known to have gall-stones, which were, erhaps unwisely, not dealt with at the same time as the astrectomy. Since the end of the review period we ave performed a further 114 operations with 3 deaths lose together. Our mortality has therefore risen to 1·4% or 640 cases.

METHOD OF FOLLOW-UP

Though nearly all the patients included in this review vere interviewed by one or other of us at regular intervals, ve have come to the conclusion that a carefully composed questionnaire yields data more susceptible to bjective analysis and allowing comparisons of greater alidity than can be gained in conversation; for at nterviews not only do questions vary in the way they re put to the patient, but also his answers are likely o be influenced by the knowledge that he is, or is not, n the presence of the surgeon who did his operation. Our analysis has therefore been made on the basis of written questions to each of which alternative answers re offered—e.g., "Have you, since your operation, uffered from wind pain? YES, OCCASIONALLY OR SLIGHTLY, NO. Did you have wind pain as distinct from lcer pain before your operation? YES, OCCASIONALLY OR SLIGHTLY, NO. If so, is it now BETTER, THE SAME, WORSE? (Cross out two answers in each case.)"

After questions about ulcer pain, wind pain, vomiting of food, regurgitation of bile, heartburn, diarrhœa, attacks of weakness, giddiness, sweating, &c., size of meal taken without discomfort, and progress in body-weight, the patients are asked: "Do you find that, since your operation you are, all things considered, 1, CURED AND NORMAL; 2, MUCH BETTER; 3, A LITTLE BETTER; 4, NO BETTER; or 5, WORSE? (Strike out four of the alternatives and write nothing in.)"

Patients seem to have no difficulty in deciding whether to put themselves in category 5 or 4 or 3, but the choice between 2 and 1 caused some indecision. The more cautious were afraid, after years of relapse before operation, to pronounce themselves permanently cured, even though free from symptoms so far. We should have done better to call these two categories NORMAL AND APPARENTLY CURED and MUCH BETTER BUT NOT NORMAL. Possibly in the large groups dealt with psychological factors have evened out.

TABLE I—CATEGORIES SELECTED BY PATIENTS IN ANSWER TO THE QUESTION: "TAKING EVERYTHING INTO CONSIDERATION, DO YOU FIND YOURSELF, SINCE YOUR OPERATION, 1, CURED AND NORMAL; 2, MUCH BETTER; 3, A LITTLE BETTER; 4, NO BETTER; or 5, WORSE?"

Category	1	2	3	4	5	1 or 2	3, 4, or 5
	Percentages						
All lesions:							
Radical gastrectomy (222) ..	42	47	9	1·8	0·5	89	11
Policy group (513)	53	42	4	0·4	0·8	95	5
Duodenal ulcer:							
Radical gastrectomy (125) ..	46	41	10	1·6	0·8	87	13
Policy group (353)	54	41	4	0·6	0·8	95	5
Gastric ulcer:							
Radical gastrectomy (75) ..	36	56	7	1·3	0	92	8
Policy group (105)	49	47	3	0	1	96	4
	Not percentages						
Anastomotic ulcer:							
Radical gastrectomy (9) ..	5	4	0	0	0	9	0
Policy group (25)	13	10	2	0	0	23	2

Patients who could not be followed up fall into two groups: (1) those who will not coöperate, either because they are well and cannot be bothered or because they have done badly and are dissatisfied and resentful; and (2) those who have left the district for an unknown address and are not reached by follow-up communications. By persistence and personal visits we eliminated the first group, but were left with 7 in the second and have had to omit them from our calculations. Of 4 patients who died during follow-up, from causes unrelated to ulcer, the results for 3 have been included up to the date of the last review; but the 4th died within a few months, of carcinoma of the bronchus, and is excluded.

All these figures refer to the policy group. In the high-gastrectomy group we were rather less successful, for 15 patients remained untraced. 7 others died, 4 of causes unrelated to ulcer and 3 of unknown causes. 4 of these had not been followed for long enough before death to be included. We were thus left with 222 satisfactory follow-ups for analysis in this group out of 241 survivals.

ULCER RECURRENCE

No proven recurrent ulcer has yet appeared in the "policy" series; but there are 4 patients (0·8%) whose symptoms have never been relieved by their operations. In the high-gastrectomy group 2 proven recurrent ulcers developed and 3 other patients did not get relief from their symptoms from the start (2·2% in all). We may therefore claim that there is as yet no very significant difference in success, as regards control of ulcer disease, between routine radical gastrectomy and the selection policy.

SIDE-EFFECTS AND SATISFACTION WITH RESULTS

The clinical failures of gastric surgery are nowadays far more often due to the side-effects of operation than to ulcer relapse. The incidences of the various symptoms remaining, or appearing for the first time, after operations

TABLE II—SYMPTOMS OCCURRING DURING FOLLOW-UP

(Percentages of Alternative Answers Selected by Patients in Questionnaires (478 D.U., 180 G.U., 36 D.U., and G.U., 34 A.U., 7 Others))

Operation	No. of cases	Ulcer-like pain			Colic or wind pain			Vomiting of food			Regurgitation of bile			Attacks of weakness, &c. ? Dumping ? Hypoglycæmia			Size of meal able to be taken without discomfort				Symptomless	Symptomless gained weight and category 1
		No	Sl.	Yes	No	Sl.	Yes	No	Sl.	Yes	No	Sl.	Yes	No	Sl.	Yes	L.	M.	S.	O.		
$^{4}/_{5}$–$^{7}/_{8}$ gastrectomy ..	222	92	3	5	58	12	30	88	7	5	79	4	17	53	10	37	15	57	26	2	39	25
Policy group ..	513	96	2	2	79	8	13	92	3	5	86	5	9	75	10	15	25	63	12	—	58	44
Policy group:																						
$^{2}/_{3}$ gastrectomy ..	245	96	2	2	82	10	8	92	3	5	85	8	7	77	8	15	16	68	16	—	61	47
$^{1}/_{2}$ gastrectomy and vagotomy ..	228	97	1	2	75	7	18	92	2	6	85	3	12	73	12	15	32	58	9	—	55	41
Gastro-enterostomy and vagotomy ..	40	97	2	—	90	2	7	100	—	—	87	2	10	77	12	10	22	70	7	—	52	37

Sl., occasional or slight. L, large. M, medium. S., small.

The hydatid complement fixation test and the intradermal test have both been employed for more than forty years to assist in the diagnosis of hydatid disease While the usefulness of the two tests has been generally acknowledged, and one or other or both much used in other countries, there is little in the literature to show that, outside Australia, the careful work of Hamilton Fairley (1922) is fully appreciated Certainly in this country, as far as can be ascertained, the importance of using standard reagents does not seem to be generally accepted

This communication is intended to redirect attention to the need for standardisation of the reagents for both the hydatid complement-fixation and the intradermal tests and to demonstrate their enhanced value (admittedly in a small number of cases) in primary diagnosis, when an accurate " standardised " technique is followed

COMPLEMENT-FIXATION REACTION

Bordet and Gengou (1901) showed that when a suspension of *Pasteurella pestis* reacted with a plague antiserum in the presence of complement there was complete fixation of this latter substance This complement-fixation reaction was first known as the Bordet-Gengou phenomenon Further experiments demonstrated the specificity of the reaction and that other bacterial antigens and their homologous antisera fix complement in the same way The specificity was rated very high and the test was employed by Bordet and Gengou in 1906 as the final proof of the authenticity of *Hæmophilus pertussis* (Bordet Gengou bacillus) as the causal agent of whooping cough

Later observations by Gengou (1902) showed that the sera of animals immunised with dissolved protein, when brought together with their specific antigens, likewise formed combinations which fixed complement, and this led to a much wider application of the test During the same year that Wassermann, Neisser, and Bruck (1906) produced their classical paper on the serological diagnosis of syphilis, the application of the Bordet-Gengou phenomenon to the diagnosis of hydatid disease was described by Ghedini (1906) The most important of the early studies were, however, undertaken by Weinberg (Weinberg and Parvu 1908, Weinberg 1909), and today the hydatid complement-fixation test is frequently referred to as the Ghedini-Weinberg reaction Although there are several references in the literature to the varying fixing powers of the different hydatid fluids as antigens—particularly by Sonntag (1913)—opinions differ widely about this variation It was not until Hamilton Fairley (1922) showed that the specific antigen in a hydatid fluid was derived from the developing embryo, and that the potency of an antigen was related to the number of scolices present in the cyst from which the antigen was prepared, that any progress was made towards standardisation of the test Relying on this method of assessment, Fairley found that fluids rich in scolices regularly proved to be good antigens for the complement-fixation test Pooled fluids of this sort from several cysts, handled with aseptic precautions, give very consistent results Fairley preferred to use the clear supernatant from fairly fresh fluids without filtration or the addition of preservative

Although the use of fresh sheep hydatid fluid is feasible in areas where the disease is endemic and sheep infestation heavy, it cannot be relied on in this country where hydatid cysts are not commonly found in sheep Dried extracts of scolices have proved satisfactory, but there are always difficulties in using dried antigens for quantitative complement fixation work, where the batches of sera to be examined at any one time are relatively small A number of workers in the past used phenol as a preservative for the fluid hydatid antigen, but there is little reliable information about the keeping properties of such material Hamilton Fairley (1922) reported his preference for unpreserved antigens, but other workers have found merthiolate 1 in 10,000 to be satisfactory

Experience had shown us that the complement fixing antibody-titre of human sera from patients suffering from hydatid disease remain unaltered over very long periods provided they are sterile and maintained at +4°C It was decided therefore to attempt to standardise the test by employing a standard serum to titrate hydatid antigens and to repeat these tests at regular intervals to assess their stability over long periods It was also decided to investigate the possibility of immunising suitable animals for the production of a standard serum instead of having to rely on the chance availability of satisfactory human serum We were fortunate enough to obtain a fair amount of human serum from a case of hydatid disease which possessed strong complement fixing properties, this was adopted as the provisional standard serum, and through the kindness of Dr Hilda Gardner, of the Royal Melbourne Hospital, we received a generous supply of a very good sheep antigen preserved with 1 in 10,000 merthiolate

Preliminary tests showed that this antigen in the undiluted state did not by itself fix complement, and that its optimum dilution for the test was 1 in 4 when the provisional standard gave complete fixation of complement up to a dilution of 1 in 64

The technique adopted and maintained unchanged since was as follows

All reagents were used in unit volumes of 0 25 ml All sera including standard, negative controls, and test specimens were inactivated and set out in doubling dilutions from 1 in 2 to 1 in 128 Antigen, diluted 1 in 4, and $2^1/_2$ doses of complement, were added successively to each tube After thorough mixing, fixation was allowed to proceed for eighteen hours at +4°C After standing at room temperature for one hour the hæmolytic system (5% washed sheep cells plus 5 doses of hæmolytic amboceptor) was added *The racks were incubated* at 37°C for thirty minutes and preliminary readings were taken The racks were returned to the refrigerator before the final readings on the degree of hæmolysis were recorded

Notation		
	Complete fixation	+ + +
	75%	+ +
	50%	+
	25%	±

An arbitrary standard was thus set up for the hydatid complement fixation test, both for the technique itself and the reagents employed in the test It was decided that the serum should be the standardising agent and that no antigen should be used which when diluted 1 in 4 for the test did not give full fixation of complement with the standard serum at a dilution previously determined, and which did not in undiluted form by itself fix complement or react with sera from patients not suffering from hydatid disease

It is now almost two years since we adopted this technique and over this period batches of patients' sera have been examined at approximately fortnightly intervals In these tests the standard serum has always been included as a check on the potency of the antigen employed The original antigen has been used throughout the series reported, but a number of other satisfactory antigens have been used in parallel with it as additional controls

Our previous experience regarding the stability of the complement-fixing antibodies in human sera stored at +4°C over long periods has been confirmed The titre of a number of positive sera have now been tested at intervals over a year under controlled conditions and have been found to be unchanged

Other workers have explored the possibility of immunising animals for the preparation of hydatid complement gastrectomy with vagotomy and those of five-sixths gastrectomy alone.

The experiments on animals upon which Dragstedt 1945) based his use of vagotomy in man seem indeed to point in the right direction. It is not on these, however, nor on biochemical theory that the status of the operation must rest, but upon the clinical results.

We believe that vagotomy, including division of selected branches, though it is of strictly limited application, has now established for itself an important ancillary rôle in the surgery of peptic ulcer in intensely hypersecreting people. Moderate or two-thirds gastric resection alone is adequate to prevent recurrence of ulcer in patients with normal or low secretion-rates but sometimes fails in those with gross oversecretion. The addition of vagotomy makes moderate resection a satisfactory operation in these hypersecreting patients as well. The effect of this combination on gastric secretion is not significantly different from that of radical, five-sixths, or seven-eighths gastrectomy alone, but its power to prevent recurrence appears to be at least as good and its symptomatic results significantly better.

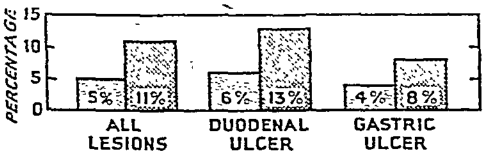

Fig 2.—Failures: percentages of patients selecting categories 3–5.

SUMMARY

The long-term results in 108 patients with duodenal ulcers submitted to vagotomy alone from four to seven years ago are reported. 60% of them continue to have good results, but the operation cannot be recommended, because, unless the effects of scarring and deformity are overcome at the same time, sustained symptomatic relief cannot be depended on.

However, vagus resection has proved and maintained its efficiency in controlling excessive acid secretion and therefore continues to have an important ancillary rôle in ulcer surgery.

During the past five years we have followed a policy for peptic ulcer in which patients are selected, according to the results of special investigations of acid secretion, either for two-thirds gastric resection alone or for a similar moderate gastrectomy with the addition of vagotomy. Gastro-enterostomy plus vagotomy has been used for a few bad-risk patients.

A method of follow-up and assessment has been used in which the patients themselves assess their results and the bias of the observer is eliminated.

The results of our policy, ascertained in this way in 526 cases, are compared with those of 241 radical (from four-fifths to seven-eighths) gastric resections used for similar lesions during the same period and similarly assessed (figs. 1 and 2).

Though both methods of treatment have achieved a high order of success, the "policy group" has shown a lower incidence of every side-effect and a higher proportion of satisfactory results during the period reviewed. The mortality in the policy group was 1·1%.

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THE SERUM ANTIBODY RESPONSE IN ALASTRIM

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In the outbreak of alastrim in the Rochdale district of Lancashire in the spring of 1952 there were more than 150 cases. Many of the patients, particularly in the earlier weeks of the outbreak, had not been vaccinated; and these cases offered an opportunity to investigate the antibody response to the infection. From 19 unvaccinated patients 21 sera were obtained and examined with three objectives: (1) to compare various laboratory methods for detecting antibody; (2) to ascertain the time of appearance of antibody in relation to onset of symptoms; and (3) to assess the specificity of the antibody response.

In patients suffering from alastrim or smallpox who have never been vaccinated the estimation of antibody in the serum may be a useful diagnostic procedure. In the Rochdale outbreak it was so used to make a retrospective diagnosis in patients who had recovered and for whom other laboratory diagnostic techniques could not be used. For the detection of antibody the complement-fixation test has been commonly employed: the serum is tested against an antigen prepared from smallpox or alastrim crusts, from vaccinia-infected tissue from rabbits or from egg membranes infected with vaccinia, variola, or alastrim viruses (Downie and Macdonald 1950). The test for antihæmagglutinins has become popular of recent years and has been used for the estimation of antibody in the serum after vaccination (Nagler 1944) as well as in cases of smallpox (Collier et al. 1950). The neutralisation test, made by injecting a mixture of virus and patient's serum into the skin of rabbits or on the chorio-allantoic membrane of chick embryos, also gives satisfactory results (Loutit and McClean 1945, Blattner et al. 1943). We used all these three methods in examining each of our 21 sera.

Previous work from this and other laboratories had shown the close serological relation between the viruses of variola, vaccinia, alastrim, and cowpox, using sera from immune animals. The sera from some of the alastrim patients were therefore tested against these viruses to find out whether the response to infection in man was more specific than that of experimental animals. Obviously the results might have some bearing on the value of laboratory tests in the differential diagnosis of alastrim, smallpox, and generalised vaccinia.

MATERIALS AND METHODS

Sera

All sera were stored in the refrigerator at about 4°C. Before use they were inactivated by heating at 57°–58°C for twenty minutes.

Viruses

One strain of each of alastrim, smallpox, vaccinia, and cowpox viruses was used. The alastrim strain was recovered

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MR. JOHNSON, MR. ORR: REFERENCES—*continued*

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TABLE V—RESULTS OF SERIAL TESTS IN THREE PATIENTS AFTER REMOVAL OF CYSTS

Clinical condition	Date	Complement fixation result in serum dilutions							Remarks
		2	4	8	16	32	64	128	
Liver and lung	1945	Strong positive titre unknown							Cyst removed from liver
	Dec 5 1950	+	±	−	−	−	−	−	Casoni ± ? recurrence
	Feb 12, 1952	+++	+++	+++	+	−	−	−	Definite recurrence Cyst found in l Casoni ++
Liver	June, 1951	+++	+++	+++	+++	+++	++	±	Operated on, May 1951
	Feb 1952	+++	+++	++	+	+	−	−	No symptoms Casoni +
	Sept, 1952	+++	++	+	−	−	−	−	No signs or symptoms
Liver	Dec 5 1950	+++	+++	++	±	−	−	−	Cyst removed
	Feb 13 1952	−	−	−	−	−	−	−	No symptoms or signs

These have been omitted from the table because the fluid itself had not been examined for scolices and antigenicity, and the blood-serum had not been examined for complement-fixing antibodies

Of 49 patients examined for diagnosis before any exploratory needling or operation, 20 were found to have negative skin reactions and hydatid complement-fixing antibodies could not be demonstrated All these patients were found to be suffering from a condition which was definitely not hydatid disease The remaining 29 were proved by operation to have hydatid cysts, but whereas 27 (93%) gave positive complement-fixing reactions only 25 (86%) gave positive skin reactions

A primary uncomplicated cyst of the liver may contain a fluid very rich in scolices but there may be little leakage into the circulation with only moderate serological reactions Table III shows the results in such a case On the other hand a patient who had a cyst removed one year previously and was then operated on again for removal of a further cyst gave a type of reaction which may be the result of escape of antigen at first operation plus the effect of the new cyst developing (table IV)

TABLE IV—RESULTS OF TEST IN PATIENT WITH HYDATID CYST WHO HAD HAD ANOTHER CYST REMOVED A YEAR PREVIOUSLY

Antigen	Serum	C F T result
Standard	Standard	1 in 64
Standard	Patient's	1 in 64
Patient's	Standard	1 in 8

Skin test strong positive

Table V below illustrates the results of serial tests performed on these patients after operation for removal of hydatid cysts, one of which shows a fall in complement-fixing antibodies followed by a rise as a new cyst developed The other two cases of single cysts of the liver with no evidence at present of any new cyst development show continuous falling titres

DISCUSSION

Since Hamilton Fairley (1922) showed that the antigen content of a hydatid fluid depended on the presence of scolices, it has been obvious that a sterile cyst will not contain antigen and that serological reactions will not be positive in patients with cysts that do not contain scolices Information about the frequency of sterile cysts is meagre, but they cannot be very common in man

In only 1 case in the present series was a human fluid found to be completely devoid of antigen, although several appeared to have very little Scolices are not always to be seen in fluids submitted for examination, because only the clear supernatant may be sent In the past, before we adopted standard reagents and technique, it was not always possible to assess the value of negative complement fixation and intradermal tests The present series is small, but there was only the 1 case with negative serological reactions in which the evidence at operation showed that the patient was suffering from a hyda cyst In this small series chance may have played a p in determining the favourable results, but there was selection of cases beyond the exclusion of those wh complete investigations, including the actual demonst tion of the presence or absence of a hydatid cyst, had been carried out In no case in which the final diagno was not hydatid disease was the skin test or the comp ment-fixation reaction found to be positive Th results compare very favourably with previously record results, but, apart from the series recorded by Fairley a Kellaway (1933), there was little information about t potency or supply of the reagents used The Austral workers found the intradermal test to be somew more sensitive than the complement-fixation test, figures, in which the reverse was found, cannot regarded as significant in view of our small numb The actual titration of complement-fixing antibody the patients' serum with standardised reagents, now t their stability has been demonstrated, appears to us have advantages which may extend the value of the t beyond the diagnosis of the primary cyst Some evide is presented to show that after the excision of the prim cyst the complement-fixing titre tends to fall slowly will rise again if further cysts develop It is obvious t additional experience is required before this sugge is accepted without reserve as having value in progno

SUMMARY

A technique employing accurately standard reagents for the serological diagnosis of hydatid dise is described

In a series of 49 cases where the exact diagnosis made at surgical operations, 20 non-hydatid cases g negative complement-fixation and intradermal reactio and 28 of the 29 proved cases gave positive serolog reactions with a slight advantage to the compleme fixation test (27 positive complement fixation test 25 positive Casoni)

We have to thank Dr Naomi Datta for help in the prep tion of the provisional standard sera We are also grat to the doctors who have sent us detailed reports on t cases, and particularly to Dr G Wetherley Mein for careful measurements of skin reactions

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TABLE III—COMPLEMENT-FIXATION TESTS WITH CHLOROFORM-EXTRACTED ANTIGENS

Serum from case of	Serum titres* with antigens of			
	Alastrim	Variola	Vaccinia	Cowpox
Alastrim	40	40	20	20
,, ...	40	40	20	20
,, ...	80	40	40	20
,, ...	80	40	80	80
Variola	80	80	40	40
Vaccination	20	40	40	40
Generalised vaccinia	80	80	80	80
Cowpox	40	20	20	80

*Expressed as reciprocals.

is of doubtful significance, and less than 30% is within the range of fluctuation about the mean shown by serum-virus mixtures containing replicate samples of the same serum. Serum no. 3 we would therefore regard as negative and serum 1 as a doubtful positive in the neutralisation test. It would appear from these results that neutralising antibody is the earliest to appear and that this, though perhaps varying in different patients, may be detectable as early as the fifth day after the onset of symptoms. Similar findings have been obtained in this laboratory with a larger number of smallpox sera (results to be published). Although no sera from these alastrim cases were obtained more than forty-three days after the onset of illness, our tests on smallpox sera have shown that neutralising antibody can be found years after an attack at a time when antihæmagglutinin and complement-fixing antibody can no longer be detected. The present findings confirm our previous experience that the order of reliability of these techniques for antibody estimation is neutralisation>antihæmagglutinin>complement-fixation. It may be noted that in the examination of smallpox and post-vaccination sera Collier et al. (1950) obtained higher titres of antihæmagglutinin than those shown in table I. The apparent difference is exaggerated by their method of calculating titres (in terms of the dilution of serum in the total volume of fluid per tube). Had we adopted this method, the titres recorded in this paper would have been increased threefold. Their hæmagglutinin was an extract of "smallpox lymph" prepared in buffaloes and may well have been a more sensitive indicator than our extracts prepared from infected chorioallantois.

Specificity of the Antibody Response

The investigations on this point were made with the complement-fixation and neutralisation techniques. The difficulty of obtaining active hæmagglutinins from alastrim, variola, and cowpox material precluded the use of antihæmagglutination titrations for assessing specificity of antibody.

Complement-fixation.—In these tests infected chorio-[illegible] mbranes were used for the preparation of [illegible] :ause this was the only tissue which could [illegible] be used as a source of antigen for all four viruses. The results of tests with 13 of the alastrim sera are shown in table II. There is little evidence of selective reactivity of the sera with the alastrim antigen. The slightly higher titres obtained with the variola and cowpox antigens are to be attributed to the greater reactivity of these two preparations. Likewise, complement-fixation tests with human sera obtained after vaccination or after recovery from smallpox or cowpox showed a similar lack of specificity. It has been suggested (MacCallum 1952) that with human convalescent sera chloroform-extracted egg antigens give complement-fixation reactions sufficiently specific to differentiate the antibodies resulting from smallpox and cowpox infections. Table III shows the results of tests with egg antigens that had been extracted overnight with chloroform to make 20% by volume. There is here also little evidence of specificity, except perhaps with the cowpox serum, which reacted to slightly higher titre with the homologous antigen; and this antigen gave, on the whole, lower titres with the variola and alastrim sera than did their homologous antigens. The differences, however, were slight and not in our opinion sufficiently great to make the use of this type of antigen of differential diagnostic value in the examination of convalescent sera from patients infected with those viruses.

TABLE IV—NEUTRALISATION OF ALASTRIM, VARIOLA, VACCINIA, AND COWPOX VIRUSES BY CONVALESCENT SERUM (CASE NO. 17)

Serum dilutions	Per cent. virus surviving (derived from pock counts)			
	Alastrim	Variola	Vaccinia	Cowpox
1/5	1	9	20	13
1/50	87	82*	90	120*
1/500	115	85	87	95
Control serum 1/5 ..	100	100	100	100

*These figures fall within the range of variation with normal serum-virus mixtures.

Neutralisation tests.—With immune sera prepared in animals, neutralisation tests with undiluted sera had not served to differentiate viruses of the pox group (McCarthy and Downie 1948). However, when the sera were tested in dilutions, higher neutralisation titres were usually obtained against the homologous virus (Downie and McCarthy 1950). The serum from one of the alastrim patients was therefore tested in tenfold dilutions against the four viruses, a normal human serum being used as control. The figures in table IV record the percentage of surviving virus as compared with the control and not the percentage neutralisation as in table I. There is significant neutralisation of all the viruses by 1/5 serum dilution but none with serum dilutions of 1/50 or 1/500. It is doubtful if the differences in the percentages of surviving virus with the 1/5 dilution of serum are significant; for it has been our experience that post-vaccination sera usually show better neutralisation of variola than of vaccinia virus, and in our previous experimental studies alastrim virus appeared to be more readily neutralised than other pock viruses by heterologous and homologous immune sera (McCarthy and Downie 1948, tables I and II).

DISCUSSION

Of the techniques used in the examination of the sera from alastrim patients, the neutralisation test was the more sensitive in that antibody was found in earlier specimens of serum which were negative by the complement-fixation test. It is to be noted, however, that in the neutralisation tests the serum was used in a dilution of 1 in 2, whereas 1 in 5 was the lowest dilution tested by complement-fixation. It seems likely that the fall in temperature and improvement in the patient's condition which occurs about the fourth or fifth day of illness is related to the production of antibody (Downie 1951), and by the neutralisation technique antibody may be found in the blood very soon after clinical improvement occurs. Such antibody is presumably the excess over that fixed by virus antigen in the tissues and body-fluids. For diagnostic purposes, however, the neutralisation test is not so conveniently carried out as is the complement-fixation test. The test for antihæmagglutinins, which is certainly as sensitive as complement-fixation, requires freshly prepared hæmagglutinin, because this antigen deteriorates within a few weeks at ordinary refrigerator temperature. On the other hand complement-fixing antigen may be kept under similar conditions for years without deterioration. Moreover, as complement-fixing antibody usually disappears within a year after vaccination, the complement-fixation test is a useful diagnostic procedure in suspected cases of smallpox who have been vaccinated more than twelve months previbeen jaundiced For some five years he had had nasal catarrh and cough, productive of a small amount of greenish sputum, and in July, 1948, these conditions had worsened About the same time he began to suffer from conjunctivitis In November, 1948, cutaneous pigmentation was noticed by the patient, first on his trunk and later down his thighs midway to his knees In December, 1948, his voice became husky and he felt generally but vaguely unwell

On examination he was found to have scattered lesions of dermatitis herpetiformis, some of which were infected In addition he had a "raindrop" type of brownish pigmentation of his trunk and upper thighs There was hyperkeratosis of his palms which may in part have been occupational His liver was enlarged to one hand's breadth below the costal margin (fig 1) and was hard but not tender There was no abnormality in the cardiovascular, respiratory, or central nervous systems and no evidence of peripheral neuritis

Investigations—He was admitted to hospital on April 4, 1949, and investigations gave the following results serum-bilirubin 0 95 mg per 100 ml , alkaline phosphatase 7 9 units, thymol turbidity 5 units, serum proteins 7 4 g per 100 ml (albumin 3 6 g , globulin 3 8 g), prothrombin concentration 90%, blood-urea 40 mg per 100 ml , urea-clearance 105% of the average normal function Radiography of the chest showed no abnormality

Treatment and Its Results—He was given a high-protein diet with vitamin supplements and there was a gradual reduction in the size of the liver, which ceased when it was three fingers breadth below the costal margin

As excretion of that part of a dose of inorganic arsenic which does not enter into combination in the tissues is complete in ten to fourteen days (Taylor 1948), the urinary arsenic excretion was not estimated until arsenic had been withheld for three weeks The excretion was then estimated by Mr Harri Heap, Manchester city analyst, and the amount of arsenic in each of 6 twenty four hour specimens was found to be within normal limits This having been ascertained, a course of dimercaprol was commenced in an attempt to free the combined arsenic Intramuscular injections of 3 mg per kg body-weight were given four hourly for forty eight hours and then twice daily It will be seen from fig 2 that the urinary excretion of arsenic increased considerably The injections were continued until, after seventeen days, there was no further significant excretion

No toxic effects were caused by the dimercaprol, but the patient had some pain at the injection sites During treatment there was a return of his sense of well being and the liver edge receded to one finger's breadth below the costal margin

Multiple puncture vaccination with calf lymph was performed for the dermatitis herpetiformis (Cecil 1947) and a good primary take was obtained A few days after vaccination the skin lesions cleared

On discharge the patient felt well enough to open a business of his own When last seen on Sept 20, 1950, he had remained well The dermatitis herpetiformis had returned soon after discharge, but the lesions had been few and scattered and much less than when the condition was under treatment with arsenic There had been no change in the hyperkeratosis of the palms or in the pigmentation of the skin The liver edge had now reached the costal margin but remained easily palpable and the liver surface was quite hard and apparently smooth On his last attendance the th turbidity was 4 units whilst the plasma proteins to 8 98 g per 100 ml with fibrinogen 0 44 g , albumin 4 3 and globulin 4 24 g.

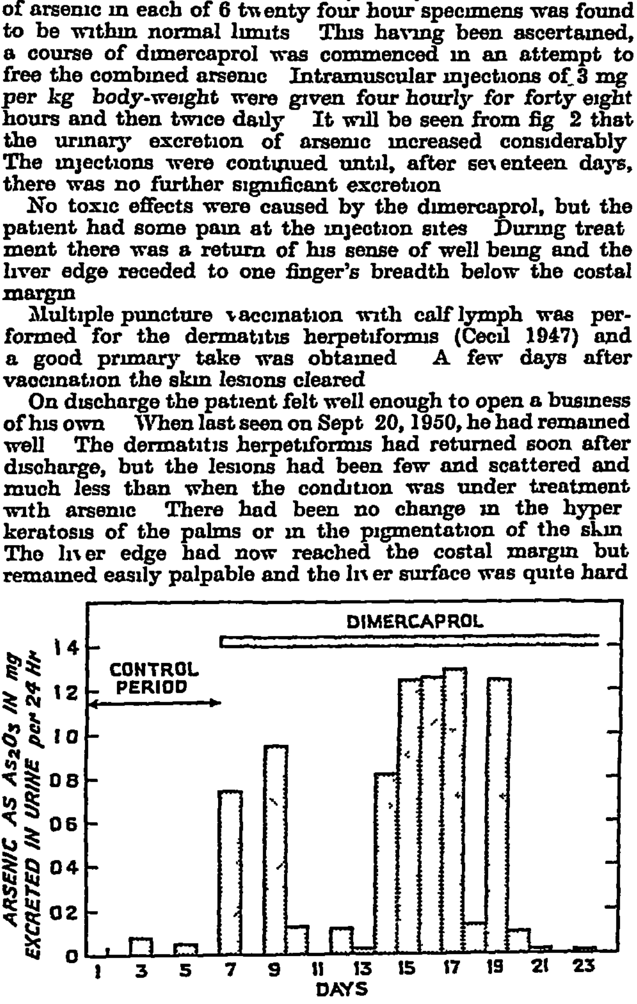

Fig 2—Urinary arsenic excretion before and during administration of dimercaprol

DISCUSSION

Inorganic arsenic, after absorption, passes to the l where a considerable proportion is stored , the rema reaches the general circulation, and that part w does not become fixed in the tissues is excreted, al entirely by the kidneys, in ten to fourteen days retained arsenic has attached itself to SH- contai protein components of the pyruvate oxidase sys The high toxicity of trivalent arsenicals is due to t ability to form stable arsenical-ring compounds such proteins (Eagle et al 1946) Thus arsenic by poisoning the function of cells, not their struct

Dimercaprol was discovered as a result of work car out on the thesis that simple dithiol compounds m form relatively stable ring compounds with triva arsenicals and consequently might compete effectively arsenic with dithiol tissue proteins This thesis first proposed by Stocken and Thompson and t work is referred to by Peters (1948) In prac dimercaprol has been found not only to combine w free arsenic but also to remove arsenic from it combination (Eagle et al 1946, Carleton and Peters 19 The latter reaction may be represented as

Tissue protein arsenic + dimercaprol → dimercaprol t arsenite + tissue protein

It is of this latter property that we have taken advant in treating our patient It should be noted, howe that cell damage may be irreversible even if the ars be removed (Taylor 1948)

We believe this to be the first report of the u dimercaprol in toxipathic hepatitis due to chr inorganic arsenic poisoning In the absence of a hist of jaundice or of other factors liable to cause hepat we do not feel that the toxipathic hepatitis in our pati can be dissociated from his ingestion of arsenic

The urinary excretion of arsenic had been wit normal limits before treatment , yet when the pati was given dimercaprol he excreted considerable amou of arsenic in the urine This confirms previous obser tions that dimercaprol can remove arsenic from combi tion with tissue proteins There is some evidence t the arsenic removed by dimercaprol is that part whic causing most damage (Carleton and Peters 1946), and reasonable to suppose that the arsenic removed fr our patient was interfering with his pyruvate oxidat system The liver is, of course, intimately concer with carbohydrate metabolism, and this may expl the high storage-rate of arsenic in the liver and t tendency to hepatitis

For a period while our patient was under treatme the level of urinary arsenic excretion indicated blo levels which would have been associated with sympto of acute arsenical poisoning if the arsenic had not be circulating as an innocuous dimercaprol thioarsenite

Reference must be made to the work of Koppanyi a Sperling (1947), who found that when rabbits were gi sodium arsenite followed by dimercaprol an explosive reacti developed The effect did not occur with arsenates or w arsphenamine It was certainly not due to the final dim caprol thioarsenite, and Koppanyi and Sperling thought was perhaps caused by toxic intermediate compounds T wondered whether, in cases of poisoning with arsenite su as Fowler's solution, the protective action of dimercap might not be accompanied by similar unpleasant side-effec No such side effects were seen in our case

Despite the beneficial effects of therapy, we think likely that the patient's liver has sustained permane damage After eighteen months it remained har though there had been much reduction in its size ow to the removal of fat The plasma globulin was hig at 4 24 g per 100 ml and diffuse hepatic fibrosis w

DETERMINATION OF PROTHROMBIN

Many different methods have been used. Three main methods are here briefly discussed.

Quick's (1945) one-stage method and later modifications thereof (Link-Shapiro, and others) have been most commonly used. Theoretically one can argue against this method that the results depend not only on the amount of prothrombin in the plasma but also on the amount of proaccelerin and proconvertin (Owren 1947, 1951). When the method is used as guidance for dicoumarol treatment, this will not have any important bearing on its dependability, because the concentration of proaccelerin is on the whole hardly influenced by dicoumarol (Owren 1950, Bjerkelund 1950), and the concentration of proconvertin largely follows that of prothrombin during the treatment (Owren 1950, Owren and Aas 1951).

The values found by Quick's method are usually given as prothrombin time in seconds or as prothrombin index. For the reasons mentioned above this is unfortunate and has caused much confusion. A great deal would be gained if everyone, at least in medical papers, could give the prothrombin value as a percentage of the normal. This would make it possible to compare and assess methods and results, which at present is difficult or impossible. Further, in the Quick method the prothrombin time can be converted to prothrombin percentage by the use of a normal curve. The most correct normal curve is constructed by dilution of normal plasma with prothrombin-free human plasma. From this the prothrombin time in different dilutions from 100% down to 10% is decided (Wright and Foley 1947, and others). The curve is logarithmic.

The two-stage method originated by Warner et al. (1936) and later modified by Owren (1947), Ware and Seegers (1949), and others has been generally found too complicated for clinical use, though it is used by a few laboratories. No further mention will be made of it here.

The most practical and dependable method for clinical use is without doubt Owren's one-stage method (Owren 1947, 1949). In contrast to Quick's method, the variations in the concentration of proaccelerin have no influence here. Though Owren's method was at first described as a specific method of prothrombin estimation, later investigations (Owren and Aas 1951) showed that in its original form the method is in reality a combined determination of prothrombin and the new factor proconvertin ("P and P method"). As mentioned above, proconvertin under dicoumarol treatment largely follows prothrombin; the method is therefore ideally suited to the control of dicoumarol treatment and is steadily gaining favour. For details of the method the reader is referred to the above-mentioned papers.

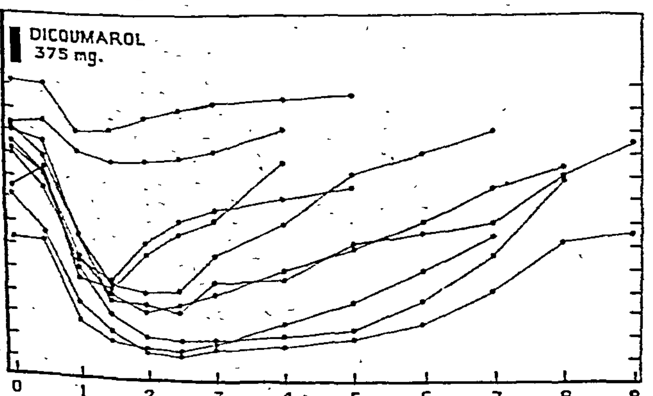

Fig. 1—Effects of dicoumarol 375 mg. on ten healthy persons, showing (1) sensitivity to dicoumarol varies widely, (2) maximal effect develops late, and (3) effect is prolonged.

EFFECT OF DICOUMAROL ON MAN

The main effects of dicoumarol on man are demonstrated by a clinical experiment illustrated in fig. 1 (Bjerkelund 1950). This shows the fall in the prothrombin value of 10 normal persons who received 375 mg. dicoumarol orally. It also shows that: (1) the sensitivity to dicoumarol varies greatly from person to person; (2) the effect appears relatively late, the maximum being first seen after 36–72 hours; and (3) dicoumarol has a long-lasting effect, a dose of 375 mg. lasting in some people up to eight days. These three properties of dicoumarol are most important when it is used therapeutically, and they must be kept in mind in determining the dosage.

When dicoumarol treatment is to be started, one can seldom predict whether the patient is sensitive or resistant to it. The body-weight is no guide, for there is no definite relation between the weight and the requisite dose. The patient's age and general condition may give a hint, because older patients and patients in poor general condition are more sensitive than younger and more robust persons; but even this cannot be depended on; nor has the patient's initial prothrombin value any constant relation to his tolerance of dicoumarol.

That liver disease diminishes the tolerance towards dicoumarol is well known. It has also been shown that the onset of acute hepatitis during prolonged treatment with dicoumarol greatly increases the sensitivity; hence the maintenance dose must be reduced to a fraction of the original dose (Bjerkelund 1951). In liver disease, however, dicoumarol treatment is usually not indicated.

In practice it is therefore wisest to assume that one cannot foretell a patient's resistance toward dicoumarol. Consequently there is no reason to vary the initial dosage for different patients. On the contrary, there are grounds for using fixed initial dosage, because after two or three days the effect of the initial dosage will give the first indication of the patient's tolerance.

We have found that 250 mg. on the first day and 125 mg. on the second day are suitable initial doses, if the treatment is started in the morning. 200 mg. is given if the treatment is started in the afternoon or evening, and 100 mg. is given next morning, because the doses will be closer to one another. (The patients treated in the medical departments at Oslo Municipal Hospital are for the most part older patients with heart ailments. In departments with younger patients, it would, perhaps, be advisable to give somewhat larger initial doses.) Blood for prothrombin estimation is always taken before giving the first dose of dicoumarol. The blood can be examined later with other samples. This is permissible with Owren's method, since the ox plasma used in this method contains a surplus of labile proaccelerin. It is essential to have the patient's prothrombin value registered before treatment is started, because it gives the initial point of the prothrombin curve, which is our most important guide during treatment.

The importance of charting the prothrombin values and the dicoumarol doses for each patient under treatment cannot be exaggerated. If one has once become accustomed to determining dicoumarol dosage by means of such a curve one cannot imagine doing it in any other way. The curve gives us at once a picture of how the day's prothrombin value compares with the previous ones. We can see the effect of the previous days' doses of dicoumarol, and can decide whether they have been sufficient, too small, or too large. One must strongly emphasise that it is not the effect of yesterday's dose but of the many more patients would complain of symptoms in hospital, but the lochia tend to obscure the bleeding at defæcation, and the pain is often attributed to perineal sutures or their recent removal In the present series there were 6 cases in which symptoms came on between the twelfth and thirty-ninth weeks of pregnancy

CASE-RECORD

The following case-record shows how painful anal fissure can be (prolapsed piles were also present) and how very large hæmorrhoids may be cured spontaneously six weeks after delivery

A multipara, aged 27, was admitted, when thirty four weeks pregnant, complaining of "an attack of piles" She said she had had hæmorrhoids for six years On examination two very large hæmorrhoids were seen, one anterior and one posterior In addition there were two acute fissures anteriorly and one posteriorly The hæmorrhoids also prolapsed after replacement, which was extremely painful, in spite of the application of an anæsthetic ointment It was therefore necessary to dilate the anus digitally under anæsthesia After this the stools were kept soft with mist magnesii hydroxidi *B.P* $^{1}/_{2}$ fl oz (14 ml) nocte, and a no 2 St Mark's dilator was passed twice daily lubricated with ung cinchocainæ co *B P C* This relieved the patient's symptoms considerably, but she had to remain in hospital until her spontaneous delivery at term There was no perineal laceration Six weeks after delivery she attended the postnatal clinic, and the only abnormality was a long mucosal and skin tag. It was arranged to excise this when the baby was weaned

PARITY

A primipara is obviously more liable to perineal damage The commonest cause of anal fissure is trauma, and in this series there was no case of a patient with more than two previous deliveries having an anal fissure, 35 patients were primigravid, and 10 had had one previous pregnancy

ANAL FISSURE IN RELATION TO PERINEAL DAMAGE

Perineal damage	Method of delivery	Fissures	Antenatal symptoms
No laceration	Spontaneous	11 cases	2 cases
Episiotomy	Spontaneous	12 ,,	
Episiotomy	Forceps	13 ,,	2 ,,
1st-degree tear	Spontaneous	3 ,,	1 case
2nd degree tear	Spontaneous	4 ,,	1 ,,
	Cæsarean section	2 ,,	

The accompanying table shows that, excluding cases in which symptoms were present before delivery and 2 cæsarean sections, there was damage to the perineum in 28 out of 39 cases 23 of the cases with damage to the perineum had episiotomy, and in 11 cases this was associated with forceps delivery The forceps rate over the period studied was 13 1% in primipara and 3 5% in multipara The episiotomy rate in these two groups was 34 9% and 13 1% respectively

TREATMENT

Treatment was on the lines described by Gabriel (1948) Patients were instructed to maintain a good fluid intake, and constipation was treated with mist magnesii hydroxidi *B P* Liquid paraffin was avoided Digital application of ung cinchocainæ co *B.P C* or ung benzocainæ co *B.P C* twice daily round the anal margin was prescribed in the first instance The ointment was always used before defæcation If this did not bring relief, a no 2 St Mark's dilator was used, lubricated with one of these two ointments, and passed twice daily 34 patients were cured by use of ointment alone, 10 required the use of a dilator, and the case described above required stretching of the sphincter In no other case was surgery or injection of the sphincter necessary, but since this time intractable cases have been seen and referred to the surgical department for treatment The symptoms usually abate within a few days, and the fissure heals completely within two or three weeks In some cases fresh fissures appear a few weeks after apparent cure 3 patients included in this investigation did not atten the follow-up clinic but are presumed cured There di not seem to be any great difference between ung cinchocainæ co *B.P C* and ung benzocainæ *B.P C* i effectiveness, the impression is that the former is le liable to give rise to pruritus

DISCUSSION

Pregnancy, labour, and the postpartum period off many opportunities for the formation of fissure Constipation is common in the antenatal period and may b associated with the excessive use of purgatives Insufficient fluid intake, weak abdominal muscles, and a painf perineum may also lead to constipation in the puerperiu In addition the ritual enemata of the first stage of labou with rectal examinations and the distension of the anu and perineum in the second stage of labour, are ætiologica factors

From the present investigation it can be said that th more traumatic the delivery the more likely is fissure t occur, and that anterior and multiple fissures are ver common in puerperal women This is understandabl and agrees with the views put forward by Lockhart Mummery (1934) He described the external sphincter a consisting of two lateral halves In front the halve are continuous, but posteriorly all the fibres do not joi end to end but are for the most part placed parallel wit each other This arrangement of fibres leaves the posterior commissure least supported, whereas the nex weakest place is the anterior commissure In women th anterior commissure receives less support than in me owing to the presence of the vagina In labour it is mo likely that the anterior commissure will be damaged especially if the perineum is torn or episiotomy is performed This probably explains the large number o anterior fissures seen in the present series

As would be expected, anal fissure is most common i the primiparous patient and is often related to forcep delivery and to perineal damage The commonest tim for symptoms to appear is after discharge from hospital This may be explained by the patient leading a ver sedentary life in hospital and not noticing any increased discomfort on defæcation, especially if she has perineal sutures In the postpartum period the sphincter i nearly always extremely lax and it does not regain it tone until the patient is discharged from hospital. It was thought that patients after discharge might not keep up their fluid intake to the six pints a day recommended in hospital, and that this predisposed to constipation and subsequent fissure In view of this the influence of breast-feeding was investigated, but no significant conclusion was reached The fall in the œstrogen level after delivery may also adversely affect the mucosa of the anal margin, making it less resistant to trauma

It is important to realise that many patients attending the postnatal clinic have distended rectal veins 16 patients complaining of anal fissure had this condition but as soon as the fissure was cured they became symptom-free owing to the tendency of hæmorrhoids to spontaneous remission during the postpartum period In six months only 3 patients were seen at the postnatal clinic with hæmorrhoids requiring injection Hæmorrhoids cause great discomfort in the antenatal period and in the early puerperium, but it must be emphasised here that most of these patients will be spontaneously cured of their hæmorrhoids six weeks after delivery

To confirm the last fact 100 patients were examined in the wards from the first to the tenth day of the puerperium Prolapsed piles are very common, and fissures, although sometimes seen, are difficult to find owing to the excessive corrugations of the anal margin and the presence of lochia Further, the fissures give rise to very little discomfort, owing to the great laxity of the anal sphincter at this time, and, if there is any discomfort perineal sutures or their recent removal will be blamed

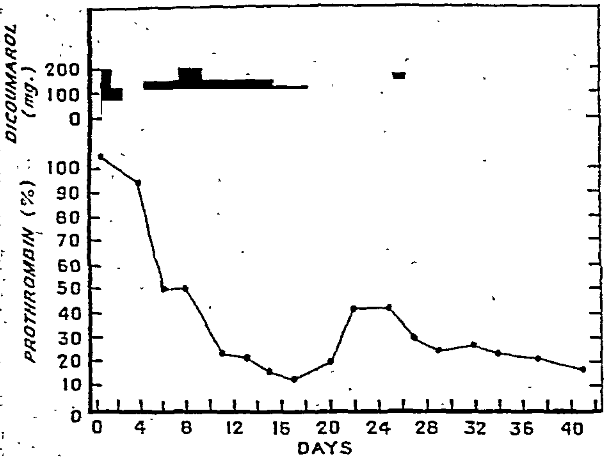

Fig. 5—Adjustment of dosage of dicoumarol according to effect on prothrombin in a man, aged 54, with coronary thrombosis and very resistant to dicoumarol.

By immediately making small adjustments in the dosage in keeping with minor fluctuations in the prothrombin curve, the prothrombin value will be kept as near constant as possible. If one waits for the next laboratory report before adjusting the dosage, one will often find that meanwhile the prothrombin value has risen far above the therapeutic range. This means that a much larger dose must be given, and there will be a delay in reaching the maintenance dosage required to produce a stable prothrombin value.

For this reason it is essential for the dose of dicoumarol in each tablet to be small. In Norway tablets of 25 mg. of dicoumarol are used. Even with these small tablets it will usually be impossible to reach a constant prothrombin value with a definite number of whole tablets each day; often the tablets have to be broken. Variations of 10–20 mg. weekly in the dosage can prove sufficient to change the prothrombin curve. This matter is more fully explained below, in the discussion of long-continued treatment.

CONTACT BETWEEN LABORATORY, PHYSICIAN, AND PATIENT

Quick and dependable contact between laboratory, physician, and patient is essential. Figs. 2–8 show that the prothrombin value is not estimated daily, as has been usual in most hospitals in the past, but at intervals of two or three days. In practice this has proved fully sufficient in view of the long-lasting effect of dicoumarol and the fact that the dosage is based on the shape of the curve and not on the current prothrombin value. Thereby the laboratory is saved much unnecessary work, and the patient many venepunctures. We estimate the prothrombin values three times weekly—on Monday, Wednesday, and Friday. As soon as the laboratory results are to hand, each patient's curve is brought up to date. From the curve, the physician determines the dosage for the two or three following days. The dosage is marked on each patient's diagram and at the same time entered in ward books for the nurse who gives out medicines each morning. Sometimes, as a result of an increase in prothrombin values, it is desirable to give a patient an extra dose on the same day, besides the one he has already received. In such cases the physician gives a direct order to the nurse on duty.

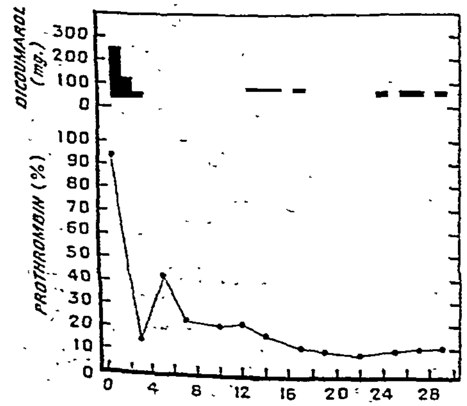

Fig. 6—Secondary rise of prothrombin value owing to too great a reduction of dicoumarol dosage after initial dose, and subsequent adjustment of dosage to keep prothrombin value in therapeutic range in a man, aged 52, with coronary thrombosis.

The system here outlined has proved very satisfactory in practice. It is a great advantage if one can limit the determination of prothrombin to three times weekly.

LONG-CONTINUED TREATMENT OF AMBULANT OUTPATIENTS

Today no article about dicoumarol dosage is complete without mentioning the question of continued treatment of ambulant patients after they have left hospital. In the past two years, in our department of Oslo Municipal Hospital, we have given such treatment to many patients with (1) coronary thrombosis and myocardial infarction, (2) mitral-valve stenosis with auricular fibrillation and a tendency towards embolism, and (3) thrombo-embolic episodes from other causes. It has proved possible to give adequate dicoumarol treatment to ambulant outpatients with estimation of the prothrombin values every week or fortnight. Usually the prothrombin values ought to be estimated weekly from four to eight weeks after the patient's discharge from hospital; later every fortnight will suffice in most cases. It is an advantage to be able to start the treatment while the patient is in hospital, so that the correct maintenance dosage can be reached before he is discharged. On the other hand, there is no objection to starting treatment on outpatients provided that the prothrombin value is estimated and charted every second or third day until the suitable maintenance dosage has been discovered.

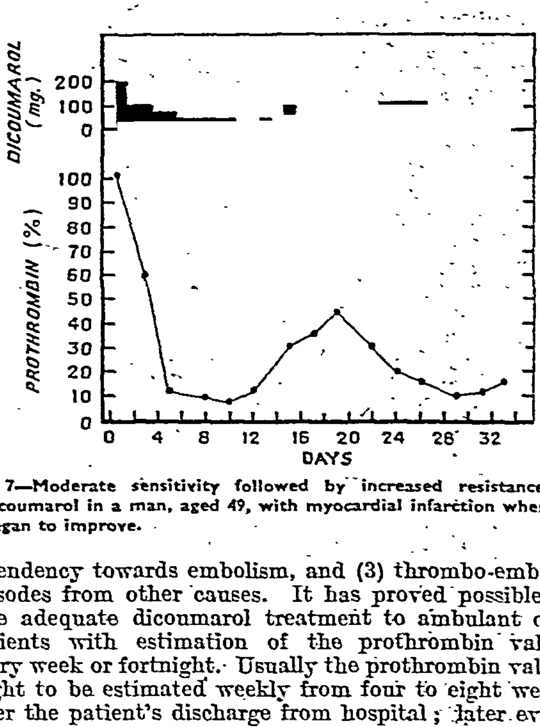

Fig. 7—Moderate sensitivity followed by increased resistance to dicoumarol in a man, aged 49, with myocardial infarction when he began to improve.

Fig. 9 shows the treatment administered, with estimation of the prothrombin value every fortnight for a year in a patient with coronary thrombosis. Throughout that time the prothrombin value remained in the optimum therapeutic range, with only small fluctuations up to 10%. These minor fluctuations must at once be met with an adjustment in the dose, if the best therapeutic effect is to be maintained. The figure shows clearly that an increase or decrease of 25–50 mg. at the fortnightly adjustment of dosage is sufficient to effect the desirable change in the prothrombin curve. If one could give addimarrow biopsy showed hypercellularity, with megaloblastic erythropoiesis A diagnosis of pernicious anæmia in relapse was made

Treatment —The patient was confined to bed for a period of observation and was given a normal ward diet A mixture of 100 ml of R D E -treated gastric juice (see below) and 10 µg of vitamin B_{12} (‘Cytamen,’ Glaxo) was given at 9 P M daily, three and a half hours after the last meal of the day, for five days by mouth

Results of Treatment —Changes in the hæmoglobin values and red cell and reticulocyte counts are shown in fig 2 A reticulocyte response of 35% was observed on the fifth day after treatment began On the fourteenth day the red cell count had risen to 3,600,000 per c mm from an initial level of 1,600,000 per c.mm This represents an optimum response (Ungley and Campbell 1949)

THE GASTRIC JUICE

Student volunteers were used as a source of gastric juice

Collection —A Ryle's tube was passed after an overnight fast, and the fasting juice was discarded Histamine phosphate 0 3 mg was given subcutaneously, and gastric juice was aspirated until 150 ml had been collected from one or more volunteers Before the gastric juice was pooled, a sample was taken from each volunteer and tested with Topfer's reagent for the presence of hydrochloric acid Only gastric juice containing free hydrochloric acid and no bile or blood was used

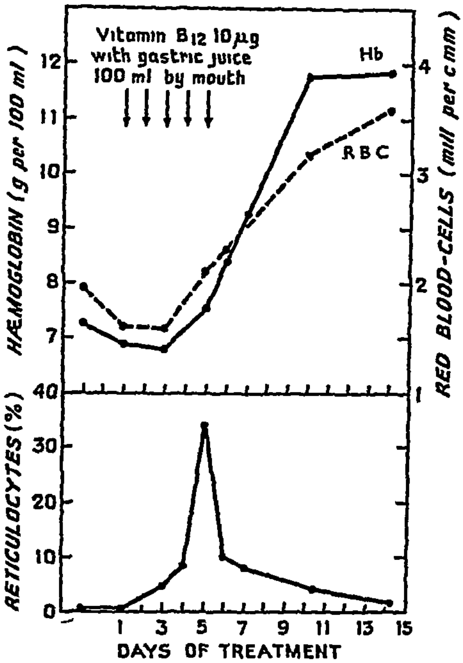

Fig 2—Reticulocyte response, increased amount of Hb, and increased red-cell count after treatment with oral vitamin B_{12} and human gastric juice treated with R D E

Treatment of Juice —The collected juice was covered with a layer of undissolved mucus The 150 ml sample was transferred to a sterile jar and stirred mechanically, while sodium hydroxide was added drop by drop until pH 6 0–6 5 (the optimum range for R D E) was reached The gastric juice was then spun in a horizontal centrifuge at 3000 r p m for fifteen minutes Neutralisation led to the solution of most of the surface layer of mucin After centrifugation 100 ml of the supernatant fluid was mixed with 10 ml of calcium-acetate saline solution (Stone 1949) and with 3000 units of purified R D E prepared by the method of Ada and French (1950) This mixture was then incubated in a water bath at 37°C for an hour, at the end of which samples of the original untreated supernatant fluid and the R D E -treated material were titrated against five agglutinating doses of indicator virus (T MEL) by the technique of Burnet (1948)

The accompanying table shows the results obtained with five samples of gastric juice given to the patient Destruction of the mucous substrate was virtually complete

DISCUSSION

The fact that an optimum hæmatological response was obtained in classical pernicious anæmia treated with oral vitamin B_{12} and neutralised gastric juice incubated with R D E indicates only that, if the intrinsic factor is a mucoprotein, its biological activity is not modified by treatment with R D E In the case of urinary mucoprotein it is known that full action of R D E, while destroying all capacity to react with viruses, leave the serological character unchanged The action is limited and specific, and our failure to obtain inhibition of intrinsic factor by R D E does not in any way diminish the significance of Glass's important work Increased knowledge of the function of these substances is clearly of fundamental importance to the understanding of the physiology of the alimentary tract

RESULTS OBTAINED IN TITRATION OF TREATED AND UNTR GASTRIC JUICE AGAINST INDICATOR VIRUS

Date	Designation	Inhibitor titres to 5 agglutinating doses of T ME	
		Before R D E treatment	After R D E treatm
May 9, 1952	A	5120	<
„ 10, 1952	B	3000	<
„ 11, 1952	C	2560	<
„ 12, 1952	D	3000	<
„ 13 1952	E	6000	<

Pernicious anæmia is uncommon in patients of this age The case demonstrates the value of gastric biopsy in substantiating diagnosis in megaloblastic anæmias thought to be addisonian

SUMMARY

A young woman with classical pernicious anæmia in relapse was treated with oral vitamin B_{12} and human gastric juice acted upon by receptor destroying enzyme (R D E) A normal therapeutic response was obtained

Although there is good evidence that intrinsic factor in gastric juice is a mucoprotein, it is not one which is inactivated by R D E , thereby differing in its properties from gonadotrophin and mucoproteins derived from respiratory-tract cells

We are grateful to Dr Ian Wood, head of the clinical research unit, for his help and advice in this work, and Dr E S Finckh, pathologist, for his histological studies

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“*The time is overdue for more active participation by physiologists as consultants to clinical services in teaching hospitals Such a development could become a tremendous boon to clinical medicine I think that physiology would profit equally thereby there might come to be two groups of physiologists—the experimentalists in general physiology as now, and an equally important division, whose members would spend a definite, if not a major, portion of their time in the wards and laboratories of teaching hospitals Physiologists have machine shops for the development of tools necessary in the prosecution of their experiments Why not machine shops in which the physiologist may develop precision instruments for the study of disease and its care in man? What if physiology did become the handmaiden of medicine? Would physiology suffer? I do not think so*”—OWEN H WANGENSTEEN, *Proc Mayo Clin* 1952 27, 532

DISCUSSION

It should be evident from the reasons given above at maintenance dosage is more desirable than intermittent dosage because (1) it is more logical; (2) experince has proved it to be a practical and adequate method administering dicoumarol in hospitals; and (3) it is made possible a safe and effective treatment for [illegible]ts. It is therefore difficult to under- [illegible] and Weiner (1951) advocate intermittent dosage. Despite their great experience their guments in this connection do not seem sound.

They demonstrate in a diagram the treatment of one patient ith intermittent doses. Three doses are given with ten-day tervals, the first 600 mg. and the second and third 400 mg. ich. They claim to have obtained satisfactory results with iese doses. (The fluctuations of the prothrombin values en in the diagram cannot be ascertained by the reader, r the values are not given in percentages of the normal.) n order to compare the two methods of administration, the atient then receives 50 mg. daily for five days (equalling 00 mg. with ten-day intervals) as a maintenance dosage. No large initial dose which could bring the prothrombin value the therapeutic range is given.) As the mentioned mainenance dosage is insufficient to decrease the prothrombin alue satisfactorily, Shapiro and Weiner administer 100 mg. aily on the following four days; in fact they double the dose. he prothrombin value then decreases after a couple of days o a dangerously low level. I have shown here how even inor changes in the dosage can increase or decrease the rothrombin value considerably. It is therefore not surprising hat doubling the dose has the effect already mentioned. If he same principle were used for intermittent dosage, Shapiro nd Weiner would certainly also have produced very low rothrombin values by suddenly administering double doses ith the same time interval.

It seems clear that intermittent dosage is entirely unsuitable for treating ambulant patients with infrequent estimations of prothrombin.

CONCLUSION AND SUMMARY

One must conclude that at present there is only one rational method of giving dicoumarol—namely, maintenance dosage.

For this purpose an exact and dependable method of estimating prothrombin is necessary. Owren's method is especially recommended.

It must be kept in mind that the effect of dicoumarol appears slowly, lasts long, and varies greatly between one patient and another (fig. 1).

The same initial dosage (250 mg. on the first day and 125 mg. on the second day) may be used for all patients. The effect of the initial dosage is seen after two or three days and gives the first indication of the patient's tolerance. Thereafter the dosage should be adjusted according to the shape of the curve of prothrombin values (not the current prothrombin value). Large variations in the dosage from day to day should be avoided as much as possible while trying to reach the correct maintenance dosage.

Dependable contact between laboratory, physician, and patient is essential.

The dicoumarol dosage should be adjusted immediately even to minor fluctuations, not only in treating hospital inpatients but also in treating ambulant outpatients with infrequent estimations of prothrombin. An increase or decrease equalling 2–4 mg. a day is often enough to provoke a distinct fall or rise in the prothrombin curve after 8–14 days.

If an immediate anticoagulant effect is desired, heparin should be used with dicoumarol until the prothrombin value has reached the therapeutic range.

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HYDATID DISEASE

SEROLOGICAL REACTIONS WITH STANDARDISED REAGENTS

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LIEUT.-COLONEL, R.A.M.C. RETD; DIRECTOR OF LABORATORIES

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F.I.M.L.T.

From the Central Public Health Laboratory, Colindale

HYDATID disease is not generally considered to be a common condition in this country; but the fact that the Central Public Health Laboratory has issued during the last two years more than 600 doses of antigen for the intracutaneous or Casoni test suggests that the possibility of the disease is not infrequently considered when there is radiological evidence of a mass in the thorax or abdomen. Doubtless the test is often undertaken as a routine exclusion test; for in only 90 of these cases was information and/or material obtained for additional investigation. Of these, 28 were reported as having a completely negative Casoni reaction and adequate information was given for regarding the condition as other than hydatid disease. The remaining 62 cases were fully investigated, complement-fixation reactions were performed, and the final diagnosis was supported by the results of surgical procedures.

The usual definitive host of the *Echinococcus granulosus* is the dog, and the intermediate hosts are commonly cattle and sheep, although other mammals, including man, may serve. Dogs whose feeding is uncontrolled, and particularly farm dogs which may have access to local slaughterhouses, are more liable to harbour this tapeworm. Farmland in and around the farm may be heavily contaminated with egg-laden fæces, and the coats of all animals lying or rolling on such contaminated ground will be likely to pick up ova. People handling these animals may readily transfer the ova to their fingers, and unless a high standard of personal hygiene is maintained it is not difficult for the ova to gain entrance to the alimentary canal and set up an infection by the liberated embryo migrating to some organ or tissue where the hydatid can develop fully. This indirect route is generally regarded as a commoner way for human infections to be contracted than by direct contact with an infected dog.

A large proportion of the cases of hydatid disease seen in this country appear, from their history, to have been contracted overseas; but a significant number can be traced to South Wales. Wolfe (1943) found that 0·5% of the sheep killed in one slaughterhouse in Cardiff were infected with hydatid cysts. Among the 62 cases investigated in our series there were 42 cases of proved hydatid disease, and one-quarter of the patients lived in Wales, while nearly half had spent periods of their life in the Middle or Far East.

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Reviews of Books

Viral and Rickettsial Infections of Man

2nd ed Editor THOMAS M RIVERS, M D, director of the hospital, the Rockefeller Institute for Medical Research Philadelphia and London J B Lippincott 1952 Pp 719 60s

THE second edition of Rivers is about half way in size between some recent pocket-size textbooks of virology and a well-known portmanteau-size reference book It combines successfully the readability of the former with the erudition of the latter In his preface Dr Rivers suggests that the book may fulfil a need of medical students and practising physicians, but it seems unlikely that many of these busy people will have time to study another new specialty in the detail provided here The book should appeal much more to bacteriologists, research students, and others interested in learning or teaching virology, and to physicians and public-health workers specialising in the treatment of infectious diseases It is beautifully printed and illustrated and should be a great help to many would-be virologists in distress

This omnibus of virology carries contributions from many well known experts (In this case an expert is one who has spent considerably more than the customary one year period studying his subject) The first nine chapters describe general aspects of the study of virus diseases, physical, chemical, and serological techniques, methods of cultivating viruses in fertile eggs and tissue cultures, epidemiology, interference between viruses, and diagnosis Then follows an excellent chapter on bacteriophages, which earn their inclusion in a textbook of viral infections of man by the important light they have thrown on methods of virus multiplication After these lengthy preliminaries we come to the individual virus diseases, and it is good to see that for once the patient and the epidemic receive more attention than the virus This book is supported by a grant from the National Foundation for Infantile Paralysis, which may perhaps explain the greater respect paid to neurotropic than to respiratory virus diseases Chapters on hæmagglutination by Hirst, epidemiology by Maxcy, rabies by Johnson, and yellow fever by Theiler are all that could be wished for An otherwise excellent chapter on poliomyelitis is spoilt by its cursory treatment of tissue culture techniques in the study of this disease Some chapters tend to be more autobiographical than is desirable in an objective account of research, and here and there will be found odd sins of omission and commission This edition is brought up to date with accounts of cat scratch fever and of diseases caused by the Coxsackie viruses, and it is obvious that a big attempt has been made to refer to all the latest advances

Osteo-arthritis of the Hip

W ALEXANDER LAW, O B E, M D, F R C S, assistant orthopædic surgeon, London Hospital, associate surgeon, Robert Jones and Agnes Hunt Hospital, Oswestry. London Butterworth 1952 Pp 87 25s

ALTHOUGH this little monograph surveys briefly the causes and treatment of osteo arthritis of the hip, it is mainly concerned in reflecting Mr Law's well-known interest in its management by vitallium cup arthroplasty In a very personal account of case-histories and technique he shows just what success can be obtained by meticulous attention to the details of case-selection, operation, and aftercare, though perhaps he does not make it sufficiently clear that this procedure is essentially one for the superlative technician, and that, in average hands, the acrylic prosthesis may yield good results with less expenditure of effort

Le trachome

ROGER NATAF, ophtalmologiste des Hôpitaux, membre associé de l'Institut Pasteur de Tunis Paris Masson 1952 Pp 426 Fr 3700

THE name of Dr Nataf and that of his collaborator Dr Cuenod is already well known to ophthalmologists for biomicroscopical investigations of the conjunctiva, which has included much work on trachoma Now Dr Nataf, working at the Institut Pasteur of Tunis, gives us a complete account of trachoma in all its possible ramifications, even including its medicolegal aspects Dr Jean Sedan also contributes a chapter on the physiopathology of the trachomatous eye

In the British Isles trachoma is hardly a problem for few new cases arise, and treatment is almost confined to the late complications of trachoma contracted elsewhere, but in the Middle and Far East trachoma remains the major ophthalmic scourge, responsible for more blindness than any other ophthalmic disease The medical world at large will, therefore, be grateful to Dr Nataf for his excellent monograph, which gives us all the benefit of the 25 years he has spent studying this condition

Manual of Electrocardiography

B F SMITH, M D, professor of clinical medicine, Baylor University College of Medicine New York and London Elsevier Press 1952 Pp 215 32s

THIS is a description of electrocardiography reduced to the smallest compass, but every word is to the point The principles are clearly set out and applied to the explanation of many abnormal tracings, giving the student for higher examinations and the general physician an insight into the way in which most abnormalities are caused This will also be appreciated by the cardiologist who can also occupy himself by considering how he would explain those changes, particularly in the T waves not covered by the author There is little to criticise, but the advice on precordial leads is out of date, some of the tracings are of poor quality and in none of them are the waves labelled, and there are a few typographical errors A quarter of the book contains tracings from patients, accompanied by the post-mortem reports, but without comment or explanation, the reader being left to make his own correlation This is an excellent feature, but the final chapter, entitled "Pen Pictures of Cardiology," is out of place

Infant Development

The Embryology of Early Human Behaviour ARNOLD GESELL, M D London Hamish Hamilton 1952 Pp 108 21s

OVER a period of thirty-five years, Dr Gesell has produced no less than twenty-five books on his chosen subject, besides the films he has used to an increasing extent in demonstrating facets of early human development *Infancy and Human Growth*, which appeared a quarter of a century ago, was an important pædiatric landmark, and did much to stimulate other workers in the same field With the passage of the years, and the development of cinematography, the author's publications appear to have become, to an increasing extent, running commentaries, and to describe the present volume as "the book of the film" would be less inaccurate than when a similar description is applied to, say, *Kidnapped* or *War and Peace* The style at times is perilously near the pompous, and many will prefer the author's earlier writings

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Symptoms and Signs in Clinical Medicine (5th ed Bristol John Wright & Sons 1952 Pp 480 35s)—It is five years since the last edition of Dr E Noble Chamberlain's popular textbook appeared As before, there are many illustrations most of them clear, well chosen, and helpful to the text Many chapters have been revised and one or two completely rewritten, including that on medical operations and investigations, a particularly useful part of the book A new feature, much to be welcomed, is a short glossary showing the origin and meaning of many of the words which all students have to meet for the first time

The book is likely to remain a valued friend to student, houseman, and practitioner

Gynecologic and Obstetric Pathology (3rd ed Philadelphia and London W B Saunders 1952 Pp 595 50s)—Prof Emil Novak's well illustrated textbook emerges in good form from a thorough grooming at the hands of its careful author The sections on carcinoma of the cervix, hydatidiform mole, chorionepithelioma, and several other topics have been revised to express modern opinion, and there is an informative new chapter on diseases of the breast—an organ which gynæcologists have only recently discovered The pictures are as good as ever, and nearly a hundred new ones appear in this edition—some of them replacing less successful earlier versions of the same subjects

TABLE I—COMPLEMENT-FIXING TITRES OF CYST FLUIDS

Antigen	Standard serum dilution						
	2	4	8	16	32	64	128
heep I	+ + +	+ + +	+ + +	+ + +	+ + +	+ +	−
„ II	+ + +	+ + +	+ + +	+ + +	+ + +	+ +	−
„ III	+ + +	+ + +	+ + +	+ +	±	−	−
uman I	+ + +	+ + +	+ +	±	−	−	−
„ II	+ + +	+ + +	+ +	±	−	−	−
„ III	+ + +	+ + +	+ + +	+ ± +	+ + +	+ + +	±
„ IV	+ + +	+ +	+	−	−	−	−

xing antibody. and Hiles (1926) reported that horses nd rabbits were unsatisfactory. We ourselves have xamined the sera of horses with hydatid infestation nd have not found any significant complement-fixing ntibody; but we have not attempted to immunise these nimals with suspensions of scolices. Our experience with abbits has confirmed Hiles's (1926) findings that a high roportion of the sera from uninoculated rabbits conained some natural substance which in the presence of ydatid antigen fixed complement.

Guineapigs, although not convenient animals for the reparation of large amounts of immune serum, proved o be suitable. A batch of selected guineapigs was herefore given a series of injections of a suspension of round-up scolices from a fresh hydatid fluid and then led out. The sera were tested individually and without xception found to have reasonably high titres of complenent-fixing antibody. They were later pooled for final esting and use as a standard serum.

Attention has already been drawn to the method of ssessment of antigenic potency employed by Hamilton airley (1922) and the consistent results he reported in omparative tests on pooled sheep-cyst fluids rich in colices. While this may be true with large pools of heep's fluid, we have not found that individual cyst luids from either ovine or human sources give such onsistent results. Table I shows the complement-fixing itres of a number of fluids (all of which appeared to be equally rich in scolices) when examined with the same standard serum.

Fluids deficient in scolices, however, were consistently poor as antigens. Two fluids from horses, one from a sheep, and one from a human source failed to fix complement with the standard serum diluted more than 1 in 2, and several human fluids have proved to have very low antigen content.

TABLE II—ANALYSIS OF 62 CONSECUTIVE CASES OF SUSPECTED OR KNOWN HYDATID DISEASE IN WHICH THE FINAL DIAGNOSIS WAS CONFIRMED BY EXAMINATION OF THE CYST FLUID OR BY SURGICAL OPERATION

Type of case	Total no.	C.F.T. and skin test positive	Only C.F.T. positive	Only skin test positive	Both tests negative
Primary uncomplicated cyst of liver—					
Before operation	23	18	3	1	1*
1 year or more after operation..	4	1	2	0	1†
Cyst of lung—					
Before operation	6	6	0	0	0
1 year or more after operation..	7	7	0	0	0
Mesenteric cysts—					
After operation	1	1	0	0	0
Bone—					
After operation	1	1‡	0	0	0
Suspected hydatid proved at operation to be due to other causes..	20	0	0	0	20

C.F.T. = complement-fixation test.
*No antigen found in cyst fluid.
†Both skin test and C.F.T. positive 18 months previously.
‡C.F.T. + + 1 in 64; Casoni positive with one antigen, negative with 2 others.

INTRACUTANEOUS TEST

The history of the intracutaneous test for hydatid disease, introduced by Casoni in 1911, is very similar to that of the complement-fixation test in regard to the varying opinions as to its reliability.

The variation in the potency of different hydatid fluids was recognised, but the reason for this was not appreciated until Hamilton Fairley (1922) showed that the antigen was derived from the scolices. The potency of the Casoni fluid prepared by Kellaway and K. D. Fairley (1932) was assured by using hydatid fluid from uncomplicated sheep cysts rich in scolices and then by extensive comparative clinical trials in selected patients. This method of standardisation is still undertaken by the workers at the Royal Melbourne Hospital, Australia. In this country it has not been easy to follow this practice, owing to the difficulty of obtaining satisfactory supplies of sheep antigen. Kellaway and Fairley indicated that human antigens were less satisfactory than those from sheep, and Graña (1945), in an extensive review of the literature, expressed the same opinion. They may well be right; indeed one or two human fluids in our series which proved to be equal to the standard antigen in the complement-fixation test were found to be less sensitive in the skin test. Nevertheless it has been possible to obtain some human fluids which, both by the complement-fixation test and by parallel skin tests in suitable patients, have been found to be the equal of the standard sheep fluid.

TABLE III—COMPLEMENT-FIXATION AND SKIN TESTS. CASE OF UNCOMPLICATED CYST OF LIVER

Antigen	Serum	C.F.T. result
Standard	Standard	1 in 64
Standard	Patient's	1 in 16
Patient's	Standard	1 in 64

Skin test: weak positive.

In this country most readings of Casoni reactions are, of necessity, undertaken by different observers; and this makes it difficult to give comparable values to the records received, even when careful measurements of the skin reactions are taken. Using three antigens of the same potency, when assessed as complement-fixing reagents, there has been appreciable variation in the results of the parallel skin tests as recorded by different observers.

The difficulty of obtaining consistent results in the reading of any skin sensitivity tests by different observers, even when it is feasible to standardise a large batch of the antigen with a fair degree of accuracy, has been made clear in the recent report of an M.R.C. National Tuberculin Survey (Medical Research Council 1952). In the case of the Casoni test, where the supply of any one batch of antigen may be strictly limited, the difficulties are even greater, more especially when the only ancillary laboratory test depends on an antigen-antibody reaction which may not represent exactly the same complex as those involved in the intradermal reaction.

On 5 occasions, in which the complement-fixation reactions were positive in serum dilutions of 1 in 16 or more, the patients were skin-tested with two different antigens. The two antigens appeared to be equally potent when examined with the standard serum for complement-fixing antibodies, yet in each case only one gave a definite positive skin reaction. In 4 cases antigen I was superior but in the 5th case antigen II was reported to be the one giving the positive reaction.

In comparing the value of the intradermal test with the complement-fixation test in hydatid disease we have, in table II, included only those cases in which the records and clinical histories have been reasonably complete and in which both tests were performed. During the period there were 4 cases reported as having negative skin reactions in which a hydatid cyst was found at operation.

patient arrangements, and at the Middlesex Hospital Brigadier HARDY ROBERTS has found it helpful to hold outpatient staff conferences, which can sometimes solve problems previously deemed insoluble

Unfortunately it is very hard to organise improvements in an outpatient department (or in any other concern) which is already overburdened by numbers, and, though most references to hospital are perfectly reasonable, it is possible that practitioners could help to make conditions better if they exercised their right of consultation a little more sparingly Sir JAMES SPENCE found that a meeting with general practitioners to discuss doctors' letters was well received, and if B M A meetings were held to consider local problems they would bring out many constructive criticisms and help everyone concerned Alternatively, the subject could be considered by the local liaison committee, where such exists Another and very important means of reducing the pressure on consultative outpatient departments is to provide "direct access" for practitioners to pathological and radiological investigations—an arrangement which is greatly appreciated and rarely abused In practice it is found that the special departments have very little extra work to undertake

In all such arranging, the standpoint of the patient needs to be kept in mind Good signposting is a help to the newcomer, and so is the assistance of receptionists in the entrance-hall to promote the regular flow of patients with their notes The use of trained nurses for such work is quite unjustifiable, and the duties of outpatient nurses should be restricted to assistance with medical procedures Wherever possible departments should come to the patient and not vice versa thus a circuitous journey to the pathological laboratory may be avoided if accommodation is provided in the outpatient department where the common pathological tests can be made Similarly ancillary medical staff such as dietitians should have accommodation in the department to enable them to attend various clinics But the main consideration is that good facilities for outpatient consultation should enable the consultant both to provide guidance to patient and doctor and at the same time to reinforce the patient's confidence in what is being done for him

Prevention of Rheumatic Fever

RHEUMATIC fever is a manifestation of infection of the upper respiratory tract with group-A *hæmolytic* streptococci More than twenty years of epidemiological and immunological investigation support this statement, and, although we know disappointingly little about the details of the relationship, present methods of preventing rheumatic fever are based on the inference that control of streptococcal respiratory infection will reduce the incidence of primary and recurrent rheumatic attacks The results of clinical trials of prophylaxis with sulphonamides or penicillin suggest that this inference is justified

In the United States streptococcal infections and rheumatic fever reach a peak during the early spring The American Heart Association's committee which has been studying the prevention of rheumatic fever has therefore chosen this moment to publish its recommendations, which are being widely distributed to doctors, medical societies, health departments, and medical ancillaries, as part of a general campaign for the prevention of this disease The statement, which we reproduce on p 285, is a useful and simple account of the use and hazards of sulphonamides and penicillin in the treatment of streptococcal respiratory infections in general, and in the prevention of streptococcal infection in rheumatic subjects In England and Wales the peak of streptococcal infections comes later in the year than it does in the United States both scarlet fever and rheumatic fever are usually commonest during the last quarter of the year[1] The American statement is none the less a timely reminder of what can be done the application of a general policy designed to prevent rheumatic fever in this country remains of the first importance, for, quite apart from recurrences induced in rheumatic patients, rheumatic sequelæ probably complicate 1–2% of streptococcal upper respiratory infections The main points made by the committee are now well established, but they cannot be given too much emphasis In the *treatment* of streptococcal infections, intramuscular procaine penicillin, given early and continued until the organisms are eradicated from the throat, has amply proved its worth[2] Sulphonamides are not recommended, and oral penicillin gets second place for though it is known to be useful its reliability for this purpose has not yet been sufficiently widely assessed In the *prevention* of streptococcal infection in rheumatic subjects, the population at risk includes all those under the age of 18 who have had rheumatic fever or chorea, and also all those over this age who have had an attack within 5 years, for the risk of recurrence seems greatest within this period[3] The problem here is a much bigger one than that of treatment prophylaxis should be applied continuously within these age-limits—an expensive business—and partly for this reason the choice of the American authorities has fallen on sulphadiazine Patients in hospital recovering from acute rheumatic attacks may be successfully launched on their course of sulphadiazine, but their supervision as outpatients afterwards calls for considerable organisation Toxic effects, though rare after the first 8 weeks of prophylaxis, should be watched for, routine examination for signs of rheumatic recurrence should be carried out, and it is probably desirable to test the urine occasionally to make certain that the drug is being taken Although resistant streptococci have appeared—with devastating results—when mass prophylaxis has been applied to closed communities under Service conditions,[4] in the individual rheumatic patient taking sulphadiazine at home the risk is not nearly so great

But sulphonamides have their shortcomings, and the superiority of penicillin in exerting a bactericidal rather than bacteriostatic action, in effectively eliminating the streptococcal carrier state, and in only rarely producing penicillin-resistant streptococci has prompted a search for practicable methods of penicillin prophylaxis Penicillin has been given orally, but there are disadvantages it is a more

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TOXIPATHIC HEPATITIS DUE TO FOWLER'S SOLUTION

A CASE TREATED WITH DIMERCAPROL

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Thomas Fowler published in 1786 his "Medical ports of the effects of arsenic in the cure of agues, mitting fevers, and periodic headaches" and therein troduced the solution of 1% arsenic trioxide which has nce borne his name. This solution is now little used general medicine but is often prescribed as a palliative r dermatological conditions. Our purpose here is) to draw attention to its toxic effects and (2) to discuss e treatment of toxipathic hepatitis with dimercaprol.

TOXIC EFFECTS OF FOWLER'S SOLUTION

Peripheral Neuritis.—Déjerine (1883) showed that e nerve condition characteristic of arsenic poisoning as a multiple neuritis essentially similar to alcoholic euritis. The "biochemical lesion" responsible is n inhibition of the pyruvate oxidase enzyme system avrilescu and Peters 1931). This system may be hibited negatively by lack of the co-enzyme thiamine itamin B_1) or positively by the combination of trivalent rsenicals with SH- groups in protein components of he system. Arsenical poisoning thus produces a olyneuritis similar to that seen in thiamine deficiency.

Pain and paræsthesiæ may be intense. In addition o the usual mixed form, with motor and sensory paralysis here is a pseudotabetic form with little motor paralysis Ross and Bury 1893, Harris 1926). The cranial nerves re occasionally involved (Kinnier Wilson 1940). The apidity with which symptoms may appear is illustrated y a case quoted by Harris (1926) in which severe polyeuritis with bilateral wrist and foot drop followed the aking of Fowler's solution 15 minims t.d.s. for six eeks. Recovery is said to be complete in 97% of cases. ut it may be delayed for two years or more.

Epitheliomata.—Inorganic arsenic is now known to ave carcinogenic properties, and Goeckerman and Vilhelm (1940) state that a 1 in 40,000,000 solution of rsenic will change embryonal cells to tumour cells. Arsenical keratoses, first described by E. Wilson (1868). sually occur on the palms and soles but may occur lsewhere. They are prone to malignant change and uch change may be multiple. Epitheliomata are in act said to develop in 20% of keratoses. Ayres and Anderson (1934) examined the palms and soles of each patient with a basal-cell epitheliomata and by this means detected unsuspected cases of chronic inorganic arsenical poisoning. Goeckerman and Wilhelm (1940) mention an interesting case of malignant papillomata of the bladder and ureter in which the lesions were found to contain crystals of arsenic sulphide, and these were present twenty-one years after the patient had taken Fowler's solution over a long period.

Toxipathic Hepatitis.—This term was introduced by Himsworth and Glynn (1944) to describe the hepatic lesion produced by the direct action of a noxious agent, whether a chemical such as inorganic arsenic or a living organism such as the virus of infective hepatitis.

Experimental work on the effect of inorganic arsenic on the liver was done by Ziegler and Obolonsky (1888), Wolkow (1892), Stoeber (1936), and von Glahn et al. (1938). Similar results were obtained by all observers. In rabbits and guineapigs fatty change in the liver cells were seen after a few days; they progressed to necrosis in two weeks, and shortly after this there was an increase in connective tissue with proliferation of bile-ducts in the animals which survived. Such a process in man would lead to diffuse hepatic fibrosis or to multiple nodular hyperplasia, depending on whether zonal or massive necrosis had taken place.

The first report suggesting that hepatic damage could be caused in man by inorganic arsenic was that of Bang (1774) under the title of "De hydrope ex ingesto arsenico observatio." Cases of cirrhosis due to this cause have since been described by Hutchinson (1895), Geyer (1898), Hamburger (1900), Sturrock (1900), Reynolds (1901), Stockman (1921), O'Leary et al. (1928), Rolleston and McNee (1929), Weir (1930), Chapman (1931), Osterberg (1935), and Cannon (1936). The most recent report is that of Himsworth who, in his Lowell lectures of 1947, cites the case of a woman who had taken Fowler's solution for twenty years for psoriasis and fourteen years later was found to have hepatic cirrhosis. No other ætiological factors were evident.

Though it is now fully established, both experimentally and clinically, that inorganic arsenic may cause toxipathic hepatitis and fibrosis of the liver, this is not clearly indicated in standard textbooks. Cushny (1947), for example, mentions that "some swelling of the liver and jaundice may occur but these are not generally well-marked"; Price (1946) merely says that "ascites and general œdema occur towards the end"; and neither Taylor (1948) nor Cecil (1947) describe liver damage in inorganic arsenic poisoning.

CASE-REPORT

A 40-year-old butcher was first seen on March 31, 1949, with an indefinite complaint of lack of joie-de-vivre.

History.—For the previous nineteen months he had suffered from dermatitis herpetiformis, the onset of which had been closely related to an emotional upset. Treatment with a mixture containing Fowler's solution 4 minims given three times daily had commenced in December, 1947, and the amount had been increased to 6 minims in January, 1948, to 7 minims in September, 1948, and to 8 minims in January, 1949. The total intake of Fowler's solution had been 144 drachms, which contains 80 grains of arsenic trioxide. This treatment had kept the skin lesions under control but they had never cleared.

His diet was good and his alcohol intake amounted to no more than an occasional glass of beer. He had never

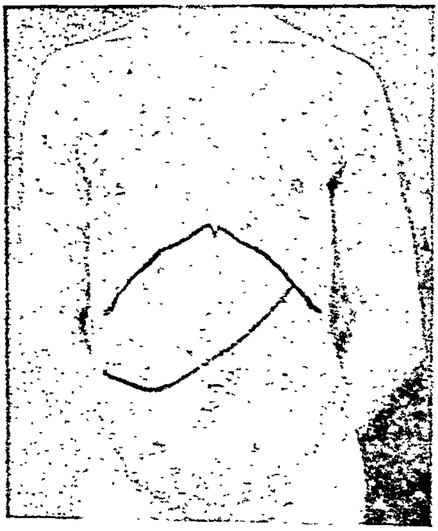

Fig. 1—Showing dermatitis herpetiformis, raindrop pigmentation, and liver enlargement.

It is true, no doubt, that society wishes to be avenged on evil-doers , for in this way an inner tension is released and public anger is assuaged Those seeking to restore judicial flogging also take this human desire for vengeance into account Some, indeed, argue that this kind of emotional release helps to prevent aggression appearing in less controllable forms—as war, for instance But history does not seem to support this opinion in the days of abominable public executions—burnings, quarterings, breaking on the wheel—wars were as common as now, and the atrocities done in wars of our own day have been of the same ugly pattern as those done at the sacking of ancient cities On the contrary, an appetite for cruelty grows by what it feeds on wide experience of brutality does not fit a man to be humane Moreover the enjoyment of other people's suffering is, like other vices, infectious people respond insensibly to the standards of those around them, and can be oriented to base pleasures quite as readily as good ones Whether an execution is actually seen or merely imagined, the mental effect is qualitatively the same, and in our view the perpetual public preoccupation with the condemned cell and the gallows is harmful to the mental health of society

To the English, at any rate, revenge is seldom a fully satisfying experience , it carries too much guilt with it In the case of Bentley the public sense of guilt seems to have been strong—far stronger than the desire for vengeance The youth of the prisoner, the fact that he did not fire the shot, and that he was angry and excited when he shouted to Craig, have carried weight with a generation which is beginning to have a shadowy new conception of the nature of adolescence In this first change of life the endocrine imbalance is expressed in symptoms ranging from noisy laughter, group enthusiasms, fantasy, exhibitionist attire, and transient homosexual attachments to such graver manifestations as manic and schizoid episodes, delinquency, and crime In the case of the Trowbridge boys a fantasy is suggested by their purchase not only of firearms and knives but of a tent, and some similar factor may have been at work in Bentley's case An element of fantasy in a crime neither excuses nor fully explains it, but it may throw some light on the mechanism Daydreaming generally puts the dreamers into positions of success and power, but these are attained quite as often through virtue, courage, and brilliance as through lawlessness or oppression of others If fantasies of easy success through ruthless action persist to an age when they should have been outgrown and are expressed in antisocial deeds, where does the blame lie ? Granted free will, much of it lies, of course, on the youth himself He has chosen his antisocial fantasies, and has resisted good advice and other influences guiding him into socially acceptable behaviour On the other hand, society shares the blame for not providing him with worthier objects for his fantasies, for not giving the good advice with more authority and enthusiasm, and for failing to train him successfully in citizenship Part of the emotion over Bentley's fate can doubtless be identified with a morbid taste for executions, acceptably disguised , and part sprang from an illogical idea that (since he did not fire the shot) the rules of fair play had been infringed But part at least was an acknowledgment of society's share in the responsibility and that is as it should be

Annotations

CONTROL OF DRUG SALES

It is manifestly undesirable that pharmacological potent substances should be freely accessible to t public The supply of poisons has been restricted f over a century , but the rise of chemotherapy, a notably the introduction of the sulphonamides a penicillin, increased temporarily the tendency to se medication with compounds that should be used wi care Soon the sulphonamides were scheduled as poisons and in 1947 a special Act was passed to curb the ind criminate use of penicillin Under this Act the sale a supply of penicillin products was restricted so that th could be obtained only on prescription or for treatmen by, or in accordance with the directions of, a medic practitioner Later a similar ban was placed on strept mycin, aureomycin, and chloramphenicol Now th Therapeutic Substances (Prevention of Misuse) Bill ha been introduced into the House of Lords, to modify th Penicillin Act by permitting any therapeutic substan to be subjected to the provisions of that Act if it appear "to be capable of causing danger to the health of th community if used without proper safeguards" An specific substance would be controlled by regulation b only after consultation with the Medical Research Counc The prospective regulations will presumably make litt change in medical practice, since the Penicillin Act itsel has had no hampering effect , but these regulations wi help to save the public from mishaps through uncontrolle use of substances whose supply cannot be regulate under the poisons law—phenylbutazone, for exampl may be named in them The Bill also seeks power t relax the regulations of the Penicillin Act so that it ca be used for agricultural purposes—presumably th fattening of livestock

MATING AMONG VIRUSES

The demonstration by Delbrück and Bailey[1] tha bacteria simultaneously infected with two different ba related bacteriophage strains yielded progeny wit characters derived from both "parent" phages wa received with unusual interest At once a great deal o speculation on the methods of virus reproduction wa aroused Hershey and Rotman[2] kept the pot boilin briskly with their detailed studies of the mating habit of a group of bacteriophages From an analysis of th numbers of recombinants among the progeny fro different "parent" phages, they were able to construc what are virtually chromosome maps for the particula "genes" which they investigated The possibility o carrying out similar studies with influenza viruses ha lately been engaging the attention of Burnet and hi colleagues in Melbourne

Burnet and Lind[3] found that when a mixture of a influenza virus (MEL) with a neurotropic influenza varian (NWS) was inoculated intracerebrally in mice it wa possible to recover from the mouse brain a virus bearing the serological characters of MEL and the neurotropic properties of NWS They suggested that recombination analogous to that described for bacteriophages, had take place But there was another possible explanation fo these results , the "recombinant" might simply hav been a neurotropic mutant of MEL which would grow happily in the mouse brain, the mutation being in some way favoured by the presence of the NWS In an attemp to exclude this possibility, Burnet et al[4] have now looked for evidence of recombination in viruses grown

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robably in progress. Himsworth (1947) emphasises he difficulty of deciding clinically when the stage of ncomplicated fatty infiltration has passed and the tage of fibrosis has definitely begun. The matter can e settled by liver biopsy, but there were non-medical ontra-indications to this investigation in our patient. Himsworth believes that diffuse hepatic fibrosis may ake decades to develop and he remarks that it is ompatible with years of reasonable health. Our patient will probably remain in good health until symptoms of portal hypertension appear.

Reactions to Fowler's solution may cause death or ong illness, and there is now, we believe, no justification for the long-continued administration of arsenic in general medicine. If advantage is to be taken of the [illegible] effect of Fowler's solution in dermatological [illegible], the necessity for careful clinical control must be appreciated. This will involve, as a minimum, examination for hyperkeratosis, inquiry regarding the subjective symptoms of peripheral neuritis, and abdominal examination to detect liver enlargement due to fatty infiltration. If, in a busy dermatological department, careful follow-up is not practicable, it is most unwise to use inorganic arsenic at all.

SUMMARY

The important toxic reactions to Fowler's solution are discussed with particular reference to toxipathic hepatitis.

A case of hepatitis due to administration of Fowler's solution for dermatitis herpetiformis is described.

Treatment with dimercaprol resulted in the urinary excretion of considerable amounts of arsenic, with subjective and objective improvement, but diffuse fibrosis is likely to be the sequel to the administration of arsenic to this patient.

Fowler's solution should not be used without consideration of the risks, nor without careful clinical control.

We wish to express our thanks to Mr. Harri Heap, former city analyst for Manchester, for the considerable amount of work he so willingly undertook in carrying out the urinary analyses for arsenic, and to the Department of Medical Photography, Manchester Royal Infirmary, for the photographs.

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POSTPARTUM ANAL FISSURE

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Anal fissure is common in pregnancy and the puerperium. Goodsall and Miles (1900) suggested that parturition causes overstretching of the anal mucosa, which is thus rendered more susceptible to trauma. Lynch (1914) and Smith (1939) noted that rupture of the perineum in childbirth predisposes to anal fissure. De Lee and Greenhill (1943) state that anal fissures are a common sequence to the stretching of the anus during labour.

MATERIAL

Many patients attending the postnatal clinic at this hospital six weeks after delivery complained of anal symptoms. An investigation was therefore started in which such patients were examined for abnormalities in the anal region. The patients studied attended the postnatal clinic between December, 1950, and May, 1951. Of 642 patients booked to return to this clinic six weeks after delivery 424 attended and were questioned.

RESULTS

Of the 424 patients questioned 50 (11·8%) complained of pain or bleeding or both on defæcation. The following lesions were discovered :

Anal fissure	45 cases (10·7 % of total cases seen)
Hæmorrhoids	3 cases
Thrombosed hæmorrhoids	2 cases

Many patients were found to have skin tags round the anal canal, but only the lesions responsible for the patients' symptoms are included.

These figures show that anal fissure is responsible for most of the symptoms, and that the patient's complaint of "having piles" should always be regarded with suspicion. She will almost certainly have a fissure.

SITES OF FISSURES

The fissures were sited as follows :

Single fissures		*Multiple fissures*	
Anterior ..	15	Anterior	26
Posterior ..	8	Posterior	24
Lateral	1	Lateral	3
Total ..	24 cases	Total	21 cases
(54 % of total cases of fissure)		(46 % of total cases of fissure)	

In this series 62% of the single fissures occurred anteriorly. Multiple fissures were found in 21 (47%) of the women with fissures. Anterior fissure is agreed to be more common in women, but the proportion of anterior fissures in women seen varies from 8% (Pennington 1923) to 40% (Bacon 1943); most writers favour the lower figure. Goodsall (1892) mentioned that in 8% of his female patients both anterior and posterior fissures were present. Multiple fissures are common after parturition : two fissures were seen in 12 cases, three in 7 cases, and four in 2 cases. Gabriel (1948) states that multiple fissures are only occasionally met with, and in a series of cases of fissure at the Mayo Clinic (Buie 1937) found that 0·1% were multiple. But multiple fissures are common after parturition: two fissures were seen in 12 cases, three in 7 cases, and four in 2 cases. It must be emphasised that the fissure is seldom large, and very careful inspection of the anal margin is necessary in suspected cases.

ONSET OF SYMPTOMS

All the patients were questioned about the onset of symptoms, and their answers gave the following figures :

Antenatal	.. ..	6 cases
Postpartum	0–4 days	11 cases
	5–9 days	2 cases
	10–14 days	17 cases
	15–40 days	9 cases

The patients were discharged home on the ninth or tenth day of the puerperium, and most of them noticed symptoms within a few days of returning home. Undoubtedly with one contrast medium does not necessarily indicate sensitivity to another, they think that the standard intravenous test is of doubtful value in assessing the liability to a severe reaction In all, 17 deaths after intravenous pyelography have been reported, these have all followed administration of diodone Considering the great number of examinations performed every year, the margin of safety is large

TUBERCULOSIS IN NEW YORK AND LONDON

BOTH in New York[1] and London[2] the half-century up to 1950 has been marked by reviews of changes in the tuberculosis situation The unsatisfactory hygienic conditions of the 19th century, with large outbreaks of acute epidemic diseases causing many deaths, led to great sanitary advances at the end of the century In New York between 1900 and 1950 the population increased from 3½ million to 8 million, largely as a result of immigration, in 1910 40% of the population were foreign-born The Manhattan area was already crowded at the beginning of the century, and its population has increased little In the London county area the population declined from 4½ million to less than 3½ million between 1913 and 1950, owing mainly to migration from the crowded central areas to the suburbs, the population of Greater London, including the dormitory zone, has increased during this period, though not to the same extent as in New York Such major movements of population must affect the age-structure of the population, and hence also the epidemiological picture of tuberculosis Migration occurs especially among young adults New York has grown by immigration of this group from Europe especially, while in London it is predominantly the young adults that are likely to be rehoused outside the county boundaries

In both areas the death-rate from tuberculosis fell greatly during the half-century—in New York by about 90% from 280 to 29 per 100,000 The rate in London in 1900 was lower (223 per 100,000), but had not fallen to the same extent by 1950, when it was 40 per 100,000 The two wars had a greater effect on tuberculosis mortality in London than in New York, in the second war the fall in this rate in New York was hardly checked, whereas in London the rate rose steeply Evacuation raised the London rate artificially, since "the tuberculous were evacuated to a much less extent than healthy persons" The death-rate has shown the greatest fall in childhood, and comparatively little improvement in old age The control of bovine tuberculosis—by eliminating tuberculosis in cattle in New York State, by pasteurisation in London—has played a large part in the reduction of childhood mortality

In London compulsory notification of cases of tuberculosis was started in 1911 in New York "registration" of cases has been carried out since 1894, but was not complete before 1910 Since then the annual notification-rate has declined in each city, but this decline is much less than that of mortality, and it was interrupted during the war periods in both New York and London

The New York report describes differences in tuberculosis mortality between various racial groups The unfavourable record of the coloured population in this respect is well known, but there are distinct and consistent differences between the white groups of European origin The lowest rate is in the "native born" group, but presumably this includes a large number of children and is not really comparable with the various "foreign-born" groups In 1920 the highest mortality-rates were in those born in Ireland and Scandinavia, the lowest in those (mostly Jews) born in Russia Similar relationships are evident in the figures for 1890 and 1930

These reports show that, while there are fundamental similarities in the tuberculosis records of New York and London, detailed comparisons are not justified because of differences in population structure as regards race and age The New York report is especially valuable in bringing together in tabular form all the available records concerning tuberculosis in the city Both reports show that considerable progress has been made in reducing tuberculosis mortality, especially in childhood and we may echo the final hope of the authors of the New York report that by the end of the century tuberculosis will be rare at any age

ELECTRO-ENCEPHALOGRAPHY FOR BOXERS

SUPPORTERS of boxing often point out that severe injuries may be inflicted in sports which are not so often challenged as being dangerous, but, as we have remarked,[1] one of the boxer's main aims is to disable his opponent The medical subcommittee of the British Boxing Board of Control has laid down the conditions for compulsory examination A professional boxer must be examined after he has taken a count or after a fight has been stopped for any reason, and if he loses four consecutive fights a representative of the board interviews him and his manager But clinical examination, however frequent, cannot prevent occasional fatalities, and once in a while a death, such as that of M Pratesi, of France, a few months ago, revives the discussion whether these precautions are adequate The B B B C seems to take the view that no other method has yet been proved superior, but one suggestion to which thought is being given is that periodical electro-encephalographic (E.E G) examinations should be made

This procedure has been adopted in Colorado[2] where it was decided that every professional boxer should have an E E G examination (*a*) once a year, (*b*) within two weeks of a knockout, and (*c*) frequently if his record was abnormal In all, 24 men have been studied An increased prevalence of dysrhythmia was found in 8 of them, and there was some indication that those who had been knocked out showed a greater disturbance than those who had not Older men had, on the whole, fewer disturbances than younger ones In 1 case where the E E G abnormality was progressive the boxer was suspended Busse and Silverman[2] conclude that compulsory periodic E E G examinations contribute to the safety of boxers

Many workers in this field would disagree, for it is by no means certain that changes reflected in the E.E.G would not be discovered clinically This doubt is especially great in cases of acute injury, but one exception is the subdural hæmatoma which, though clinically "silent," may produce focal or general E E G changes In the Colorado investigation overbreathing was carried out routinely, and sleep records were taken when possible but no mention is made of blood sugar levels, and the allowances made for age changes are not clear On the last point it might be argued that some, at least, of the abnormalities described could be due to maturation defects In Gibbs's[3] opinion a diffuse abnormality is of no diagnostic value in post traumatic cases He states that (*a*) focal abnormality suggests brain damage, but absence of focal abnormality does not exclude it, (*b*) if a general abnormality is present three to four months after a mild injury the chances are sixteen to one that this abnormality antedated the injury, and (*c*) in post-traumatic cases the E.E G may be normal in the presence of known brain damage (of 160 patients with normal E E G s 3 had neurological evidence of damage) But Busse and Silverman's series is too small to point conclusively ly 6 cases of fissure in the antenatal period are scribed, although this condition is probably more mmon, but I have not had access to all the antenatal tients. The diagnosis of fissure in these cases is rticularly important if pregnancy is not to become a isery.

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[1] A Half Century's Progress against Tuberculosis in New York City 1900-1950 By G J DROLET and A M LOWELL Published by the New York Tuberculosis and Health Association, 386 Fourth Avenue New York 16 N Y

[2] Half a Century of Tuberculosis in London a review of changes and trends since 1900 Reprinted from the Report of the County Medical Officer of Health for the year 1950

[1] *Lancet* 1950 i 1006

[2] Busse E W Silverman A J *J Amer med Ass* 1952, 149 15[illegible]

[3] Gibbs F A *J clin Psychopath* 1916, 8 58

The recognition of anal fissure in pregnant and puer-eral women is important. Improvement will come by e avoidance of constipation in the antenatal and ostnatal periods, by great care in the use of enema ringes and at rectal examinations, and by the avoidance f damage to the anal margin by tears or episiotomy. In me cases, however, a timely episiotomy will reduce the amage to the perineum and anal mucosa. All patients hould be questioned, before discharge from hospital, bout discomfort or bleeding on defæcation, especially f forceps have been used. Instructions should also be iven, before discharge from hospital, for the patients o report at once if rectal symptoms appear before they re due to attend the postnatal clinic.

SUMMARY

45 cases of anal fissure are described in 424 women ttending a postnatal clinic (incidence 10·7%).

Hæmorrhoids are rarely responsible for rectal symptoms ix weeks after delivery.

Multiple fissures are common and were seen in 21 cases 46%).

Anterior fissure occurred in 15 (62%) of 24 cases with single fissure.

The causes, prevention, and treatment of anal fissures are discussed.

I wish to thank Mr. O. V. Lloyd-Davies for his help and advice in the preparation of this paper.

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GASTRIC MUCOPROTEIN AND INTRINSIC FACTOR

RESPONSE OF PERNICIOUS ANÆMIA TO ORAL VITAMIN B_{12} PLUS NORMAL GASTRIC JUICE TREATED WITH RECEPTOR-DESTROYING ENZYME

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THE chemical nature of intrinsic factor has long been a baffling problem and it is of great interest that Jerzy Glass and his colleagues at the New York Hospital have recently claimed that Castle's hæmopoietic principle is associated, if not identical, with a gastric mucoprotein (Glass et al. 1952).

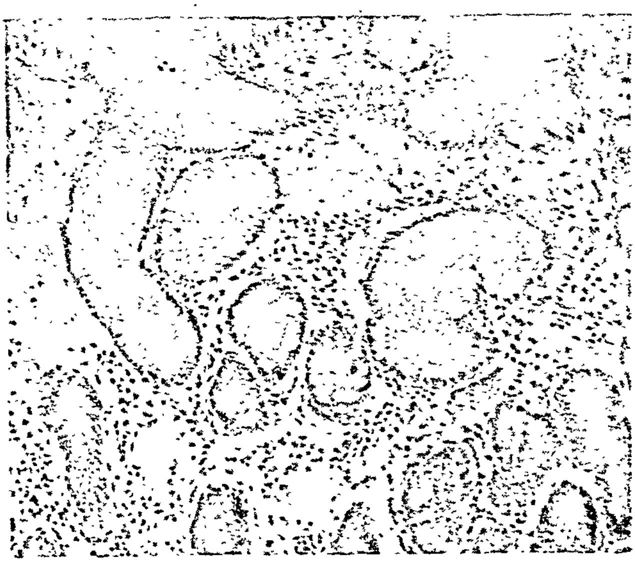

Fig. 1—Gastric biopsy showing mucosa reduced in width; surface epithelium partly columnar and partly goblet-cell in type, with pits leading to a few coiled tubules entirely composed of non-specific cells; infiltration of lamina propria with lymphocytes and plasma cells. Appearances are those of gastric atrophy characteristic of pernicious anæmia. (Hæmatoxylin and eosin. × 250.)

In 1947 Burnet and Stone discovered a soluble enzyme which was derived from *Vibrio choleræ* and could either modify or destroy the influenza-virus receptors on erythrocytes and on cells susceptible to experimental infection. A long series of investigations, reviewed by Burnet (1951), established that this receptor-destroying enzyme (R.D.E.) like that on the viruses themselves, was a mucinase acting on a considerable range of soluble mucins, including some of those present in egg-white, meconium, saliva, and human gastric contents. The chemical nature of the reaction is not yet established, but Gottschalk (1951) has provided evidence which points strongly to an action on the carbohydrate moiety of the mucoproteins in egg-white and urinary inhibitor. In addition to destroying the power of mucoproteins to react with influenza viruses the enzyme produces a sharp change to a less electronegative state in the electrophoretic mobility both of red cells and of soluble mucoproteins. Whitten (1949) reported the very interesting finding that R.D.E. could destroy the biological activity of the mucoprotein gonadotrophic hormone.

In view of this apparently specific action on a variety of mucoproteins it was of interest to see whether the gastric mucoprotein believed by Glass to be the intrinsic factor would lose its activity after treatment with R.D.E.

CASE-RECORD

A woman, aged 29, was admitted to the Royal Melbourne Hospital on May 12, 1952. She had been successfully treated with liver extract for "anæmia" in Yugoslavia in 1949 but had allowed her injections to lapse for eighteen months, she had become weak, tired, and breathless on exertion.

On examination she was very pale and slightly icteric. Her tongue showed moderate papillary atrophy. There was no evidence of subacute combined degeneration of the spinal cord.

Investigations revealed the classical features of pernicious anæmia. A histamine test-meal showed complete achlorhydria, and a gastric biopsy, obtained by the method described by Wood et al. (1949), showed atrophic mucosal changes typical of addisonian anæmia (fig. 1). A blood-count showed Hb 6·8 g. per 100 ml.; red cells 1,600,000 per c.mm.; white cells 6000 per c.mm.; packed-cell volume 30%; mean corpuscular volume 150 c.μ; mean corpuscular Hb 36 μμg.; mean corpuscular Hb concentration 26%. A blood smear showed considerable macrocytosis and variation in size of the red cells, with numerous poikilocytes. A sternal-a characteristic histological picture of swollen elastic tissue Electron microscopy showed that in fact there was no increase in elastic fibres in this condition, but that the collagen fibres were abnormally short it is these collagen fibres that take up the elastic stain On the other hand, not all abnormal collagen stains like elastic fibres In Werner's syndrome, where the electron microscopes shows grossly degraded collagen in the skin, histologically the elastic staining is normal

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* Rockefeller Foundation Fellow.
† Aided by a grant from the National Health and Medical Research Council.
‡ Drug Houses of Australia Fellow.

The discrepancy between the results of histological staining and electron microscopy, and its convincing explanation by the Leeds workers, throws some light on the nature of the morphological changes in the skin with age It also underlines the inadequacy of staining techniques alone as a means of interpreting the morphology of connective-tissue lesions in general It is reasonable to hope that the simple technique of enzymatic digestion, used in conjunction with quantitative biochemical analysis and, where feasible, with electron microscopy, may give much help in the elucidation of connective tissue disease

SIGNS OF PAIN

Pain, being essentially subjective, is not easily assessed It has objective counterparts, such as wincing, reflex withdrawals, vocal expressions, sweating, and changes in respiration, heart-rate, and blood-pressure, for example, in association with ischæmic muscular pain Alam and Smirk[1] recorded increases in blood-pressure and heart-rate, and Thompson and Gellhorn[2] reduction in electrical skin resistance But such changes vary greatly from one person to another, and are slight or absent with mild or moderate pain, and in gauging the action of an analgesic drug it is important to remember that this drug may influence the accompaniments of pain by mechanisms unrelated to those which underlie its relief

Wolff et al[3] have distinguished between pain perception and the reaction pattern to pain The reaction pattern involves withdrawal, fear, flight, or anxiety and is associated with visceral reactions such as those already mentioned Its association with pain is extremely variable, indeed the reaction pattern may be induced by mere apprehension of pain, as when sitting in a dentist's chair The most important way in which morphine relieves pain is by preventing the usual reaction pattern, even though pain is still perceived and recognised as such Thus analgesic drugs are best judged by recording the patient's own words, and the reliability of this evidence can be tested by careful control of the nature and doses of the drugs given[4]

Dr Phyllis Croft[5] has reported on the reflex tachycardia from painful stimuli in rabbits and in man She suggests that the "cardiac pain reflex is a reliable and convenient method of assessing pain perception . particularly useful in conditions of curarization" Here the "cardiac pain reflex" does not mean, as one might suppose, that pain arises in the heart, but that the heart-rate responds by an increase when a nocuous stimulus is applied to the skin Furthermore, the word "perception" should mean awareness of something and has no meaning when a person is unconscious In the second stage of anæsthesia the patient is unconscious and unaware of pain, yet his heart-rate and blood-pressure may be increased by nocuous stimuli Dr Croft has sought to correlate in rabbits and in man the electrical changes in the brain with pain perception Much might be learnt from such observations, but only by making them in man Conditions in which animals *feel* pain cannot be determined except by extrapolation from human experience Sherrington,[6] discussing reactions to harmful stimuli in animals, said "In all this experimental work on animals the observer has to work through signs of subjective states incomparably inferior in most instances to the verbal communication establishable with an intelligent human being", and Lewis[7] observed that "We have no knowledge of pain beyond that derived from human experience" This of course means, not that animals do not suffer when they show the behaviour characteristic of human beings in pain, but that in this field man is the measure of all things

COLD CARDIAC SURGERY

Although many uses have been suggested for general or regional refrigeration in clinical medicine, the results have been disappointing[8] "Hypothermia," however, has recently aroused the interest and ingenuity of the experimental surgeon Bigelow and his colleagues,[9] for example, have demonstrated experimentally the way in which cooling of the patient's body may the cardiac surgeon When the body-temperature dogs was reduced to 20°C (68°F), the cardiac inflow could be interrupted for long enough to permit the heart to be opened and its interior examined Delorme described how cooling of the blood-stream seemed to be practicable method of lowering the respiratory activity of the cell without endangering life He found that dogs whose body-temperature had been reduced to 25 (77°F) were able to survive long continued reduction in blood volume, as well as suspension of blood flow Lewis and Taufic[8] have now reported that they could make, and subsequently close, atrial septal defects under direct vision in hypothermic dogs 27 out of 29 dogs survived the operation for production of the lesion and these defects were successfully closed later in out of 26 of these animals These experimental findings have been excitingly translated into clinical reality using the same technique as in dogs Lewis and Taufic have successfully operated on a five year old girl with an atrial septal defect She was anæsthetised and wrapped in refrigerated blankets until, after two hours and minutes, her rectal temperature had fallen to 28 (82 4°F) The blankets were then removed and the operation began The cardiac inflow was occluded for 5½ minutes, and a 2 cm septal defect was closed under direct vision The operation lasted 58 minutes and the patient's rectal temperature after this time was 26 (78 8°F) She was restored by immersion in hot water at 45°C (113°F), and after 35 minutes her rectal temperature had risen to 36°C (96 8°F), when she was removed from the bath She did well after the operation, and left hospital 11 days later The cardiac murmur had gone

This technique has all the makings of a major advance in cardiac surgery But Lewis and Taufic observed ventricular fibrillation in some of their dogs after operation, and this possibility, and doubtless others, will need careful consideration

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The executive board of W H O met in Geneva on Jan 27 to nominate a successor to Dr Brock Chisholm director-general of the organisation, whose term of office expires on July 21 They chose Dr Marcolino Gomes Candau, of Brazil, who is at present assistant director of the Pan-American Sanitary Bureau in Washington The nomination will be put before the sixth World Health Assembly which opens in Geneva on May 5

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Medical Societies

ROYAL SOCIETY OF MEDICINE

nction of the Hospital Outpatient Department

THE sections of medicine and of general practice of e Royal Society of Medicine met together on Jan. 27, der the chairmanship of Dr. E. P. SCOTT, to discuss e Function of the Hospital Outpatient Department.

Sir JAMES SPENCE pointed out that the outpatient partment was a place of many functions. The general actitioner referred patients to hospital for consultative vice or specialist examination, sometimes only to get l of a troublesome person or because the patient asked for What the hospital offered might be a true consultation a clinical display for students, together with specialist chnical examinations of eyes, ears, &c., a casual- eatment department, and follow-up clinics. It was a eting-ground not only of patient and doctor but also students, nurses, almoners, and clerks, who all had eir different views of it. The department was usually the hospital cellars, lined with lavatory tiles, lodged e a poor relation in the space which could not be used r wards. He thought it a great pity that in the com- tition between the dispensaries and infirmaries in the th and early 19th centuries the infirmaries had won. aving captured the outpatient work the hospitals had en made it subsidiary to inpatient care, fitting it into amped quarters and appointing junior men to do it. many provincial suburban practitioners today had ill- uipped and unsuitable surgeries it was partly because ey had copied what they had seen as students in the tpatient departments of their teaching hospitals. In e present time of rapid change it was important to ink out what such a department should be, instead of ontinuing blindly along the old beaten track. Let us ttle the priorities, make some experiments, and try to ut improvements into practice.

Sir James said he believed that, above all, the outpatient epartment should offer a true consultation on the lines f private practice. General practitioner and consultant hould be personally acquainted. and the patient should e fully introduced by a telephone conversation between hem. Failing that, a good letter should be sent. Best f all was if the practitioner could attend with his patient. he consultation must be completely private—just the onsultant with the patient and his own doctor—and no urses, almoners, or clerks should be allowed in the room. n teaching hospitals a maximum of two students might ssist the consultant, with the patient's permission, which would be given in 90% of cases. But there should be no linical teaching except between cases. Students had lenty of other opportunities to learn physical signs nd pathology. What they could gain only from the utpatient clinic was the example of an experienced erson handling a human situation, making not only a medical diagnosis but an estimate of the patient's view f his own illness, and the level on which explanation and advice could best be offered to him. The purpose of a consultation was to explain to, and advise, the patient as well as his general practitioner. Sir James said that when after a consultation fraught with emotion he saw the captain of the university football team wiping a tear from his eye he knew that it had been valuable to this student as well as the patient.

Dr. R. J. F. H. PINSENT gave a general practitioner's view, by which a hospital visit was only an incident in his patient's medical life. He chose his consultants by the kind of reports they sent back, and tried to get to know those he approved of. In one year he had 2176 first attendances at his surgery, and referred 412—nearly a fifth—to a hospital. About 60 of these patients were referred to the casualty department, which was better equipped than he for minor operations. Medical, surgical, and ear, nose, and throat clinics each received over 11%, while 9% saw the dermatologist. Some of these cases were for diagnosis, others for special investigation, radiography, or physiotherapy. He arranged consultations by telephoning the hospital's appointments bureau, which was, however, shut at the time of his evening surgery. But the real trouble was the delay in getting reports back afterwards. He instanced a young man with a presumed peptic ulcer for whom on Oct. 29 he arranged an outpatient appointment. The consultant saw the man on Nov. 3 and ordered a barium meal. Radiographs were taken on Jan. 7, but no report on them was forthcoming by Jan. 27. Meanwhile the patient, who called at his surgery regularly for news, was looking better. He had bought a book on the cure of ulcer at a railway bookstall and was treating himself, apparently with good results. Hospitals ought to send out letters and reports the same or the next day, on paper of a standard size for easy filing.

There were too few clinical assistantships for general practitioners; no form of postgraduate education did them more good. They ought to be always welcome as visitors to the outpatient department in any case, with or without their patients, so that it became a common ground where consultant and practitioner met and combined specialised knowledge with human understanding. The practitioner might thus also be brought into schemes of research. Another link could be formed by inviting hospital registrars to visit evening surgeries—valuable experience for them now that a would-be consultant could no longer begin his career in general practice. But though the outpatient department should become a medical centre for the district, it should not absorb the personal health services run by local authorities. Preventive medicine lay in the general practitioner's sphere.

Brigadier G. P. HARDY-ROBERTS said that the hospital administrator's job was to try to keep everyone happy; but this was only possible if doctors appreciated the administrative difficulties. General practitioners sometimes sent patients without mentioning which consultant's advice (or even which clinic) they wanted, or the relative urgency of the case. Consultants were sometimes unpunctual or absent without warning. They ought to indicate to lay staff what bookings they wanted, and it was good if they could develop a "waiting-room consciousness." Marshalling the patients was work for porters, and for educated girls who must be taught that smiling and lack of shyness were part of their job; providing these girls with white coats helped this; and porters were more efficient if given good uniforms and ordered to polish their buttons. Documentation was humbler work, for less intelligent girls. Nurses must be kept for nursing duties. Periodical staff conferences with representatives of each of these three divisions and of the consultants and registrars helped to smooth out difficulties. It would be very valuable if these conferences could also be attended by a representative of the general practitioners who used the hospital.

From the general discussion several important points emerged. If more outpatients are to be seen, as modern conditions require, the consultant must accept responsibility for running his clinic. At the same time some of the patients, particularly some of the elderly, referred to the medical outpatient department do not really want to see a doctor, but benefit from attending a social club organised by the outpatient department; and this saves the consultant's time. Apparently not every clinic separates old from new cases, nor is it yet clear to all that a case may be urgent for economic as well as medical reasons. Organisation varies a good deal from hospital to hospital, and the best practices should be more widely known and imitated.

seen † Prior to the start of prophylaxis, beta hæmolytic streptococci should be eradicated by proper treatment of the patient (See methods of penicillin therapy recommended above)

How Long Should Prophylaxis be Continued ?

In children, at least to the age of eighteen , in all those above this age, for at least five years from their last attack

Should Prophylaxis be Continued During the Summer ?

Yes

PROPHYLACTIC METHODS

Sulphadiazine

This drug has the advantage of being easy to administer, inexpensive, and effective (other newer sulphonamides are probably equally effective) Although resistant streptococci have appeared during mass prophylaxis in the armed forces, this is rare in civilian populations.

Dosage —From 0 5 to 1 0 g taken each morning throughout the year The smaller dose is to be used in children under sixty pounds

Toxic reactions —These are infrequent and are usually minor However, in any patient being given prophylaxis with sulphonamides consider all rashes and sore throats as possible toxic reactions to the drug, especially if they occur in the first eight weeks of prophylaxis The chief toxic reactions are .

Skin eruptions

(*a*) Morbilliform, much like measles Continue drug with caution

(*b*) Urticarial Best discontinue treatment

(*c*) Scarlatiniform, often associated with sore throat and fever Unsafe to continue drug

Blood reactions .

Leucopenia Discontinue if white blood count falls below 4000 and polynuclear neutrophils below 35% because of possible agranulocytosis which is often associated with sore throat and a rash Because of these reactions, weekly white blood counts are advisable for the first two months of prophylaxis (The use of sulphonamides therapeutically for any reason in this period should be preceded by a white blood-count) The occurrence of agranulocytosis after eight weeks of continuous prophylaxis with sulphonamides is extremely rare

Penicillin

Although experience with oral penicillin for the prophylaxis of rheumatic fever is more limited than that with the sulphonamides, the antibiotic promises to be a safe and effective prophylactic agent Oral penicillin has the desirable characteristics of being bactericidal for hæmolytic streptococci and of rarely producing serious toxic reactions It has the disadvantages of being more costly than sulphadiazine and because of the need of giving it on an empty stomach, of being somewhat more difficult to administer Oral penicillin represents an alternative drug for rheumatic fever prophylaxis It is especially important to use this agent for those who do not tolerate sulphadiazine

Dosage —Although other routines of administration may prove satisfactory, the following schedules are suggested *200,000 to 250,000 units two times daily is recommended* Since penicillin is best absorbed on an empty stomach, the time of administration should be 1/2 to 1 hour before a meal or at bedtime A single dose of 200,000 to 250,000 units before breakfast is less preferable

Toxic reactions —(1) Urticaria (2) Reactions similar to serum sickness—they include fever and joint pains and may be mistaken for rheumatic fever (3) Angioneurotic œdema Although many individuals who have had reactions to penicillin can subsequently take the drug without trouble, it is safer not to use penicillin, if the reaction has been severe and particularly if angioneurotic œdema has occurred

TEACHING OF SOCIAL AND MEDICINE

THE Royal College of Physicians, through its and Preventive Medicine Committee, has been ing methods of teaching social and preventive me and comparing present conditions with those describ in the committee's first interim report of 1943[1] The progress report published last month observes that chairs of social or preventive medicine have now been created in almost every provincial university, thus going towards fulfilling the committee's earlier hope that every medical school would eventually have a department of social and preventive medicine

PROVINCIAL SCHOOLS

Turning first to the provincial medical schools, the committee found that almost everywhere the number of hours' teaching directly devoted to social medicine had been doubled , and in general the curriculum in social medicine is spread over the three clinical years Some departments are directed by a whole-time professor who has one or more active medical officers of health on his staff , others are directed by a medical officer of health as part-time professor or lecturer, with whole-time university lecturers carrying out most of the teaching programme There is remarkably little difference between the two arrangements, the report continues, and one way or the other "the programmes of the different provincial schools show an encouraging improvement," although "a detailed examination suggests that in some of them there are still serious gaps in teaching practice. The importance of occupational health and industrial medicine is generally accepted, but some schools are unable to give these subjects as much teaching time as they would wish Personal hygiene and environmental hygiene have a place in the undergraduate curriculum of every provincial school, but the amount of time devoted to them is relatively small The report commends the statistical departments which are appearing within, or in close association with, some departments of social medicine

> "Theoretical statistics is a subject often included in the social medicine curriculum, but more as a matter of convenience than on grounds of compelling logic As a rule, however there is no alternative provision for teaching this subject and in the absence of a separate Statistical Department the attachment of a Statistical Section to a Department of Social Medicine is usually a good working arrangement"

LONDON SCHOOLS

The arrangements in London are very different partly because the schools do not have to give postgraduate teaching in public health, which is provided by the London School of Hygiene and Tropical Medicine and by the Royal Institute of Public Health Apart from courses of formal lectures for undergraduates, the London schools aim to teach by integrating social aspects of illness with clinical subjects and pathology The report quotes the dean of one London school "Social medicine cannot and should not be taught to the undergraduate student as a special subject" It seems that the undergraduate schools in London are undertaking social medical research in the way that many of the provincial schools are doing The committee conclude "it appears that generally speaking the consolidation of social medicine as a subject in the curriculum in London lags behind the best provincial arrangements Epidemiology in the wide sense does not appear to be treated systematically at any point in many London schools"

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† In patients receiving A C T H or cortisone be cautious that other infections are not masked since the prophylactic dose is inadequate to treat such concurrent illnesses as pneumonia or meningitis

[1] See *Lancet* 1943, ii 546

THE LANCET

LONDON: SATURDAY, FEB. 7, 1953

Outpatients

LOOKING at the country as a whole, the state of tpatient departments is unsatisfactory both to tients and to doctors. The reasons are not hard to d. In the old days the care of inpatients had first iim on the limited resources of voluntary hospitals, d consequently the outpatient department was ten cramped and sometimes badly placed in some rt of the hospital, such as the basement, which uld not conveniently be used for other purposes. w of the municipal hospitals had developed any itpatient services at all, and the pressure thus rown on neighbouring voluntary hospitals was often ry heavy and quite out of proportion to their imber of beds. Before the war, many hospitals iver caught up with local expansions of population— the heyday of pre-war building, Middlesex county as expanding at the rate of 1000 people a week— id the failure to provide sufficiently for new demands the cause of some of our present difficulties. (Even iday, when we build new towns we do not build new ospitals to serve them.) Since the war many hospitals, pecially in Greater London, have been faced with a rowing demand for outpatient facilities, but have een severely restricted in any kind of new conruction. It is hardly surprising, therefore, that a eneral dissatisfaction with existing arrangements for utpatients should have been evident when these were iscussed at the Royal Society of Medicine's meeting hich we report on p. 275.

The functions fulfilled by an outpatient department re various and sometimes numerous. They provide he patient and his doctor with the opinion of a onsultant; they enable special diagnostic investiations to be made; they may accommodate services uch as eye-testing; they may include supervisory linics for patients with particular diseases such as næmia or diabetes, and for those whose progress ifter treatment, is being watched; and in some iospitals they are of course used for teaching. Their most important service to the community is probably the provision of a second opinion, which should be based on a careful history and thorough examination, with necessary investigations, followed by adequate discussion with the patient. Some would say that transmission of the results of the various investigations to the patient's doctor, and the application of a diagnostic label, are of less moment than the reassurance and help the patient will get from a proper consultation. But unfortunately, with excessive pressure on outpatient departments, the patient-consultant relationship is bound to become impersonal, and what is perhaps the most valuable function is not properly performed. In the eyes of the public, for whom the National Health Service has been organised, delay in securing an appointment is another grave defect. Before the war, outpatients often had to wait some hours before they were seen; but at least their initial attendance was not postponed for some weeks, as all too often happens under the system by which patients are given appointments for particular dates.

At the Royal Society of Medicine, Sir JAMES SPENCE laid stress on the need that outpatient departments should provide a true consultative service, and he laid down conditions under which this could be achieved. The patient, he said, should be properly introduced by letter or telephone; a specific appointment should be arranged; the history should be taken privately without a nurse in attendance; and at a teaching centre not more than two students should be present, and then only with the patient's consent. No teaching should be done in the presence of the patient, who should have the consultant's undivided attention. The consultant must not be content with making a diagnosis, but must explain and discuss the malady in terms that the patient clearly understands, carefully eradicating any misconceptions the patient may have formed. And finally a prompt report must be sent to the general practitioner. To some of Sir JAMES's hearers, who do their work in crowded outpatient departments where fifty or more patients attend in one session, some of these conditions must have seemed hopelessly unattainable. But even if the ideal consultation cannot be achieved at present, its acceptance in principle would be a sound basis for much-needed reorganisation in hospitals, and also perhaps a contribution towards improving conditions of general practice. Sir JAMES SPENCE believes that radical improvement in the outpatient departments of teaching hospitals is essential if we are to give medical students satisfactory standards. He thinks that the inadequacy of the consulting-rooms to be found in many practices is related to the inadequacy of the accommodation for outpatients at the hospitals where the practitioners were taught.

Even without new buildings many outpatient arrangements could be appreciably improved by careful reorganisation and attention to detail. In working appointment systems, which have been usefully studied by investigators of the Nuffield Provincial Hospitals Trust,[1] it is important to separate old and new patients, and the consultant should accept some responsibility for timing in his particular clinic. The number of appointments should be carefully related to the number of doctors working in the department, and unnecessary work should be eliminated by returning patients to their own doctor as soon as possible. (Many of the less senior members of hospital staffs probably have no idea how greatly many practitioners resent having patients removed by the hospital from their immediate care, when they have asked only for some diagnostic procedure.) The division of administrative responsibility between the hospital secretary, records officer, outpatient sister, and medical staff has often hindered necessary changes in routine, and, though the responsibility is essentially a medical one, the medical staff may properly organise a subcommittee, coöpting others who may be concerned. These should include a local practitioner, whose point of view may be invaluable, and who can speak from experience of, for example, the advantage of having reports written on notepaper that fits easily into the National Health Service envelope. The hospital secretary, if he takes a keen personal interest, can do much to promote the smooth running of out-

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[1] Welch, J. D., Bailey, N. T. J. *Lancet*, 1952, i, 1105.

DISCUSSION

The stage of pregnancy at which pulmonary tuberculosis is first diagnosed materially affects the prognosis, and McIntyre and Armstrong (1948) have shown the high mortality among patients first found to have active pulmonary lesions in late pregnancy and in the puerperium Clearly, a higher proportion can be diagnosed by radiology than by clinical examination alone The medical officer of health for Glasgow (1949) reports that tuberculosis is the commonest cause of death in Glasgow children under the age of 5, and now that B C G inoculation is becoming more widely used, the importance of detecting all cases of tuberculosis is greater than ever

Routine Wassermann tests are performed in all antenatal clinics, and Eisele et al (1942) found a positive W R in 0 87% of the women in their complete series This figure is much the same as the proportion of tuberculous chests discovered by X-ray examination, which varies between 1 2% and 3 0%, with active lesions present in 0 6 to 1 1% It must be remembered that *in the present series of 29 cases, tuberculosis had been* diagnosed before pregnancy in only 1 case

Few antenatal clinics undertake routine X-ray examination of the chest The disadvantage of the straight X-ray film is the expense, each film costs approximately 6*s*, and with a discovery rate of about 2 5% the cost per positive film would be £6, which is out of the question at the moment Moreover, the present shortage of X-ray film makes this form of investigation impossible in this country.

Alternative methods of diagnosis are tuberculin testing, screening, and mass or miniature radiography Tuberculin testing seems cumbersome and involves several visits for the patients In the series described by Ianne and Muir (1939) 14% of the women failed to return for the reaction to be read, and 11% of the reactors did not return for radiography Moreover, since 41–47% were positive and required X-ray examination, the total expense is little less than that of a survey using X-ray films from the start

Screening was used by both Eisele et al and Jacobs (1946), and both seem to have found it satisfactory Films were taken for permanent record in positive and suspicious cases Israel and Hetherington (1941) stated that the accuracy of diagnosis by fluoroscopy was as high as 96–99%

Eisele et al said that mass radiography probably sacrificed accuracy to a point where it was equal to or below that of fluoroscopy However, the method is being used for antenatal patients in some areas, and further reports would be valuable Miniature radiography is also reported to be relatively cheap and accurate

Screening or mass or miniature radiography seem feasible methods Certainly, the claims of the antenatal patient must be considered in allocating our limited radiological facilities The welfare of mother and child may ultimately rest on the antenatal chest examination of the mother, and, since a high proportion of tuberculous lesions escape detection by any other means, routine X ray examination of all antenatal patients is the ideal at which to aim

SUMMARY

Routine X-ray examination of the chest in 541 unselected antenatal patients showed evidence of tuberculosis in 29 cases (5 3%), and in 4 (0 74%) of these patients the disease was definitely active Another 8 patients had inactive disease, but after confinement 2 of them showed definite activity and 2 possible activity Of the remainder, 4 patients had healed fibrotic lesions and 12 had calcified pulmonary lesions In only 1 of these cases was tuberculosis known to be present before the radiological examination

A high proportion (94%) of the women who were asked to attend for X-ray examination did so

The early diagnosis of tuberculosis is particularly vital in pregnancy, and disease discovered in late pregnancy and in the puerperium has a relatively high mortality One of the various radiological methods of diagnosing pulmonary tuberculosis should be used as a routine antenatal measure

I wish to thank Dr Hugh Stirling, obstetrician in charge, for his advice, and Dr J Z Walker, director of radiology, and his staff for their help

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Deaths during the Fog

More details about the effects of the thick fog which covered many parts of the country from Dec 5 to 9 are given by Dr J A Scott, medical officer of health to the London County Council, in a report to the council's public-health committee In the week ended Dec 13, 1952, 2484 deaths were registered in the administrative county of London, the figures for the preceding three weeks were 753, 853, and 945, and for the following three weeks 1523, 1029, and 1372 (the apparent drop to 1029 was due to the usual delay in registration at Christmas Dr Scott compares the number of deaths in the week of the fog with the figures for other weeks during the cholera epidemic of 1866, the great fog of 1873, and the influenza epidemic of 1918

Week ending	*Aug 4, 1866 (cholera)*	*Dec 20, 1873 (fog)*	*Nov 9, 1918 (influenza)*	*Dec 1 19*
Deaths registered (per million population)	876	713	1085	713
Normal number of deaths for period and season (per million population)	150	470	300	30
Excess of deaths over normal	126	213	785	443

Though the death-rates in the two fogs were much the same, the increase in 1952 was considerably greater because of the fall in the normal winter death-rate since 1873 The increase is greater than that in the worst week of the cholera epidemic

An analysis of all the deaths registered in the County of London between Nov 15 and Dec 27 shows that the increase was more pronounced among babies and old people, but all ages were affected The causes of the increase were almost entirely deaths due to circulatory or respiratory diseases in the week ended Dec 13 there were 10 times as many deaths from bronchitis as would have been expected from the preceding three weeks' figures, and on this basis deaths from influenza increased sevenfold, from pneumonia nearly fivefold, and from pulmonary tuberculosis over fourfold

DAILY ATMOSPHERIC SMOKE AND SULPHUR DIOXIDE AVERAGES AT COUNTY HALL LONDON S E 1

Day	Smoke (mg per c m)	Sulphur dioxide (parts per million by volume)
Dec 3	0 61	0 220
4	0 49	0 111
5	2 64	0 751
6	1 15	0 855
7	1 46	1 339
8	1 46	1 339
9	1 22	0 472
10	1 22	0 472
11	0 32	0 221

Smoke is expressed as mg of black suspended matter per cubic metre of air The figures for Dec 7 and 8 and Dec 9 and 10 are averages for the 48 hours stly method and the drug has to be given on an mpty stomach. Serious toxic reactions, however, e rare. Until lately parenteral penicillin has not een thought feasible for such long periods of rophylaxis, but the recent introduction of a particu-rly long-acting preparation (N,N′-dibenzylethylene-amine dipenicillin G) brings penicillin prophylaxis ithin the bounds of practicability. This drug enzethacil or 'Bicillin') has no significant toxicity, nd has the advantage of being very sparingly soluble ts solubility in water is equivalent to about 200 units f penicillin per ml.). FLETCHER and KNAPPETT[5] ave now investigated the use of this compound, and TOLLERMAN and RUSOFF[6] in New York have eported a trial of its use as a prophylactic in heumatic children in hospital. Both investigations how that it is possible to maintain low serum levels f penicillin continuously in an encouragingly high roportion of individuals by means of simple intramuscular doses spaced at intervals of as long as a ortnight. The serum levels attained are variable, nd may be very low or even intermittent. It is ossible that this might favour both the emergence f resistant strains and the development of drug ypersensitivity; but neither of these troubles has o far proved to be a serious complication. In the American trial, the value of the drug as a prophylactic against rheumatic recurrences was not established, or although none occurred, there was only one recurrence in untreated patients in the same hospital during the period of the trial. Further experience is therefore required to estimate its value in prophylaxis. But it might be hard to justify a trial of this kind in Great Britain, where it is widely believed that recurrences of rheumatic fever are quite uncommon—an opinion that cannot be challenged without extensive follow-up data. At all events, it is well to remember, in the light of the American Heart Association's statement, that there are gaps in our knowledge of the natural history of rheumatic fever in this country.

Law and Public Feeling

LAWS are at best rules of thumb, designed to do, under average conditions, the "greatest good to the greatest number." There will always be some criminal cases where the outcome leaves the public conscience uneasy. Is it logical to hold an adolescent fully responsible for his actions at 18 but not at 17? Naturally not. Many factors influence his stage of maturity, including his genetic endowment, his endocrine development, his education and training, his emotional experiences, and his own choices. Yet the law must rule a line somewhere, and declare that roughly speaking most people are responsible for what they do at and after such and such an age; and until we encounter a case such as that of Bentley and Craig we are prepared to accept that this should be so. When the margin is narrowed, however—when a young man of 19 is sentenced to death for inciting another, in a moment of violent excitement, to shoot—we are obliged to ask ourselves whether in holding to the letter of justice we are letting the spirit escape. The issue of the *Times* which announced the execution of Bentley also carried a report of two boys at Trowbridge who have been stealing from safes and churches, who have used stolen money to buy firearms, knives, and a tent, and who resisted arrest, striking the police officer in the face and abdomen. Their ages are 16 and 14, and they have been sent for three years to an approved school, where they will have a 3 to 1 or 4 to 1 chance of reform. The discrepancy between their punishment and that of Bentley (whose offence was of the same order though of greater degree) seems startlingly wide. Against these considerations we have to set another: we are properly proud that our police do not ordinarily carry firearms, and if we ask them to face the risks this entails we must stand by them fully when such arms are used against them. It is generally held that the only way to do this is to deal severely with anyone who attacks them, and that in such cases the prerogative of mercy should not be exercised. According to law and practice, therefore, Bentley was justly hanged. If we think that nevertheless justice was not done, then we do not like the law or the practice. There is an 18th-century record of a boy of 11 who was justly hanged for a small theft. We have since found that law both intolerable and unnecessary.

These perhaps are not directly medical concerns; but the psychological atmosphere evoked by the recent execution certainly is. What are the motives which bring five hundred people to the gates of a prison where a man is being hanged? What lies behind the public emotion which this case has excited? Does such an experience do people good or harm? Answers to these questions must be largely guesswork, but there are some small pieces of evidence on which to base a guess. The *Manchester Guardian* correspondent who watched the scene at Wandsworth saw, among those present, members of an association formed for the abolition of capital punishment, who sang a hymn and a psalm; a woman who had lived in the same street as Bentley; a man who had attended the last fifteen such occasions, who said "Nice fresh June morning and a little more sun, that's what you want really"; and four people who had taken a taxi from Birmingham in order to be there. Thus this relatively small crowd contained representatives of the types who used to flock to public hangings and burnings: those who used the event to protest against the law as it stood, and who tried to bring the condemned man some message of religion; those who derived a *frisson* from a macabre occasion; those whose idle curiosity was not bridled by any sense of embarrassment; and no doubt others who came to see what it was like, or because a friend had brought them, or because they thought it could not really happen, or because they were passing at the time and saw the crowd, or because they thought we had grown a lot too soft with criminals and things needed tightening up. None of these motives—except the first and the last, which can be defended by argument at an intellectual level—deserves respect; and it was because the country as a whole did not respect them that public executions were given up. Nevertheless it is clear that the same motives still operate, and would doubtless be manifest on a much larger scale if sanctioned and encouraged by public opinion. Restitution of public executions would suffice to restore the audiences.

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5. Fletcher, A. P., Knappett, C. R. *Brit. med. J.* Jan. 24, 1953, p. 188.
6. Stollerman, G. H., Rusoff, J. H. *J. Amer. med. Ass.* 1952, 150, 1571.

exercised undue influence, they should not let the fact that he was a doctor weigh with them but should come out boldly and find him guilty of the coercion Medical practitioners may wonder how long it has been since juries have shown themselves especially tender towards doctors The plaintiff in the recent litigation is to be congratulated on the jury's view of his conduct As, however, the court ordered all costs to be paid out of the estate, and as the trial had occupied six learned counsel for nine days, it may be that the deceased's estate of some £22,000 will suffer serious erosion

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Occasional Survey

URTICARIA

SCIENTIFIC terms, like currency, are subject to "inflationary trends" overusage may debase a respectable term until it is almost meaningless Moreover, the circulation of pseudoscientific counterfeits throws suspicion even on the original legal tender, so that those who wish to speak and write precisely shrink from using such terms This fate has befallen "allergy," a word introduced in 1906 by von Pirquet [1] Its meaning should be confined to specific and acquired changes in the capacity of the body to react after exposure to living or inanimate agents But it has come to be used often for non-specific changes in the intensity of this reaction, or as if it were synonymous with hypersensitivity Allergy includes diminished or absent reactions as well as excessive ones, it is the opposite, not of "hypoergy," but of "normergy" Allergy is essentially an immunological process, and may affect the whole organism or only a part—for example, the skin in urticaria

THE MECHANISM OF URTICARIA

But urticaria, the skin's defence against threats to its vascular endothelium, is not necessarily an allergic manifestation The sting of a nettle contains histamine and acetylcholine [2] and so invariably causes wealing But this is not allergy, nor is bronchospasm caused by a gaseous or particulate irritant, nor the sneezing and nasal congestion induced by pepper These are normal, temporary, localised, and protective reactions by the organism to a particular threat Acetylcholine, codeine, morphine, and atropine have a histamine like action and also release histamine, so that urticaria caused by these drugs is at most only partly allergic [3]

In some people a drug or food may cause urticaria, usually acute or subacute, possibly recurrent, and related to antigen antibody reactions and the release of histamine Heat, light, cold, and mechanical stimuli may cause lesions indistinguishable from those produced by antigen-antibody reactions, and it is probable that these forms are brought about by a chemical agent, possibly acetylcholine In particular, urticaria caused by heat, exercise, or emotion has been linked, by Grant et al [4] and by Hopkins,[5] with acetylcholine, probably released by the parasympathetic system

In chronic or recurrent urticaria the most careful search usually fails to reveal an antigenic cause The severe subcutaneous variety known as "giant urticaria" is, as the name "angioneurotic œdema" implies, traditionally regarded as a neurotic condition The importance of emotional changes in the production of urticaria was emphasised by Stokes et al,[6] who thought that such disturbances were solely responsible for 12% of urticaria in their series, and partly responsible for 83% Various terms, such as "psycho-allergy," "allergy to life," and "emotional anaphylaxis" have been coined for these phenomena If there is a specific alteration in the reaction of these patients, it is not an immunological response to a specific antigen but rather a regression to an habitual morbid emotional pattern of feeling towards persons or events Roessle [7] suggested the term "pathergy" to cover a non-specific broadening of the basis of reaction These forms of urticaria are not related to the allergic varieties unless the colloquial meaning of allergy is accepted, and unless resentment at the protein of another human is taken as a manifestation of allergy Urticaria caused by such an emotion is "pathergic", and a wider use of this term might disperse a lot of the fog which obscures the meaning of the word allergy If there is such a thing as an urticarial personality it is not immediately obvious, for the wealing is linked with morbid fantasies not readily discovered by direct questioning, but only revealed by the spontaneous and unprompted choice of expression made by the patient in describing significant events

The regional defence mechanisms of lining membranes and the skin are, in the normal (normergic) individual, temporary emergency measures to deal with powerful irritants The pathergic individual uses them to deal with relatively trivial stimuli and for more persistent long-term needs He has acquired the habit of reacting to danger passively and in the same way as to regional assault Love, anger, or fear, if frustrated, are converted to longing, hate, and passivity, and the regional type of reaction is sustained This autonomic cholinergic form of urticaria is engendered from the archipallium, whereas the antigenic histamine form arises in the skin itself Feelings of helpless and passive resentment, often with masochistic fantasies, seem to be directly related to the outbreaks The retreat into fantasy is a feeble substitute for an advance into action or words Subsequent events which recall the earlier emotion laden situation may cause relapses The acetylcholine released acts on the arterioles whereas histamine acts on the capillaries, possibly explaining the larger subcutaneous lesions of giant urticaria

Graham and Wolf [8] say that a dilated capillary is, ipso facto, a more permeable one, and they produce evidence to show that arteriolar dilatation alone, without the intervention of histamine, may cause urticaria Trauma, even the pressure of clothing, may then by histamine release further lower the threshold of wealing and so localise the eruption to certain areas Graham and Wolf describe a correlation between the discussion of emotional episodes and outbreaks of urticaria Intense resentment about events to which the individual felt, for one reason or another, incapable of reacting in a positive way was the common starting point

Sometimes an urticaria apparently caused by an antigenic food or drug is in fact precipitated by a mental association with some emotional event which coincided with the first time the food or drug was taken In these circumstances, the food or drug is a specific mental, but not antigenic, precipitant

Fatigue also contributes to the production of urticaria, for it lowers the threshold of wealing Overwork, infection, or malnutrition may be significant, but it is the tiring effects of unsettled emotional conflicts that may particularly disturb autonomic function and increase the sensitivity of the individual's reactions to antigens and events alike, so that hyperergy, the commonest form of allergy, results Adrenaline depletion and failure to remove histamine may well be part of the mechanism by which this allergy develops Rose and fertile eggs. They found that similar recombinants ıld be recovered from chick brains after inoculation MEL and NWS on to the chlorio-allantois. In addition, idence was produced that recombinants resulted from uble infection of cells with these viruses under conions where simple mutation of MEL was most unlikely. Burnet et al. next turned their attention to the luenza strains MEL and WSE, which they could disıguish from one another by six different characters. ıe two viruses were grown together in eggs under nditions where recombination might be expected to cur, and the progeny were examined for the six differtial properties. Out of a litter of 41 viruses, 22 were actly like the parent MEL and 4 like the parent WSE. ıe remaining 15 showed a remarkable reciprocal terchange of properties. Only two of the six properties anged over and they were transferred together, so at only two types of recombinant were found. This sult excludes a random reassortment of characters as explanation of the recombination: it suggests rather at in a casual encounter in the same cell the two ruses may have exchanged some superficial characterics only. It is clear from this work that the cell wall no longer an impenetrable curtain which can protect e virus from the biologist's inquisitive gaze.

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MEDICINE IN UGANDA

A WEEK or two ago we commented on the dryness the report of the Sudan Medical Services.[1] Further the Nile ink seems to flow more freely; the report r 1951 of the Medical Department of Uganda[2] is much more lively account. This report not only gives good summary of the work accomplished, but sets out language easily intelligible to the layman the problems efore doctors in the protectorate and their relation to cial and economic conditions.

Although demands for more curative services continue nabated, some African communities are beginning to ppreciate the importance of prevention and are asking r additional health workers. Local authorities are howing an increasing interest in the control of endemic iseases, especially leprosy, yaws, and bilharziasis. t present in Uganda about 3s. per head is spent on he health services each year, whereas the corresponding igure in Great Britain is £8. More money is needed o pay for new services, but these services will also eed men and women suitably trained to run them; many African candidates for training as nurses, midwives, and medical assistants lack a proper vocational outlook. The majority of the diseases which give rise o the heavy demands for increased curative resources are due to defective nutrition, defective housing and sanitation, inadequate water-supplies, and dangerous personal habits. The treatment of many complaints can only be palliative with heavy recurrent costs and with little effect on the patients' disabilities or on the loss of man-power. Some African local authorities tend to equate medicine only with penicillin and similar powerful drugs; yet it should be possible without very heavy expenditure to reduce the prevalence of some of the more disabling diseases: how healthy Uganda can be is shown by the fact that in 1951 not one of the 21 deaths in the European population of about 5600 was attributable to a tropical disease.

Discussing venereal diseases, the report says that "most of the treatment given for syphilis is largely a waste of drugs," since few patients (in one district less than 1%) who start treatment completed the minimum course of injections. Further "schemes of venereal disease treatment having the avowed object of making it easy for the sufferer to get rapid relief, with no concomitant attempts to discourage promiscuity or encourage family life, are of little value to the community." Kwashiorkor is, of course, widespread in Uganda, and much of our knowledge of this disease comes from the Mulago Hospital. A real attempt is being made to tackle problems of maternal ignorances which contribute much to its ætiology. Health education is "centred around the women, aiming at the encouragement of domestic hygiene, clean food, good dietary balance and the mother's pride in and love for her child. Most of this teaching has to be given at rural welfare centres, as health visiting is made difficult by the extent to which the population is scattered. A qualified health visitor is at work in a rural area in Buganda."

The medical staff are to be congratulated on a most readable report which can be commended to any young person who is embarking on a career either in government service or in business in Uganda. A map and a few photographs would help readers unfamiliar with the country.

REACTIONS AFTER EXCRETION UROGRAPHY

SIDE-REACTIONS to the injection media used for excretion urography are well known in all X-ray departments; they are usually mild and transient. Inman[1] has lately tried to classify these reactions in relation to the media normally used. Two drugs are in common use: diodone *B.P.* ('Pyelosil,' 'Perabrodil,' 'Uriodone,' 'Pylumbrin') and iodoxyl *B.P.* ('Pyelectan,' 'Uropac,' 'Uroselectan B,' 'Urumbrin'). Diodone is supplied as a 35% or 50% *w/v* solution and has a pH of 7 to 8; and iodoxyl is a 75% *w/v* solution with a pH of 8·5. For adults the dose of each is 20 ml. Diodone has the outstanding advantage that it can be administered subcutaneously or intramuscularly, if a suitable vein is not available. The solution is usually diluted with sterile water to 15% and administered with hyaluronidase to speed absorption. The iodoxyl compounds, on the other hand, cause tissue necrosis and cannot be given in this way.

From his observations of over 600 patients investigated by intravenous pyelography, Inman finds that the side-reactions fall into two main groups: *general reactions* (vomiting, flushing, and unusual sensations of heat and taste) and *local reactions* (pain at the site of injection or up the arm owing to venospasm, tissue necrosis, and local venous thrombosis). Local reactions were much commoner with iodoxyl. Venospasm occurred in 39% of the 189 patients who were given iodoxyl, but in only 1% of the 286 who had diodone. Inman points out the importance of venospasm and its possible relation to subsequent venous thrombosis: Kemp[2] reported a significant number of cases of venous thrombosis in patients seen 10–14 days after intravenous pyelography. But venous thrombosis is not necessarily confined to patients who show venospasm.

General reactions were equally prevalent with diodone and iodoxyl, suggesting that they have a common cause not directly related to the pharmacological properties of these two drugs. In a group of 12 patients given diodone, Inman demonstrated that the skin-temperature of the forehead rose by 0·8°–2·2°C, and returned to normal after 30–45 minutes. Evidence of mild idiosyncrasy to diodone was found in 1% of the patients: there was puffiness of the eyes and an urticarial or papular skin rash, which were easily controlled by adrenaline. Simultaneous administration of atropine or diphenhydramine ('Benadryl') helped to reduce the number of general reactions—probably, Inman believes, by diminishing vagal stimulation.

Inman suggests that for routine use diodone is the better drug, except in patients with a history of allergy, when iodoxyl is advisable. His conclusions are supported by Mullen and Hughes,[3] who point out that a reaction downstairs—i e, *further south—but it isn't* So I have to remember that whereas Capetown is south of Durban on the map, the ward named Capetown is above—i e, further north—than the ward named Durban

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[1] *Lancet*, Jan. 24, 1953, p. 200.

[2] Annual Report of the Medical Department of Uganda Protectorate for 1951. Entebbe, 1952. Pp. 84. 3s.

[1] Inman, G. K. E. *Brit. J. Radiol.* 1952, 25, 625.

[2] Kemp, F. H. *Ibid*, 1940, 13, 291.

[3] Mullen, W. H., Hughes, C. R. *Amer. J. Roentgenol.* 1952, 68, 903.

The new *labels may* be *easy* for the young men, or for those with a more elastic geographical outlook, but we older ones find them confusing Ward labellers might take heed of the way streets in New York are named—e g, West 42nd Street There the name gives some clue as to where the street is, but with us the ward's name gives no clue to its location

All the same there may be advantages in calling a room by a *name* I remember a *retired* physician who labelled his room and workshop "Liverpool" so that his housekeeper could truthfully say, when he did not want to be *disturbed*, "I'm sorry, but he has gone up to Liverpool"

* * *

The silence of the night was broken by the creaking of boards in the hotel corridor Someone was stealthily making for my room, and I did what anyone would do in like circumstances—hid my head under the bed-clothes A gentle tap on the door reassured me Pulling myself *together*, I *called out* "*What is it?*" A *female voice* replied "It's a heifer"

After a suitable pause to allow this strange communication to register, the voice continued "Joe would like you to look at her" Joe, the farm bailiff, is an old friend of mine, and I agreed to go After all, I thought, there's no harm in having a look

Joe Sorry to get yer airt, Doc, but there's summat up with yon

Self It's all right, Joe Where is she?

Joe Dairn t'lane

We went down the lane in pitch darkness, without a torch I was on holiday, of course, without the tools *of my trade*, *all I had was head, hands, and general* principles Inspection, palpation, percussion, auscultation—I could manage so much, at least As it happened, the last came first, for I soon heard a sound like the dialling tone, a curious blend of menace and misery, which enabled me to locate the patient Since it was too dark to see anything, I cautiously palpated an unidentifiable part of the beast between its head and its tail Whatever it was, it felt doughy, and light pressure produced a sound like the crackling of thorns under a pot How I wished someone had written an article on "Doughiness and crackling in heifers"! Instinct told me that the signs boded no good, and I ventured my opinion

Self You're right, Joe, there's summat up

Joe Ay, doc, ah were sure there were, and if yer ask me she's 'ad it, and she won't last till morning

Self That's it, Joe, she's had it I suppose heifers are much more lively than this when they're well?

Joe Oh ay, quite different than this

Self That's what I thought This one's very ill, and I *don't think she'll last long* *Can we do anything for her?*

Joe *Oh no, not at this time o'night* Thanks ever so much for coming There's nowt like a second opinion

No, I thought, there isn't, and if my diagnosis was rather indefinite, it was no worse than many another, and my prognosis at any rate was right

* * *

The last patient of a busy surgery on a cold, wet, evening was a rather dirty, rhinorrhœic boy of 8, who had clearly been too timid to take his proper turn in the queue Without a word he handed me a scrap of paper, which read

"Doctor—Do you give Horlicks on the National Health? I was run down recently and bought a bottle but I have now finished it, and it did me good *If it is allowed will you please* give a prescription

Yours truly,

Mrs ———

P S—This boy needs his finger lancing"

The dramatic simplicity of the last line contained an accurate diagnosis, so I was able to ensure that at least one member of that family slept more soundly that night

Letters to the Editor

"UNFIT FOR MILITARY SERVICE"

SIR,—I am concerned *at the apparent* increase certificates lightly given by medical practitioners, general and specialist, stating that a patient is to do his National Service It is not the numerical increase that worries me so much as the unthinking *often unfortunate way in which these certificates* given, so that considerable harm is done on all *I am able to see both sides of this* because I hold civilian appointment and, quite separately, an advisory one to one of the Services

The harm is first done to the patient, who forms view that either he or Service life is unhealthy, usually quite absurd, and in fact Service life is often saving of a nervous and coddled young man

Secondly harm is done to the parents, who probably have visited the doctor and often paid a fee with purpose of acquiring such a certificate, and who develop a paranoid outlook to life in general and Service in particular when their son is asked to after all

Thirdly, harm is *done* to the Service, because situation often leads to a Ministerial inquiry and question in the House of Commons, and the whole may become political, with the added suggestion Service doctors are poor clinicians In fact clinical ability in Service doctors has probably never higher in peace-time than it is *now*

It is of course most valuable to have a balanced experienced opinion on a National Serviceman from own doctor or a competent specialist I have noticed that those doctors who have known something of Service life themselves never give the *type* of certificate about which I am concerned

My particular interest brings me into contact certificates about "blackouts" and headaches Nothing is more helpful than a good description by an unbiased observer of an attack of unconsciousness, and nothing more harmful than the last certificate I read which stated "I have examined X Y Z who is suffering from neurocirculatory asthenia and is quite unfit for form of military service" The signature was grand in its self-description, and in fact the boy was suffering from mild attacks of migraine which had not interfered with his earning capacity (£14 a week)

My plea is for more care and thought in the giving these certificates, particularly in cases of vasomo syncope, which is often due to muscular flabbiness for which the physical training of Service life is one the best forms of treatment

London, W 1

A BARHAM CARTER

CHILD-WELFARE CLINICS

SIR,—Most general practitioners will agree with conclusions in the article by Dr George and his collaborators (Jan 10), but the suggestion that few of them at present equipped *to do* child-welfare work is what surprising Since they deal every day with very conditions which are seen once a week at the and have the added advantage of knowing the family and how it lives, they can hardly fail to have experience

Some already hold afternoon sessions for infants children because so many mothers prefer their doctor's opinion to the clinic medical *officer's* advice in many cases is the same, but it is trusted when given by the well known general practitioner than by the seldom-seen clinic doctor

An increased capitation fee, or indeed any incentive, would encourage *more to do the same* Whether they work in their own surgeries or in the local authority premises is immaterial, and would depend on the opposite direction; and until more evidence is railable it does not seem necessary to urge compulsory E.G. examination of all professional boxers in this untry.

AMYLOIDOSIS

In classical amyloidosis of parenchymatous organs, nyloid is deposited in the skin to a degree which is rely more than microscopical. In the form known as typical or primary systematised amyloidosis, however, ere is striking clinical involvement of the skin or ucous membranes in about half the cases. Naturally ese patients are seen by dermatologists and attract ttention in dermatological circles; but the importance f the syndrome to general physicians has been lately own by Goltz.[1]

Primary systematised amyloidosis differs from classical lardaceous" disease in several respects. It is not sually associated with chronic suppurative disease. The myloid deposits are mainly in and around blood-vessels n connective tissue and muscle, sparing the parenchyma f liver, spleen, and kidneys. Microscopically the amyloid akes up the usual stains, such as methyl violet or congo ed, only with difficulty, and special techniques may be equired to demonstrate it. The skin of the face, neck, xillæ, hands, and perineum shows a variety of changes. t may be studded with papules, which are so discrete nd translucent that they resemble blisters. The infiltration may be diffuse, giving the skin a sclerodermatous or myxœdematous appearance. The resemblance to hypothyroidism may be enhanced by pallor and loss of hair. Hæmorrhages occur into papules or into skin which is clinically normal. Macroglossia is often striking and, together with xerostomia resulting from involvement of the salivary glands, may seriously interfere with chewing and swallowing. The surface of the tongue may be smooth or crowded with pseudovesicles. Involvement of the larynx may cause hoarseness.

The patient's initial complaint may be of breathlessness due to amyloidosis of the heart muscle or valves. Indeed, death in this condition is often the result of cardiac failure. Voluntary muscle may be infiltrated, causing weakness and severe pain, and where the gut is involved there may be constipation, diarrhœa, or even fatal hæmorrhage. Some cases show Bence-Jones proteinuria and non-invasive plasmocytosis of the bone-marrow. This finding is of particular interest, for true multiple myelomatosis may be associated with amyloidosis which may assume the "primary" type of distribution. Wells [2] described a case of primary systematised amyloidosis showing benign plasmocytosis of the marrow. There was no Bence-Jones protein in the urine, but an abnormal beta globulin was detected in the serum. He regarded the marrow changes as reactive—i.e., the result of the disease-producing mechanism—rather than causative. Nevertheless, he treated his patient with urethane, but without benefit.

Some people regard amyloidosis in general as a disease of disordered immunity. Classical amyloid disease develops in association with chronic infection, such as tuberculosis or syphilis; and it also occurs in animals used for the production of antisera. The young doctor who died of primary systematised amyloidosis [3] was sure that he was hypersensitive to milk, and he said he was better when he stopped taking milk and milk products. Another patient was strongly sensitive to egg.[4] Some people believe that the plasma cell is the site of antibody production, and plasmocytosis of the marrow has been shown to coincide with maximum antibody production in hyperimmunised rabbits. This plasmocytosis associated with the appearance of abnormal serum globulins was reported in two cases of sulphonamide sensitivity.[5] The subject is further complicated by the occurrence of localised forms of amyloidosis—for instance, in the heart or skin. Freudenthal [6] described amyloid in a variety of distinctive skin lesions, including epithelioma and nævi. He also gave the name lichen amyloidosus to a condition resembling at times lichen planus; this condition lacks the distinctive pathological lesions of lichen planus, but heavy amyloid infiltration is one of its features. It produces intractable irritation, which is not a symptom of primary systematised amyloidosis.

It may be that we are caught in the terminological trap referred to by Trotter [7] in a discussion of skin myxœdema. The latter term is used in the sense of a generalised disease—i.e., hypothyroidism—or to mean a tissue change detected microscopically. In "amyloidosis" we are comparing a variety of conditions, some generalised and fatal, others purely local, in which the only common factor is a similar tinctorial quality. It seems certain that there are several "amyloids," differing in physical state and probably in chemical composition. Further chemical and cytochemical work is required to enable us to identify comparable states of amyloidosis.

AGE AND SKIN STRUCTURE

The skin of elderly people is characteristically wrinkled and thin, especially in exposed sites, and shows an obvious loss of elasticity. Histological stains nevertheless reveal an apparent increase in the elastic-staining tissue from these sites, although both conventional histology and electron microscopy [8, 9] agree that the chief component of normal human dermis is collagen. Much work with the electron microscope has centred on connective tissue, with the structure and genesis of collagen as its focus.[10] Tunbridge and his colleagues,[11] at Leeds, have now used electron microscopy to investigate the more general fibrous structure of normal human skin, and particularly the changes in elasticity accompanying ageing and certain inherited skin abnormalities. They found only small numbers of elastic fibres in normal skin, and they attribute its "elasticity" to the flexibility of the network structure of the collagen fibres. As others have reported, these fibres are long, banded, straight or smoothly curved fibrils of uniform width, and they are associated with a small amount of fluffy amorphous material which can be removed by trypsin treatment. This is probably the interfibrillar cementing material or ground substance.

Senile skin from exposed sites gives a different picture. There is a considerable increase in amorphous material but not in elastic fibres. The collagen fibres themselves are often short, kinked, and frayed. Treatment with trypsin removes not only the amorphous material, but also the misshapen collagen fibrils and the material responsible for the increased elastic staining, so that only normal collagen fibrils remain. It was also found that normal skin takes up more elastic stain after treatment with pepsin, which attacks collagen. From these results, it is reasonably concluded that in senile skin there is no increase in elastic tissue, but rather a degeneration of some of the collagen fibrils, whereby they acquire a capacity for taking up elastic stain and a susceptibility to the action of trypsin. The puzzling feature is that these changes seem to develop only in skin taken from exposed areas of the body. A similar change was found in pseudoxanthoma elasticum—a rare disease whose manifestations include a general looseness of the skin, a tendency for striæ to form, and

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1. Goltz, R. W. *Medicine, Baltimore*, 1952, 31, 381.
2. Wells, G. C. *Brit. J. Derm.* 1952, 64, 169.
3. Baker, G. P., de Navasquez, S., Maclean, K. S. *Guy's Hosp. Rep.* 1949, 98, 95.
4. Lindsay, S. *Amer. Heart J.* 1946, 32, 419.
5. Robertson, T. *Amer. J. Med.* 1950, 9, 315.
6. Freudenthal, W. *Arch. Derm. Syph. Berlin*, 1930, 162, 40.
7. Trotter, W. R. *Proc. R. Soc. Med.* 1947, 40, 703.
8. Gross, J., Schmitt, F. O. *J. exp. Med.* 1948, 88, 555.
9. Schmitt, F. O., Hall, C. E., Jakus, M. A. *J. cell. comp. Physiol.* 1942, 20, 11.
10. See *Lancet*, 1952, ii, 774.
11. Tunbridge, R. E., Tattersall, R. N., Hall, D. A., Astbury, W. T., Reed, R. *Clin. Sci.* 1952, 11, 315.

that the effective number of skin antigens may well turn out to be reducible by means of special drugs It can only be advantageous to know in advance the possible implications of research into the use of such drugs

London, N W 2 I J GOOD

PRACTICAL PENICILLIN

SIR,—In 1947 when in general practice, I treated patients suffering from boils and carbuncles with systemic penicillin[1] At that time I used the oil-wax suspension (1,250,000 units in 10 ml) I gave a single dose of 10 ml I treated patients with otitis media, both in the acute and chronic phases, with the same oil-wax suspension, but I gave them the 1,250,000 units in four daily doses of about 300,000 units each[2]

My treatment differed from that described by Mr Cohen (Jan 24) in that, apart from the application of a piece of gauze or lint on any discharging area, there was no local treatment

For over a year now I have been in the habit, if the patient did not respond to penicillin injections within thirty-six hours, of giving aureomycin, which I found to be far the most effective antibiotic in staphylococcal infections Aureomycin has the added attraction that it can be taken by mouth

During the last twelve months I have not resorted to incision at all In 2 cases, however, when the induration had subsided I was able to aspirate the pus

Enfield I GOTTLIEB

THE MEDICAL SERVICES IN THE KOREAN WAR

SIR,—Dr Binning (Jan 24) has expressed anxiety that whole blood was not available for Commonwealth medical units It would indeed be strange if such were the case, but let me assure him that whole blood is supplied by the United States Medical Services to all United Nations medical units

The point which I am sure the writer of your article wished to make was that American policy was to give whole blood rather than plasma to types of cases in which we prefer to give plasma

Osborne House East Cowes
Isle of Wight N CANTLIE

ŒSOPHAGEAL CONTRACTION AND CARDIAC PAIN

SIR —In your issue of Dec 6 Dr William Evans presents an impressive series of fluoroscopic observations on the motility of the œsophagus and its possible relation to "cardiac-like" pain Although in a certain number of the patients described the pain may be related to œsophageal dysfunction, the pathological significance of some of the observed phenomena must be questioned

The "œsophageal arrhythmia" discussed by Dr Evans sounds very much like "tertiary contractions" which Templeton and others have described in many people, especially in the older age-groups, with a normal œsophagus In their extreme form these contractions have been called "curling" and appear not to have any pathological significance, though they are sometimes associated with œsophageal diverticula or carcinoma

Dr Evans further attributes the observed retrograde propulsion of barium to probably antiperistaltic waves So far as I know, no one directly recording œsophageal motility has ever found true antiperistalsis, and the return of barium towards the upper œsophagus may be explained on the basis of rebound of the bolus, which is propelled forward by peristalsis and encounters a physiological block in its path (call it cardiac sphincter, œsophago gastric junction, or what you will) Two of my colleagues (Ingelfinger and Kramer) and I have studied œsophageal motility with simultaneous fluoroscopic observations and direct pressure recordings with balloons or an electrical recording device Although we have seen a good many cases where barium flowed cephalad, we have never observed retrograde progression of pressure waves

The temporary halt of the barium meal at the diaphragm or just above it is a normal event of varying duration in different subjects

Finally, the partial or total pinching off of the œsophagus 1–2 cm above the diaphragm again is a normal phenomenon seen in every subject on deep inspiration From a few fluoroscopic observations in subjects where a small tenuous dome is seen to project above the diaphragm and attach at the site of the pinchcock, we have favoured the theory that this pinching off is due to the action of the phrenico œsophageal membrane at the site of its attachment to the œsophagus

Department of Gastroenterology,
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Hospitals, Boston, U S A GUILLERMO C SANCHEZ

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[1] Gottlieb I *Lancet* 1947, ii 808

[2] Gottlieb I *Brit med J* 1948 i, 121

ACTION OF PARATHYROID HORMONE

SIR,—Your leading articles of Jan 10 on hyperparathyroidism and nephrocalcinosis (idiopathic renal acidosis) certainly emphasise the complexity of the problem when both kidney and parathyroid are involved in one syndrome I should like to draw attention therefore to an observation which I made last year in the veterinary field, and which may be pertinent

Renal osteodystrophy (rubber jaw), a not uncommon condition in the dog,[1] is assumed on good evidence[2] to be *primarily a renal disease The lesions of osteitis fibrosa* which subsequently develop are associated with hypertrophy of the parathyroids,[1–3] and apparently the degree of hypertrophy and overactivity of the gland is directly related to the stage of the renal lesion[2] The cause of this lesion is so far unknown, but in dogs there is a high incidence of *Leptospira canicola* infection, which is known to produce nephritic lesions resembling those in osteodystrophy[4] Apparently in man there is no single similar condition that occurs so regularly or follows so unvarying a course Incidentally the canine condition was first described by Dr Tom Hare before the Royal Society of Medicine[5]

Last year I attended a trio of cases which constitute an unusual coincidence or alternatively provide food for thought regarding associated renal parathyroid syndromes in the dog The cases will be described elsewhere, but briefly the *facts are as follows*

In one set of kennels three closely related dogs (sire 5 years, son 3 years, stepdaughter 3½ years) were destroyed within a period of 6 weeks All had uræmia arising from chronic nephritis Of the two younger dogs one showed advanced coincident osteitis fibrosa (renal osteodystrophy), the other bilateral renal calculi The sire was found to have pronounced hypertrophy of one adrenal gland No lesions were *found in any* of the dogs except those in the kidneys There is good evidence that the calculi had been present in the bitch at under 1 year of age

Renal calculi are rare in the dog, although cystic calculi are common[6] Primary parathyroid tumour has never been satisfactorily demonstrated in the dog to my knowledge It is tempting to suggest that in this case also (as in that showing osteitis fibrosa) a primary renal lesion preceded the mineral imbalance, leading in one instance to calculus formation and in the other to bone dystrophy As to the hypertrophy of the adrenal in the third case, I make no comment, but I have previously suggested[1] that examination of this gland in cases of chronic nephritis in the dog especially when associated with osteitis fibrosa, might demonstrate hypertrophy if

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[1] Hogg A H *Vet Rec* 1948 60 117

[2] Platt H *J comp Path* 1951 61 188 197

[3] Ojemann J G Osteodystrophia Fibrosa Amsterdam 1943

[4] McIntyre W I M Montgomery, G L *J Path Bact* 1952 64 145

[5] Hare T *Proc R Soc Med* 1934 37 789

[6] Krabbe A Paper read at the Annual Congress of the British Veterinary Association, 1949

Special Articles

REVENTION OF RHEUMATIC FEVER

AMERICAN HEART ASSOCIATION'S STATEMENT *

HEUMATIC fever is a recurrent disease which can be rented. It is now generally agreed that both the al and recurrent attacks of the disease are usually ipitated by infections with beta hæmolytic strepto- i. Therefore, the prevention of rheumatic fever and matic heart-disease depends upon the control of ptococcal illnesses. This may be successfully accom- hed by (1) early and adequate treatment of strepto- al infections in all individuals and (2) prevention of ptococcal infections in rheumatic subjects.

gnosis and Treatment of Streptococcal Infections

n the general population at least 3% of untreated ptococcal infections are followed by rheumatic fever. ong certain individuals, especially those with previous umatic fever, the incidence is much higher. Adequate early penicillin treatment, however, will prevent st attacks of rheumatic fever and eliminate strepto- ci from the throat.

DIAGNOSIS OF STREPTOCOCCAL INFECTIONS

n most instances it is possible to recognise strepto- cal infections by their clinical manifestations but oratory tests may assist in establishing the diagnosis.

idemiology

he seasonal pattern and presence of similar cases in the nmunity or household may be helpful. For example, ptococcal infections in the northern United States are st common from January through June. Likewise, a case scarlet fever in one child would suggest that a sore throat another has the same ætiology.

mptoms

a) Sore throat—onset sudden, in the tonsillar area, not the trachea.

b) Headache—common.

c) Fever—variable, but generally from 101° to 104°F.

(d) Abdominal pain—common, especially in children. Not common in adults, but does occur.

(e) Nausea and vomiting—common, especially in children.

(f) These symptoms are usually *not* present: (1) simple ryza, (2) cough, (3) hoarseness.

gns

(a) Red throat—frequently beefy red, but if seen early the dness may be mild.

(b) Exudate—usually present.

(c) Glands—swollen, tender tonsillar glands at angle of jaw.

(d) Rash—scarlatiniform (characteristic of scarlet fever; t common).

(e) Discharge—otitis media and sinusitis indicated by erous or purulent) aural or nasal discharge are frequent mplications of streptococcus pharyngitis.

aboratory

(a) White blood-count—generally over 12,000 and in ildren frequently over 20,000.

(b) Throat culture—positive for hæmolytic streptococci.

herapeutic Response

Almost without exception patients with streptococcal fections are vastly improved within 24 hours after penicillin as been started and the temperature normal, or nearly so. his therapeutic response is characteristic and if it does not occur, the chances are much against the disease being due to hæmolytic streptococci.

TREATMENT OF STREPTOCOCCAL INFECTIONS

In order to be effective, treatment should be started immediately when a streptococcal infection is suspected and continued for sufficient time to eradicate the streptococci from the throat.

Penicillin is the drug of choice for treating streptococcal infections. Both the oral and the intramuscular routes of administration have been utilised successfully for penicillin therapy of streptococcal infections. Intramuscular injections have been proved to prevent rheumatic fever. The data on the value of oral penicillin as a preventive is less complete.

Oral administration in contrast to intramuscular administration has these advantages: (1) it is not as distasteful to many patients; (2) it requires fewer physician visits. It has these disadvantages: (1) larger amounts of penicillin must be used; (2) it is difficult to administer to vomiting or refractory children; (3) in some adults it gives rise to persistent diarrhœa and pruritus ani; (4) it is difficult to be sure that treatment is continued for sufficient time and given in proper relation to meals to be effective.

Recommended Schedules

Intramuscular penicillin.—(1) Children—one intramuscular injection of 300,000 units of procaine penicillin with aluminium monostearate in oil every third day for three doses.

(2) Adults—one intramuscular injection of 600,000 units of procaine penicillin in aluminium monostearate every third day for three doses. (Note: Less preferable, but usually effective—two doses as above at three-day intervals.)

Oral penicillin.—(1) First five days: 200,000 to 300,000 units one half to one hour before meals and at bedtime (total of 800,000 to 1·2 million units per day in four divided doses; smaller amount children, larger amount adults).

(2) Second five days: 200,000 to 250,000 units one half to one hour before meals (total 600,000 to 750,000 units per day in three divided doses). (Note: To be effective, therapy should be continued for the entire ten days even though the temperature may return to normal and the patient may feel better within one or two days.)

Combination of intramuscular and oral penicillin.—Therapy may be begun with one injection of penicillin (300,000 units of procaine penicillin with aluminium monostearate in oil) and then, beginning three days after the injection, continued for an additional seven days with oral penicillin according to the schedule (2) outlined above.

Other medication.—(1) Aureomycin is less effective than penicillin in controlling streptococcal infection but is especially useful in those sensitive to penicillin. Dosage: Total 10 mg. per pound of body-weight in four divided doses daily for two days. Cut dose in half for remaining eight days of therapy.

(2) New preparations of penicillin. These may be effective and even preferable to the treatment schedules outlined, but at present they have not had sufficient trial to warrant their recommendation.

(3) Other antibiotics. At present there is inadequate data on their value.

Not recommended for treatment.—(1) Penicillin troches or lozenges, (2) penicillin followed by sulphonamides, (3) sulphonamide drugs. (Note: Recurrences of streptococcal infection should be treated as primary attacks.)

Prevention of Streptococcal Infections

GENERAL RULES FOR PROPHYLAXIS

Who Should be Treated?

All individuals under the age of eighteen who have had rheumatic fever or chorea and all those over this age who have had an attack within five years.

When Should Prophylactic Treatment be Initiated?

At the end of the second week of the attack of rheumatic fever or at any time thereafter when the patient is first a firm inelastic layer of fascia This fascia is particularly strong and closely applied to the muscles in the lower third of the leg A leak outwards from this musculo-fascial structure would be effective in transmitting the raised pressure inside the fascial sheath outwards, irrespective of whether the rest of the valves within the pump were normal or abnormal

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* Prepared by the association's council on rheumatic fever and congenital heart-disease. The statement is signed by: BURTIS B. BREESE, M.D., chairman, committee on prevention of rheumatic fever; MARJORIE T. BELLOWS; EDWARD E. FISCHEL, M.D.; ANN KUTTNER, M.D.; BENEDICT F. MASSELL, M.D.; CHARLES H. RAMMELKAMP, jun., M.D.; EDWARD R. SCHLESINGER, M.D. Copies are obtainable from the medical director of the association, 44, East 23rd Street, New York 10, N.Y.

In conclusion I should like to stress two points First, the presence of an ulcer in a leg presents a diagnostic problem in sorting out the factors responsible for it, some of the factors are arterial ischæmia, infection, trauma, general disease, or venous incompetence which may lie in the superficial veins, deep veins, or communicating veins, or a combination of these three The younger group of patients are usually extremely keen to have any operative treatment which holds out hope of cure The older patients do extremely well on supportive treatment, as is well known

Ulcer of the leg is such a common, everyday disease, and is socially so unpleasant and economically so important, that the subject deserves a good deal of interest and research

St Thomas's Hospital
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F B COCKETT

BOVINE TUBERCULOSIS AND HUMAN TUBERCULOSIS

SIR,—Mr Pitcher, in his letters of Dec, 6 and Jan 24, makes the mistake of estimating the incidence of pulmonary tuberculosis from notification statistics He overlooks the fact that improved case-finding could account for the increased morbidity-rates he quotes Indeed, one is tempted to suggest that the counties whose health authorities were astute enough to advise attestation of dairy herds are the counties where improved case-finding methods are likely to have been encouraged and developed

The uncertain remote benefits of drinking tuberculous milk must be compared with the certain immediate risks of primary infection Only the survivors of such infection will enjoy any increased resistance to tuberculosis Therefore, before publicly advocating oral vaccination with virulent bovine bacilli, Mr Pitcher should examine and quote the mortality-rates from non-respiratory tuberculosis (especially in young children) in the counties he has studied

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Nunthorpe near Middlesbrough

J P ANDERSON

TUBERCULIN SENSITIVITY

SIR,—The interesting paper by Dr Edwards and Dr Palmer (Jan 10) illustrates the value of qualitative examinations of the tuberculin reaction, but they do not seem justified in suggesting that the low-grade sensitivity to tuberculin shown by children in Egypt and India may be due to non-tuberculous infection It is well known that sensitivity to tuberculin can vary greatly Bluhm [1] found that it diminished with healing of tuberculous lesions Reversion to complete insensitivity in those who had previously reacted is a recognised phenomenon and has occurred, according to Rich,[2] in between 2% and 21% of the persons studied Indeed, although this is rare, it is possible to suffer from moderately active tuberculosis without having a positive tuberculin reaction [3 4] At the other end of the scale there are those who, although not suffering from tuberculosis react to tuberculin in fantastically high dilutions Lyle Cummins [5] found Africans who were positive to 1/10,000,000 tuberculin, and his work has been confirmed by others Europeans rarely react so strongly, and of 50 tuberculous patients in my hospital not one was positive to 0· of 1/1,000,000 tuberculin when tested recently

If the capacity of Africans to react to tuberculin w taken as a standard, the reaction of Europeans w be uniformly "low-grade", but this would not b reason for suggesting that the European reaction w non specific in origin It seems more logical, the to conclude that for reasons that are not yet ob tuberculin sensitivity may vary widely between diff groups of people, than to conclude that an orga other than the tubercle bacillus is responsible whe tuberculin reaction is minimal

Surely, however, the crucial question is the cl significance of variation in the tuberculin reaction is generally agreed that acutely sensitive Africans more liable to tuberculous disease than those who not react strongly to tuberculin, and that loss of se tivity does not by any means indicate loss of resista to infection It will be most important therefore in the future Dr Edwards and Dr Palmer can indic the mortality and morbidity rates from tuberculosis the various groups of children who have been the subj of their present research It seems unlikely that th implication can have escaped the notice of such care workers Certainly the protective value of B C G vacc tion, from a statistical point of view, would be grea enhanced if many of those who were vaccinated w already highly resistant to tuberculosis

Dungannon Chest Hospital,
Dungannon co Tyrone

E F JAME

STREPTOMYCIN-P A S HYPERSENSITIVIT

SIR,—May I make some comments on Dr Mars paper on this subject [1]

It seems that his patient showed hypersensitivity t p aminosalicylic acid (P A S), streptomycin, chloramphe penicillin, and a local anæsthetic solution, and that he sugg the aggregation of P.A S , streptomycin, chloramphenicol, a the unspecified local anæsthetic into one group of rea agents—"substances containing a benzene ring with attached amino or nitro group" He then suggests th penicillin is in a second group, with a common factor w streptomycin, for both these substances are said to b "complex proteins derived from moulds" Furthermore, remarks on the alleged importance of m aminophenol P A S hypersensitivity

When one patient shows hypersensitivity to several dru it is hard to decide whether one is dealing with a mixture specific reactions or whether there is a true "cross reacti By the term "cross reaction" I mean the development in th organism of a capacity to react abnormally to one or m different chemical structures, each quite different in stru from the original reactive agent By the term specific react I mean a reaction invariably dependent on a part chemical structure, and the specific structure does n necessarily include the entire molecule

From my own and from published observations it see that in patients who show skin hypersensitivity to P.A.S definite hypersensitivity reactions have been demonstra when pure salicylates, phenols, carboxylic acids of benze and carboxylic acid phenols are applied to the skin. A those tested have been hypersensitive to various prim aromatic amines (using the term "aromatic amine" for th compounds composed of an amino group directly attached to benzene ring but not including those with an amino g only in a side chain) I have not yet seen a reaction in su patients after the application of either secondary or ter mixed aliphatic aromatic amines Moreover, I do not kn of any reactions to benzene derivatives containing amino amido groups in side chains only, unless the structure the compound suggested the likelihood of its in vi transformation to a primary aromatic amine

Though a primary aromatic amine structure seems esse to the skin reaction caused by P A S , it is also clear that qu simple additions to the structure will alter such reactions For instance, a patient whose skin was hypersensitive to P.A.S reacted severely to the application of aniline, but more mil to 1, 4 benzenediamine, and not at all to p aminobenz

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[1] Bluhm I *Tubercle* 1948 29 73
[2] Rich A R Pathogenesis of Tuberculosis Oxford 1951
[3] Lichtenstein M R *Amer Rev Tuberc* 1947 56 198
[4] Mascher W *Ibid* 1951 63 501
[5] Lyle Cummins S *Tubercle* 1948 29 68

[1] Marsh, K *Lancet*, 1952, ii 606

Public Health

OUTINE X-RAY EXAMINATION OF THE CHEST AT AN ANTENATAL CLINIC

Audrey Freeth
M.B. Lond., M.R.C.O.G.
ST ASSISTANT OBSTETRICIAN, EASTERN DISTRICT HOSPITAL, GLASGOW

Radiology is acknowledged as the best of the routine eans of examining the chests of apparently healthy ople, and its use in this way is particularly valuable in e care of pregnant women. We decided to look for nsuspected tuberculosis by making X-ray examinations the chests of mothers attending an antenatal clinic a district where tuberculosis was common; and this per describes the results.

EARLIER SURVEYS

It is hard to compare the figures that have been tained by previous surveys of this kind, because of the ifferent standards used in deciding which patients to nclude. For example, Eiscle et al. (1942) excluded all omen known to have tuberculosis—a group of 62 with inimal fibrotic lesions, and a further group with rimary calcified complexes. However, the figures of cker and Bryant (1943) are comparable with the results f Eisele et al. Roe (1946) does not include primary alcified lesions, and Jacobs (1946) excludes 39 women ith calcified shadows only. Graham (1941) mentioned hat 206 women in his series were "contact" cases with alcium deposits in the hilum and lung parenchyma. Both Perlberg (1940) and Dawson (1945) included calcified pulmonary lesions. Bickerstaff et al. (1951) said that ver half the cases they discovered were diagnosed as minimal lesions, and over one-third as moderately or far advanced, and that two-fifths of the cases were probably active; these figures, they concluded, "indicate the significance of what was classified as tuberculosis."

The results of these and other earlier investigations are set out in the table.

TUBERCULOSIS IN GLASGOW

In Glasgow the death-rate from pulmonary tuberculosis in 1949 was 1010 per million population, compared with 590 in Scotland as a whole, and 403 in England and Wales. The medical officer of health for Glasgow (1949) says that the mortality-rates have remained high since the early years of the late war, largely because of more deaths among young women between the ages of 15 and 25 (and even up to 35), and because of more tuberculosis among men over the age of 45. The total number of cases of pulmonary tuberculosis notified in Glasgow in 1949 was 2829; 1374 (43%) were women, of whom 1196 (87%) were of child-bearing age (15–45).

McIntyre and Armstrong (1948) treated 150 Glasgow women who became pregnant while suffering from tuberculosis between January, 1947, and March, 1948. During this time 16 women (10·7%) died and 14 (9·3%) became worse. In 42 cases the disease was first discovered during the pregnancy, and in 38 of these the disease was active: 7 of the women with active disease died (all of them had been discovered late in pregnancy); and a further 3 women, diagnosed in the puerperium, also died.

THE PRESENT INVESTIGATION

The clinic chosen for our investigation is in a working-class area. In this area women known to have tuberculosis are referred to a special unit when they become pregnant, and these cases were excluded from our series. Apart from this, there was no selection of patients in the series. As it happened, only 1 woman with known tuberculosis reported to the clinic during the investigation; all the other cases found were unsuspected.

During their first visit to the clinic 576 patients were asked to attend for X-ray examination of the chest, and 541 (94%) did so. One 15 by 12 in. A.-P. film was taken. Patients showing active or healed tuberculous lesions were asked to attend for a second film three to six months later, and 69% did so. Of the 541 films taken, 477 were normal. The other 64 (13·4%) showed some abnormality.

Evidence of tuberculosis was found in 29 women (5·3%), and another 4 had calcified glands, with no lung changes. Of the 29 tuberculous cases, 12 showed only calcified areas in the lungs, while the remaining 17 (3·1%) showed active, inactive, or fibrotic lesions. In 4 cases the disease was definitely active (0·74% of the total), and a further woman, who was reported to have lesions of doubtful activity, declined further investigation: 8 cases showed inactive lesions, and 4 had healed fibrotic lesions.

The active and inactive cases were re-examined after delivery. The 4 active cases were reported to be unchanged. Of the 8 inactive cases, 2 failed to attend for examination, 2 had become active, in 2 others activity was doubtful, and in the remaining 2 the condition remained unchanged.

The other abnormalities found included mitral stenosis (6 cases), emphysema (2), old pleurisy (3), peri-apical pleural thickening (2), and inflammatory changes (6).

RESULTS OF PREVIOUS SURVEYS BY ANTENATAL X-RAY EXAMINATION OF THE CHEST

Author, place, and time	Method	No. in survey	No. with evidence of tuberculosis	No. with active disease	—
Eisele and Mann (1938), Eisele et al. (1942); Chicago, 1934–41	Screening	10,968	172 (*1·6%*)	74 (*0·6%*)	Excludes known tuberculosis and primary calcified complexes
Tucker and Bryant (1943); Chicago, 1939–42	Screening	1000	29 (*2·9%*)	18 (*1·8%*)	Comparable with figures of Eisele et al.
Graham (1941); California, 1937–39	Radiography	800	30 (*3·7%*)	8 (*1%*)	24 had significant parenchymal disease. Excludes 206 "contact" cases with calcium deposits in hilum and parenchyma
Perlberg (1940); Jersey City N.J., 1938–39	Screening	2834	130 (*4·5%*)	3 (*0·1%*)	18 inactive, 14 suspicious cases, and 95 healed primary lesions
Dawson (1945); Dunedin, N.Z., 1942–44	Radiography	1000	30 (*3·0%*)	6 (*0·6%*)	Includes 25 calcified lesions only in lungs
Roe (1946); Uxbridge Chest Clinic, Middlesex, 1943–45	Radiography	1088	10 (*0·9%*)	2 (*0·18%*)	3 inactive and 5 suspicious cases. Excludes primary calcified lesions
Jacobs (1946); Paddington, London, 1943–46	Screening	4430	107 (*2·4%*)	38 (*0·9%*)	Excludes 39 cases with calcified shadows only
Bickerstaff et al. (1951); Muscogee, Georgia, 1946–49	Miniature radiography	3576	43 (*1·2%*)	14 (*0·4%*)	In the 14 active cases tuberculosis was unsuspected

Five hours after treatment was started cortisone became available, 100 mg was given intramuscularly and 200 mg orally Meanwhile general improvement had continued, and the blood pressure was now 90/60

Cortical extract was now omitted, but deoxycortone was given in 10 mg doses twice daily for another week, and cortisone in gradually decreasing doses for five days Antibiotics were given for a further four weeks, as the illness was marked by a relapse of fever with a joint effusion in the third and fourth weeks

The patient was discharged five weeks after admission He has been followed up for five months, during which he has maintained excellent health and has been free from all sequelæ The blood-pressure on discharge was 115/70, and subsequent readings have been substantially the same

Investigations

Blood culture on admission grew meningococcus type II Lumbar puncture on the day of admission yielded turbid cerebrospinal fluid under a pressure of 230 mm of water, containing large numbers of polymorphs and a few gram negative intracellular diplococci, culture was sterile A blood count showed Hb 84%, white cells 5500 per c.mm (neutrophil polymorphs 79%, eosinophils nil, lymphocytes 9%, monocytes 5%, metamyelocytes 6%, myelocytes 1%) Lumbar puncture and blood culture a week after admission gave normal results in all respects

The blood electrolytes were investigated repeatedly, but were within normal limits except for a slightly low sodium level (315 mg per 100 ml) on the first day

Urinary 17 ketosteroids, estimated on the tenth, twelfth, and thirteenth days, amounted to 2 2, 2 9, and 2 8 mg per day, three and a half months after discharge the value was 5 2 mg per day

In this case the diagnosis of the Waterhouse-Friderichsen syndrome (sometimes a matter of doubt) was probably as well authenticated as can be expected in the absence of confirmation at necropsy Dr Stanley Banks kindly read a précis of the case notes and agreed to this diagnosis In his opinion it was a case of meningococcal septicæmia of the mixed encephalitic and adrenal type [1]

One might ask why these cases on recovery from acute illness do not require long-term replacement therapy as in Addison's disease our patient only had adrenal cortical extract for three hours, cortisone for five days, and deoxycortone for a week Histological study of the adrenal from a fatal case, however, showed that although the cortex was grossly damaged about a third to a quarter of it was affected only by œdema, being probably capable of functional recovery had the patient survived In this respect the low values for urinary 17-ketosteroids in our patient are interesting He was postpubertal, but even three and a half months after his illness excretion was rather low (5 2 mg per twenty-four hours)

Of particular interest was the apparent excellent response to large intravenous doses of adrenal cortical extract given over a short time—120 ml in three hours Cortisone was only available later, when anxiety for the survival of the patient was much less, though it probably contributed to the recovery Possibly, where adrenal cortical extract has previously failed in these cases [2 3] the dose has not been large enough

Whether the beneficial effect of the adrenal cortical extract should be credited to the deoxycortone content of the extract or to other substances is not clear These preparations are, I understand, assayed biologically by their action on the blood electrolytes Eucortone probably contains cortisone, though only in negligible amounts But these adrenal cortical extracts, besides the known crystalline compounds of the perhydrocyclopentenophenanthrene series (such as cortisone, deoxycortone, and progesterone of the 21 carbon pregnene group, androsterone of the 19 carbon etiocholane group, œstrone, and other 18 carbon phenols) contai amorphous residue which is chemically unidentifi From the work of Kendall [4] and others [5] it seems th this residue produces powerful physiological effects, these may be of therapeutic value in states such as Waterhouse-Friderichsen syndrome

I am indebted to Dr E N Allott, Dr H S Banks H V Morlock, Dr G Nelson, and Dr G F Thomas help with this case report

London, N W 6 I A Macyt

TABLET-IDENTIFICATION BOX

Sir,—The experience of producing a tablet identifica box for this hospital has demonstrated the difficul and possible danger in trying to use only a box f this procedure I suggest that anyone who is conte plating such a box should consider the following poi

The box should be produced with the coöperation of pharmacist, if not by him alone He can readily ob *complete set of locally prescribed coloured tablets from* retail pharmacists In my opinion white tablets, wh *coated or plain, scored or otherwise marked,* are b excluded

The total number of coloured potent tablets and caps for this area is about fifty, so that our box is little m than pocket-sized

When the capacity of the box is decided, the tablets a capsules can be arranged according to colour and sh The following precautions will then be necessary

1 A warning should be attached to the box stating it should only be used in conjuction with two m reliable sources of information (*a*) the doctor w prescribed the tablets, who should have a filed rec of them in his surgery, and (*b*) the chemist who d pensed the tablets, whose name and address will found on the container if the parent produces this
2 The colourings of tablets, more especially the o non proprietary ones, are liable to variation wi limits, and brightly coloured tablets of green and can change sufficiently in a perspiring parent's hand make identification by colour alone most difficult

These points ought to be brought to the attenti of every new house physician The box then beco a safe as well as a useful additional source of informati

Kent and Canterbury Hospital,
Canterbury JOHN C SMITH

PERFORATION OF COLON AFTER BARIUM ENEMA

Sir,—With reference to the letter which was publi under the above head from Mr. A V Pollock on Jan. I was not consulted before publication, and I sh welcome an opportunity of correcting one or two wr *impressions which the letter has created*

The patient in question was admitted to the West Lon Hospital under my care As registrar to my surgical u Mr Pollock performed the routine sigmoidoscopy, which later followed by the passage of a barium enema into peritoneal cavity through a rent in the sigmoid colon Pollock assisted me with the first operation at which laceration of the sigmoid was sutured and cæcostomy p formed, but he had left the hospital before the splenic flex was resected The patient is still in hospital and his recov is not yet beyond doubt

It is my intention to publish a full account of t case in due course

London, W 1 G F GRANT BATCHELOR

*** We have shown the above letter to Mr Pollock, w replies "I naturally wrote to Mr Batchelor asking permission to publish this case *Hearing* nothing over a week I left his name out of my communicati believing that he did not wish to be associated with case which reflected no credit on me The facts of t case are exactly as stated in my letter of Jan 10' Ed L

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1 Banks H S McCartney, J E *Lancet*, 1943 i, 771
2 Nelson J Goldstein N *J Amer med Ass* 1951, 146, 1193
3 Faloon W W Reynolds, R W Beebe R T *New Engl J Med* 1950, 242 441
4 Kendall H C *Proc Mayo Clin* 1940, 15, 297
5 Tait J F Simpson, S A, Grundy, H M *Lancet* 1952 i

The chemical branch of the L.C.C. public health partment make daily measurements of the amount of oke and sulphur dioxide in the atmosphere at County ll and elsewhere. Some of the results obtained at time of the fog are shown in the accompanying table. e maximum averages were reached over the weekend ling at 10 A.M. on Monday, Dec. 8. These figures re higher than any that have been traced in the L.C.C. ords, which, for sulphur dioxide, date back to 1932.

In a report to the borough's public-health committee, . E. H. R. Smithard, medical officer of health for wisham, says that 228 deaths were registered in wisham in the fortnight ended Dec. 20, compared h 76 and 95 deaths in the corresponding fortnights 1951 and 1950 respectively. Of those who died in this tnight, 130 were men and 98 women; 104 were over age of 75, and all but 8 were over 45. A striking ture of the Lewisham figures was the abnormally ge number of deaths in the Sydenham registration trict, as compared with the other two districts in the rough. Dr. Smithard suggests three possible explanans:

(1) An older population in the Sydenham area.

(2) A denser fog caused by geographical configuration.

(3) A more poisonous fog due to greater atmospheric llution in that part of the borough.

rther inquiries are being made. Dr. Smithard mentions e new and popular type of slow-burning fire, which commonly stoked up to keep it going all night, as a ely cause of increased atmospheric pollution.

Influenza

In the week ended Jan. 24 there were 132 deaths om influenza in the 160 great towns of England and ales, compared with 72 in the preceding week. This ings the total number of deaths from influenza in the eat towns this year to 255; at this time last year e total was 110. The outbreak is still confined to the uthern half of England, with a large number of cases the London area. Of the 132 deaths in the week ded Jan. 24, 78 were in the London and South Eastern gions; and 112 of those who died were aged 55 or ver. Only localised outbreaks have so far been reported om the north of England and Wales.

Dr. William Bonne, director of the W.H.O. division f communicable diseases, describes the epidemic as ild in all countries. The A-prime virus which has been olated in several countries seems to be closely related o the virus responsible for the outbreaks in the winter f 1950–51.

Emergency Bed Service.—Last week applications for admision to hospital for general acute cases averaged about 350 day; but by Monday of this week the daily total had ropped to 293. On Tuesday the red warning was replaced y a yellow warning, even though the proportion admitted n the previous week was 88%—a level at which no warning sually operates. It was thought that the improved position as largely due to the excellent response by hospitals to last eek's red warning, and that the need for special measures ontinued.

Estimate of Births

The Registrar-General[1] estimates that in the quarter ending March 31 this year live births in England and Wales will number 170,000. The provisional estimate for the quarter ending June 30 is 165,000, giving an estimated total in the first half of this year of 335,000. Last year births in the first two quarters numbered 173,503 and 174,089, making a total of 347,592.

Statistics for England and Wales in 1952

The Registrar-General[2] has reported provisional statistics for England and Wales in the year 1952 and for the fourth quarter of that year. These figures, along with the corresponding figures for 1951, are as follows:

Rate	*Whole year*		*Fourth quarter*	
	1952	*1951*	*1952*	*1951*
Live birth (per 1000 pop.) ..	15·3	15·5	14·3	13·9
Stillbirth (per 1000 total live and still births)	22·6	23·0	23·1	24·2
Death (per 1000 pop.).. ..	11·3	12·5	12·4	11·0
Infant-mortality (per 1000 related live births)	27·6	29·7	29·0	28·5

The stillbirth and infant-mortality rates for the year are the lowest ever recorded in this country.

Medicine and the Law

A Patient's Bequest

THE law recognises that the confidential relationship of doctor and patient (like that of solicitor and client and certain other relationships) establishes an opportunity of influence. In Estate of Smith deceased, Creditor *v.* Markowicz,[1] a doctor put forward as plaintiff a will of 1949 which he had himself made for an old lady, his patient, aged 89. Under this will he was to obtain substantial benefit. The defendant, Mrs. M., was executrix and beneficiary under a will of 1947 which had been drawn for the old lady by her solicitors. There were two questions for the jury. First, at the time when the will of 1949 was executed, did the deceased know and approve its contents? Secondly, was the execution of the will procured by the undue influence of the doctor? As Mr. Justice Barnard put the problem to the jury—was the doctor an honest man who behaved foolishly or a wicked man who took advantage of his position as a doctor to get money out of the old lady? After a prolonged hearing and after deliberating in their room for eighty minutes the jury found in favour of the doctor.

As already stated, the doctor-and-patient relationship is deemed analogous to that of solicitor and client. A solicitor can obtain benefits under a will which he draws up for a client; but if the benefits are substantial he will be expected to show that the testator was capable of making the will and knew and approved its contents and was not subjected to undue influence. Professional prudence will persuade the solicitor to send the client to another solicitor who can give independent advice and who will make a proper note of the instructions received and the advice given. In Radcliffe *v.* Price (1902) a gift by a patient to a doctor was set aside on the ground that the patient had no independent advice, even though there was no suggestion of pressure or of weak intellect. There is, however, a curious legal difference between the case of a gift made during life and a legacy under a will. The former courts of equity thought that the natural influence arising from such relationships as those of doctor and patient, exerted by those who possessed it for the purpose of obtaining benefit for themselves, was undue influence. With wills, as was stated by Lord Penzance in Parfitt *v.* Lawley (1872) in a passage read by Mr. Justice Barnard to the jury, it is otherwise. Such relation may lawfully be exerted to obtain a legacy so long as the testator understands what he is doing and is a free agent. In the recent litigation there was much argument as to the onus of proof. The learned judge quoted the judgment of Sir Gorell Barnes in Spiers *v.* English (1907) to the effect that the onus is not "specially heavy" upon a person who obtains and puts forward a will in his favour. "I doubt whether the fact of his having been instrumental in making a will under which he substantially benefits makes any difference to the presumption of law." Mr. Justice Barnard told the jury that to be satisfied that there had been undue influence they must be satisfied that, when the transaction had been finished, the testatrix would have said "it is not my wish: I had to do it"; there must be coercion.

One intriguing remark fell from the judge's lips. If, he said, the jury were satisfied that the doctor had

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[1] Registrar-General's Weekly Return for England and Wales, no. 3, 1953. H.M. Stationery Office. Pp. 19. 1s.

[2] Registrar-General's Weekly Return for England and Wales for the week ended Jan. 17, 1953. H.M. Stationery Office. Pp. 19. 1s.

[1] *Times*, Jan. 23.

If no other syringe is available in an emergency the technique can be adapted for intravenous injection. Advantage is taken of the recoil by maintaining gentle pressure on the rubber piston while the vein is being sought. The release of this pressure (insufficient to inject solution) will draw blood from a vein.

From my own experience, the glass container is best dipped into hot or boiling water for a moment before use. This serves two purposes: the solution is warmed and the injection is infinitely less painful; the rubber piston is thereby caused to run smoothly down the glass cylinder, instead of stiffly or in jerks.

Stockport D N BARBER

UNUSUAL PNEUMONIA

SIR,—In common with other physicians I have recently seen many cases of pneumonia, and I think it is worth recording some unusual features in these cases.

They have all resembled the usual descriptions of virus pneumonia in so far as they have had (1) mucoid sputum and (2) no leucocytosis. They have, however, differed considerably from the usual accounts of virus pneumonia in so far as (1) pleural pain has been prominent, (2) physical signs have been gross, and (3) sterile pleural effusions—usually comparatively small and encysted—have often complicated the illness.

London, W 1 M H PAPPWORTH

Parliament

Therapeutic Substances Bill

IN the House of Lords on Jan 27 the Therapeutic Substances (Prevention of Misuse) Bill was read a first time. The Bill makes further provision as to the substances other than penicillin to which the Penicillin Act, 1947, may be applied by regulations, and provides for the relaxation in certain cases of the restrictions imposed by that Act. The Bill is discussed in an annotation on p 280.

QUESTION TIME

Adoption of Children Inquiry

Replying to a question, Sir DAVID MAXWELL FYFE, the Home Secretary, said that he and the Secretary of State for Scotland had decided to appoint a committee to consider the present law relating to the adoption of children and to report whether any, and if so what, changes in policy or procedure were desirable in the interests of the welfare of children. His Honour Sir Gerald Hurst, Q C, would be chairman of the committee, and Miss J M Northover, of the Home Office, the secretary.

Surgical Boots

In answer to a question, Mr MACLEOD stated that in England and Wales during the twelve months to May 31, 1952, 48,071 pairs of surgical footwear were issued, costing approximately £400,000. In the seven complete months since then 19,435 pairs had been prescribed.

Pneumoconiosis Benefits

Dr BARNETT STROSS asked the Minister of National Insurance whether he would make a statement concerning the pneumoconiosis benefit scheme giving, to the nearest date, the number of applications made for benefit, the number of cases examined and still outstanding and the number receiving benefit following examination.—Mr R H TURTON replied: The following is the information asked for:

PNEUMOCONIOSIS AND BYSSINOSIS BENEFIT SCHEME 1952

(Period from March 10, 1952 (commencement) to Jan 3, 1953, inclusive)

—	Total disablement	Death	Total
Applications received	5586	860	6446
Claims allowed	2179	458	2637
Claims disallowed	2153	237	2390
Claims under examination	1254	165	1419

Obituary

GEOFFREY DOUGLAS HALE CARPENTER

M B E, D M Oxfd

Professor Hale Carpenter well exemplified a pecu British product, the doctor naturalist who allowed w was at first a hobby to become the pivot of his ca In this respect he was a disciple and follower of Edward Poulton, and Oxford with its traditions be his spiritual home. He was not entirely bound entomology and it was his understanding of all for wild life that brought him international fame.

Hale Carpenter was born at Eton 70 years ago and received the main part of his education at Oxford zest for entomology was inherited from his fath master at Eton, who was also a distinguished natur and a fellow of the Royal Society. Having chos medical career he took a second-class honours de natural sciences from St Catherine's Society, Oxford 1904. With a university entrance scholarship he th entered St George's Hospital, where after qualifying 1908 he served for a year as house-surgeon and h physician.

In 1910, on entering the Colonial Medical Service studied tropical medicine at the London School Tropical Medicine under Sir Patrick Manson and C Daniels. It was this experience that decided his fu for almost immediately after obtaining the certi of the school with honours, he was appointed to th Royal Society's Sleeping Sickness Commis Uganda. At Entebbe he found his true métier in th stimulating company of Sir David and Lady Br Harvey, Mackie, and Hamerton, who had joined to in the great research on the relationship between tryp somes, tsetse flies, and the magnificent mammalian fa of Central Africa. Carpenter's special attention directed to the tsetse flies; but in his researches on th habits he studied reptiles and crocodiles as well. Du the 1914–18 war he served as a medical officer in E Africa.

In 1920 he was appointed special officer in charge the sleeping-sickness campaign in Uganda. He was th obvious choice for the post, for which he was fitted b inclination, training, and experience. His reputatio may well be judged by the results he obtained, for it largely due to his work that trypanosomiasis is no lo a scourge there. This appointment ended in 1930 wh he retired from the Colonial Service.

The following year found him in Ngamiland, at th extreme northern border of the South African Un where in the Okavango and Chobe swamps a foc human trypanosomiasis (*Trypanosoma rhodesiense*) h been discovered and where tsetse flies (*Glossina mors* abounded. Returning to Oxford he was appointed H professor of zoology (entomology) in 1933. Hav entered this academic career he was little seen in med circles, but during the late war he lectured on tro medicine to troops stationed near Oxford.

His many scientific publications were mainly on th entomology and the bionomics of tsetse flies, but he w greatly attracted by the phenomenon of mimicry butterflies, moths, beetles, hornets, and other in and he quoted examples also in birds. In 193 published a monograph on this subject. Two pop books of his, which contain a wealth of information *A Naturalist on Lake Victoria* (1920), and *A Natur in East Africa* (1925). As a speaker he was much so after, for his addresses had an appeal, in their dive and interest, far beyond mere entomological stu During these years he often visited London to attend th meetings of the various zoological and entomolo societies. He served as vice-president of the Linnea Society (1935–36), and as president of the Royal Ento gical Society (1945–46). After he retired from his ch in 1948 he spent more time than ever in his garden Cumnor Hill. He died on Jan 30.

Professor Buxton writes: "His many friend remember Hale Carpenter for his charming, enthusi manner and his very wide interest in natural hi It was this that led him to seek work in Uganda in 19 soon after he qualified. He was an excellent choic what was wanted was a doctor to study the distributi of sleeping sickness around Lake Victoria, and

ne[9] showed that the histamine content of the skin
creased 200 times by adrenalectomy. Staub[10]
ves that adrenaline and histamine are partners in a
pensatory mechanism which regulates the blood-
sure. The prompt response of many forms of
ergy to adrenaline injections confirms in a practical
the importance of this cutaneous barostat.

TREATMENT

early the treatment of urticaria is not a matter of
g an anti-histamine drug, and if that fails trying
her. Rational treatment must be based on a search
a specific antigen and for a possible connection
veen the urticaria and the patient's attitude to
ts. If the patient feels that the last straw has fallen
ome way on his back, this straw may, in his mind's
loom as large as a lash that weals his back.

einberg,[11] dealing with common misconceptions in
treatment of allergic conditions, said that although
-histamines may show their greatest effect in urticaria,
nany severe cases and in certain stages of urticaria
are by no means helpful; and they have no effect
ome people, even with the mildest type of manifesta-
Most anti-histamine drugs are powerful local
sthetics, and the anæsthetic and adrenergic effects
independent of the anti-histamine activity.[12] They
y act by blocking antigen-antibody junctions or, as
lerat[13] believes, by displacing tissue histamine from
cell receptors and liberating it into the blood, where
is partly adsorbed and detoxicated by the cellular
nents of the blood, and partly neutralised by
ulating anti-histamine.

istaminic antigenic urticaria may respond well to
i-histamine drugs, but adrenaline, the best of all anti-
tamines, is still the most valuable remedy in the worst
es. It is essential to remove the source of antigens if
ssible—whether drug, food, or the products of micro-
ganisms. Until this has been done, the anti-histamines
uld be regarded as palliatives. In drug urticaria—
e to penicillin, for example—the wealing may persist
a time in spite of the withdrawal of the drug, and
ti-histamines are especially useful in these circum-
nces.

If the urticaria seems to be of cholinergic autonomic
igin, the anti-histamines are likely to give disappointing
sults (though they may relieve irritation), for anti-
stamines are usually ineffective against acetylcholine.
hese drugs are used today as much for their antipruritic
operty as for their anti-histamine effects, but the doctor
ho uses them in this way should do so deliberately and
t deceive himself by imagining that their palliative
fect is due to their action against histamine in patients
ith non-histaminic or only partly histaminic urticaria.

The anti-histamines may relieve the irritation but
ot the wealing in pathergic autonomic urticaria, but
milar or better results may be obtained by hypo-
alamic sedatives of the barbiturate group. Some
lief may also be obtained for these patients by a
orning dose of amphetamine sulphate to encourage
he release of emotional tension through action or
ords.[14] Rest, although theoretically indicated, is of
o certain value in chronic urticaria, and, after all, it only
elieves a secondary cause. These measures are merely
alliative and symptomatic, in the same way that the
se of anti-histamines in histaminic urticaria is palliative
f the source of antigens is not removed. Lasting relief
an only be expected from exorcism and abandonment
f the morbid fantasies.

In England Now

A Running Commentary by Peripatetic Correspondents

According to Professor Konrad Lorenz,[1] whom we were all happy to welcome to London this week, the present remarkable relationship of man and dog goes back to the time when dogs joined wandering tribes of primitive huntsmen as scavengers of any surplus mammoth flesh. After a few generations the dogs began to pay for their board by acting as guards and hunting aides. Ultimately some dogs ceased to be capable of living independently and came to accept Man as a substitute for their pack-leader—a healthy symbiosis which survives to this day in most homes of suburban England. But though Lorenz has illuminated many facets of dog behaviour, personal experience of three charming but quite diabolical dachshunds has convinced me that there is much about dogs that has yet to be explained.

George, the ringleader of this unholy alliance, whose mother came from Bangalore, presents a baffling and often sinister pattern of behaviour, part intelligence and part instinct, which is quite beyond me, a mere doctor, to understand. At the age of 18 months he has succeeded in becoming a master of overdogmanship; for example, he always goes rabbiting with his younger colleague and returns smooth and shiny, not a hair out of place, carrying a rabbit, while his companion, who is covered from head to foot with mud and is clearly regularly employed as a ferret, trots humbly behind, hoping he may be allowed perhaps a mouthful. And yet they appear to be on the best of terms; students of political philosophy may be able to explain this.

The other evening George resented a delay in his meal, and was found, five minutes before our guests arrived, standing in the middle of our carefully contrived dining-table décor licking the polished glasses, which activity he forsook, on our approach, to stare coldly past us. Considering his length of leg and the height of the dining-table, we considered this a remarkable physical as well as intellectual feat.

During a scuffle in the kitchen the youngest dog secured and triumphantly, if slowly, consumed a teat from the baby's bottle. George's rage and frustration were wonderful to witness; he made his observations, planned his crime, and awaited his opportunity; and nine days later, when the appropriate drawer was inadvertently left an inch or so open, he secured a brand new teat in 'Cellophane' wrapper. His happiness was complete, and we wonder what Dr. Freud might have made of this. I feel that this particular human tribe must soon accept George as its pack-leader; it could perhaps do worse.

* * *

WHENAS IN SULKS

"I've had a quite magnificent idea,"
Said Robert Herrick. "I have asked Anthea
—A charming girl with poise and no boloney
I always think; I've also asked Oenone,
Electra, Dianeme, and Corinna,
And all those rosebud-gathering girls to dinner.
I wonder if we ought to ask Perenna?
She doesn't look so well with all that henna . . ."
He faltered, smiling nervously at Julia,
Observing that she looked a shade peculiar.

* * *

"I'm just going to Capetown." "I'll see you in Montreal." Such words are heard in the main corridor of my hospital probably even more often than at a large airport. All this is because the names of Commonwealth cities have replaced numbers for labelling the wards. The change, though no doubt a broadening influence in our life, is not all gain, for the numbers indicated geographical location. Thus the three floors at the north end of the hospital were North 1, North 2, and North 3, and the small ward attached to the lower ward was generally called "North 1 little end." The two floors of the medical block are now Durban and Capetown. It would have been easier if Capetown was ing services general surgery, general medicine, ophthalmology, otorhinolaryngology, orthopædics, pædiatrics, obstetrics, gynæcology, outpatient, laboratory, pharmacy, and radiology Special facilities are provided as follows neuropsychiatry, Burderop Park, urology, Burderop Park and South Ruislip, orthopædics, Burderop Park, cardiology, South Ruislip, allergy, Wimpole Park A mortuary service is provided at each of the four hospitals, or information may be had from the nearest American station Any doctor wishing to use these arrangements for the investigation or treatment of American patients should get into touch with the appropriate hospital or the nearest hospital

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[9] Rose, B., Browne, J. S. L. *J. Physiol.* 1938, 124, 412.
[10] Staub, H. *Schweiz. med. Wschr.* 1946, 76, 818.
[11] Feinberg, S. M. *J. Amer. med. Ass.* 1951, 147, 617.
[12] Huttrer, C. P. *Experientia*, 1949, 5, 53.
[13] Pellerat, J. Thesis, University of Lyons, 1945; *Congr. Méd. franç.* Paris, October, 1947.
[14] Kendig, E. L. *Sth. Med. Surg.* 1945, 107, 366.

[1] King Solomon's Ring. London, 1952.

A STUDY OF CHILD DEVELOPMENT

In 1951 a long term study of the physical and mental development of normal children, from birth to the end of adolescence, was begun by the Institutes of Education and Child Health of the University of London The investigation now has a sample of about 100 babies, who are seen at regular intervals Expectant mothers (and their husbands) are interviewed during pregnancy, and are asked to cooperate by bringing their babies to the child study centre at the Foundling Hospital, Coram's Garden, Brunswick Square, W C 1, and by receiving research workers in the home Few parents have refused to help, and it is planned to take in further samples at intervals, until the total number of children is about 250,

At each visit to the centre, the mother is interviewed about the child's health, experience, and behaviour, since her last visit She is asked about the kind of routine she follows for feeding, sleeping, elimination, for example, and the child's reaction to it, about the child's level of development in locomotion, manipulation, speech, and imitation, and about early signs of temperament and personality as evidenced by behaviour with strangers, readiness to cry, and responses to different members of the family Objective tests and observations are also made and a full clinical examination is made As the children grow older note will be taken of school progress, and its relation to earlier stages of development

INDIA'S HEALTH PROBLEMS

Under the new constitution the 28 States of the Indian Union control their own public health programmes The central government acts in an advisory capacity in furthering progress through national and international conferences, conducting and promoting research through national institutes, setting up uniform medical and drug standards, and training teachers for medical colleges Emphasis is shifting from curative to preventive medicine, and research is being conducted in tuberculosis, cancer, malaria, cholera, and other tropical diseases Unicef and W H O have aided greatly by providing both experts and funds Four international teams are active in anti malaria work, and Unicef has sponsored three tuberculosis centres in Delhi, Patna, and Trivandrum to train personnel, as well as prosecute research Unicef has also worked out a comprehensive plan for child welfare and maternity clinics to secure uniform sanitation and nutrition measures to lower the maternal and infant mortality rates, and to ensure the health of future citizens Both Unicef and W H O are collaborating with the Central and Bombay governments in erecting a penicillin factory near Bombay

B C G vaccines manufactured in a factory near Madras are being used in mass inoculation programmes by more than ninety teams operating throughout the country The Council of Medical Research, in collaboration with W H O, is to seek precise data on the epidemiology of tuberculosis in India, and to assess the efficacy of control measures under local conditions The Rockefeller Foundation has donated funds to the Indian Cancer Research Centre in Bombay, to meet working expenses of a laboratory for studies in human variations

Since 85% of India's population lives in villages, rural health measures are naturally receiving increasing attention The State governments are amalgamating villages in units, or blocks, to be served by dispensaries and in remote areas by mobile vans manned by a doctor and a pharmacist Moving pictures on basic hygiene and diet habits, as well as leaflets and pamphlets, are carried by mobile units. Sound track broadcasts are conducted in village meeting places The States are strengthening measures by centralising work under health officers appointed for each district They going ahead with safe water supply schemes and con of sewage plants Madras, for example, has a five-yea for rural areas, and a twenty-year project for providing and sewage plants in all towns with populations of 10 over Madhya Pradesh, Bihar, Bombay, Uttar P and Orissa are following suit, taking up the pro environmental hygiene, and furnishing piped water, dr and wells in towns and villages

To combat the serious shortage of doctors, nurses, and trained personnel, medical training facilities all over country are being expanded, and many institut following the pattern of colleges in West Bengal and Pradesh wherein "double shift" teaching systems force for the training of twice as many doctors Old p tioners are being offered refresher courses, and spec training is available for orderlies, attendants, and mid Colleges have been upgraded and given State grants, the number of yearly admissions has been stepped up.

The first attempt to raise nursing to professional s was started with the establishment of the Nursing Col Delhi, offering courses of university standard Special de in dietetics and nutrition are being awarded Also, gr schools have begun training public health engineers, pioneer in this field being the All India Institute of Hy and Public Health The All India Medical Institute in due course, provide the nation with qualified adm trators in medical and allied professions It has f for postgraduate research linked with the Council of Me Research

National standards are being laid down for the pr of nursing, pharmacy, and dentistry Industrial labour enjoys the advantage of medical service, coupled with benefits through the new employees' insurance act provident funds The central health ministry is now w on measures for a pure food and drug law

TELLING THE LAYMAN ABOUT MALARIA

The subject of malaria is so overloaded with techn terms that it taxes the wisdom and memory of even the m earnest student Prof George Macdonald[1] has pre an up to date, clear, and concise account of this so constructed and phrased as to be intelligible to th reader This is a difficult undertaking in which he succeeded admirably, it will be read with pro sanitarians, planters, miners, and others The epide logical types of malaria are discussed, and the condi and mosquito carriers in some selected areas described principles of malaria control are set forth, whilst over pages are devoted to residual insecticides Finally there two appendices—one dealing with the malaria parasite a the other with mosquitoes—couched, as far as possib unscientific language and illustrated by outline figures

A MEDICAL MISSIONARY

Reared in Illinois, the son of a Congregational minister, James McCord had, from boyhood reading of the travels of Livingstone and Paul Du Chaillu, been fired with the ambi to go to Africa His plans to achieve this by becoming missionary were nearly frustrated by his shyness and ina to preach, but his future wife suggested that he might as a medical missionary, and this he eventually did[2]

He landed at Durban in 1899 with his wife and two sm children, and his book gives an interesting picture of a med missionary's life up country He had to learn the Zu language and win the confidence of the natives, who w accustomed to the crude methods of their witch-doc He found that the more nauseous a medicine was, the more Zulu patients would believe in it and benefit from it, i then resembled most closely the magic remedies the wi doctor dispensed The appalling suffering and loss of l especially of mothers and young children, resulting from t natives' ignorance, and their exploitation by the crafty ignorant witch doctors, is graphically described

Later on, Dr and Mrs McCord moved back to Durban eventually—in the face of bitter opposition from some of ditions. (In many villages, for example, the surgery often far more suitable than the hired room in the ish hall which houses the clinic.) The main point to put the responsibility for child health where it ongs—with the family doctor.

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[1] London School [illegible] Bulletin no [illegible] November, 1[illegible] Planters & Miners by G[illegible] Ross Institute of Tropical Hygiene

[2] My Patients were Zulus By James B McCord M D, with J Scott Douglas London Frederick Muller 19[illegible] Pp 16[illegible]

Whickham,
ewcastle upon Tyne.

ANDREW SMITH.

SIR,—In 1944 the late Dr. Dalrymple Smith, of chmond, and I wrote a memorandum on the care of e child in the future health service which was almost ntical with the suggestions of Dr. George and his lleagues except that we carried the care back to e antenatal period. Since we wrote that, I have come convinced that such an association of general-practioner pædiatricians (or, as we called them, family actitioners) with a group of general practitioners would feasible only in the group practices of small market wns, where 4–8 practitioners cover the whole area. In ral areas and in densely populated urban areas (where ere seems little tendency toward the *spontaneous* rmation of group practices) I am sure that the general actitioner should become the family doctor and give th preventive and curative advice.

If we split up the life of "the whole man," the doctors tending him in the different phases will never learn how e care or lack of care of the infant and the child can fluence the future well-being of the adult. Faulty advice d unsuitable treatment may be perpetuated by the ilure to recognise its effects. Such a situation arises ready with regard to advice on infant feeding given by ersons who never see the baby after the first few weeks. ack of knowledge of the subsequent failures leads to mplacency and rule-of-thumb methods.

Another point that it would be well for us to remember that it is not the practitioner who treats the child, but he mother. I am sure that there are many doctors who re "interested in children," and give much thought to heir diagnoses, lines of treatment, and prognoses, but who fail utterly to gain the confidence of the mothers. This is usually because they give them orders, instead of nviting the mothers to observe the children for them. The best way of gaining the confidence of mothers is to know them well before and during the time their babies are born.

The best way to ensure happy and thoughtful parents for the next generation is to follow our present patients carefully from childhood through adolescence to manhood and womanhood.

York.

F. CHARLOTTE NAISH.

SIR,—I hope that Dr. Tabbush's suggestion that general-practitioner services should be split up on an age-group basis at a point halfway through childhood will not be seriously entertained. His justification of this attack on the "concept of the family doctor" appears to rest solely on the statement that in certain families different members of the family are looked after by different doctors already.

It would be a bad mistake to assume too lightly the inevitability of the defects of the past and present, and to make administrative arrangements which would ensure their perpetuation. The present division of responsibility for the health of children between general practitioners, child-welfare services, school medical services, and hospital outpatient departments is such a defect. This encroachment on the responsibility of the family doctor is to a large extent the result of the failure of the old National Health Insurance system to cater for dependants of bread-winners: many parents could not afford to pay private fees, and children therefore got no medical care unless ill enough to warrant a visit to an outpatient department or admission to hospital; and general practitioners thus lost much of the experience they would otherwise have gained in dealing with childhood ailments and problems. The child-welfare services grew up in an attempt partially to fill this void; but when in 1948 a universal medical service, available to all citizens of and visitors to this country was introduced, the opportunity arose of filling this void more satisfactorily from another direction. Since 1948 there has been no particular economic reason why children should not receive all the medical care they require from the family doctor; but habits change slowly.

It has been my experience, when working in a children's outpatient department in London, that we spend much of our time dealing with problems which need never have been the subject of a consultation if the family doctor had had the time, the inclination, and the opportunity to observe the symptom in its home environment. In these outpatient sessions we hear many of the criticisms of our colleagues in general practice to which your correspondent refers: but this is not a matter solely of the extent of these doctors' specialist knowledge of children's diseases. If a doctor has failed to give satisfactory service to a child, the same has usually applied to his dealings with adult members of the family: but we most of us tend to worry more about our dependants, and especially our children, than about ourselves; and a responsible parent who is thus dissatisfied will immediately seek whatever other help is available, whether in a welfare clinic or in a hospital outpatient department. But these are second choices; everybody's first choice would be a responsible doctor, proud of his job of looking after the whole family.

The attitude to medicine which sees nothing fundamentally wrong in the splitting up of general-practitioner services by age-groups will, if applied in other fields, lead directly to a service in which the general practitioner ceases to hold the major responsibility for the health of the family, and acts solely as an agency for a variety of narrow specialties; and to a state of affairs in which the patient only gets satisfactory service to the limited extent that he is a machine which develops remediable mechanical faults. Surely the ideal service is one in which the patient's contact with specialist branches of the profession is solely through a responsible family doctor by whom opinion is sought and to whom opinion is given, as has always been the case in the best private practice. Like all ideals this is not universally attainable, but it is none the less worth striving for. We shall not approach it by throwing it overboard.

All of us who work for children wish to do our best by them, but we must look carefully ahead; and I am sure that your correspondent has not seen the precipice over which he would lead a Gadarene herd.

In our maturing health service only the continuing personal service, which the family doctor alone can give, can protect the patient from what most of us regard as a characteristic evil of our time, but which is probably universal, and which was certainly sufficiently well recognised by critical observers of the first Elizabethan age for Shakespeare to describe it for all time as "the insolence of office."

The Hospital for Sick Children,
Great Ormond Street,
London, W.C.1.

DAVID LAWSON.

SKIN BANKS

SIR,—Prof. L. S. Penrose has recently drawn my attention to Mr. M. F. A. Woodruff's reply[1] to my letter.[2] Mr. Woodruff has raised some arguments which I must admit do seem to be cogent, suggesting that the number of independent skin antigens in man is unlikely to be as low as 20. Nevertheless I think it would be a pity if the criticism of my letter were to obscure the points that are uncontroversial. The general theoretical results could be applied to any homografting or homotransplanting work in animals or man. It is also worth noting

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[1] *Lancet*, 1952, ii, 779.
[2] *Ibid*, p. 289.

Simpson Smith Lecture

Sir Clement Price Thomas will deliver this lecture on Thursday, June 11, at the Medical Society of London, 11, Chandos Street, W 1, at 4 30 P M He is to speak on Benign Tumours of the Lung

Lasker Award in Cardiology

Dr Paul Dudley White, of Boston, Massachusetts, has been named by the Albert and Mary Lasker Foundation and the American Heart Association as the first winner of the annual Albert Lasker award "for distinguished achievement in the field of cardiovascular diseases"

N A P T. Prize

The prize of 100 guineas offered by the National Association for the Prevention of Tuberculosis for the best essay by a public health medical officer on Modern Measures for the Control of Tuberculosis as Practised by Local Health Authorities has been divided between Dr H D Chalke, a divisional medical officer of the London County Council, and Dr E R Hargreaves, deputy medical officer of health, Cornwall County Council

St Thomas's Hospital Musical Society

A performance of the Mass in C Minor by Mozart will be given in St Sepulchre Church, Holborn, on Tuesday, Feb 24, at 8 15 P M No tickets are required

Safety of Old People on the Roads

The Pedestrians' Association is holding a conference in London on this subject on March 7 The speakers will include Dr Trevor Howell, director of the geriatric unit of St John's Hospital, Battersea, and Dr C A Boucher, of the Ministry of Health Further particulars may be had from the secretary of the association, Mitre House, 44, Fleet Street, E C 4

We understand from Sir Heneage Ogilvie that his duties as praelector in the University of St Andrews during the present session will only necessitate one week's residence in Dundee and absence from London

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EMERGENCY BED SERVICE —In the week ended last Monday applications for general acute cases numbered 2065 The proportion admitted was 88 47% On Tuesday a red warning was superseded by a yellow warning

Sir Alexander Fleming, F R S, Mr H Osmond Clarke, and Prof R R Macintosh, are to be members of a W H O teaching mission which is to spend two months in India at the request of the Indian government The team of 15 doctors, led by Dr Samuel Z Levine, of New York, was to reach Madras on Feb 5

A Tribute to a Great Surgeon Gathorne Robert Girdlestone which first appeared last year (see *Lancet*, 1952, i, 1313) has been reissued in a second edition Copies (1s 3d each) may be had from the compiler, the Rev P Stewart Browning the Chaplain's Office, Pembury Hospital, Pembury, Kent

A fourth draft British standard for X ray protective gloves for medical diagnostic purposes (CO(ELE)8420) has been issued by the British Standards Institution Comments on this draft should be sent before March 10 to Mr H L Griffiths secretary of technical committee ELE/55, at the institution, 24, Victoria Street London, S W 1

Appointments

BOAS, BRUNO, M D Berlin asst ophthalmologist Ashton under Lyne General Hospital and Lancashire Cheshire and Derbyshire local authorities

COWAN JACK M B Edin, D M R D consultant radiologist Monsall and Booth Hall hospitals, Manchester

EDMUNDS, V E M D Lond, M R C P part time clinical asst cardiographic department Charing Cross Hospital London

MCFARLAND J C, M D Lpool F R C S E, D I H, D L O part time consultant otorhinolaryngologist, Southport Promenade Hospital

NASH F W, M D Lond, M R C P consultant pædiatrician St Tydfil's Hospital, Merthyr

TROUNSON N, M B whole time consultant pathologist, Coventry group of hospitals

North-East Metropolitan Regional Hospital Board.

BLADES, [illegible] [illegible]tist (consultant), St [illegible]

HAMER [illegible] [illegible]e surgeon (consult[illegible]

HUTTON, J N T M B Durh D [illegible] part time anæsthetist (consultant) St Leonard's and St Matthew's hospitals

McLAUGHLIN F F, L.R.C.S I, D O.M.S part time ophthalmic surgeon (consultant) Tilbury and Riverside hospitals

PEARCE H A, M B Lond F R C S part time surgeon (consultant) S E Essex group of hospitals

Diary of the Week

FEB 8 TO 14

Monday, 9th

INSTITUTE OF [illegible] Queen Square W C
5 P M Prof [illegible] Visual Agnosia
INSTITUTE OF [illegible] Denmark Hill S E
5 30 P M Dr E Stengel Lecture demonstration
MEDICAL SOCIETY OF LONDON, 11 Chandos Street, W 1
8 30 P M Dr W E Snell, Mr V C Thompson Recent Ad[illegible] in Treatment of Pulmonary Tuberculosis

Tuesday, 10th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S W 1
5 P M Dr W R S Doll Bronchial Carcinoma (First of [illegible] Milroy lectures)
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W C 2
5 P M Mr T E Cawthorne Surgery of the Temporal Bo[illegible] (Hunterian lecture)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street, W C 1) Miss Honor B Fell, F R S [illegible] Culture in Biological and Medical Research
ROYAL SOCIETY OF ME[illegible] W 1
5 30 P M *Section of* [illegible] C B McKerrow, Dr D V L[illegible] Assessment [illegible] Respiratory Function
8 P M *Section of Psychiatry* Prof E E Krapf Ageing
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street W C 2
5 30 P M Mr A K Monro, Hypostatic Eczema and Ulcer[illegible]
WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Mary[illegible] Lane W 1
5 30 P M Mr G C Knight Treatment of Head Injury
CHELSEA CLINICAL SOCIETY
8 30 P M (South Kensington Hotel, 41, Queen's Gate Ter[illegible] S W 7) Mr John Betjeman, Sir Heneage Ogilvie [illegible] Gilbert Harding The Importance of Leisure
MANCHESTER MEDICAL SOCIETY
5 P M (University of Manchester) *Section of Surgery* Mr E [illegible] Simmons *Cancer of the Rectum*

Wednesday, 11th

UNIVERSITY OF LONDON
5 P M (London Hospital Medical College, E 1) *Prof A* [illegible] (Paris) Factors of Abnormal Development
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Benign Tumours of the Corium
INSTITUTE OF UROLOGY, St Paul's Hospital Endell Street W C 2
5 P M Mr A R C Higham Enuresis
MANCHESTER MEDICAL SOCIETY
4 30 P M *Section of Pathology* Dr M C G Israëls The [illegible] *loses*
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW [illegible] St Vincent Street, Glasgow, C 2
5 P M Dr R R Willcox *Treponemal Diseases (John* [illegible] lecture)

Thursday, 12th

ROYAL COLLEGE OF PHYSICIANS
5 P M Dr Doll Bronchial Carcinoma (Second of two Mi[illegible] lectures)
ROYAL COLLEGE OF SURGEONS
5 P M Mr W Hynes Results of Pharyngoplasty by M[illegible] Transplantation in "Failed Cleft palate" Cases (Hunterian lecture)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Prof P C C Garnham Life Cycle of the Mal[illegible] Parasite
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children G[illegible] Ormond Street W C 1
5 P M Dr E M Creak Behaviour Problems in Early Childh[illegible]
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Diagnostic Techniques
ROYAL ARMY MEDICAL ([illegible] S W 1
5 P M Dr Raymond [illegible] Group of Fever[illegible]
ST GEORGE'S HOSPITAL [illegible] Hyde Park Co[illegible] S W 1
5 P M Sir F [illegible] [illegible]atry demonstration
ALFRED ADLE[illegible]
8 P M (11, [illegible] Dr M N Pai Indicatio[illegible] Hyp[illegible]
[illegible] TION 114, Mount Pleasant, Liverpool [illegible]ards Present Position of Surgery [illegible]ssels
[illegible] [illegible]mall's Wynd Dundee) Prof J [illegible] McLeod F R S Observations on Nature of Anaerobic Infections and their Control

Friday, 13th

ROYAL COLLEGE OF SURGEONS
4 P M Mr L E C Norbury The Hunterian Era—It Influ[illegible] on the Art and Science of Surgery (Hunterian Oration)
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Gordon Benign New Growths
ROYAL MEDICAL SO[illegible] 7 Melbourne Place, Edinburgh
8 P M Sir Cle[illegible] Thomas Carcinoma of the Lun[illegible]

Saturday, 14

SOUTH EAST ME[illegible] [illegible]EGIONAL TUBERCULOSIS SOCIETY
11 A M (Lon[illegible] Hygiene and Tropical Medicine)
Dr Neve[illegible] [illegible]onchitis

mined by the technique adopted by Gilmour[7] for parathyroid in man or that of Platt[2] in the dog. ed Stoeltzner[8] many years ago in his "adrenal ry" stated that disease of these glands was a cause steomalacia. At one time it was also said that in hypertrophy of these glands was observed in nic nephritis.[9]

arwick. A. H. HOGG.

TUBERCULOSIS MORTALITY

IR,—In your leading article on this subject (Jan. 24) have misrepresented a statement in my paper.[10] a say:

> "Russell states that previous investigations based on the ohort method of study have emphasised the dependence of ulmonary tuberculosis mortality in adult life on that xperienced by the same age group in childhood."

iat I actually wrote was:

> "The conclusion reached by previous cohort investigators s that the magnitude of the phthisis mortality in adult ife is shaped or determined to a greater extent by the onditions of life in childhood than by happenings in or bout the year of death."

As regards your later comment on the influence of ildhood environment on adult phthisis, I would say at according to the Kermack theory one would expect continuance into later life of the high positive correion shown to exist up to age 25. As will be seen in ble IV, the association disappears and the correlation th contemporary environmental conditions becomes finitely the more important.

Institute of Social Medicine, Oxford. W. T. RUSSELL.

PSYCHOSIS WITH ISONIAZID THERAPY

SIR,—I wish to report the following case.

A man, aged 26, and weighing 48 kg., was admitted to iad Hospital on Dec. 11, 1952, with bilateral caseo-pneuonic tuberculosis. He was given isoniazid ('Rimifon') in daily dosage of 6 mg. per kg. body-weight, with streptoycin 1 g. every other day. His condition improved greatly; s appetite was always good, though he complained of odominal pain, constipation, and drowsiness.

On Jan. 14, 1953, he developed mental symptoms. He as very irritable and had hallucinations and delusions. ometimes he cried and put his hand on his head, and later ll into a confused muttering and impulsive movements. xamination showed exaggeration of the tendon reflexes; he cerebrospinal fluid was normal. There were no skin, ral, or gastro-intestinal manifestations of pellagra, but ince it seems that isoniazid inhibits the action of nicotinic cid in the formation of co-enzymes necessary for cell etabolism, we decided to stop isoniazid and to give icotinamide.

Administration of nicotinamide was started on the same ay with 100 mg. intramuscularly and 50 mg. by mouth every hours. By the 3rd day the patient's condition had greatly mproved, and on the 4th day he was completely cured of his sychosis: he was quiet, and his reflexes were normal; his appetite was good, and he no longer complained of abdominal pain or constipation.

This case, together with that described by McConnell and Cheetham,[11] proves that isoniazid in a daily dosage of 6 mg. per kg. is not always without ill effects in an undernourished patient who is not given enough nicotinio acid to balance the action of isoniazid. Nicotinamide should be given in such cases to prevent the organic cerebral impairment described by Hunter.[12]

Riad Hospital, Riad,
Soadi-Arabia.

M. ZABAD.

THE ANKLE BLOW-OUT SYNDROME

SIR,—I also would like to congratulate Mr. Cockett and Mr. Elgan Jones on their excellent article of Jan. 3. It is outstanding as a contribution to the literature about leg ulcers because it consists mainly of factual observations. Mr. Krafft's letter (Jan. 24) is not so well founded on fact, but his opinions and theories have their value. Previous correspondence on this subject has shown that many agree with him that firm bandaging will allow an ulcer to heal, and I would like to ask Mr. Cockett whether he could record the pressure in the veins below, beneath, and above such a bandage, and thus supply Mr. Krafft with more facts on which to base his theories.

Alnmouth, Northumberland. G. L. LEATHART.

SIR,—It is extremely unfortunate that Mr. Krafft should have read in the paper by myself and Mr. Elgan Jones statements which are not there! We do not claim that an incompetent perforating vein or veins is the cause of every ulcer. Nor did we say anywhere that incompetence is always found only in the perforating veins in cases of post-thrombotic ulcer. Such a statement is obvious nonsense.

In drawing attention to this particular site of venous valvular incompetence it is important to realise that it may be, and often is, a part of a much more extensive incompetence in the leg. It may be associated with post-thrombotic valve destruction in the deep veins of the calf or of the whole length of the leg. The anatomical path by which clot in the calf veins may find its way into the perforating vein, and thus cause this particular local venous incompetence, was pointed out in the last part of our paper, and has been observed several times since. For this reason we would expect incompetence of the perforators to be a fairly constant result of deep vein thrombosis, and this we have in fact found. Now in these legs with extensive valvular destruction in the deep veins from ankle to groin, due to old femoral thrombosis, the ulcer is only one component of the post-thrombotic syndrome; the other two components are postural œdema, and postural pain and aching in the lower leg. Our experience of the results of deep-vein ligation (extending over about 20 cases to date) has been reasonably clear-cut. The aching in the leg is always relieved; the swelling is often improved, but is never made worse; the ulcer is seldom affected much. If the swelling is made worse by deep-vein ligation, then probably a competent vein has been tied in error. One of the great difficulties in this work so far has been the lack of a simple, easy technique for showing for certain whether valves are present and functioning in the femoral vein. This difficulty has been met by the introduction of the Valsalva technique of venography. (This technique is shortly to be described in the *British Journal of Radiology*.) Thus it was this notable failure of deep vein ligation to control ulcers which set us looking for a more local cause underneath them. Moreover, well over half of our ulcer cases show numerous competent valves in the femoral vein at venography. To argue that, in spite of the valves being there, they are perhaps not as competent as they should be seems to us to be begging the question.

Finally there are a small group of cases in which an incompetent perforating vein draining into a mass of dilated venules beneath the ulcer is the only venous lesion demonstrable in the limb. This was so in the case dissected and described in our paper; and we have had several fully investigated cases since then, which have been operated upon. To suggest that such a state of affairs can have little to do with the ulcer, and to base this solely on a complicated mechanistic theory of action of the calf pump, seems to us inadmissible. Mr. Krafft overlooks the vital point in the structure of the calf pump—namely, the fact that it is a large muscle within

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7. Gilmour, J. R. The Parathyroid Glands and Skeleton in Renal Disease. London, 1948.
8. Stoeltzner. *In* Special Pathology and Therapeutics of the Diseases of Domestic Animals. London, 1938; vol. 3, p. 191.
9. Goldzieher, M. A. The Adrenals. 1929.
10. *Med. Offr*, 1952, 88, 269.
11. McConnell, R. B., Cheetham, H. D. *Lancet*, 1952, ii, 959.
12. Hunter, R. A. *Ibid*, p. 960.

this theoretical principle In the first four days of salt depletion, his subjects lost weight in parallel with their loss of sodium, indicating that the osmotic pressure of body-fluids was being conserved at the expense of volume Later on, however, the body-weight fell only slowly, while the sodium-loss continued, so that the serum sodium fell In clinical salt depletion, the serum-sodium is usually low, indicating a rather advanced sodium depletion, we shall discuss later the bearing of this fact on therapeutic methods

Although the volume of extracellular fluid can be plausibly related to the osmotic activity of its sodium and associated anions, evidence has accumulated of serious deviations from osmotic equilibrium within the body Analysis of cell fluid shows a higher concentration of base than in the extracellular fluid, which led Peters (1947) to postulate the existence of " osmotically inactive base " within cells, Elkinton et al (1948) have accepted this concept, and brought forward evidence of discrepancy between shifts of cation and of water across the cell wall, suggesting that the proportion of cell base which is inactive may change from time to time A more radical approach is that of Robinson (1950, 1952), who discards osmotic determination of body-water distribution in favour of a continued active process of water extrusion from cells, which keeps the intracellular osmotic pressure consistently higher than that in the surrounding medium Robinson showed that tissue slices would remain in equilibrium with " isotonic " media only so long as their oxygen uptake was normal, when metabolism was depressed by cyanide or by oxygen-lack the cells took up water even from " hypertonic " solutions up to an osmolarity of 0 58 osmols per litre Similar active transport mechanisms are invoked by Ussing (1952) to explain the low sodium content of cells in a medium of high sodium content such as extra cellular fluid The active expulsion of sodium ions sets up a potential difference across the cell wall, and the high potassium content of cells can be attributed to a passive flow down an electrochemical potential gradient Terner, Eggleston, and Krebs (1950) have shown that brain tissue maintains its potassium content in a saline medium containing oxygen, glucose, and L glutamate, if any of these is missing from the medium, potassium leaves the cells, returning when the missing item of substrate is restored The lower sodium and higher potassium content of fœtal, as compared to maternal, erythrocytes in the sheep, has been related to the more rapid glycolysis and greater oxygen consumption of the fœtal erythrocyte (Hallman and Karvonen 1949) These examples may illustrate a tendency to explain apparent anomalies of body-fluid distribution and composition in terms of active processes, dependent on the energy of tissue oxidation, rather than in terms of classical physiochemical equilibria The final balance between these modes of thought has certainly not yet been struck As William James says in another context, the sciences " habitually advance by zig-zagging from one absolute formula to another which corrects it by going too far the other way "

Regulation of Body-fluid Tonicity and Volume

Although the composition of body-fluid is both complex and variable from one phase to another, it is possible to find evidence of a control of the general parameters of body-fluid which transcends the detailed operations on separate ions and molecules There is a suggestion from McCance's experiments that osmotic tonicity is more jealously guarded than the volume of body-fluid, and this is borne out when we consider the characters of the regulatory processes which normally govern body fluid It is a fair generalisation that the body reacts quickly to stimuli which modify the tonicity of body-fluids, but more slowly to those which modify volume without change in tonicity, this is perhaps best shown by the very different response of a normally hydrated subject to water and to 0 9% salt solution An increase in body-fluid tonicity stimulates both thirst (Wolf 1950) and the output of posterior-pituitary antidiuretic hormone (A D H) (Verney 1947), a decrease in tonicity inhibits thirst and A D H output Both responses are rapid, and the excess water load is eliminated, or the deficit made good, within an hour or two Neither response, at least in man, need involve any change in the solute content of the body This close and rapid regulation of osmotic tonicity implies that changes in the volume of body-fluid shall be attended by corresponding changes in the total solutes of the body, except in so far as intracellular solutes may gain or lose osmotic effect or have their osmotic action overborne by change in intensity of active shifts of electrolytes and water For the present, we may be justified in accepting changes in sodium balance as representing changes in osmotically active solute If we do this, we gain the impression that control of the volume of body-fluid is much less close and rapid than that of body tonicity For one thing, expansion of the volume of body-fluid by saline provokes only a slow and incomplete diuretic response, unless the subject has been preconditioned by a water load, in which event he has a water rather than a saline diuresis (Ladd 1950) Moreover, on a diet of constant sodium content, and with minimal sweating, the sodium balance shows quite wide fluctuations, the equivalent of as much as a litre of body-fluid (Black and Thomson 1951) If one can assess the sensitivity of a regulating mechanism in terms of permitted percentage variation in the quantity regulated, it would appear that the regulation of tonicity, at least by the A D H mechanism, is considerably more sensitive than the regulation of extracellular fluid volume, the phase of body fluid most directly related to the sodium balance The A D H mechanism is sensitive to a change of about 1% in the tonicity of the blood supplying the hypothalamus (Verney 1948), whereas variations of the order of 6% of extracellular fluid or 2% of body-fluid, are accepted, without immediate response, by the mechanism regulating volume

It may not be altogether a coincidence that we know a good deal of the regulation of tonicity, whereas that of volume largely eludes us A rapidly acting mechanism can be studied by short critical experiments, whereas a slowly acting mechanism, especially if it is bedevilled by diurnal variation (Stanbury and Thomson 1951), yields its secrets more reluctantly, and with greater chance of random error I do not know if this is a valid reason, or merely an excuse, for the collective failure of natrophiles to expose a mechanism of regulation comparable in elegance to the A D H mechanism, it may be that we still await our Verney The essence of the problem clearly lies in the regulation of output of sodium and potassium in the urine, for there is no evidence of any intake regulation of these ions comparable to the thirst mechanism for water I have lately reviewed the factors which determine sodium excretion (Black 1952), and shall now merely reiterate the conclusions that variation either in glomerular or in tubular activity may be critical under different conditions, and that the body possesses efficient mechanisms of sodium conservation, which is mainly effected by enhanced tubular reabsorption of sodium We do not clearly know what change in body fluid composition or distribution triggers off this mechanism, nor indeed anything of the way in which the message reaches the tubule cell Adrenal hormones are known to increase sodium reabsorption in the renal tubule, but definite evidence of their participation in the normal response to a low salt diet is still lacking The regulation of potassium excretion has been reviewed in some detail by Berliner (1950), here again we are far from understanding the mechanisms involved On a

TMENT OF PNEUMOCOCCAL MENINGITIS

—I have read with interest the article by Dr. and Dr. James.[1] Excluding 3 deaths within y-four hours of the start of treatment, they have ed a recovery-rate of 100%.

experience in Nyasaland has been very different.

e April, 1951, I have had 10 cases of pneumococcal gitis under my care; 6 were in children between d twelve years of age, the remainder being in adults. had only 2 recoveries, 1 a child and 1 an adult. ent consisted in a daily intrathecal injection of units of penicillin with 100,000 units intramuscularly rly. This was supplemented with 'Sulphatriad' or diazine 1 g. four-hourly after an initial loading dose. ese patients had been ill for three or four days before g to hospital. They usually improved at first; but a week the theca became blocked, and in 2 cases llin was administered by cisternal puncture with no vement.

ave tried intrathecal streptomycin and oral chlor-enicol with no better results. Up to date I have no means of improving on our 80% mortality-rate. r as I am aware, most doctors in Central Africa had similar experience; and Dr. E. R. Cullinan, recently visited Nyasaland, informed me that he gained the same impression in other parts of Africa g his tour as Nuffield visitor.

ave never given penicillin in as large a daily dosage 1,600,000 units used by Dr. Gibson and Dr. James. ld not like to increase the intrathecal dose, as even 50,000 units convulsions have occurred.

rican Hospital,
ba, Nyasaland.

J. W. D. GOODALL.

SEARCH FOR SICKLE-CELL TRAIT

s,—I read with great interest the article by Dreyfuss and his colleagues[2] on the search for sickle-rait in Yemenite Jews.

few months ago I had the same difficulties that these stigators describe. Using the moist stasis method criver and Waugh[3] I investigated more than 200 nesian patients (taken at random from the General ral Hospital at Djakarta). Of the 216 patients nined in this way, 2 were found positive for sickling he blood. Moreover, a private patient of mine with ominal crisis was also found positive.

ssuming that the method of Scriver and Waugh was ific and that a positive result indicated a sickle-trait or sickle-cell anæmia, I believed that I had d the sickle-cell trait in Indonesians. However, her examinations of the blood of the same patients e inconsistent results. Sometimes I obtained positive lts and at other times negative results in the same ients. I have since found more positive tests for ling with the same lack of consistency.

s a routine all the slides to be used were cleaned in romate/sulphuric-acid mixture for two days, then washed unning water. They were then placed in distilled water twenty-four hours and finally transferred to absolute hol, where they remained until use.

n one occasion I used a batch of slides which had been ated as described above except for the cleaning with omic acid. This batch of slides gave many positive results h blood of different patients taken at random from the spital. However, using another batch of slides these ne patients gave negative results. I collected the slides ich gave positive tests and examined my own blood on m. As a control, slides which had given negative results h the blood of the same patients were also tested with blood. All the slides which gave positive tests with the ferent patients' blood gave also positive tests with my od, and all the negative ones gave a negative result. the test-tube method of Beck and Hertz[4] my blood and that of these patients did not show sickling. Addition of ascorbic acid (2% or 5%) or bisulphite (2%) to the blood under liquid paraffin did not give sickling. Using the other sides of the slides with a positive preparation I could get the blood of all my laboratory workers to sickle. I concluded that something on the slide (a chemical substance?) caused the sickling. Sometimes the whole preparation showed a full development of the abnormal cells, but very often the sickling appeared in localised areas. The sickling usually appeared after twenty-four hours (sometimes earlier or later) but never immediately as in the test with glue.[5] It was further found that incubation was not necessary, and a positive result could also be found without sealing the preparation and without preliminary stasis of the blood.

If a slide with positive test is washed not too vigorously with water, the same slide can again give a positive test with any blood; but after vigorous washing and brushing the test becomes negative. Moreover, washing in bichromate solution did not assure that a slide would not give an erratic result.

I am of the opinion that the method of Scriver and Waugh, without control, should not be used as a routine test; for it is very difficult to be sure that a slide is entirely free from the sickling substance, which (even in traces) causes sickling of the blood of any person.

When I read the article by Caminopetros[6] on sickle-cell anomaly as a sign of Mediterranean anæmia, I suspected that the factor described above caused the sickling in most of his tests, though perhaps not in all. If so, the difference between the findings of Dr. Caminopetros and those of Dr. Choremis[7] on the sickle-cell trait in Athens can easily be understood. The same suspicion arose when I read the article by Dr. Dreyfuss and his colleagues.

A more detailed description of my investigation will be published later.

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LIE-INJO LUAN ENG.

DEATH AFTER ANÆSTHETIC WITH HYPOTENSION

SIR,—Dr. Bodman's example of modern anæsthesia (Nov. 29) and Dr. Belfrage's comment (Dec. 13) suggest this question: How many such patients would be alive and well today had they had chloroform on a bit of lint? In the old rag-and-bottle days did we really kill as many as now succumb to "advances" in anæsthesia?

I have spent twenty-five years in the tropics, in Africa and on ships, where chloroform, given by an untrained nurse or dispenser, is the only general anæsthetic available; and well it serves us. Yet, I am told, there are persons with the D.A. who have never given it in their lives.

And another thing; what was the cost of all this, compared with that of a few drachms of chloroform?

G. L. ALEXANDER.

CARTRIDGE-TYPE HYPODERMIC SYRINGE

SIR,—The introduction of the cartridge-type hypodermic syringe is an obvious sequel to the use of a similar instrument in dental surgery for many years.

The method is hardly suitable for intravenous injection as the plunger cannot be deliberately withdrawn. The accidental "recoil" of the plunger following injection is well illustrated by the simple test of injecting a small amount into a bottle of ink. The quantity of ink which flows up the needle and enters the phial on the release of the plunger has to be seen to be believed.

Attention has already been drawn to this drawback in *dental journals*, for it is obvious that cross-infection could easily result if a cartridge left over from a half dose were used on a second patient.

Gibson, C. D., James, D. G. *Lancet*, 1952, ii, 1203.
Dreyfuss, F., Ikin, E. W., Lehmann, H., Mourant, A. E. *Ibid*, p. 1010.
Scriver, J. B., Waugh, T. R. *Canad. med. Ass. J.* 1930, 23, 375.
Beck, J. S. P., Hertz, C. S. *Amer. J. clin. Path.* 1935, 5, 325.

[5] Isaacs, R. *Science*, 1950, 112, 716.
[6] Caminopetros, J. *Lancet*, 1952, i, 687. See also *Ibid*, pp. 1068, 1212.
[7] Choremis, C. *Ibid*, p. 1069; *Ibid*, ii, 42.

sodium loss is limited by increased renal formation of ammonia (Gamble et al 1923) In renal disease and in Addison's disease (Jimenez-Diaz 1936), ammonia formation is impaired and acidosis may then lead to continued loss of sodium Sodium excretion may also be increased deliberately by mercurial diuretics, and this may on occasion lead to a "low salt syndrome" even in the presence of œdema (Schroeder 1949)

Abnormal Physiology

We have seen that sodium, with its associated anions, is the osmotic mainstay of extracellular fluid, and shrinkage of the extracellular fluid can account for the most significant features of sodium depletion It is true that in severe sodium depletion the osmotic standard is relaxed somewhat, permitting a fall in the serum-sodium concentration, and this may account for some clinical manifestations such as cramp and lowered intestinal motility (Streeten 1950) It is also true that the impact of sodium depletion on the extracellular fluid phase could be modified by contributions of sodium from inside the cells and from bone, but I know of no studies showing that these collections of sodium can in fact function as sodium reserves, and at present we may justifiably look on sodium depletion as exerting its main effects by reducing extracellular fluid volume Both plasma and tissue fluid are diminished in amount Hypovolæmia with reduced cardiac output leads to inadequate circulation, reflex vasoconstriction may maintain the central blood-pressure for a time, but in severe sodium depletion the blood pressure falls The vasoconstriction varies in different circulatory areas, so that cerebral blood flow is well maintained, but the splanchnic and renal blood flow are reduced to an even greater extent than the cardiac output Glomerular filtration is reduced, and nitrogen retention follows The urine usually contains only traces of sodium and chloride, not only is the amount of sodium presented to the tubules lowered with the filtration rate, but the tubules reabsorb sodium more completely The depletion of tissue fluid is clinically obvious, but we know little of its effects on function, by modifying the internal environment unfavourably, it may contribute to the increased "wear and tear" of protein which was shown in McCance's experiment by increased urea production This is speculation, and other causes for increased protein breakdown are just as likely —for example increased glucocorticoid production in response to stress, and dilution of intracellular fluid pari passu with the fall in plasma sodium which commonly attends sodium depletion

Clinical Features

The various manifestations of sodium depletion cannot be forced into a single clear-cut clinical syndrome, for they are profoundly modified not only by the primary disease but also by the concurrent state of water and acid-base balance and by the rapidity of onset and the magnitude of the sodium depletion At the cost of some violence to the facts—perhaps no greater than is commonly offered in the separation of "disease entities" from the continuum of human morbidity—we may distinguish the syndromes of acute sodium depletion, chronic mild sodium depletion, and chronic severe sodium depletion

Acute sodium depletion arises when non saline fluids are used to replace rapid losses of saline fluids, such as sweat or the exudate from burnt areas It is seen when severe exertion is undertaken in the tropics, or in comparable artificial environments Severe cramp is the outstanding symptom, and can be alleviated by ingestion or injection of salt Under tropical conditions I have seen a "salt frost" on the skin but the absolute loss of sodium in a few hours cannot equal the large losses of sodium sustained by patients with vomiting and diarrhœa, who often are free from cramp It is well recognised clinically that high water intake potentiates the symptoms of acute sodium depletion, and it probably does so by entering the cells to produce a mild degree of water intoxication (Rowntree 1922)

Chronic mild sodium depletion, as judged by moderately lowered serum sodium levels in the absence of clinical dehydration, is found in sufferers from "heat exhaustion" and from chronic wasting disease, notably tuberculosis Ladell et al (1944) described a syndrome observed towards the end of the hot season in the Persian Gulf, in which the patients suffered from loss of appetite and energy, and had low serum sodium levels, but there was no clinical dehydration, and no signs of acute sodium depletion such as cramps and vomiting They designated this syndrome "heat exhaustion, type II," in contrast to the other type of heat exhaustion observed by them in which the patients were obviously dehydrated Both syndromes improved when salt supplements were added to the diet Although low serum sodium levels have likewise been noted in chronic illness, there is no similar evidence that the low serum sodium is directly responsible for symptoms Sims et al (1950) suggest that the primary change may be a fall in intracellular osmolarity, and that the fall in serum sodium represents an accommodation to this There is no shrinkage of extracellular fluid volume, and no retention of sodium by the kidneys, addition of salt to the diet has little effect on the serum sodium level or general clinical state

Chronic severe sodium depletion is what is generally referred to, not altogether happily, as "dehydration" The term dehydration can be criticised on the grounds of ambiguity, and because it emphasises *water* depletion whereas clinical dehydration is most commonly related to primary sodium depletion, the loss of water being secondary to this Our clinical judgment of the hydration of the body is based largely on inspection and palpation of the subcutaneous tissue, whose fullness and elasticity depend on its content of extracellular fluid A primary water depletion is spread over both intracellular and extracellular fluid, whereas sodium depletion has its impact on the extracellular fluid alone, the impression of dehydration from a given degree of sodium depletion will thus be greater than that from a comparable depletion of water itself In spite of these semantic objections, the term "dehydration" does convey a familiar clinical picture, which I maintain is that of severe sodium depletion Its features have often been described, and are well recognised I do not propose to conduct you once again over this well trodden road, but rather to bring forward evidence that the magnitude of the sodium depletion which underlies clinical dehydration has often been underestimated, and in consequence sodium replacement has been inadequate I shall first consider the methods at our disposal for assessing sodium depletion

Assessment of Sodium Depletion

We may distinguish between prospective and retrospective methods of assessing the depletion of sodium, or indeed of other bodily constituents The prospective method, in which we measure the negative balance of sodium as it accumulates, is obviously only applicable in experimental studies, in which we can assume a normal initial sodium household, and can observe the induced distortion from its beginning The errors of this method are limited to those inherent in balance technique Retrospective assessment of depletion involves the measurement of the positive balance of sodium, or other substance, which accomplishes repair of the depletion The validity of this method depends on the assumption that a normal state has in fact been reached at the conclusion of the observations, an assumption which may not hold where repair of a depletion has been accelerated by giving supplements of the defective material For ologist to investigate the biology of the tsetse fly *na palpalis*. He was able to do both and to show ne disease occurred in villages that were close to the of woodland in which the insect bred: but if there n area of grass and reeds without bush between llage and the Lake, then sleeping sickness would be even though the odd fly could be found among the . He was never idle: in his spare time he made s of Central African butterflies, and on insects which dible or not, as tested on pet monkeys. In between and in the latter part of his life he became an nely skilled gardener."

e Carpenter married in 1919 Amy Frances, youngest ter of J. F. Thomas-Peter. There were no children.

Mr. S. A. COURTAULD

Courtauld's death on Jan. 28 brings to mind his benefactions to research and education, especially gh the Middlesex Hospital.

interest in this work was aroused by his association he late Dr. Campbell Thompson, who was dean of the al school during the 1914–18 war. Campbell Thompson cceeded by Mr. A. E. Webb-Johnson, now Lord Webb-on, who early recognised that the future of the London al schools lay in their association with the University ndon, and was therefore at great pains to obtain endows for university chairs in the key subjects. One of ourtauld's first benefactions was to endow the chair of my, after which he gave a sum of money to encourage ewly founded department of biochemistry, then housed e Bland-Sutton Institute of Pathology. In the early biochemistry was expanding very rapidly, and the of the Middlesex Hospital Medical School saw that ew department could not permanently be housed in the l-Sutton Institute. Mr. Courtauld provided a further antial sum of money to erect the Institute of Biochemistry, in June, 1928, the institute that bears his name was ed.

is building, composed of five floors, provided the n-needed space for extension of the department. Many e time thought it far too big to be associated with a ital, and fears were expressed as to whether its accomation would ever be put to full use. But today it is ded and indeed has recently been considerably extended hat the equivalent of practically another floor has been d. The accommodation is still inadequate for the large ber of research-workers already in the institute and also ying for admission.

r. Courtauld's benefactions did not finish here. He owed a chair of biochemistry and before the war gave a of money to provide beds for a special unit for clinical arch. These beds were governed by quite novel regulas in that they could be controlled by one of the medical ol professors in conjunction with members of the honorary f.

o the outsider Mr. Courtauld appeared rather a distant re who made his benefactions in a somewhat impersonal nner. His main motive, however, was a desire to apply great wealth to the right causes. He thought a great l before giving money, and took the advice of his friends, ticularly that of Lord Webb-Johnson; but once having de up his mind, he would support a project of his choosing the utmost of his ability. He was a classical scholar of lliance, having published a translation of the *Odes of race* which went into several editions, and he was a mber of the Horatian Society. He also had an encyclodic knowledge of 18th-century literature.

Dr. **Clifford Beale**, consulting physician to the London est Hospital, died at his home in London on Jan. 31 the age of 101. At the end of the last century he was e of the earliest supporters in this country of the en-air treatment of tuberculosis. He was elected the fellowship of the Royal College of Physicians of ondon in 1890, and he was the senior fellow.

Births, Marriages, and Deaths

BIRTHS

AVIES.—On Jan. 22, to Dr. Winifred M. Davies (née Haigh), wife of Dr. D. M. Davies of Meadehurst, Glebelands Road, Prestwich —a son.

Notes and News

"DUAL APPOINTMENTS"

At present those doctors (such as chest physicians and psychiatrists) who are employed full time but divide their work between a hospital and a local health authority are appointed on a part-time basis to the staff of both authorities. This arrangement has not worked well in practice, and the Ministry of Health in agreement with the County Councils' Association, the Association of Municipal Corporations, the London County Council, and the British Medical Association has now suggested a different procedure.[1] Where the two jobs together make up a full-time job the Ministry proposes that instead of being employed by the two authorities the doctor should receive a full-time salary from the authority which makes the greater use of his services. The authority that pays him would then arrange to provide the other authority with certain services. In the agreement between the authorities the doctor who would carry out these services need not be named. This arrangement between the two authorities would not affect the pay of the doctor concerned.

After Feb. 6 all new appointments to these dual posts will be made on this basis. The contracts of doctors engaged on a provisional basis while these negotiations were pending should be adjusted to conform by May 1, 1953, or at the expiry of any agreed period of notice. Where the new arrangement is more favourable to the doctor the adjustment should be retrospective to the beginning of his provisional appointment. Doctors who hold appointments of this kind on a permanent basis may choose whether they will continue with their present contracts or change to the new arrangement. A committee has been set up, consisting of representatives of the B.M.A. and the employing authorities, to which doctors and employing authorities can turn for advice. It may be addressed at the Ministry of Health, Savile Row, London, W.1

A FUND FOR POLIOMYELITIS RESEARCH

Since it was founded in 1939 the Infantile Paralysis Fellowship has done much to help its 8000 disabled members. During the difficult war years the fellowship wisely restricted its work to the welfare of those who had been crippled by the disease; but it has always wished also to share in the work of prevention, and last year it felt the time had come to extend its interests. After discussions with the Ministry of Health, the Royal College of Physicians of London, and the Royal College of Surgeons of England it was decided to set up a separate body, the National Fund for Poliomyelitis Research. This body was officially inaugurated by the Lord Mayor at a meeting at the Mansion House on Dec. 17. Its vice-presidents include Sir Russell Brain, P.R.C.P., Lord Horder, F.R.C.P., and Sir Cecil Wakeley, P.R.C.S.; and Dr. Reginald Bennett, M.P., Mr. Somerville Hastings, M.S., M.P., Prof. J. M. Mackintosh, F.R.C.P., Dr. Barnett Stross, M.P., Prof. J. Trueta, M.D., and Lord Webb-Johnson, F.R.C.S., are members of the council. The aims of the fund are "to promote and finance research into the causes, cure, prevention and treatment of poliomyelitis; and research into the methods of rehabilitation of those disabled from polio." It is emphasised that the fund will only spend money at the advice of the medical profession. Donations will not be unwelcome, but anyone who sends a minimum annual subscription of a guinea will become an associate of the fund and receive reports of its work. The fund's secretary is Mr. Duncan Guthrie, 41, Spenser Street, London, S.W.1.

MEDICAL ARRANGEMENTS FOR U.S. SERVICE PERSONNEL IN ENGLAND

The U.S. Service authorities in Britain have issued the following information for the guidance of doctors attending American military personnel or their dependants.

There are four U.S. Air Force hospitals in England: (1) the 59th Medical Group, Burtonwood, near Warrington, Lancs, serving the Liverpool region (tel. Warrington 3000, ext. 1070, 1060); (2) the 5th Hospital Group Burderop Park, near Swindon, Wilts, serving the Oxford area (tel. Wroughton 391); (3) the 3rd Hospital Group, Wimpole Park, near Royston, Cambridge, serving the East Anglia area (tel. Arrington 381); and (4) the 494th Medical Group, South Ruislip, Middx, serving the London area (tel. Waxlow 4300, ext. 112, 113, 114). Each of these hospitals has the follow-these fluids in a few days are not uncommon in severe diarrhœa, paralytic ileus, and postgastrectomy duodenal fistulæ. Coller et al. (1938) measured the loss of "salt" in various patients with lesions of the upper gastro-intestinal tract. In one patient the measured loss amounted to 79.8 g., representing 1360 m.eq. If in fact it was chloride which was measured, this would be an overestimate of the sodium loss, but the article does not indicate that this was so. Similar losses of sodium can occur in patients with watery diarrhœa, in one patient with steatorrhœa the fæcal loss of sodium over twelve days amounted to 1127 m.eq. Evidence of the large size of sodium deficit can also be gained from the amount of sodium which can be given in repair of the deficit. I have already quoted a man who received 1400 m.eq. of sodium by infusion without becoming clinically or biochemically "over salted." Another patient with protracted vomiting was given 1700 m.eq. of sodium in a single infusion, without ill effect, and with a fall in his blood-urea from 152 mg. per 100 ml. to 38 mg.

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[1] Ministry of Health Circular 3 53, R.H.B.(53)11, B.G.(53)12, H.M.C.(53)10.

An indirect estimate of the sodium deficit can also be gained from the serum sodium level, and this is of special practical value in that it can be made before treatment is begun. I would remind you that in experimental sodium depletion the level of serum-sodium is conserved for a time, and then falls when the sodium deficit becomes considerable. This fall in serum-sodium is attended by the entry of water into the cells, as was demonstrated in the animal experiments of Darrow and Yannett (1935). It might be supposed that, since sodium in the body is largely confined to the extracellular fluid, the sodium deficit could be arrived at by multiplying the fall in serum-sodium by the extracellular fluid volume. In fact, however, we must use the total body-water in our estimate, and not the E.C.F. volume, the shift of water into cells maintains the E.C.F. sodium concentration at a level which does not directly reflect the loss of sodium from E.C.F. For example, a patient who has lost half his E.C.F. sodium might be expected to have a fall in serum sodium of 70 m.eq. per litre, but the observed fall in serum-sodium is only about a third of this, since there is about twice as much intracellular as extracellular fluid. This can be expressed in another way, perhaps more directly relevant to treatment, by saying that the effective volume of distribution of injected sodium approximates the total body-water rather than the extracellular fluid. In support of this contention, I have calculated the "volume of distribution" of sodium injected as hypertonic saline, using some of our own results (Black, Platt, and Stanbury 1950), and additional data provided by Dr. S. Oleesky (personal communication). When the total amount of injected sodium is divided by the observed rise in serum-sodium, we have the effective volume of distribution of sodium. In 11 subjects, this averaged 54.7 litres, with 99% confidence limits of 33.6–75.8 litres. This is not of course a practical method of measuring total body water, for the error of the difference between two serum sodium levels is high, but my point is that the average figure approximates the total body-water, and is significantly different from any possible value for extracellular fluid volume.

Entry of water into the cells is not the only factor which keeps the serum-sodium at a higher level than would correspond exactly to the sodium deficit, there is also the loss of water which inevitably attends the depletion of sodium. This is very variable from one patient to another, for although sodium is usually lost in isotonic solution, the amount of water which the patient is willing or able to drink varies. The concurrent water loss will tend to minimise the fall in serum sodium, which therefore gives a conservative estimate of the sodium deficit. In the extreme case the serum-sodium may be within normal limits, or even raised, as reported by Allott (1939), by Borst (1938), and more recently by Higgins et al. (1951). The conjunction of raised serum sodium and low sodium output is often associated with brain disease or injury, in which water intake is prevented, it is distinctly unusual in the severe sodium depletion which we are discussing. When present, it is not a contra-indication to saline therapy, if the history clearly indicates salt loss, and the patient is dehydrated. Conversely, a low serum-sodium should never be the sole indication for saline therapy, we have already mentioned the hyponatræmia of chronic disease, which is not associated with overt salt loss or dehydration, and does not respond to saline therapy, nor indeed require it.

When the clinical evidence of sodium depletion is secure, the serum sodium can be used to assess the sodium deficit, it tends on the whole to underestimate it, because of concurrent water loss. The observed serum sodium in m.eq. per litre is subtracted from 140 to give the "serum sodium deficit," which gives the amount of sodium deficit per litre of body-water. The average value of 40 litres for total body-water can be used to calculate the total deficit in milli-equivalents. This is then divided by 140 to give the number of litres of isotonic solution needed to repair the deficit. If [Na] is the serum sodium level the isotonic fluid needed is given by

$$\frac{(140-[\mathrm{Na}])\times 40}{140}.$$

Even this simple formula is too precise, and it is sufficient to take a third of the "serum-sodium deficit" as our measure of the requirement of isotonic sodium solution in litres. No one who has noted the successive approximations by which this figure is derived will be tempted to regard it as other than a crude measure of the saline requirement, but even as such it has proved itself in my experience to be of some value. For reasons which I have given, it underestimates the saline requirement, and at the completion of infusion the serum sodium is usually at the lower limit of normal. Although the amount of saline prescribed in this way may be large, I have not seen any evidence of salt overloading when this formula has been used. Others have advocated the serum chloride level or the specific gravity of the plasma as guides to infusion, but the serum-chloride level is invalidated, as a measure of sodium depletion, by acid-base disturbances, and the plasma protein level may be quite misleading in debilitated patients (Abbott 1946).

It should be noted that any such assessment can give us information only on the sodium deficit, in addition to making up the deficit, we must repair continuing losses of salt as they occur, and also cover the patient's maintenance requirement of water. When possible, the best way of dealing with continuing losses of saline fluid is to return it to the patient by stomach tube, as is done in the Hammersmith régime for anuria (Bull, Joekes, and Lowe 1949), and as can sometimes be done with the secretion from fistulæ. When the fluid cannot be returned in this way, because of its nature (e.g., watery stools) or because of alimentary dysfunction (ileus or obstruction), a fluid of similar composition and amount should be given parenterally. When the fluid loss is small, and the kidneys are healthy and well supplied with blood, volume-for-volume replacement with normal saline may be adequate. When large amounts of fluid are involved, better results are obtained by using a replacement fluid with an acidifying or alkalinising effect similar to that of the fluid lost. Short of the perfectionism of analysing the fluid, and providing a tailor-made substitute, this can be done by giving a proportion of lactate, or of ammonium chloride, in the infusion fluid. Cooke and Crowley (1952) have made a useful practical approach to this problem by devising solutions suitable for replacing ng white citizens—established the McCord Zulu Hospital, e natives were given good medical treatment, and where girls were trained as nurses. The necessity for training s in medicine, so that they might return to their own smen and help to break down the prejudice against the tific prevention and treatment of disease, led to another acted struggle with diehards among the whites; but tually, shortly before the second world war, the training ılus as medical aides who could work under the supern of white government doctors was begun.

ie book contains several colourful case-reports, including of a lithopædion and one of ruptured urethra. Dr. McCord especially interested in surgery and midwifery, and one surmise that he had considerable ability, and profited by vast experience. When he retired in 1940 at the age of nty, he left Natal and the Zulus permanently indebted to orty years of service. Throughout the book his religious fs are nowhere stated, but their effect is abundantly ent in the usefulness of his career.

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versity of Oxford

n Jan. 22 the degree of D.M. was conferred on F. J. Flint Thomas Stapleton.

versity of Cambridge

n Jan. 24 the following degrees were conferred:

.D.—K. B. Dickson, A. C. C. Hughes, D. G. James, T. A. np, P. F. Lucas.

.B., B.Chir.—G. L. S. Rankin.

iversity of London

r. F. E. Bruce, M.SC.(ENG.) Lond., S.M. Harvard, has been ointed to the university readership in public health ineering at the Imperial College of Science and Technology.

yal College of Physicians of London

At a comitia of the college held on Jan. 29, with Sir Russell in, the president, in the chair, Dr. R. S. Stacey was ointed examiner in pharmacology, and Dr. D. Hunter d Dr. C. A. Keele members of the Joint Formulary Comttee. Dr. D. A. Long was appointed Milroy lecturer for 54.

The following having satisfied the censors' board were cted to the membership:

E. D. Acheson, B.M. Oxfd, Katharine M. S. Ainley-Walker, I. Oxfd, J. F. T. Allison, B.M. Oxfd, T. H. Barrie, M.B. Lond., N. Beck, M.D. Belf., Bryan Bevan, B.M. Oxfd, major R.A.M.C., mir Kumar Biswas, M.B. Calcutta, Joyce B. Burke, M.D. Lond., H. Capel, M.B. Lond., J. M. Cliff, M.B. Camb., surgeon lieutenant ., J. D. De Jong, M.D. McGill, J. E. Forster, M.B. Camb., Michael arington, M.B. Camb., E. W. Hughes, M.D. Lond., A. F. Knyvett, B. Queensland, R. C. Lewis, M.B. Lond., C. J. Lucas, M.B. Lond.

Licences to practise were conferred upon the following ho have passed the final examination of the conjoint board:

B. L. Anderson, L. P. Balfour-Lynn, R. H. Bartley, Yvonne G. eeching, Mary A. M. Beeney, F. A. F. Biddle, A. R. Bellen, M. S. Boyd, Margaret H. Bradshaw, Joan T. Bruce, Jessie A. S. D. urns, A. G. N. Calder, R. Y. Calne, H. T. Chadwick, H. W. V. harlton, Norman Crook, Agnes M. S. Curry, Sylvia J. Darke, P. H. ennison, P. G. Dunbar, W. A. Elkin, Helen R. Ellis, J. E. Evans, L. Evans, Sheila M. Forbes, R. F. Fouche, N. B. Gillison, H. R. ompertz, R. M. H. Gompertz, A. H. Gretton, M. C. Guard, ureen E. Hall, A. G. Harrison, M. D. Heyman, M. D. Hickman, E. C. ., R. J. Hutchinson, Shirley M. Inman, E. M. M. Jackson- J. A. Jemson, D. C. Jenkins, J. K. Johnson, C. G. Keith, vrence, R. E. Lovelace, K. G. Lupprian, Irene M. McAndrew, A. McClelland, H. G. McDonald, J. A. McHardy, W. M. IcIsaac, E. N. McKenzie, M. C. G. Mantell, John Marryat, Gillian G. latthews, L. J. Miller, Margaret E. C. Mitchell, G. L. Money, B. Moorhead, K. E. Murray, F. G. M. G. Myer, J. S. Norell, J. Parry, N. E. Pitts, M. F. Porter, J. F. Pritchard, Donald Ricketts, W. H. Rout, J. A. Rozario, K. E. Schmidt, Rita W. hannon, C. S. Sheldon, F. G. A. Shenton, Gurbachan Singh, John Stark, I. A. Stewart, B. A. Thompson, R. W. Tooley, A. D. Tuddenham, B. A. Tudgay, J. L. Turk, Maire P. Wallington, J. W. S. Webb, F. L. Whalley, Dorothy J. Whitney, J. R. Williams, A. G. Winfield, D. W. Wood, J. C. Worswick, A. P. J. Wynne-Jones, J. R. Young, K. J. Zilkha.

The following diplomas, and those mentioned in our issue of Jan 17 (p. 151), were conferred jointly with the Royal College of Surgeons.

D.A.—Ian Jackson.

D.I.H.—Dhundiraj Nilkanth Bhatavadekar, W. T. Buckle, P. N. B. Peacock, Dattatraya Ramadwar, E. S. O. Smith.

D.P.H.—T. C. R. Archer, E. M. Ensor, Syed Jawhar, G. S. Kambourian, Alan McGregor, Asoke Kumar Mitra, W. T. D. Ray, J. E. C. Robinson, J. P. Scrivener, F. J. Wickremasinghe, O. S. Williams.

Tributes to the late Philip Mitchiner

The Royal Medical Benevolent Fund has received £163 in donations made in tribute to the late Mr. Philip Mitchiner.

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on Jan. 31, with Mr. A. A. Gemmell, the president, in the chair, Leverhulme research scholarships for 1953 were awarded to D. C. A. Bevis, Ian Donald, and Ian Macdonald.

The following were elected to the membership:

D. M. Brodie, Patrick Bruce-Lockhart, D. S. Burris, K. G. Cockburn, S. B. Cooper, Janette G. Cowie, H. J. G. De Villiers, H. G. Dixon, Margaret M. Downes, E. M. Edwards, J. R. Elliott, A. H. Foate, G. S. Foster, A. E. Fyfe, G. H. Garfield, J. M. Gate, G. L. Gleeson, Louis Goldman, N. G. Gourlay, Michael Grant, R. W. Grayburn, J. M. Holmes, G. C. S. Hunter, Valentine M. Husband, Sarah I. Jacob, R. A. Kenihan, Kamala Khadenga, H. H. Kirk, B. V. Kyle, J. C. McCawley, John Macpherson, J. S. McVeigh, Jean Murray-Jones, T. J. Murphy Myles, L. M. Norburn, E. M. O'Dwyer, Selvam Panchalingam, R. M. M. Pratt, M. J. M. Solomons, W. K. Sutton, T. A. Thompson, R. S. Wurm.

Royal Society

Dr. F. M. R. Walshe, F.R.S., will deliver the Ferrier lecture of this society for 1953 on Dec. 10.

International Society of Orthopædic Surgery and Traumatology

This society is holding a congress at Berne from Aug. 30 to Sept. 3. The principle subjects chosen for discussion are Scoliosis and Surgery of the Hand. Further particulars may be had from the secretary-general of the society, Dr. J. Delchef, 34, rue Montoyer, Brussels.

Ergonomics Research Society

From Monday, April 13 to Thursday, April 16 at the Department of Human Anatomy, University of Oxford. this society is holding a symposium on Human Performance—Its Measurement and Limitations. Further particulars may be had from H. Murrell, Spinneys, Marlpit Lane, Headless Cross, near Redditch, Worcs.

Institute of Almoners

The annual general meeting of this institute will be held on Friday, March 13, at 6 P.M., at B.M.A. House, Tavistock Square, London, W.C.1, when Mr. L. Farrer-Brown, secretary of the Nuffield Foundation, will speak on Professionalism in the Health Service.

Society for the Study of Addiction

Prof. E. M. Jellinek, SC.D., consultant on alcoholism to the World Health Organisation, will give the fifth Kelynack lecture on Tuesday, Feb. 17, at 5 P.M., at Westminster Hospital Medical School, Horseferry Road, London, S.W.1. He will speak on International Aspects of Alcoholism.

British Association of Sport and Medicine

The first annual general meeting of this association will be held at Westminster Hospital Medical School, London, S.W.1, at 5 P.M., on Friday, Feb. 27, when Sir Adolphe Abrahams will speak on its aims and policy. Doctors interested in the medical aspects of sport will be welcome. Further information may be had from Dr. William Tegner, the hon. secretary of the association, c/o the British Olympic Association, 95, Mount Street, W.1.

Institute of Social Medicine

The address of this institute is now Social Medicine Unit. 8, South Parks Road, Oxford.

Horse Shoe Club

This organisation for promoting Anglo-American medical relations is anxious to compile a list of American doctors temporarily resident in this country. Names should be sent to Dr. C. S. Nicol, the hon. secretary, St. Bartholomew's Hospital, London, E.C.1.

Claiming Sickness Benefit

Owing to the influenza epidemic, doctors in some areas, particularly in the south of England, may not be able to see their patients without some delay. The Ministry of National Insurance reminds people claiming sickness benefit that they must notify the local National Insurance office of their illness within three days of its onset. But if a patient has not yet received a medical certificate he may send a note (written by himself or by a relative or friend) giving his name, address, National Insurance number, and the date on which the illness began. The formal claim on the doctor's "first medical certificate" should follow as soon as the doctor has been seen, and in any case within 10 days of the start of the illness.

D D D. THERAPY IN CUSHING'S SYNDROME

H L Sheehan
M D, D Sc Manc, F R C P, F R C O G

V K Summers
M D Lpool, M R C P

John Nichols
Ph D North Carolina

From the Pathology Department, University of Liverpool

D D D has the formula 2,2 bis-(parachlorophenyl)-1,1 dichloroethane, and is an insecticide related to D D T In 1948 and 1949 Nelson and Woodard reported the important discovery that, when dogs are given this substance by mouth in a dosage of about 20–50 mg per kg body-weight, the deeper layers of the adrenal cortex atrophy and disappear Within about a month, only the zona glomerulosa and a narrow outer part of the zona fasciculata remain Nichols and Gardner (1951) confirmed these findings and found that the dogs became relatively insulin-sensitive, though there was no disturbance of electrolyte balance Nichols and Sheehan (1952) described the development of the histological changes in the adrenal cortex, and studied the related disturbances of carbohydrate metabolism They found that such dogs could not be made diabetic with alloxan, but remained resistant to potassium intoxication

Such a striking and very specific destruction of the deep layers of the adrenal cortex raised the possibility that D D D might have considerable therapeutic value in patients whose symptoms indicate a hyperfunction of these layers—e g, adrenal virilism or Cushing's syndrome, and possibly some cases of diabetes or hypertension The difficulty was that dogs are the only laboratory animals known to develop the adrenal lesion as a result of treatment with D D D This substance had not previously been given to man, and thus there was no information as to whether it had any effect on the human adrenal The investigation to be described shows that, with the particular dosage used, D D D does not produce any significant clinical effect on Cushing's syndrome, and that at any rate it does not cause any permanent adrenal atrophy in this condition Nevertheless it is to be hoped that the investigation of chemically related substances will lead to the development of a method of reproducing in these patients the same degree of atrophy and reduction of function of the adrenal cortex as can be obtained in the dog

TABLE I—MEAN FIGURES OF GLUCOSE TOLERANCE AND INSULIN-TOLERANCE TESTS BEFORE D D D THERAPY

Test	Minutes				
	0	30	60	90	120
Glucose tolerance (mg per 100 ml)	83	161	172	149	102
Insulin tolerance (mg per 100 ml)	86	70	72	80	71

The patient treated in the present study was made fully aware of the experimental nature of the treatment, of the possible beneficial effects, and of the completely unknown risks We should like to record our thanks for her willing cooperation

INVESTIGATION

The patient married at the age of 20 She had no pregnancies, and menstruation continued regularly Her weight remained at its normal level of 109 lb, her height being 62½ inches Apart from a short attack of hepatitis when she was 23, her health was good until the onset of the endocrine disturbance At the age of 24 menstruation ceased and she gradually developed a classical and severe Cushing's syndrome during the next two yea She was admitted to hospital when she was 27, complaini of a rapid increase of weight, change in facial appearan lack of energy, occasional headaches, and sometim slight swelling of the feet

On examination she had the characteristic red "mo face," with moderate growth of hair along the side of the j and a little over the chin, considerable obesity, mainly of t trunk, purple striæ on the sides of the abdomen, and buffalo hump over the shoulders (see figure) Her weight w 154 lb There was mild acne of the face and trunk The pul hair was of masculine distribution The clitoris was r enlarged The uterus was small and the endometrium atroph Radiologically the skull appeared normal and there was decalcification of the spine or long bones, the left kidney h a double pelvis and ureters The blood pressure ranged betwe 200/135 and 185/120 mm Hg The electrocardiogram w normal, apart from a negative T_3

Several blood counts gave mean figures as follows 107%, red cells 5,500,000 per c cm, and white cells 98 per c mm Kepler tests showed good diuresis, with a uri output in the 2nd hour more than double the volume of t night urine, the Kepler index ranged from 56 to 116 Th basal metabolic rate (B M R) was −16% and −21% Ther was a moderate increase of nitrogen excretion in the urin and the urinary excretion of 17-ketosteroids and 11 oxycort coids was above normal (These and other biochemic findings are shown in table III) The patient was relativel resistant to insulin The mean figures of two glucose toleranc tests after a dose of 50 g of glucose by mouth, and of thre insulin-tolerance tests after an intravenous injection o 7 5 units of insulin, are shown in table I

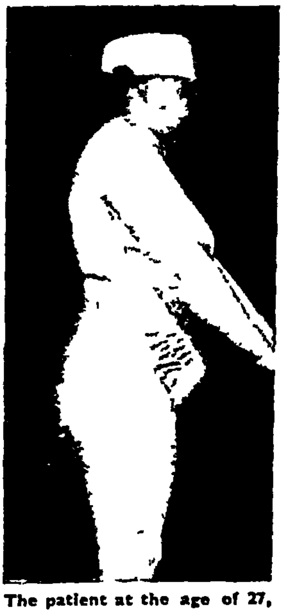
TABLE II—MEAN FIGURES OF GLUCOSE TOLERANCE AN INSULIN TOLERANCE TESTS AFTER COMPLETION OF SECO COURSE OF D D D

Test	Minutes				
	0	30	60	90	12
Glucose tolerance (mg per 100 ml)	117	200	202	184	12
Insulin-tolerance (mg per 100 ml)	175	122	160	160	15

Treatment

The patient was studied for an observation period o 12 weeks before the administration of D D D was begun Her weight gradually increased to 168 lb

The first course of treatment with D D D lasted 18 days The dosage was 1 06 g daily, equal to 13 3 mg per kg body-weight, the total amoun given in this course was 19 g administered by mouth as 10% solution in oil of arachis There was no recognisable clinical effect The blood-pressure continued in the range of 210/120 to 190/110, and the weight increased to 176 lb The only biochemical change was a fall in the serum-sodium level Glucose-tolerance tests and insulin tolerance tests gave curves substantially the same as before treatment



The patient at the age of 27, showing the striæ on flanks and abdomen

An observation period of 39 days followed, in case delayed effects of D D D might appear No such effects were seen The blood-pressure ranged from 200/120 to 180/120 The patient was next given a second course of treatment, which lasted for 30 days The dosage was 2 84 g daily, equal to 34 6 mg per kg, the total amount in this course was 85 g The drug was again given dissolved in oil of arachis No clinical effects were observed, apart from the fact that the blood-pressure was

BODY-FLUID DEPLETION*

D. A. K. BLACK
M.D., B.Sc. St. And., F.R.C.P.
TURER IN MEDICINE IN THE UNIVERSITY OF MANCHESTER

VHEN physicists ascend from Natural to Metaphysical losophy, they show us a world whose apparent solidity nerely the paradoxical expression of a changing flux mponderable particles. Process likewise masquerades structure in biology and medicine, and nowhere more than in the fabric of body-fluid. Our notions of mical equilibrium within and between the different ases of body-fluid are being displaced by concepts ed on a "steady state," which requires the expense of rgy to maintain its precarious stability. Bertalanffy 50) has summarised the characters of steady states, nting out that in open systems such as living organisms increase of entropy—which men call death—is oided only by the continued import of energy-rich stances. In this way, the organism can locally and nsiently defy the second law of thermodynamics, intaining a bubble of organisation in an environment increasing disorder.

The relevance of a dynamic approach to the study of dy-fluid becomes apparent when we consider either e very different composition of fluid within and outside e cells, or the rapidity with which changes induced in e phase of body-fluid evoke responses in other phases. milarly, methods of study have evolved from the timation of plasma composition through the classical lance techniques to the present time, in which the timation of volumes of distribution of chemically or ysically labelled markers gives us the means of sessing rapid changes in body-fluid distribution. In is first lecture I shall discuss some general aspects of ody-fluid in relation to the treatment of clinical fluid epletion; in the second lecture I shall deal more ecifically with experimental and clinical depletion of otassium, the predominant cation of intracellular fluid.

Total Body-water

Changes in the water content of the body can be stimated from the body-weight and fluid balance; but he total amount of water in the living body at any time an only be assessed by dilution methods. In principle, a measured amount is given of a substance which quickly diffuses through the whole of body-water; when equilibrium has been reached, the concentration of this substance in plasma water is determined, and the total volume of distribution of the substance can then be calculated. In practice, corrections have to be made for nequalities of distribution, and for excretion of the test substances during the interval between administration and the attainment of equilibrium. Urea, thiourea, antipyrine, and deuterium have all been used for this purpose. The antipyrine method (Soberman et al. 1949) agrees fairly well with estimations based on deuterium given as "heavy water." The most extensive studies with deuterium come from F. D. Moore's team at Boston (Edelman et al. 1952). They show clearly that the water content of the body decreases as age advances, and that in the same age-group men have a higher water content than women, as a percentage of total body-weight. This sex difference is probably largely a matter of the different fat content of the two sexes, for the "lean body mass" is surprisingly constant in composition (McCance and Widdowson 1951). In Moore's series, the percentage of water in the bodies of 34 young men (ages 17–34) ranged from 53·3 to 70·3, with a mean of 61·1%; the mean body-water in 18 young women was 51·2%. Dilution methods, even with deuterium, depend on equilibrium of the test substance with body-fluid; so in accepting their results we owe much to their general agreement with the results of an analytical tour-de-force carried out by Widdowson, McCance, and Spray (1951). By chemical analysis of the cadaver, they found 61·8% water in a man of 25, and 56% water in a woman of 45.

Physical State of Body-fluid

When we cut across normal tissue from which the blood has been allowed to drain, no fluid escapes, although the tissue looks moist, and we know it contains more than half its weight of water. We are obviously dealing with something which resembles a jelly rather than a water-filled sponge. Protoplasm has long been known to be a gel; and the recent intensive study of the extracellular supporting tissues, reviewed in the Goulstonian lectures last year (Kellgren 1952), has shown us that they, too, are probably in the gel form. The firmness of the gel depends largely on the degree of polymerisation of glycoprotein, and in rapidly growing tumours or in the symphysis pubis of pregnant guineapigs the "ground substance" is much more fluid (Gersh 1949–50). A simple increase in the extracellular tissue fluid, as in œdema, is also associated with the appearance of watery fluid, but the transformation from gel to sol may be incomplete, as suggested by the variable success of Southey's tubes in withdrawing œdema, and the different "feel" of œdematous tissues from case to case. Small molecules and ions diffuse rapidly through gels, but larger molecules such as inulin may be impeded; an inulin infusion takes five hours to attain equilibrium with extracellular fluid (Schwartz et al. 1949), whereas hypertonic salt has diffused through the extracellular space within twenty minutes (Black, Platt, and Stanbury 1950). Even if, as seems likely, body-fluid is in fact a solid of high water content, we can continue to use this, the accepted term, in a Pickwickian sense.

Distribution of Body-fluid

The basic division of body-fluid is effected by the aggregate of cell walls. Extracellular and intracellular fluid differ radically in their ionic composition; by comparison, plasma is strikingly similar in composition to extravascular extracellular fluid, which for brevity's sake we may call interstitial fluid. As a first approximation, it may be said that the partition of body-fluid into extracellular and cellular fluid depends on the relative amounts of sodium and potassium in the body; while the partition of extracellular fluid into plasma and interstitial fluid depends on the total mass of plasma-protein, whose osmotic attraction counterbalances the hydrostatic forces tending to expel fluid from the capillaries. The total extracellular fluid can be measured by the volume of distribution of inulin after equilibrium has been attained by long-continued infusion; Schwartz et al. (1949) in seven normal men found values ranging from 14 to 18% of body-weight, with a mean of 16·2%. Cell fluid can be measured only by the difference of estimates of extracellular fluid and total body-fluid; comparison of inulin and deuterium results gives a mean figure of 45% of body-weight. In infants, a much higher proportion of body-fluid is extracellular (Widdowson and Spray 1951).

Sodium forms more than 90% of the base of extracellular fluid (E.C.F.) and the osmotic pressure of E.C.F. depends almost entirely on its electrolyte content. Claude Bernard's vision of an osmotically stable internal environment thus implies a close relation between E.C.F. volume and E.C.F. total sodium. In his Goulstonian lectures, McCance (1936a) described experimental work on man which showed both the validity and the limitations of

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* The first Goulstonian lecture for 1953, delivered before the Royal College of Physicians on Jan. 13. The second lecture will appear in a forthcoming issue.

In our opinion the true values are very close to the figures given, though they might be a little lower Assuming the maximum errors both in the estimations and the correction, the true values cannot possibly be less than half the figures given "

DISCUSSION

This experimental therapy was undoubtedly a complete failure from the clinical aspect The biochemical findings during the second course of D D D treatment raised the slight possibility that there might at that stage have been some increased adrenal production of deoxycorticoid-like substances and a decreased production of androgens Histologically there was, however, no evidence that the adrenal cortex had been affected in any way by the treatment.

The problem arises of why, in man, D D D does not produce atrophy and loss of function of the deeper zones of the adrenal cortex

In the dog D D D certainly accumulates in the adrenal cortex as well as in the adipose tissue It is not known whether D D D produces its effect on the dog's adrenal by direct toxic action in the gland or whether it blocks the action (or the production) of corticotrophic hormone Nevertheless it is clearly important to know whether D D D is accumulated in the adrenal gland and adipose tissue of man in the same way as it is in the dog

Before the onset of her illness the patient weighed 50 kg and was of normal nutrition, she would have a normal amount (say about 5 kg) of adipose tissue distributed in her body If it is assumed that her subsequent increase of weight was nearly all due to fat, she presumably had about 45 kg of adipose tissue when the specimens of tissue were obtained for analysis Thus it may be calculated that there was a total of 16 g of D D D in the adipose tissue of the body at the time of the first biopsy (7 weeks after she had taken 104 g), and 6 g at the time of the second biopsy (11 weeks after receiving a further 23 g)

To compare the results of animal experiments with the present case, the figures may be considered in terms of the amount of D D D per 100 g of fat Finnegan et al (1949) gave D D D orally to dogs in a dosage of 25 mg per kg for four weeks Immediately at the end of this period the dogs had 30–88 mg of D D D per 100 g of fat If the dosage had been 35 mg per kg, it may be inferred that the dogs would have had 40–120 mg of D D D per 100 g of fat at that time These workers have shown that D D D is slowly broken down, some of the metabolic products may remain for a time in the fat, but others are excreted in the fæces and urine Thus, after the administration of the drug is discontinued, there is a progressive and gradual reduction in the amount of D D D in the fat

The present patient was given 35 mg of D D D per kg for 4 weeks The immediate concentration in the fat is not known, but after an interval of 7 weeks there still remained 35 mg of D D D per 100 g of fat During the last course of treatment she was given about a quarter of the amount given in the second course After a further interval of 11 weeks, there was 14 mg of D D D per 100 g of fat These findings suggest that in man the initial accumulation of D D D in the fat had probably been roughly about the same as in the dog, and that the lower figures when the biopsy specimens were taken resulted from the gradual metabolism of the D D D in the fat

Finnegan et al found that the adrenals of the dog contained 0–21 mg of D D D per 100 g of tissue when the fat contained 30–88 mg of D D D per 100 g In the present patient the amount of D D D per 100 g of adrenal tissue was about a third of that per 100 g of fat There is therefore nothing to indicate any important difference between the rate of accumulation of D D D in the adrenal of man and the dog

The absence of any significant effect on the adren of the present patient is thus not apparently related any failure to accumulate D D D in the adrenal gland It must be considered as due to some lack of sensitivi of the human adrenal to D D D, the precise cause this remains to be ascertained

It is of interest that the toxic symptoms occurre when the D D D was given in olive oil, but not when was given in oil of arachis Possibly there may hav been some interaction with the oil, or some difference the rate of absorption This needs to be considered further work on the subject

SUMMARY

D D D is a substance which, when given experimentall to dogs, produces severe atrophy and loss of function the deeper layers of the adrenal cortex

An attempt was made to reproduce this adrenal atroph for therapeutic purposes in a patient with Cushing' syndrome She was given a total dosage of 127 g D D D in three courses of treatment

No recognisable clinical, biochemical, or histologic response was obtained

Biopsies of fat and of adrenal gland showed that D D was taken up by these tissues in the human patient amounts comparable to those in the dog The insensitivit of the human adrenal gland to D D D thus does no appear to be due to any failure of the substance accumulate there

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ISONIAZID-RESISTANT STRAINS OF TUBERCLE BACILLI

THEIR DEVELOPMENT AND STABILITY

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Strains of *Mycobacterium tuberculosis* resistant to isonicotinic acid hydrazide (isoniazid) have been produced in vitro (Steenken et al 1952, Buck and Schnitze 1952, Pansy et al 1952, Middlebrook 1952, Hobby and Lenert 1952, Rist et al 1952, Goulding et al 1952), and they occur frequently in the sputa of patients treated with the drug (Medical Research Council 1952)

During experiments in which resistant strains were produced in vitro, we found that in certain circumstances these strains were unstable both in viability and in their degree of resistance An investigation of the stability of resistant strains from patients also indicated that some of these tended to become less resistant during subculture without isoniazid, and probably to be then sufficiently sensitive to respond to therapeutic concentrations of the drug Chemotherapeutic studies in mice and guineapigs were therefore made with two of these unstable strains and a variant of H37Rv having a similar degree of resistance low-potassium diet the body is capable of conserving potassium to a greater extent than has often been supposed (Fourman 1952); but potassium conservation sets in more slowly than that of sodium (Black and Milne 1952), although in the end the urine may contain potassium in lower concentration than the plasma.

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Even this brief summary of body-fluid regulation must have brought out the central rôle of the kidneys, whose task it is to protect us from our dietary variations, privations, and indiscretions. In his Lumleian lectures last year, my chief, Prof. Robert Platt, was able to show how well the chronically diseased kidney can adapt itself to its straitened circumstances, and put up a good performance of homœostasis even when its excretory function is largely spent (Platt 1952). Unfortunately, even the normal kidneys can only continue their efficient regulation of body-fluid if the circulation through them is adequate, and if water is freely available for urine formation. Severe depletion of body-fluid withdraws the very conditions under which the kidneys function efficiently, and is to that extent self-perpetuating.

Body-fluid Depletion

In his Croonian lectures of 1946, Marriott performed a great service to medicine and surgery in elaborating the clinical distinction between water and salt depletion. My own preference is to speak of "sodium" rather than of "salt" depletion, in order to emphasise the importance of sodium in maintaining E.C.F. volume, and also to remind ourselves that the electrolyte lost in this condition is not sodium chloride but a mixture of chloride, bicarbonate, and other anions in varying proportions, depending on the particular channel of fluid loss. Although the term "salt depletion" is entirely adequate to express the important distinction which Marriott had in mind, it also suggests that salt solution, or "saline," is the correct replacement solution for E.C.F. depletion. Saline is certainly preferable to glucose solution in sodium depletion, but when large amounts of sodium have to be given —and I hope to show you later that this is often necessary —the use of saline will provoke acidosis, and a proportion of the sodium should be given in the form of bicarbonate or lactate. Van Slyke (1948) points out that "physiological" 0·9% saline is really unphysiological, as a substitute for E.C.F.

I have little to say of primary water depletion, except to emphasise the generalisation, implicit in Marriott's account, that water depletion arises from defective intake of fluid, whereas sodium depletion is mainly caused by abnormal losses of fluid. This generalisation really stems from the inevitability of water loss in sweat, urine, and expired air, in contrast to the effective conservation of sodium under all ordinary conditions. Like most clinical generalisations, it needs its proper glosses: as that in fever enhanced water loss may speed the depletion of water; and anorexia may aggravate the effects of sodium loss by enhancing the negative balance of sodium. But I think it holds true in respect of root causes.

My concern in the rest of these lectures will be with deficiencies of body-fluid which arise not from any lack of access to water—often indeed in spite of a free water intake, because of the compelling force of electrolyte depletion. Sodium depletion leads to shrinkage of the extracellular phase of body-fluid, and potassium depletion to shrinkage of the intracellular phase. Either deficiency may be complicated by change in the acid-base balance, and may even predispose to such change; but I shall discuss this as an incidental matter, even though in a few clinical contexts it may overshadow the change in total electrolyte. *Vitae summa brevis spem nos vetat inchoare longam*; and on this occasion life's own injunction to brevity is reinforced by the need to fit a large subject into little room.

Causes of Sodium Depletion

Dietary deficiency of sodium is not in itself a sufficient cause of serious sodium depletion, though it may aggravate depletion produced in other ways. Cation exchange resins are likewise ineffective in producing sodium depletion, for they do little more than prevent the absorption of dietary sodium; when cation exchange resin is added to a sodium-free diet, the excretion of sodium in the stools is not significantly increased (Mateer et al. 1951). Clinically significant sodium depletion arises only when loss of sodium from the body is abnormally great. In the tropics, and in mines and stoke-holds, the necessities of thermoregulation impose a loss of sodium in the sweat which may suffice to bring about either acute or chronic sodium depletion in otherwise fit people. In disease, sodium depletion arises either from external loss of gastro-intestinal secretions, or from increased urinary excretion of sodium. The various gastro-intestinal secretions contain about 1000 m.eq. of sodium per day, which represents about a third of the total sodium content of the body, and is five times as great as the average dietary intake of sodium. The stools normally contain less than 10 m.eq. of sodium per day; reabsorption of alimentary-tract sodium is carried out with an efficiency comparable to that of the renal tubule. Whenever appreciable amounts of gastro-intestinal secretions are lost to the body, the risk of sodium depletion arises; such losses may come from vomiting or diarrhœa, from fistulæ, or from continuous aspiration. No-one who has seen patients with cholera can doubt the effectiveness of this mechanism of sodium depletion, which can lead to circulatory collapse within a few hours; but fortunately the wastage of digestive juices is usually less extreme, and the syndrome of sodium depletion manifests itself more slowly. While gastro-intestinal disease is by far the commonest cause of clinical sodium depletion, urinary losses of sodium are not rare, and the channel of sodium loss is far less obvious than in the gastro-intestinal group. This occult quality of urinary sodium loss gives it diagnostic interest out of proportion to its absolute frequency.

Primary renal disease seldom leads to excessive sodium excretion. In most cases of renal failure, the decrease in glomerular filtration, and so in the amount of sodium presented to the tubules, is compensated by decreased sodium reabsorption (Platt 1950); the serum-sodium remains within normal limits until lowered by terminal vomiting or diarrhœa. Rare cases have been described in which renal disease has been associated with excessive sodium excretion—the "salt-losing nephritis" of Thorn et al. (1944). These may be distinguished from Addison's disease by their lack of response to deoxycortone. Apart from intrinsic renal disease, sodium may be lost to excess in the urine in Addison's disease, in osmotic diuresis, and in metabolic acidosis. Pitts (1952) presents a masterly discussion of the mechanisms by which adrenal deficiency enhances sodium excretion. In osmotic diuresis, the "loading solute," which may be either native (glucose) or foreign (mannitol) to the body, is excreted in large amount, and imposes a constraint on reabsorption by its osmotic activity; the urine volume rises, and also the rate of sodium excretion, though the concentration of sodium is diminished, unless sodium be itself one of the loading solutes, as in sodium sulphate diuresis. Clinically, osmotic diuresis contributes to sodium depletion in diabetic coma, with glucose as the loading solute (Brodsky et al. 1950). Urea may act as a loading solute in chronic renal failure (Platt 1951), and also in the water-and-salt diuresis which characterises the "early diuretic phase" of recovery from acute tubular necrosis (Bull et al. 1950). When excessive amounts of anions are produced in the body from any cause, such as increased breakdown of fat or protein, their excretion must be partly covered by base; initially this is largely sodium, but normally the

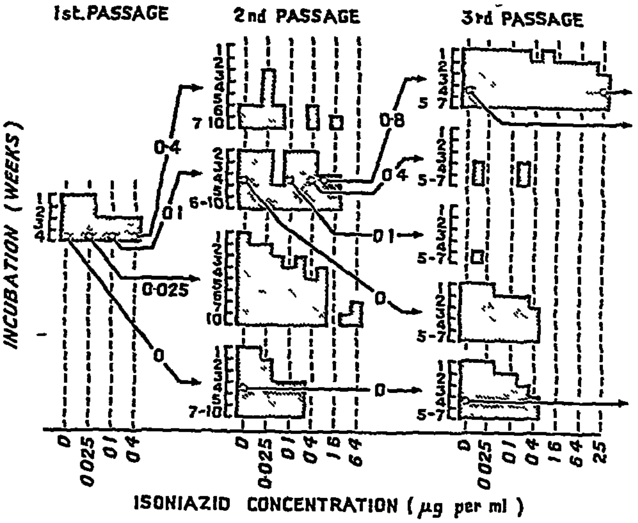

Fig 2—Results of first three passages of variant B in liquid medium

Shading indicates growth The sensitivity test on the left was inoculated with H37RV, arrows link the bottles containing the inoculum to the sensitivity tests set up from them and pass through numbers indicating the isoniazid concentration in the inoculum bottle The vertical interrupted lines are drawn at intervals of every two concentrations

cultures had poor viability Similar poor viability occurred with strain A (passage 4, fig 1), and the same tendency has also been observed in another series of resistant variants of H37RV

A further series of four passages, in each case passaging from the bottle with the highest tolerated concentration and from the bottle without isoniazid, showed (1) that it did not appear possible to obtain a resistant strain growing in more than 25–50 µg of isoniazid per ml, (2) that, apart from reversion after a single passage in isoniazid, resistant strains subcultured once without isoniazid did not lose their resistance, and (3) that the viability of the strain appeared normal after the third subculture

The variant B was finally subcultured eight times without isoniazid without any loss of resistance

Resistant Strains from Solid Medium

Serial twofold dilutions of isoniazid were made in Herrold's medium and Dubos oleic acid-albumin agar medium as described previously (Mitchison 1952) and the slopes were inoculated with 0 02 ml of a Dubos culture of H37RV and Pr, a strain recently isolated from a patient not previously treated with any chemotherapeutic agent The degree of growth after 6 weeks' incubation is shown in table I From the tubes indicated, colonies were picked off into Dubos medium without isoniazid, and after 18 days' incubation were tested for sensitivity Among the variants originating from concentrations which had largely inhibited growth, three out of nine failed to grow in the first subculture, and, of those that grew, one appeared to be of poor viability in the sensitivity test Only one of the subcultures (Pr from Dubos medium containing 1 6 µg of isoniazid per ml) definitely proved to be resistant, but one other (H37RV from Dubos medium containing 0 4 µg per ml) grew in a higher concentration after 28 days' incubation than would be expected with a normally sensitive strain

Summary

These experiments with resistant variants induced in vitro seem to show that (1) the variants rapidly revert to their original sensitivity after having been in contact with isoniazid for one subculture but do not revert after longer periods of contact, and (2) when first produced they tend to die more rapidly than do sensitiv strains

STABILITY OF RESISTANT STRAINS FROM PATIENTS

Twenty strains from patients were obtained by treating sputum with 4% sodium hydroxide and culturing on Löwenstein Jensen medium Sensitivity tests on solid medium were made on the resulting cultures From the control tube of the test, two successive subcultures were made in Dubos medium, and from the second of these, after 10 days' incubation, a further sensitivity test was made Thus the two sets of sensitivity tests were separated by three subcultures in medium without isoniazid

The results are shown in table II Of sixteen resistant strains six showed no loss of resistance, whereas ten showed a considerable loss In only one strain, however, was the final sensitivity equal to that of a fully sensitive strain, suggesting that strains with a low degree of resistance are more stable

RESULTS OF IN-VIVO EXPERIMENTS

Experiment 1

The resistance in vivo of the H37RV variant A1 was measured in mice and guineapigs To obtain a sufficient number of organisms for the test, a flask of Dubos medium containing 1 µg of isoniazid per ml was inoculated from the tube of the first passage containing the highest tolerated concentration of isoniazid

The instability following the first passage that had been demonstrated in vitro was also measured at the same time in vivo by infecting animals with the variant after a single passage in medium without isoniazid (variant A0) For this purpose a second flask of medium without isoniazid, was inoculated with the same

TABLE I—SOLID-MEDIUM SENSITIVITY TESTS OF TWO SENSITIVE STRAINS AND GROWTH AND SENSITIVITY OF SUBCULTURES FROM COLONIES ON THESE SLOPES

Strain	Medium	Isoniazid concentration in solid medium (µg per ml)							
		0	0 025	0 05	0 1	0 2	0 4	0 8	1
H37RV	D	+++	+++	+++	++	+	+	1	0
	H	+++	+++	++	++	+	1	0	0
Pr	D	+++	+++	++	+	3	1	1	2
	H	+++	+++	++	+	+	+	+	0

Strain	Derivation of colony: Medium	Derivation of colony: Isoniazid concentration (µg per ml)	Growth in liquid medium	Inhibitory concentration of isoniazid in liquid medium (µg per ml): Days incubation 7	10	14	28
H37RV	D	0	+	0 1	0 2	0 2	0 4
	D	0 4	+	0 1	0 2	0 2	0 4
	H	0	+	0 1	0 2	0 2	0 4
	H	0 1	−				
	H	0 4	+	N G	*	0 1†	0 8
Pr	D	0	+	0 2	0 2	0 2	*0 8
	D	0 05	+	0 1	0 2	0 2	0 4
	D	0 2	+	0 2	0 2	0 4	1 6
	D	1 6	+	25	25	25	25
	H	0	+	Not tested			
	H	0 05	+	Not tested			
	H	0 2	−				
	H	0 8	−				

Figures indicate number of colonies on a slope These results were read after 6 weeks incubation

+ + +, confluent growth + +, innumerable colonies +, 10–100 colonies

D, Dubos oleic acid albumin agar medium

H, Herrold's medium

N G no growth

* Growth in 0 025 µg and 0 012 µg per ml only

† No growth in control tube

example, McCance (1936b) describes one subject who lost 17·5 g. of sodium during depletion, but retained 21 g. during recovery; there was a gain in weight equal to the gain in extracellular fluid volume which would correspond to the observed increase in sodium content of the body at the end of the experiment. Again, Atchley et al. (1933) give figures showing discrepancy between loss of sodium and subsequent gain in diabetics allowed to enter acidosis and then recover.

Neither of these rather direct methods can give a practical clinical assessment of sodium depletion, for the data required for a prospective assessment are lost in the past, while the retrospective assessment would be available only when the depletion had been corrected. We are left with indirect methods, which include isotope dilution, the estimation of the serum-sodium level, and the more purely clinical assessment of dehydration and sodium loss. With isotope dilution methods, it is possible to make a fairly accurate assessment of the exchangeable sodium content of the body; but to convert this to an assessment of the depletion, it is necessary to compare this with a normal value, and here we encounter the wide range of normal variation. Nevertheless, observations on the exchangeable sodium content in clinical dehydration, supplemented by observations on the same patient after recovery, would form a useful addition to our quantitative knowledge of clinical sodium depletion. Without this background of information, the isotope method is of no present value in the clinical assessment of sodium depletion; but in five years our hunger for numerical precision may make it seem indispensable.

The clinical assessment of sodium depletion is an exercise in which no merit attaches to dissociating the evidence derived from history, examination, and chemical analysis. None of these, and perhaps least of all the chemical analysis, gives us by itself all the information which we require for considered treatment. The history should establish the channel of sodium loss, and give us at least an indication of its amount. In the great majority of these patients, sodium has been lost from the alimentary tract in an obvious way; renal loss of sodium is infrequent by comparison, and diabetes or Addison's disease have usually been recognised before the onset of dehydration. Physical examination shows the presence of dehydration and of peripheral circulatory failure; and in conjunction with the history allows some estimate of the amount of sodium depletion. By the time dehydration is just detectable clinically, there must already be a considerable sodium deficit; this may be of the order of 200 m.eq., corresponding to 1·5 litres of extracellular fluid, for Atchley et al. (1933) found such a sodium deficit in diabetics who were allowed to become acidotic but were not notably dehydrated. In acute sodium depletion with definite dehydration, as in diabetic coma, the sodium deficit is probably around 400–500 m.eq.; at any rate, Nabarro et al. (1952a) found that the retention of sodium in such patients during recovery ranged from 273 to 571 m.eq., with a mean of 455 m.eq. Much larger amounts of sodium may be lost in chronic dehydration, the result of long-continued loss of gastro-intestinal fluids. I have lately seen a patient who had been losing bile and pancreatic secretion for some weeks from a duodenal fistula. He was severely dehydrated, with cord-like veins and eyes staring from lid retraction; the serum-sodium was 118 m.eq. per litre. He was given no less than 1400 m.eq. of sodium in one protracted infusion. He was much better, with full veins and no appearance of exophthalmos, but his serum-sodium was still below normal, and his deficit had presumably not been fully corrected.

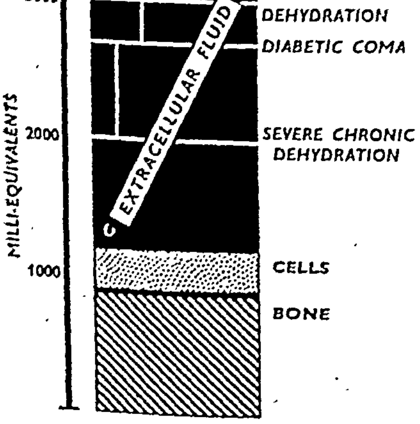

Fig. 1—Order of magnitude of different sodium deficits in relation to the normal distribution of sodium.

Given historical evidence of sodium loss, and clinical evidence of dehydration, we can get further help from chemical analysis of the blood in assessing the amount of the sodium deficit. It may be very difficult to get blood from a superficial vein, and on one or two occasions I have had to withdraw blood from the femoral vein. With a flame photometer, sodium and potassium concentrations can be estimated on 1 ml. of serum; but whenever possible the chloride and bicarbonate should also be estimated, the whole sample being taken under liquid paraffin. A raised blood-urea, hæmatocrit, or plasma-protein level is often found in dehydrated patients, but in guiding treatment they are less important than knowledge of the electrolyte concentrations.

Treatment of Severe Sodium Depletion

No special difficulty arises in the treatment of acute sodium depletion, where the sodium deficit is of the order of 500 m.eq., an amount which can be restored by giving 3 litres or so of "normal" saline. If the first litre of normal saline is given quite rapidly, say in an hour, the circulation to the kidneys is sufficiently restored in moderate sodium depletion to enable them to act selectively, excreting a higher proportion of the chloride than of the sodium. We may observe in passing that such is the normal kidney's daily task—to conserve bicarbonate in the body-fluids although our sodium intake in the diet is almost wholly in combination with chloride. It is generally accepted that amounts of sodium chloride of this order can be given without producing significant acidosis (Peters and Van Slyke 1931). When sodium depletion is already complicated by metabolic acidosis, as in diabetic coma, it is better to give one litre in three of the replacement fluid as *M*/6 sodium lactate instead of as *M*/6 sodium chloride, or "normal saline."

Chronic severe sodium depletion presents a more difficult problem in several ways—the large amount of sodium needed, the acidifying effect of really large sodium chloride infusions, the frequent co-existence of potassium depletion which may be intensified by massive sodium infusion. I shall devote the rest of this lecture to the management of this type of sodium depletion, which is almost always associated with severe and prolonged loss of gastric, pancreatic, or intestinal secretion. This is a syndrome where proper treatment should bring physician and surgeon together. The physician can often restore electrolyte balance, but is powerless to arrest the continuing fluid loss; on the other hand, the surgeon, unless he be very exceptional, may make more mistakes than the physician in trying to make this type of patient "safe for surgery."

Before advocating special measures of treatment for these patients with severe sodium deficiency, I must first try to establish that their sodium deficit is in fact 1000 m.eq. and upwards—half or more of the normal extracellular sodium content of the body. The channel of sodium loss is certainly adequate to account for deficits of this magnitude; with the exception of gastric juice, the various alimentary secretions are equivalent in sodium content to extracellular fluid, and losses of 8–9 litres of spleen of one animal infected with M2, there was no evidence of infection in the treated animals Tuberculosis was widespread in the untreated animals

DISCUSSION

In a rather ambiguous statement Steenken and Wolinsky (1952) implied that attempts to induce resistance by serial subculture in increasing concentrations of isoniazid at 14 day intervals produced little or no increase in resistance A longer period of incubation, 26–57 days in our experiments, allowed a definite and more rapid development of resistance During this period growth occurred in progressively higher concentrations of isoniazid Goulding et al (1952) and Mitchison (1952) have described the destruction of isoniazid in Dubos medium at 37°C, and it might be thought that persisting sensitive organisms were growing because the isoniazid was destroyed However, the resistance of the strains during the next passage was increased, though not always to the extent that might be expected from the isoniazid concentration originally in the inoculum bottle It thus seems likely that a combination of selection of resistant bacilli and destruction of isoniazid is responsible for the shift in the inhibitory end point found during prolonged incubation, as suggested by Goulding et al (1952)

The previous reports on the stability of artificially produced isoniazid-resistant strains have been rather confusing Pansy et al (1952) reported that variants of B C G grown once in the presence of isoniazid tended rapidly to revert to sensitivity This was also found by Szybalski and Bryson (1952) using *Myco ranæ*, and they suggested that it might have been because the resistant variant had been rapidly overgrown by faster-growing sensitive organisms Knox et al (1952) and Fisher (1952) stated that resistant variants of H37RV derived by multiple passage in the presence of isoniazid (similar to our variant B) were stable on subculture without isoniazid These reports are therefore in agreement with the behaviour of our two resistant variants A and B which were unstable only after the first passage in the presence of isoniazid The initial instability was also confirmed by the in-vivo tests, since mice infected with variant A1 were only partially protected by isoniazid, whereas mice infected with variant A0 were completely protected

Three possible mechanisms for the initial instability can be suggested

(1) When an inoculum from the growth in medium containing isoniazid was transferred to medium without isoniazid a few sensitive organisms surviving the bacteriostatic concentration were also transferred These might grow more rapidly and take the place of the resistant ones in the isoniazid free medium This explanation is unlikely since, even if the resistant strain did not multiply at all, a sufficient number of resistant bacilli would be transferred from the isoniazid free medium to initiate growth in the subsequent sensitivity test

(2) The resistant organisms may have had poor viability, and most or all of them may have been dead when transferred to isoniazid free medium Sensitive organisms, present either as survivors or (less likely) as black mutants from the resistant population might then have multiplied and taken their place This seems probable, since with both variants A and B it was shown that some of the resistant cultures appeared to be poorly viable after the first two or three subcultures in the presence of isoniazid Fisher (1952) has shown that a strain similar to B differs in its growth requirements from H37RV since it did not grow in a purely synthetic medium Further, some subcultures from colonies on solid medium containing isoniazid failed to grow on subculture, a finding also reported by Karlson and Ikemi (1952a)

(3) The process of development of resistance may not involve selection of mutants but may depend on the formation of an adaptive enzyme system not genetically determined This system, though at first unstable, might acquire stability during growth in the presence of isoniazid and be transmitted to subsequent generations This explanation involves acceptance of the theory of inheritance of acquired characteristics and appears unduly complicated

Similar mechanisms may be involved in the tendency of resistant strains from patients to lose part of their resistance It should be noted that our strains were subcultured entirely without isoniazid, hence it would be likely that they contained a proportion of more sensitive organisms which had survived the effect of the isoniazid present in the body It is therefore more probable that these sensitive

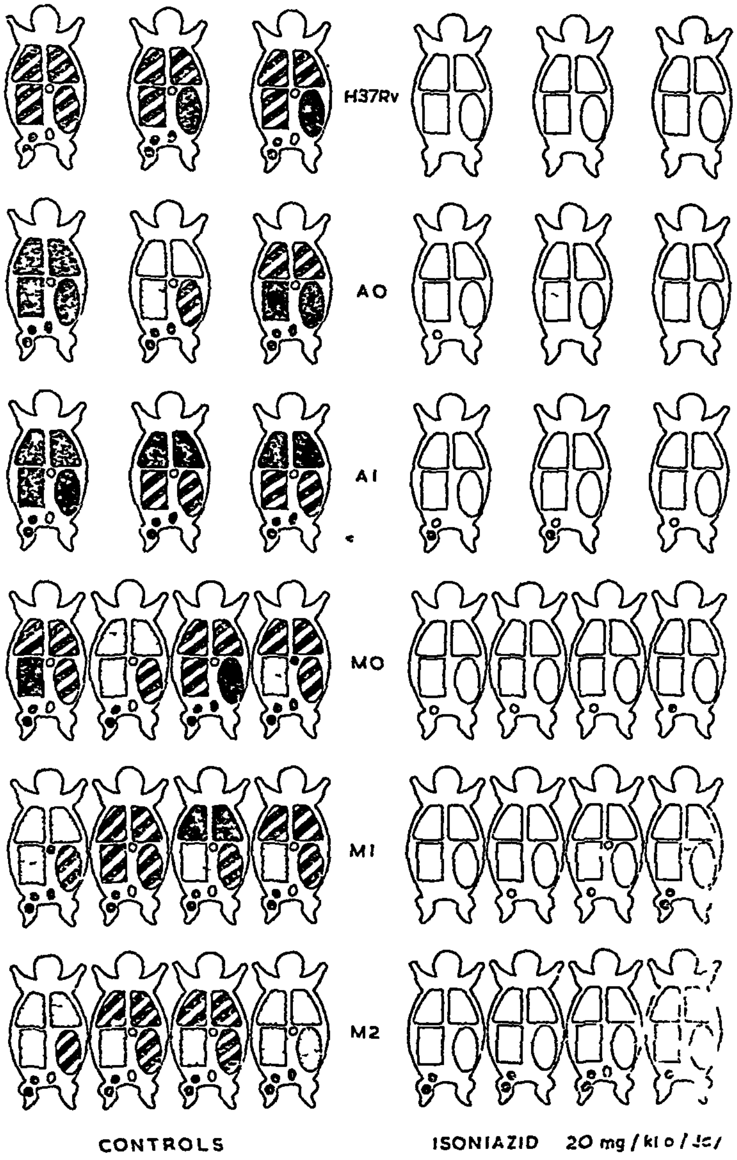

Fig 3—Chemotherapeutic experiments in guineapigs

The extent of tuberculosis in the organs is indicated by the degree of shading complete shading indicating maximal involvement, and stippling minimal involvement The liver is indicated by a rectangle, and the spleen by an oval From the right leg upwards are indicated the site of inoculation, the draining inguinal glands, the sublumbar gland, and the cœliac gland Enlarged glands are marked by open circles, which are shaded if the glands were caseous loss of gastric fluid, and of intestinal fluid respectively; these can be kept in readiness, and this avoids the delays inherent in a perpetual ad-hoc approach. The maintenance requirements of patients who cannot take food and water by mouth have been reviewed in some detail by Gamble (1951); he recommends 2 litres of 5% glucose daily to cover water losses, and to exploit the protein-sparing effect of carbohydrate. In patients who can eat and drink, thirst is the best guide to their maintenance water requirement.

These severely dehydrated patients whom we are discussing often have a sodium deficit equivalent to 10 litres or more of normal saline. When we add to this the replacement of current loss and the maintenance of water intake, it will be seen that the fluid requirement may be very high, the volume to be infused amounting to perhaps 12 litres of normal saline and 2 litres of glucose. I have suggested elsewhere (Black 1951) one expedient whereby the intravenous traffic can be kept down to a reasonable level—we may be content to allow several days for the correction of the existing deficit. Further experience has convinced me that this method may suffice for patients with moderate dehydration, but that severely dehydrated patients need more vigorous treatment, and it is specially important to restore the renal circulation as soon as possible. The large amounts of salt needed cannot be given by mouth in time, and similarly subcutaneous saline with hyaluronidase would not seem to offer sufficiently rapid replacement, in adults at least. Large amounts of hypertonic saline can be given to normal people without obvious harm; and I have also given considerable amounts of hypertonic saline to patients with anuria, who often have a low serum-sodium, and in whom it is desirable to keep fluid intake low. I believe there is a place for hypertonic saline infusion in patients with a large and definitely established sodium deficit, a low serum-sodium, and no condition which interferes with oral water intake. Such patients are not common, but I have treated 4 in the past year with 5% saline and molar lactate in amounts ranging from 500 ml. to 2 litres. In all of them the clinical improvement was definite, and there were no untoward effects. In 3 of them, I have observations comparing the amount of water actually drunk with that required to dilute the hypertonic sodium solutions down to isotonicity. Table I shows that the positive water balance, even neglecting insensible losses, was considerably less than the water needed to dilute down the hypertonic infusion; this would indicate that under such circumstances substantial amounts of water are available from the cells. In patient 3, infusion of the same amount of sodium as normal saline would have meant loading the patient with several litres of extra water, and his intracellular plethora would not have been so promptly relieved. Although the indications which I have given for hypertonic saline are limited, the results in suitable patients can be dramatic.

TABLE I—APPARENT "WATER FROM CELLS" IN PATIENTS GIVEN HYPERTONIC SALINE

Patient	Volume of hypertonic infusion (ml.)	Theoretical "water of dilution" (ml.)	Excess of water drunk (ml.)	"Water from cells" (ml.)
1	350	1400	600	800
2	1600	6400	5000	1400
3	2000	8000	2800	5200

When these large amounts of sodium have to be given, whether in isotonic or hypertonic solution, attention must be given to acid-base regulation and to potassium depletion. Large amounts of sodium chloride infusion lead to lowering of the plasma-bicarbonate, and this "dilution acidosis" (Shires and Holman 1948) may be clinically important when the renal defence of extracellular fluid pH is impaired. When there is no pre-existing acidosis or alkalosis, a fifth of the sodium in large infusions should be given as lactate, either undiluted molar sodium lactate, or diluted to one-sixth molar concentration. The proportion of lactate to chloride is appropriately modified when there is already a distortion of the acid-base balance. Many of the causes which lead to massive sodium depletion also lead to significant potassium depletion, but this may not be apparent either clinically or biochemically so long as the extracellular fluid volume is contracted by sodium depletion. As sodium depletion is corrected, the serum-potassium falls, partly because potassium excretion is increased during saline infusion (Wolf 1947) and partly because of expansion of E.C.F. volume. In 1 patient, the serum-potassium fell from 5·6 to 2·8 m.eq. per litre in twenty-four hours, during which a massive saline infusion had been given. My own practice is to give potassium salts by mouth during repair of massive sodium depletion; when this is not possible, parenteral potassium may be justified—a matter to be discussed in the second lecture.

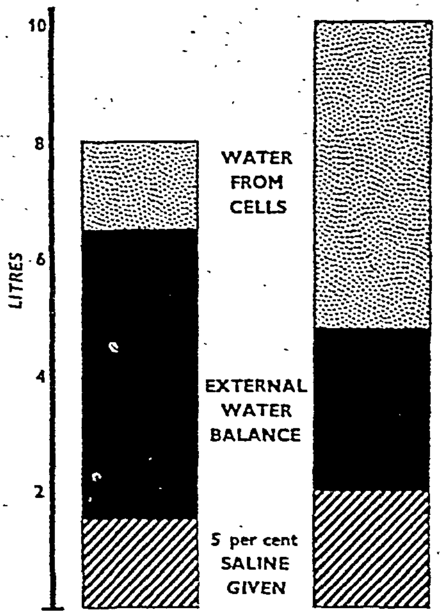

Fig. 2—Comparison of water theoretically required to dilute hypertonic saline down to "normality" with the actual positive balance of water in two patients. The difference represents water mobilised from cells during hypertonic saline infusion.

Perhaps this is as convenient a place as any to point the moral that depletion of sodium, potassium, and water are closely related to each other, and to the acid-base balance, although for purposes both of experiment and of discussion we may sometimes find ourselves forced to impose on them a spurious isolation. When we speak of "sodium depletion," I think we really imply "primary" or "predominant" sodium depletion, for secondary effects very quickly follow any loss of electrolyte or water from the body. Much of the interest of experimental studies in which a specific electrolyte depletion is induced lies in observing the secondary effects on other electrolytes and on water—a theme which I hope to develop in the second lecture. In clinical work, we have the additional complication that most depletions are mixed from their very onset, and we may be hard put to it to discover which changes are primary, and which represent secondary effects. As in most other fields of medicine, responsible experience of the clinical problems creates a healthy distrust of the corpus of knowledge and the intellectual equipment with which we presume to solve them.

"Man is the result of two thousand million years of biological evolution; he has every prospect of an equal or even greater span of psycho-social evolution before him. The human species has many grave problems before it: but it has a great deal of time in which to work them out—there may be some comfort in that thought."—JULIAN HUXLEY F.R.S., Evolution in Action. London, 1953; p. 135.

Repeated serial passages, in Dubos medium, from growth in the highest tolerated concentration of isoniazid failed to produce a strain with an inhibitory end-point higher than 25–50 µg per ml

The level of resistance of ten out of sixteen resistant strains of tubercle bacilli from patients fell substantially during three subcultures in the absence of isoniazid

Mice and guineapigs infected with sensitive strains were completely protected by isoniazid in dosage of 20 mg per kg body-weight daily When mice were infected with in-vitro resistant strains (which showed scanty colonies on solid medium containing 1 µg of isoniazid per ml. and heavy growth on solid medium containing 0 2 µg per ml) treatment with isoniazid considerably increased their survival-time Guineapigs infected with the same strains were almost completely protected, and in guineapigs a chemotherapeutic response is likely even with strains that will grow in the presence of about 1 µg of isoniazid per ml

We are indebted to Miss M Monk for technical assistance The isoniazid used in the in-vitro studies and the experiments on guineapigs was supplied as 'Nydrazid' by Messrs E R Squibb, London

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AN OUTBREAK OF STREPTOCOCCAL INFECTION IN A MATERNITY HOSPITAL

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DURING the ten weeks from Nov 1, 1952 to Jan 3, 1953, the laboratory at this hospital received 38 swabs which grew Lancefield group-A β hæmolytic streptococci This is more than the total number of similar swabs received in the preceding five years, and the outbreak is still continuing The relatively small number of times that these organisms were found between 1947 and 1952 is compatible with the decline in the number of patients admitted to fever hospitals with this type of infection Gibberd (1937) suggested that this decline, which was first noted in the period 1935–37, might be in part due to a change in virulence of the prevalent organism This suggestion was based on the observations of Colebrook and Kenny (1936) who showed that the mortality among patients admitted to the North Western Fever Hospital, London, with puerperal streptococcal infections had fallen from 22% in 1933 to 5% in 1936—before the introduction of the sulphonamides —and among the same patients the incidence of peritonitis had fallen from 7 4 to 2 6%

The present outbreak is reported because

(1) It suggests an increase in the virulence of the organism

(2) 4 of the patients, including 1 *infant*, were very ill

(3) A change in the sensitivity to sulphadiazine was observed

(4) It may be a help to other hospitals to be forewarned

On clinical grounds it was difficult to associate some of the cases with the outbreak, and this was confirmed when the result of Griffith typing became available, for it was found that 26 of the organisms isolated belonged to one type while the remaining 12 were *of different types* 26 strains of type 13 (3/B3264) were isolated 1 came from a throat swab and 13 from vaginal swabs of patients, 11 came from throat swabs of nurses and orderlies, and 1 from ward dust

BACTERIOLOGICAL METHODS

The organisms were isolated in most cases from routine high vaginal or *throat swabs* in a few cases intra uterine swabs were taken and the organisms cultured from samples of uterine contents, this method of obtaining specimens will be discussed in a later paper The swabs were spread on blood agar and incubated aerobically for eighteen hours and anaerobically for forty eight hours After incubation the plates were examined and those showing hæmolytic streptococci were subcultured into glucose broth, a plate microscope being used to help in obtaining single colony subcultures in difficult cases A further broth was inoculated with several colonies to obtain, if possible, a profuse growth in eight hours If there was an adequate growth, grouping by a modified Lancefield method was carried out, using organisms scraped from the surface of the plate This direct grouping often gave a satisfactory result which enabled isolation measures to be imposed without delay Occasionally, however, equivocal results were obtained, and in these instances an attempt was made to use the broth with the heavy, but possibly mixed, inoculum to obtain results the same evening If this proved unsatisfactory, the broth *from the single colony* subculture was used for grouping the following morning, this broth was also used to obtain pure cultures to be sent to the Central Public Health Laboratory, Colindale for typing In addition a sensitivity plate was put up by the disc technique, using penicillin (in two strengths), chloramphenicol, and sulphadiazine The sensitivity to sulphadiazine of the type 13 organisms and the other types isolated is shown in table I The majority of the organisms received from the hospital cases were resistant to sulphadiazine, but so far the strains isolated have all shown normal sensitivity to penicillin and chloramphenicol

While the methods described occasionally involved some duplication of work, they identified the group of the streptococcus as soon as possible It was interesting to note that the morphology of the colonies was a very unreliable guide to the group—for example, in one instance an organism was practically non-hæmolytic on aerobic culture and only showed its true β hæmolytic nature on the anaerobic plate, but it was nevertheless a Griffith type-13 strain isolated from one of the severely affected patients The quantity of growth, however, and in particular the presence of streptococci in pure culture were useful guides in assessing the severity of infection

The throat swabs were taken in the usual way with precautions to avoid preliminary gargles or hot drinks The plates were incubated aerobically for twenty-four hours In one case a nurse, who was swabbed as a contact and found to have no streptococci in her throat

TABLE I—SENSITIVITY TO SULPHADIAZINE

—	Type 13	Other types
Sensitive	3	3
Slightly sensitive	3	1
Insensitive	20	8

TABLE III—URINE AND BLOOD BIOCHEMISTRY

—	Period					
	From March 1, 1951, to June 20, 1951	From June 21, 1951, to July 8, 1951	From July 9, 1951, to Aug. 14, 1951	From Aug. 15, 1951, to Sept. 15, 1951	From Sept. 16, 1951, to Nov. 26, 1951	From Nov. 27, 1951, to Dec. 6, 1951
	Observation	D.D.D.	Observation	D.D.D.	Observation	D.D.D.
Daily urinary excretion:						
Urine vol. (ml.)	2000	2160	2130	2210	2100	1860
Urea (g.)	23·1	27·2	31·2	27·8	24·4	18·0
Uric acid (g.)	0·75	0·86	0·79	0·80	0·87	0·83
Creatinine (g.)	0·98	0·76	0·91	0·82	1·31	1·55
17-Ketosteroids (mg.)	15·0	17·8	14·3	9·6	11·8	13·3
11-Oxycorticoids (mg.)	1·6	2·6	2·3	2·7	1·9	4·5
Blood:						
Potassium (mg. per 100 ml.)	20·0	20·5	20·0	19·5	..	..
Sodium ,, ,,	311	280	293	253	295	329
Cholesterol ,, ,,	134	111	76	117	186	128
Urea ,, ,,	29	28	35	31	37	22

always a little lower, in the range of 180/110 to 170/120. Her weight was 182 lb. Biochemically there was again a fall in the serum-sodium level, and there was a slight reduction in the urinary excretion of 17-ketosteroids.

A further period of observation was allowed, lasting for 72 days. During this time the blood-pressure varied between 195/135 and 180/110, and the weight increased to 190 lb. The B.M.R. was −1%. Glycosuria never occurred, but there appeared to be some deterioration of her carbohydrate control mechanism. The mean figures of glucose-tolerance tests and insulin-tolerance tests at this stage are shown in table II. On the 50th day of this observation period a sample of subcutaneous abdominal fat was removed for chemical assay of its D.D.D. content. The wound did not heal for about a month, the delay being presumably due to the high production of endogenous cortisone.

TABLE IV—D.D.D. CONTENT OF TISSUES

Tissue	Date	D.D.D. (mg. per 100 g.)	
		On lipid	On whole tissue
Adipose tissue	Nov. 1, 1951	41	35
,,	Feb. 20, 1952	18	14
Adrenal gland	,,	22	5

For the third course of treatment D.D.D. was given as a 10% solution in olive oil, because arachis oil could not be obtained. The dosage was raised to 5·68 g. of D.D.D. a day, equal to 63·1 mg. per kg. On the 2nd day of treatment she was drowsy. On the 3rd day she was very sleepy and greatly depressed. She complained of headache, giddiness, and nausea, and vomited once. In view of these toxic symptoms the medicine was changed for an equal amount of olive oil containing no D.D.D.; the patient was not told that the active drug had been discontinued. She improved rapidly and was in her normal condition within 2 days. On the 3rd day of this rest period the same volume of a 2·5% solution of D.D.D. in olive oil was substituted for the pure olive oil, the patient thus being given only 1·42 g. of D.D.D. a day, equal to 15·8 mg. per kg. There was a rapid recurrence of the same symptoms as had occurred with the larger dosage. The treatment was continued for 4 days, a total of 23 g. being given in this course. Then, as the toxic effects were continuing, all therapy was abandoned. The patient again recovered to her normal state within 2 days.

After D.D.D. therapy had been discontinued her clinical condition remained unchanged apart from a further increase of weight to 197 lb. On the 76th day after stopping the treatment, nine-tenths of the left adrenal gland was removed by Mr. Philip Hawe. The gland appeared of normal size. Histologically it did not show any atrophy of the deeper layers of the cortex, or any changes suggesting regeneration after previous atrophy. There was no cellular infiltration. Small groups of cortical cells were present in places in the medulla, as is commonly seen in glands from normal people. Part of the adrenal and a sample of subcutaneous fat from the operation incision were collected for chemical assay. Healing of this wound was again slow, taking about 2 months.

After this operation she was given a reducing diet, and after 7 months her weight was 163 lb. At this time her face and abdominal striæ were slightly less red, but the operation wounds were still very red. Her blood-pressure remained in the range of 190/135 to 220/145. A blood-count was normal. The daily urinary excretion of 17-ketosteroids averaged 16·6 mg. The results of a glucose-tolerance test were as follows:

Minutes	0	30	60	90	120
Mg. per 100 ml.	114	183	210	211	143

Slight glycosuria occurred at 90 minutes. The Kepler test showed a good diuresis. The only abnormal finding in the blood chemistry was a high serum-sodium level of 385 mg. per 100 ml.

Biochemical Observations

24-hour specimens of urine were analysed three times a week during the administration of D.D.D. and once or twice a week during the observation periods. We are indebted to Mr. E. Caldecott and Mr. G. Appleton for these laborious estimations.

The technique used for the 11-oxycorticoid estimations was the formaldehyde-chromotropic acid method of Daughaday et al. (1948). This method probably does not measure more than a small fraction of the total 11-oxycorticoids, but the results are sufficiently reproducible for comparative studies of the present type. In this laboratory normal persons give by this method a urinary excretion of 0·3–0·7 mg. per day.

The mean figures of 69 urine estimations and 27 blood estimations are shown in table III. It will be seen that the high output of urine, of nitrogenous excretion products, and of 17-ketosteroids and 11-oxycorticoids was not significantly altered by the treatment. There was no fall in the serum-sodium level during the third period of treatment, possibly because the course lasted only a short time.

Tissue Chemistry

The D.D.D. content of the pieces of tissue was assayed by Dr. F. D. Collins and Mr. G. A. J. Pitt, of the biochemistry department, Liverpool University. Their report is as follows:

“The lipid extracted with ether from the specimens was nitrated, and the colour was developed with sodium methoxide in methanol-benzene mixture according to the procedure of Ofner and Calvery (1945). The intensity of absorption at 600 μ was measured in a photo-electric spectrophotometer and compared with that of D.D.D. which had been similarly treated. Samples of normal human fat, and of the pentothal and curare used at the operation, were examined as controls, with negative results. The findings in the tissues from the patient are given in table IV.

“These tissues contain in addition to the D.D.D. an interfering substance which has a maximum absorption at 500 μ and may be derived from a metabolite of D.D.D. (It is not, however, the same as that mentioned by Ofner and Calvery (1945), which has a maximum at 540 μ.) This has required a correction of the observed absorption at 600 μ; the amount of this correction cannot be assessed with absolute accuracy of the organisms isolated were resistant to sulphadiazine Sensitivity to penicillin was normal The bacteriological methods used are described, and the implications of the outbreak are discussed

We are grateful to Dr R E O Williams and his staff at the Colindale Reference Laboratory for typing our strains, to Dr A J Cashman, registrar in bacteriology, who has undertaken many of the Lancefield groupings, and to Miss J Gratwick for technical assistance

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HEXAMETHONIUM COMPOUNDS IN THE TREATMENT OF PRE-ECLAMPSIA AND ESSENTIAL HYPERTENSION DURING PREGNANCY

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MOST workers agree that hexamethonium compounds will lower the blood-pressure temporarily, and Turner (1951) thought they might prove particularly valuable in the treatment of pre eclampsia and essential hypertension in pregnant women Apart from a recent report by Mulcahy (1952), no serious attempt to determine their value or dangers during pregnancy has been published Accordingly I present an analysis of the results obtained in 10 cases

OBSERVATIONS

As the treatment might involve hazards to the mother and especially to the fœtus, it was in general reserved for cases where the prognosis for the fœtus appeared very poor and where all the usual measures had failed

Administration

Hexamethonium bromide was given either by mouth or by intramuscular injection The summary of case records (see table) shows the high dosage required when treatment was entirely by mouth Even in non pregnant patients the hypotensive dose varies considerably (Mackey and Shaw 1951), probably because of variations in absorption, and during pregnancy absorption is likely to be further impaired In non pregnant patients persistent hypotension (Hirson and Kelsall 1951) and paralytic ileus (Bourne and Hosford 1951) have been reported, and though these complications have *not yet been recorded during pregnancy*, the risk is presumably no less, and perhaps greater, in the pregnant Even a transient hypotension, with its disturbance of uteroplacental blood-flow, might kill the fœtus For these reasons oral therapy is probably

CASE-HISTORIES

Description of case	Maturity at start of hexamethonium	Dose and route	Effect on B.P.	Duration of treatment	Delivery	Fœtus	Hexamethonium estimations
1 Primigravida aged 38 B P at 16 weeks 180/110 Admitted at 21 weeks with B P 180/110 No albuminuria or œdema Poor response to rest and sedation	26 weeks 31 weeks	125 mg, increased to 500 mg by mouth 6 hrly 80 mg intramuscularly 4 hrly, increased to 150 mg 3 hrly	Nil Fair response at first Resistance developed rapidly	6 days 30 days Last injection 3 hours before delivery	Lower segment cæsarean section at 36 weeks	5 lb 3 oz Vigorous at birth Developed cyanotic attacks and died 72 hours later P M widespread purulent bronchopneumonia	Not performed
2 Primigravida aged 22 Admitted at 26 weeks with vaginal bleeding B P 180/140 Urine normal No response to rest and sedation	30 weeks	750 mg–1 g by mouth 6 hrly, increased to 1 75 g by mouth, with 50 mg intramuscularly 6 hrly	Fair response at first Resistance developed rapidly Increased dose gave reasonable control B P 120/80–140/110	20 days Treatment continued till delivery	Spontaneous at 33 weeks	3 lb 12 oz Limp but soon responded Developed signs of intestinal obstruction Transverse colostomy Died on 6th day P M, no explanation except absence of ganglion cells in a narrowed but not obstructed segment of rectum	Not performed
3 Multigravida aged 44 three normal deliveries Admitted at 26 weeks with B P 210/105 albuminuria and œdema Poor response to rest and sedation	27 weeks	1 g by mouth 8 hrly	Fair response Stabilised at 160/100	35 days Treatment continued till delivery	Spontaneous at 33 weeks	5 lb 6 oz Treated in premature baby unit Normal progress	Cord blood at delivery 9 3 µg/ml
4 Primigravida aged 25 Admitted at 34 weeks with B P 140/90, albuminuria and œdema. No response in 48 hours to rest and sedation	34 weeks	250 mg by mouth increased to 1 5 g 8 hrly	Good response after dose was increased	16 days Treatment continued till delivery	Spontaneous after artificial rupture of membranes at 36 weeks	4 lb 15 oz Treated in premature baby unit Normal progress	At delivery amniotic fluid 11 0 µg/ml, maternal blood 3 6 µg cord blood 1 0 µg
5 Multigravida aged 38 two cæsarean sections for pre eclampsia B P at 10 weeks 160/90 Admitted at 33 weeks with B P 190/110 No albuminuria or œdema No response to rest and sedation	34 weeks	60 mg intramuscularly 6-hrly increased to 100 mg 3 hrly	Initially good response Resistance soon developed Increased dose gave satisfactory control	21 days Last injection 15 hours before delivery	Lower segment cæsarean section at 38 weeks	7 lb 2 oz No meconium for 20 hours B P at birth 80/25 Progress otherwise normal	Maternal and cord blood at delivery no hexamethonium detected

METHODS

Sensitivity Tests to Isoniazid

Liquid-medium tests were done in a modified Dubos 'Tween'-albumin medium (Medical Research Council 1948) Serial twofold dilutions of isoniazid in the range 100–0·012 µg. per ml. were prepared in 3 ml. volumes in $^1/_4$-oz. screw-capped bottles. They were inoculated with 0·02 ml. of a culture in the same medium, and the amount of growth was recorded after various periods of incubation at 37°C.

Solid-medium tests were done on Löwenstein-Jensen slopes containing 0, 0·2, 1, 5, 10, and 50 µg. per ml. added before inspissation for 1 hour at 80°C. The slopes were inoculated with a 3 mm. loopful of either a Dubos culture or a suspension of approximately the same turbidity prepared by grinding up growth from solid medium in distilled water. The degree of growth was noted after 14 and 28 days' incubation.

In both methods a control culture of the sensitive strain, H37RV, was tested under identical conditions.

Production of Isoniazid-resistant Strains in Vitro

Resistant variants were obtained either from solid medium containing isoniazid after 6 weeks' incubation or by serial passage through increasing concentrations of isoniazid. This passaging was done by inoculating the series of fluid media used in the sensitivity tests and subculturing from the bottle containing the highest tolerated concentration of the drug into a fresh series of bottles, including one without isoniazid. In this way the degree of resistance was measured at each passage.

Stability of Isoniazid-resistant Variants

The stability of the resistance of the variant was measured by redetermining the sensitivity after one or more subcultures in Dubos medium without isoniazid.

In-vivo Resistance

The in-vivo resistance of the variants to isoniazid was measured in white mice (Schofield strain) and guineapigs treated subcutaneously with the drug.

The organisms were grown in Dubos medium with or without isoniazid. The wet weight of the culture was measured in a vaccine centrifuge tube, and the number of viable units—i.e., clumps of organisms developing into single colonies—was determined by the method of Fenner (1951) using oleic-acid-albumin agar. The mice (17–19 g.), in groups of twenty, were infected intravenously at the two dose levels of 1·0 mg. and 0·3 mg., and guineapigs in groups of six or eight were injected in the right thigh muscle with 1 mg. or 0·1 mg.

Each group of animals was subdivided, half being treated with isoniazid and half serving as untreated controls. Treatment was started immediately after infection and continued until the animals died from the infection or were killed at the end of the experiments. The dose of isoniazid was 10 mg. per kg. body-weight, given at both 9 A.M. and 5 P.M. daily, except on Saturdays, when only one dose was given, and on Sundays, when none was given.

Necropsies were made on the lungs of the mice, and a complete examination was made on the guineapigs. The organisms were recovered from the spleens of the guineapigs of the first experiment and tested for sensitivity to isoniazid.

RESULTS OF IN-VITRO EXPERIMENTS

Variant A

This resistant variant of the H37RV strain was produced by passaging in Dubos medium containing isoniazid; the results are summarised in fig. 1. In this medium H37RV is inhibited by about 0·025 µg. of isoniazid per ml. after 10 days' incubation (Mitchison 1952), but in the first passage growth began to appear in the bottles containing 0·8 µg. per ml. after 39 days and became heavy by 57 days. On the 57th day the growth in this tube was inoculated into the bottles of the second passage and the in-vivo sensitivity was measured in mice and guineapigs (variant A1). The results of the second passage showed that this growth was composed of resistant organisms and not of surviving sensitive organisms which had grown after the destruction of isoniazid during the long period of incubation. After 26 days' incubation the organism growing in 1·6 µg. per ml. of the second passage was passaged a third time, and the growth in the various concentrations showed that there has been a slight increase in resistance. Fourth and fifth passages made after 30 and 29 days' incubation, showed no further increase in resistance.

At the time of the third passage a sensitivity test was made on the organisms of the second passage growing in the medium containing no isoniazid. The result indicated that resistance gained during the first passage was readily lost, for even after this one passage through plain medium the organisms reverted to their original sensitivity. The in-vivo sensitivity of the organisms (variant A0) at this stage was also measured (see below). Similar in-vitro sensitivity tests made from the plain medium of third and fourth passages showed that the strain had become more or less permanently resistant. Finally, the strain from the fifth passage was subcultured seven times in plain medium without any loss of resistance.

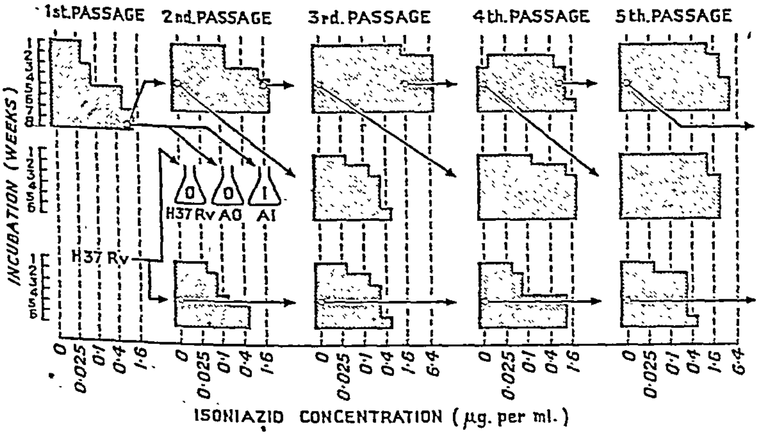

Fig. 1—Results of first five passages of variant A in liquid medium:

Top line: passages in medium containing isoniazid.

Middle line: passages to investigate stability of strains after one subculture in medium free from isoniazid.

Bottom line: H37RV controls.

The flasks illustrate the history of the variants used in experiment 1: 0, no isoniazid; 1, 1 µg. of isoniazid per ml. in medium in flask.

The stippled areas represent growth at weekly intervals in presence of various concentrations of isoniazid. Arrows link the bottles containing the inoculum to the sensitivity tests set up from them. The vertical interrupted lines are drawn at intervals of every two concentrations.

Variant B

This resistant variant was produced independently, but in a similar manner to variant A from H37RV. The period of incubation was 28 days for each passage. In the second and third passages series of bottles were set up not only from the bottles containing the highest tolerated concentrations of isoniazid but also from those with lower concentrations.

The results of the three passages are shown diagrammatically in fig. 2, from which it can be seen that organisms with a slight degree of resistance, produced by one passage in 0·1 µg. of isoniazid per ml., reverted to full sensitivity when cultured without isoniazid. Further, it shows that some of the resistant strains grew very poorly on subculture, suggesting that the and the effect of hexamethonium on these changes could be harmful rather than beneficial

Effect on Labour

In the cases where hexamethonium administration continued during labour it did not apparently alter the normal course

Maternal Side-effects

On the whole the side-effects were not significant All patients had blurring of vision, but they soon became accustomed to this None had severe constipation One showed sensitivity to bromide after two days' treatment, but this disappeared when the drug was changed for hexamethonium bitartrate

Effect on Fœtus

Young (1952) has shown that, in does, hexamethonium passes freely across the placental barrier and can very soon be detected in the liquor If a constant plasma level of hexamethonium is maintained, the hexamethonium content of the liquor increases until very soon it is well above that of the plasma It then persists in the liquor for some considerable period after the last dose has been given If the umbilical cord of the fœtus is tied, then the hexamethonium content of the liquor is very low, which suggests that it reaches the liquor via the fœtal urine Analysis of the liquor in some of our cases tends to support these observations

This accumulation of hexamethonium in the liquor may be of considerable clinical significance From the liquor which it swallows, the fœtus will presumably re absorb a certain amount of hexamethonium The more immediate action of this will be on the intestine itself, and the fœtus may thus be born with a predisposition to paralytic ileus This would explain the two cases in which the child apparently died from this cause and the further case in which there was delay in the passage of meconium This point is still unproven, however, for in a further case, where the hexamethonium content in the liquor was relatively high, the infant showed no ill effect Furthermore Mulcahy, in his series of 10 cases, did not observe any harm to the fœtus

It is also possible that any aspirated liquor would have a somewhat similar effect on the respiratory system, reducing bronchial secretion This may have been an important contributory factor in one case where the infant died from an extensive purulent bronchopneumonia As hexamethonium is only slowly removed from the liquor, discontinuance of treatment twenty-four hours before delivery is expected would do little to prevent these possible complications

CONCLUSIONS

Hexamethonium therapy during pregnancy should not be considered until the customary treatment of pre-eclampsia or essential hypertension has failed and unless the prognosis for the fœtus appears very poor Because of the risk of hypotension and the rather variable response, oral therapy should be avoided With intramuscular therapy the fall in blood-pressure is erratic and unpredictable, though it usually persists for three or four hours Resistance to the drug may develop within a few days

There is no definite evidence that hexamethonium treatment materially alters the course of the disease, but it may help to stabilise the condition It seemed to have no significant effect upon the course of labour

Hexamethonium is known to accumulate in the liquor When swallowed, it may predispose to ileus in the new-born infant and when aspirated it may reduce bronchial secretions and so favour respiratory infection

My thanks are due to Mr J V O'Sullivan, and Dr A S Duncan for permission to include certain of their case records, to Miss I M Young, who made the hexamethonium estimations, and to Prof J C McClure Browne for his encouragement and help in the preparation of this report

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CULTIVATION OF TOXOPLASMA GONDII IN TISSUE CULTURE IN MAMMALIAN CELLS

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As is known, *Toxoplasma gondii* is an obligatory tissue parasite which cannot be grown in vitro in the absence of animal tissue in the medium Meyer and de Oliveira (1945) and Mühlpfordt (1952) have described the cultivation of toxoplasma in avian tissues, but so far there has been no record of its cultivation in mammalian tissue, though mammals (including man) represent the most important hosts of this parasite

Since this method might be of interest for chemotherapeutic tests and in the study of the life history of toxoplasma, a short account is given of some preliminary experiments, made in 1948, on its behaviour in vitro in mammalian tissue

Methods—Explants of embryonic rat heart were allowed to proliferate on coverslips in Carrel flasks under a fluid medium containing 10% each of rat serum and embryonic extract in Tyrode's solution This method is similar to that used by Hawking (1946) for *Trypanosoma cruzi* After three or four days the tissue was inoculated by the addition to the flasks of a few drops of peritoneal fluid from a mouse infected with toxoplasma Alternatively, the explants were placed in the peritoneal fluid before being fixed in the flasks (Lock 1950) The coverslips were withdrawn at intervals, and the tissue was fixed with Schaudinn's solution and then stained by Giemsa's method

Results—Invasion of the host cells (fibroblasts, macrophages, and probably muscle cells) and the subsequent multiplication of the toxoplasma within them was rapid The accompanying figure shows the appearance of cultures eighteen hours after infection In these preliminary experiments the penetration of cells by the parasite was not observed and mobility of the extracellular parasites was not definitely established Under favourable conditions growth was observed up to ten days, but some cultures with numerous parasitised cells died within forty eight hours This did not appear to be due to the production of excess acid in the culture,

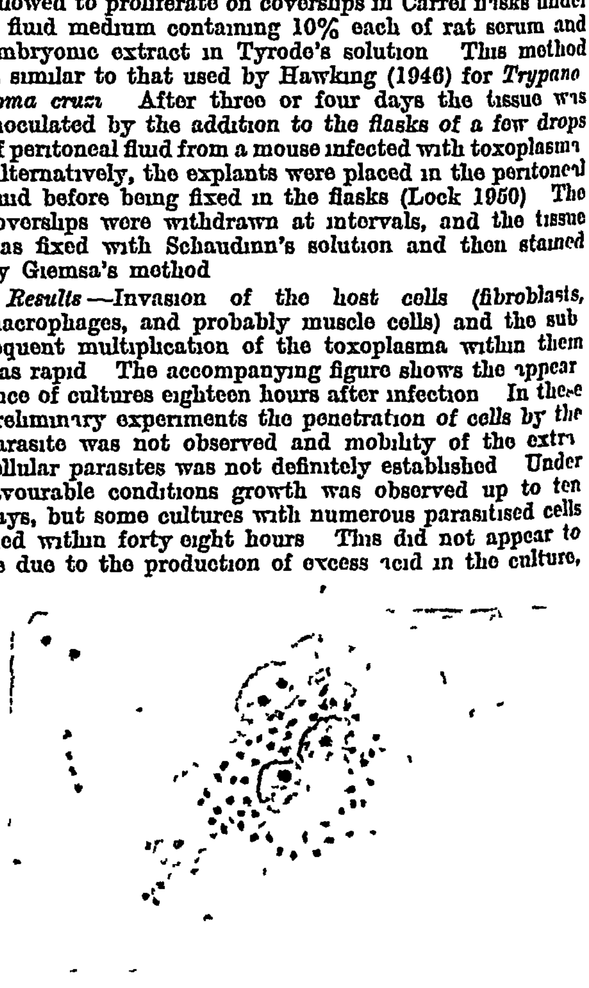


TABLE II—SENSITIVITY OF STRAINS OBTAINED FROM PATIENTS BEFORE AND AFTER THREE SUBCULTURES WITHOUT ISONIAZID

Strain	Inhibitory concentration of isoniazid in solid medium (µg. per ml.)	
	Before subculture	After subculture
St 0	0·2	0·2
Su 0	0·2	0·2
C 0	0·2	0·2
M 0	0·2	0·2
St 1	5	10
M 1	5	5
Jn 1	5	5
P 1	10	10
Ra 2	50	50
Se 1	>50	>50
Ro 1	50	5
Ra 1	>50	10
C 1	>50	10
W 1	>50	5
L 1	>50	5
Su 1	>50	1
M 2	>50	1
J 1	>50	1
Sm 1	>50	1
Jo 1	>50	0·2

The first four strains were obtained before treatment with isoniazid. The remaining strains were obtained during or after treatment with isoniazid.

The inhibitory concentration of isoniazid is that which permitted the growth of 20 or less colonies.

organisms as were used to inoculate the first flask; thus the strain had been passaged once in the presence and once in the absence of isoniazid. A third flask was inoculated with H37RV as a control.

In the absence of isoniazid, growth of H37RV and its variant A0 began to appear in 6 days, but that of variant A1, growing in the presence of isoniazid, was not visible until 19 days. On the 26th day the cultures were harvested, the wet weights of bacilli were determined, viable counts and liquid-medium sensitivity tests were made (results in table III), and mice and guineapigs (430–690 g.) were injected. The guineapigs each received 1 mg. of bacilli.

The mouse experiment was continued for 50 days, and the results are given in table IV. Isoniazid fully protected the mice infected with H37RV and with the originally resistant culture A0, which according to the in-vitro test (table III) had reverted to full sensitivity, but it afforded only partial protection against 1 mg. of the resistant culture A1.

The macroscopic appearances at the necropsies of the guineapigs killed after 37 days are shown in fig. 3. Apart from that at the site of inoculation and glandular involvement near it in two of the guineapigs injected with A1, there was no macroscopic evidence of tuberculosis in any of the treated animals, whereas the organs of untreated animals were always found to be severely affected. There was the usual histological appearance of tuberculosis in the organs of untreated animals, with early caseation in a few of the tubercles. The organs of two of each group of the treated animals were also examined histologically, and no evidence of tuberculosis was found in any of the lungs or livers, but in the section of the spleen of one animal infected with the A1 culture there were six small tubercles.

Sensitivity tests on solid medium of the organisms recovered from the spleens of the untreated animals showed them to have the same sensitivity as those injected. Only two of the nine cultures from the treated animals yielded growth, and both of these were from animals infected with culture A1; in one culture only one colony grew, and in the other there were only two colonies. The first proved to be as resistant as A1, but the second was slightly more resistant, yielding a confluent growth on 1 µg. of isoniazid per ml., and innumerable colonies on 5 µg. per ml.

Experiment 2

Strains M0, M1, and M2 were obtained from the sputum of a patient with pulmonary tuberculosis. M0 was obtained before treatment with isoniazid, and M1 40 days, and M2 62 days, after treatment with 200 mg. of isoniazid daily had begun. These strains were isolated on medium without isoniazid, and sensitivity tests on solid medium were set up from these primary cultures. Strain M1 was inhibited by 5 µg. of isoniazid per ml., and strain M2 grew well in 50 µg. per ml. Bottles of Dubos medium were inoculated from the control tube of the tests, and flasks of Dubos medium were then inoculated from these bottles. After 13 days' incubation the wet weight of bacilli was determined and a viable count on oleio-acid-albumin agar, with and without 2 µg. of isoniazid per ml., and sensitivity tests on solid and liquid media were set up. Mice and guineapigs (345–460 g.) were infected, the latter receiving 0·1 mg. each. The results of the sensitivity tests (table III) show that there had been a decrease in resistance during the subculturing of the strains M1 and M2, both now being comparable in resistance to variant A1.

The results of the mouse experiments are given in table IV. Isoniazid appeared to give complete protection against the strain isolated before treatment but only partial protection against the two resistant strains. The necropsies on the mice surviving to the 79th day showed that the lungs of the treated mice infected with M0 contained scanty tubercles, whereas those infected with M1 and M2 strains contained numerous tubercles. All the strains had about the same degree of virulence, which was better related to the viable count than to the weight of bacilli injected.

The guineapigs (345–460 g.) were infected with 0·1 mg. of the three strains and were killed after 43 days. The macroscopic post-mortem appearances are shown in fig. 3. Apart from tuberculosis at the site of inoculation and in the local glands, especially in animals infected with M2, and the presence of four microscopic tubercles in the

TABLE III—ISONIAZID SENSITIVITY OF STRAINS USED FOR EXPERIMENTS ON ANIMALS

Fluid Medium

Expt. no.	Strain	Minimal inhibitory concentration of isoniazid in liquid medium (µg. per ml.)				Number of viable units per ml. of culture	
		Period of incubation (days)				Isoniazid concentration (µg. per ml.)	
		7	10	14	28	0	2
1	H37RV	0·012	0·2	0·4	0·4	$2{\cdot}2 \times 10^7$	Not tested
	A0	0·025	0·2	0·2	0·4	$1{\cdot}2 \times 10^7$	
	A1	1·6	6·4	12·5	12·5	$3{\cdot}2 \times 10^7$	
2	M0	0·05	0·05	0·05	0·8	$2{\cdot}8 \times 10^7$	0
	M1	0·4	0·8	0·8	12·5	$1{\cdot}3 \times 10^7$	14
	M2	0·4	0·8	0·8	1·6	$4{\cdot}2 \times 10^6$	1·3

Solid Medium

Culture	Strain	Growth on solid medium containing isoniazid concentration of isoniazid (µg. per ml.)					
		0	0·2	1	5	10	50
Primary culture	M0	+ + +	0	0	0	0	0
	M1	+ + +	+ + +	+ + +	0	0	0
	M2	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
Injected into animals after 3 sub-cultures	M0	+ + +	0	0	0	0	0
	M1	+ + +	+ +	100	0	0	0
	M2	+ + +	+ + +	10	0	0	0

Solid medium tests read after 28 days' incubation.
+ + +, confluent growth.
+ +, innumerable colonies.
Numbers indicate numbers of colonies on slope.

stoppage of blood-flow through affected vessels when hypotension was induced, and regarded arteriosclerosis as a *contra indication to use of the technique* So were myocardial disease and malignant hypertension, but cases of essential hypertension benefited, and the *circulatory fluctuations arising during removal of a phæochromocytoma* might be more easily managed He felt strongly that hypotension should only be induced if it would be good for the patient It demanded skilful management, especially if it continued into the postoperative period when accidents were most likely to occur

In the ensuing discussion there was some criticism of the number of deaths, and one anæsthetist said he had abandoned pentamethonium because the slightest accident threw the patient into jeopardy. People were also troubled by the suggestion that pentamethonium averted serious surgical shock. In the Manchester neurosurgical unit the drug was used very cautiously in cases of cerebral angioma, vascular meningioma, and aneurysm *just for the 30–60 minutes* when hæmorrhage was most likely, methylamphetamine being given as soon as the risk was past Another speaker mentioned a reflex whereby lowered carotid-sinus blood pressure led to bronchial dilatation, and said that barrel chested bronchitics with laboured breathing often improved as the blood pressure fell during the action of pentamethonium

NUTRITION SOCIETY

The Psychology of Eating

Presiding at a conference held at Aberdeen on Jan 31 by the Scottish Group of the Nutrition Society, Prof **Rex Knight** said that the contributions would illustrate the five main features of contemporary psychology (1) the replacement of anecdote and the literary essay by controlled observation and experiment, (2) the unconscious nature of the tendencies underlying conduct, (3) a renewed interest in the constitution of individuals as opposed to their environmental influences, (4) the emphasis on social factors in the development of personality, and (5) the attempt to relate psychological phenomena to underlying physiological mechanisms

Reviewing the psychiatry of disturbances of eating and of nutrition Prof **W M Millar** said that the relation between the mental disorder and the abnormality of feeding was sometimes obvious, as in vitamin deficiency, but it was more often complex and obscure because it was emotional and symbolic In some mental disorders a loss of interest in life was reflected in a desire *for starvation* and death, in others abnormal fears led the patient to think that food would cause intestinal obstruction Sometimes what began as an eccentricity about food might develop into a way of life—vegetarianism, for example Emotions such as rage and fear had an undoubted though obscure influence on gastric function The rhinencephalon, which was concerned with the functions of central emotion, was capable of accrued, effective, emotional experience which was symbolic, non-verbal, and undiscriminating The rhinencephalon was not closely connected to the cerebral cortex, therefore two independent sets of thoughts could exist In this way intelligent people might be the victims of irrational *emotions and fears* In spite of much careful case taking our understanding and treatment of psychosomatic disorders was disappointing Often the patient had no conscious awareness of the stresses of life which upset his gastric function, the true nature of the relevant stress often remained obscure because neither the patient nor the doctor was willing to discuss the subject

Prof **C F W Illingworth** discussed the psycho*logical* accompaniment of peptic ulceration He agreed that there was undoubted evidence of a connection between the mental state and gastric *function*, but it was not clear how this was causally related to peptic ulceration The published observations *on the* patient Tom recorded that when Tom was defeated his gastric mucosa grew pale and his acid secretion fell When Tom was angry his gastric mucosa became hyperæmic and secreted acid But exactly the opposite results were observed in another patient, Doris, a Negro lady Most patients with peptic ulcers were of a particular temperament and type—tense, driving, active, underweight, possibly obsessional *in some degree* But the relation of this mental state to the peptic ulcer was quite unexplained Many of the mental stresses which had been adduced as causes of *peptic ulcer had been shown* by careful work not to be important—for example mental conflicts of infancy and childhood, the death of parents, unhappy homes, and divorces Perforation *of an ulcer or hæmorrhage might* follow acute psychological stresses, but this relationship was neither the whole explanation nor invariably present During the war, for example, a sharp rise in the incidence of perforated ulcers was correlated with the air raids of *1940–41* on London In Glasgow there was a similar increase in the incidence of perforations but it came just before the raids Moreover, the peaks in the graph *of acute complications of ulcer did not show* in the data for women, who suffered perhaps greater war time stresses than male civilians "We must admit that psychological stress *could* be important *but* we must not overemphasise its rôle, lest we prevent adequate investigation of other influences which might be more important

Dr **C F Rolland** emphasised that anorexia nervosa was a clinical entity but not a very common one In Prof D M Dunlop's wards at Edinburgh Royal Infirmary there had been 25 cases in fifteen years Anorexia nervosa was *the outcome of serious mental* disorder which was neither hysterical nor obsessional Often the mental cause was obscure, but if it could be discovered and explained there was reasonable hope that the patient would respond to encouragement and suggestion He quoted the case of a schoolgirl aged 16 years who was much afraid of her mother When the patient was aged 13 a girl in her school became pregnant and the resulting *scandal made a great impression on the patient* Her own plumpness of figure led to her being teased by her schoolmates to the effect that she too might be pregnant Accordingly she ate little in order to become thin, and by the time she was 16 years of age she had lost all appetite She made a good recovery in response to sympathetic explanation, encouragement, and suggestion Young spinsters were most often affected, and amenorrhœa was a *common and persistent* feature The breasts often remained well developed in spite of the general emaciation Patients under treatment must be carefully watched for tricks such as secreting food, taking cathartics, and deliberately inducing vomiting Concentrated *food* such as *calcium* caseinate *might* be coloured and offered as a medicine, ostensibly *for* the treatment of constipation Insulin, testosterone, adrenocorticotropic hormone, cortisone, and isoniazid were not of value in treatment of this condition

Dr **J M Walker** dealt with the physiological effects of smoking, a subject on which, as he told the meeting the New York City Library had over 4000 volumes Much of the evidence was *subjective, emotionally* coloured, and hard to assess Most studies dealt with acute effects His own paper dealt largely with the effects *on nutrition* When a person stopped smoking his weight increased and his appetite improved Why had smoking *this effect on appetite and weight ? Among other possibly* important effects, cigarette smoking liberated adrenaline and this raised the blood sugar, which reduced sensations *of hunger* Tentatively he suggested that nicotine also acted on the hypothalamus in much the same way as amphetamine, which also reduced appetite *In the light* of this suggestion he was interested to find that the effect of smoking on urinary output after drinking water was to

TABLE IV—CHEMOTHERAPEUTIC EXPERIMENTS ON MICE

Expt. no.	Strain	Infecting dose per mouse		Dose of isoniazid (mg. per kg. per day)	No. of mice surviving on day					Average day survival at 50 or 79 days	Appearance of lungs of survivors
		Mg.	Viable units		15	24	36	50	79		
1	H37RV	1·0	$1{\cdot}5\times10^{7}$	..	9	5	2	1	..	26·2	+ + +
				20	10	10	10	10	..	50·0	±
		0·3	$4{\cdot}6\times10^{6}$	..	10	8	6	4	..	38·7	+ + +
				20	10	10	10	10	..	50·0	±
	A0	1·0	$6{\cdot}9\times10^{6}$	..	10	5	2	0	..	26·9	..
				20	10	10	10	10	..	50·0	±
		0·3	$2{\cdot}1\times10^{6}$	..	10	10	10	10	..	50·0	+ + +
				20	10	10	10	10	..	50·0	±
	A1	1·0	$4{\cdot}0\times10^{7}$	..	2	0	0	0	..	9·5	..
				20	10	10	9	8	..	46·9	+
		0·3	$1{\cdot}2\times10^{7}$	..	10	7	6	4	..	36·7	+ + +
				20	10	10	10	10	..	50·0	+
2	M0	1·2	$6{\cdot}0\times10^{7}$	..	2	0	0	0	0	12·0	..
				20	10	10	10	10	10	79·0	+
		0·3	$1{\cdot}5\times10^{7}$	..	10	10	7	2	0	41·5	..
				20	10	10	10	10	10	79·0	±
	M1	1·2	$2{\cdot}6\times10^{7}$	..	1	0	0	0	0	9·6	..
				20	9	9	9	9	7	70·9	+ + +
		0·3	$6{\cdot}5\times10^{6}$	..	9	9	7	0	0	36·9	..
				20	10	10	10	10	9	76·2	+ + +
	M2	1·2	$8{\cdot}7\times10^{6}$	..	9	4	0	0	0	22·3	..
				20	10	10	9	9	0	55·4	..
		0·3	$2{\cdot}2\times10^{6}$	..	10	9	6	4	0	45·1	..
				20	10	10	10	9	7	71·9	+ + +

In experiment 1 both treated and untreated mice were also infected with 0·1 mg. and all survived for 50 days.

±, only slightly enlarged.
+, few small tubercles.
+ +, few large tubercles.
+ + +, many large tubercles.

organisms had largely taken the place of the resistant ones during subculture rather than that the resistant strains had poor viability. It should be noted, however, that in only one strain did the culture revert to complete sensitivity.

The experiments on animals show that the three resistant variants A1, M1, and M2 were about as virulent as the original sensitive strains, and that isoniazid did not give complete protection against them. Protection was least in mice. Although treated mice survived the period during which untreated mice died, some of them died later, and the survivors were found to have more tubercles in their lungs than were found in the lungs of the mice infected with the sensitive strains.

In guineapigs isoniazid was more effective, for there was no macroscopic evidence of generalised tuberculosis in the treated animals. Nevertheless the protection was still incomplete, for in the spleens of two guineapigs, one infected with strain A1 and the other with strain M2, there were microscopic tubercles. Further, of the eleven treated guineapigs six had a caseous abscess at the site of inoculation and caseation of the draining lymph-gland, whereas only one of the seven treated animals infected with the sensitive strains had developed a caseating gland, and none had abscess formation.

The partial protection by isoniazid against these resistant strains may be due to the inocula containing only relatively small proportions of organisms capable of growth in the concentrations of isoniazid in the tissues of the treated animals; for the sensitivity tests (table IV) showed that only a small proportion of the bacilli of the strains M1 and M2 could grow in the presence of 1 µg. of isoniazid per ml. Karlson and Ikemi (1952b) and Goulding et al. (1952) have shown that treatment with isoniazid does not affect the mortality or the development of corneal lesions in mice infected with highly resistant strains. Unpublished observations of ours show that strains only slightly more resistant than strains A1, M1, and M2 are at least as lethal in isoniazid-treated mice and guineapigs as in untreated animals. One such strain yielded heavy growth on 1 µg of isoniazid per ml., but no growth on 5 µg, of isoniazid per ml. Therefore it is reasonable to assume that bacilli capable of growth on solid medium containing 1 µg. or 2 µg. of isoniazid per ml. can grow in the tissues of animals receiving 20 mg. per kg. body-weight daily. This dosage is about five times as high as that used in the Medical Research Council (1952) trials but is nevertheless of the same order, and there is therefore some experimental evidence to support the assumption, made in their report, that strains growing in 1 µg. or more of isoniazid per ml. were resistant.

There seemed to be no essential differences between the results of the animal experiments with the three resistant strains, but apparent differences in in-vivo sensitivity in mice and guineapigs are of interest. Gray and Mattinson (1952) have shown that mouse inoculation is more sensitive in detecting small numbers of bacilli than has previously been thought, and they also showed that strain differences in mice were largely abolished if the experiments were allowed to run sufficiently long. Further, Knox et al. (1952) have pointed out that H37RV is much more sensitive to isoniazid at 35°C than at 37°C. The average rectal temperature of mice is 34·3°C (Goulding and Robson 1952) and that of guineapigs 39·1°C (personal observations). The eventual death of mice and the degree of tuberculosis in survivors infected with strains A1, M1, and M2 after relatively long periods might therefore be due to a combination of the long-term lethality of the small number of resistant organisms shown to be capable of growth in 2 µg. of isoniazid per ml. (table I, strains M1 and M2) or to the relative sensitivity of the resistant strains.

It might be argued that, since 10^7 organisms of sensitive strains appear to contain some highly resistant bacilli in vitro, similar in sensitivity to strain B (Rist 1952, Steenken and Wolinsky 1952), the inoculation of as large a dose as 1 mg. of H37RV into guineapigs in experiment 1 would lead to the death of these animals from multiplication of the resistant bacilli, or at least to the production of histologically detectable lesions. However, unreported experiments with strain B indicate that it is virulent to mice but not to guineapigs; so not all resistant bacilli may be able to set up active infection in guineapigs.

It will be interesting to see whether resistant strains of tubercle bacilli from patients treated with isoniazid tend to lose their resistance when treatment is stopped. If this happens in vivo and in manner similar to that in vitro, it might prove of benefit to treat these patients with a further course of the drug, since seven of the sixteen resistant strains which came from patients and were subcultured in the absence of isoniazid had a final sensitivity similar to or below that of A1, M1, and M2.

Finally, a comment on methods of testing the sensitivity of tubercle bacilli from patients can be made. Both Bowen and Collins (1952) and Joiner et al. (1952) have used a technique involving subculture in Dubos medium free from isoniazid before the final test in the same medium. The irregular loss of resistance that is likely to have taken place during such a procedure throws doubts on their results, and one must recommend a procedure using as little subculturing as possible.

SUMMARY

Isoniazid-resistant variants of H37RV produced in vitro rapidly reverted to sensitivity if they had been in contact with the drug during only one subculture. This was confirmed by in-vivo sensitivity tests in mice. Resistant variants passaged more than once in the presence of the drug, retained their resistance without diminution during several passages in drug-free medium.

Resistant variants tended to have poor viability during the first three passages in the presence of isoniazid, but later their viability seemed normal.

against which one should be forewarned are those liable to cause persistent sequelæ or fatalities, such as exfoliative dermatitis and agranulocytosis But we need to know their incidence, and unfortunately Dr Meyler does not give this in most cases He tells us that agranulocytosis may follow diphenhydramine ('Benadryl'), but unless we know whether it is common, or has merely been described on one solitary occasion, we are little wiser The section on acetanilide contains nothing beyond the following

> "cyanosis due to methæmoglobinæmia, hæmoglobinuria, porphyrinuria, irregular pulse, collapse, erythema Prolonged use may give rise to secondary anæmia General malaise, dizziness, palpitations, numb fingers, cardiac insufficiency, anorexia, psychic imbalance, icterus, deafness, hyperæsthesia, increased reflexes, perspiration, nausea, vomiting (Davison)"

This is not of much help Among the many side-effects of aspirin mentioned, without reference to frequency are "damage to the acoustic and optic nerves, even leading to complete deafness and blindness," hyperpyrexia, coma renal colic, necrosis of the liver, and hæmorrhagic exanthemata Often no clear distinction is made between the ill effects that inevitably follow a large dose of a drug—and these are hardly *side*-effects—and those that may follow an ordinary dose

In spite of these defects the book contains much useful information about some drugs If in future editions all the sections are brought up to the standard of the best, the book will be a useful work of reference

Annual Review of Microbiology

Vol 6 Editor Charles E Clifton Stanford, California Annual Reviews 1952 Pp 492 $6

If we have complained of previous issues of this established annual it has been because so much of their contents has been of specialised interest The volume for 1952 contains a majority of reviews which all bacteriologists may read with profit and a few which will interest any member of the medical profession Once a year is not too often for all of us to brush up our knowledge of antibiotics

Sigel's chapter on the influence of age on susceptibility to virus infections is not light reading, but most pædiatricians will find it full of suggestive observations Rickettsial infections and toxoplasmosis have received attention in many parts of the world in the years since the war, and it is useful to have all this work sorted and put in a readable form, and the same is true of Burnet's discussion of virus/red cell reactions But we hope that it is not mere jingoism which causes us to give the palm among all the distinguished contributors to Andrewes's scholarly review of the problems of naming the viruses—*or not naming them* If the standard of this volume is maintained we shall look forward to future issues

Das Inselsystem des Pankreas

Helmut Ferner, professor, Anatomical Institute, Hamburg University Stuttgart Thieme 1952 Pp 174 D M 29 70

Professor Ferner, head of the department of anatomy at Hamburg, here collects in one volume the results of many years' detailed work on the embryology, comparative anatomy, and histology of the pancreas, particularly in relation to the problems of diabetes

He has mainly favoured the Gros Schultze silver method, which can be used only on frozen or celloidin sections, to differentiate the α, β, and D cells of the islets of Langerhans He claims the β α cell ratio determined on sections so stained is characteristically depressed in diabetes, but his hypotheses take him much further He believes, for instance, that the α cells which stain with silver are precursors of β cells, in spite of the fact that mitotic figures in differentiated β cells may be found in suitable preparations Further, he thinks that the anterior pituitary secretes an *alphacytotrope Faktor*, but his evidence for this does not bear scrutiny He also develops an interesting suggestion that juvenile diabetes may be due to a maturation arrest of the transformation of α to β cells, and cites as evidence the absolute increase of α cells as well as the low β α cell ratio in many young diabetics

The book is illustrated by wonderfully detailed drawings of histological preparations, but sceptical pathologists might have preferred a greater proportion of objective photomicrographs There are particularly beautiful illustrations of the blood-supply to the islets of Langerhans

Allergy and Seborrhœa

J Avit Scott, M D, Licencié en Droit (Université de Lille) London H K Lewis 1952 Pp 100 12*s* 6*d*

Dr Scott has attempted the impossible task of comparing a pathological conception of uncertain clinical significance with a group of clinical conditions of vague pathology His disarmingly modest introduction and much of his material suggest that he has written for the beginner—who, however, is more likely to be dismayed than fortified by the greater part of the text It offers difficult and in places exasperating reading even for the dermatologist familiar with the French models upon which it is largely based

A Textbook of Pharmacology

William T Salter, M D, professor of pharmacology, Yale University School of Medicine Philadelphia and London W B Saunders 1952 Pp 1240 75*s*

This book helps to bridge the gap between human physiology and clinical pharmacology Professor Salter has been no more successful than other authors in his classification of the subject matter, but pharmacology when presented for the instruction of medical practitioners is necessarily heterogeneous His book has the merit of consistency—not a conspicuous virtue in textbooks written by numerous contributors

The pleasantly informal style recalls an American statesman's fireside chat, the sections are embellished with appropriate introductory quotations from the poets, and the reader's interest is sustained by clinical reminiscences American idiom abounds, and for the British reader this characteristic in itself makes the book delightful Professor Salter has an enviable capacity for incorporating the gist of original publications into the text without destroying the sequence of his narrative Long lists of references are appended to every chapter, but only a selection of these receive attention in the text The inclusion here and there of short paragraphs on unsolved problems is a stimulating innovation, and the synopses—running to about 200 words—at the end of each chapter will be a godsend to many students and practitioners The writer's views are conventional rather than critical, he prefers the time honoured to the sceptical approach

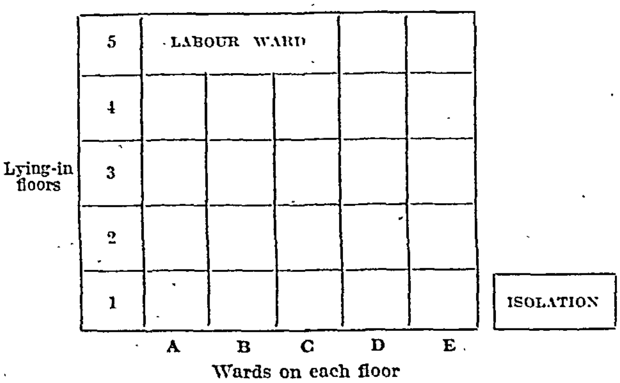
The book is sufficiently comprehensive for both the clinical student and the medical practitioner It might have been more concise and factual, but only at the risk of destroying its attractive flavour

Hypnosis in Medicine

A Philip Magonet, B SC, M D, *president*, Medical Hypnosis Association London Heinemann Medical Books 1952 Pp 104 9*s* 6*d*

Dr Magonet's purpose in writing this account of the technique and possibilities of hypnosis is to encourage doctors and medical students to explore the subject for themselves But his terminology and dogmatic approach are more likely to be acceptable to the layman The prejudice against the use of hypnosis in medical practice, which undoubtedly exists and to which he frequently refers, is unlikely to be broken down by publishing successes and forgetting failures, for the medical reader is trained not to receive suggestion but to consider evidence Hypnosis is in fact already part of the armamentarium of most psychotherapists and there seems little to justify the suggestion that it should be separated from psychotherapy as a whole

After a brief description of the early history of hypnosis Dr Magonet describes his own technique, and then devotes the bulk of his book to cases successfully treated An interesting account of the use of hypnosis in childbirth and in different kinds of insomnia gives an insight into the way in which an experienced hypnotist approaches his subject As an enthusiast for this method of treatment, Dr Magonet feels that the regrettable attitude of the medical profession towards such pioneers as Braid and Elliotson still persists and that hypnosis is still suspect as a field for charlatanry and morbid interest One can at least agree that "employed in a scientific way in accordance with well established principles" its usefulness may increase



developed tonsillitis two days later, and this proved to be due to group-A streptococcus.

HISTORY OF OUTBREAK

This hospital consists of four floors for lying-in patients, each floor having 30 beds which are subdivided into five wards of 6 beds each; the fifth floor comprises the labour-ward suite, and there is a separate isolation ward. The layout is shown in the accompanying plan.

The outbreak started in November with a few sporadic cases, the first being a nurse who reported sick and was sent off duty until her throat was clear. Fourteen days later a baby developed erysipelas and was transferred to another hospital at once. Ten days later another nurse reported sick with a sore throat which was also found to be due to a hæmolytic streptococcus; and in another nurse the organism was grown from a small infected scratch. Despite the considerable interval between these cases and the rest of the outbreak, they were of the same Griffith type and appeared on the same floor. Throat swabs were taken from all contacts, but no positive swabs were obtained, and the ward 2D was closed and disinfected after all other patients had been transferred to the isolation ward. Disinfection consisted of sealing the windows and doors with tape and spraying the ward with 40% formaldehyde; the ward was then left sealed for forty-eight hours before being opened and aired. The technique was described by White (1936) who showed that satisfactory sterilisation could be achieved in this way.

TABLE II—DISTRIBUTION OF CASES

—	1st floor	2nd floor	3rd floor	4th floor
November	—	1 nurse	—	—
	—	1 baby	—	—
	—	2 nurses	—	—
December	—	3 patients	1 patient	1 patient
	—	6 nurses	—	—
	1 case	4 patients	—	—
		1 nurse		
Jan. 1–14	—	—	3 patients	1 patient

Early in December a second group of 5 cases appeared: 3 were in ward 2D, and the other 2 on different floors. Further throat swabs were taken from the staff of the second floor and no less than 6 positive cultures were obtained. All 6 people were sent off duty, and they stayed away until 3 clear swabs had been obtained. The ward was again disinfected.

In late December another 5 cases appeared, 4 of them in the same ward, and the other on the first floor. No more positive swabs were obtained from the staff, but a blood-agar plate exposed in the ward grew a few colonies of group-A hæmolytic streptococci. In early January, 4 more cases were identified in ward 3A, where no positive cultures were obtained from the staff, and an isolated case appeared on the fourth floor. The distribution of cases is shown in table II.

In the early part of the outbreak it seemed that all the connected cases were in the same ward, the reservoir of infection being the nursing staff. After the Griffith typing became known, however, it was obvious that the isolated cases on the first, third, and fourth floors were connected with the main outbreak. If there had been cross-infection between these cases and those on the second floor, it must have taken place either in the large waiting-ward of the labour-ward suite or by way of a carrier among the staff. No evidence has been found to support the first possibility.

The clinical picture was variable, falling into three groups: mild or severe infections of the genital tract, and a miscellaneous group including a case of erysipelas. In 11 of the 14 patients who had genital-tract infections the illness was mild; a typical mild case had a temperature of 100·4°F on the fourth day, which persisted for twelve hours, with little general disturbance and rapid improvement after the administration of penicillin. The other 3 patients, however, were seriously ill for some forty-eight hours, the temperature ranging from subnormal to 105°F associated with rigors. All 3 showed varying degrees of uterine tenderness, a sign which in the pre-sulphonamide era implied that peritonitis was established. The response to penicillin and sulphonamide was much slower than in the mild cases, and the patients remained unwell for two to three days after the temperature had settled.

DISCUSSION

This outbreak of puerperal infections was far larger than anything experienced in recent years and could have been brought about by three main causes:

(1) A relaxation of antiseptic methods.
(2) An increased infection-rate in the surrounding population.
(3) An increase in the pathogenicity of the organism.

The antiseptic routine in the hospital has not been changed during the past five years. There seems to be a moderate number of cases of infection with group-A streptococci in other institutions and in the surrounding district, but the influence of rapid and effective antibiotic therapy on the infection-rate makes it difficult to assess the situation (*British Medical Journal* 1953). On the whole, however, it does not seem that the increase elsewhere is much greater than the normal seasonal rise, and in this connection it is important to note that the patients admitted from the district to the hospital isolation ward all had different Griffith types from the patients who fell ill in hospital. The infection spread from nurse to patient and back, and at the same time the ward dust became contaminated. The difficulty of controlling such a spread while continuing to admit cases, though well known in the past, has been largely forgotten of recent years. One is forced to consider whether the rise in the number of cases, and the severity of some of them, may not be due to an increase in the virulence of the infecting organism, aided by its passage through numerous hosts.

The outbreak continues, and since this paper was prepared we have had 3 more cases; one was mild, another was the most severe genital-tract infection of the outbreak, and the third was a streptococcal meningitis in an infant, the outcome of which is still in doubt. We feel it is important that this epidemic should be brought to the notice of those responsible for other maternity units in order that they may be on their guard against similar severe puerperal infections.

SUMMARY

An outbreak of 25 cases of infection with *Streptococcus pyogenes* occurred in a maternity hospital. The majority

seem to increase the duration of life any further than other treatments, they also used X rays sometimes to reduce the size of the spleen LAWRENCE[11] found that P^{32} was equally effective for chronic lymphatic leukæmia Radiophosphorus is still not much used in this country because of difficulties of supply and handling

Urethane was introduced in 1946 by EDITH PATERSON and her co-workers,[12] and it proved useful especially in chronic myeloid leukæmia STURGIS thinks that experience has shown that results with urethane are inferior to those with radiation, and it is now rarely used, mainly because of the unpleasant side effects—persistent anorexia, nausea, and even vomiting Nitrogen mustard (mustine *B P*) is still much used in this country, many reports suggest that the results are as good as with X rays, and it has the advantage over later modifications that its active phase is relatively short and its effect is therefore more controllable Its great disadvantage is that it has to be given intravenously in a running drip Drugs of this type that can be given by mouth have been introduced[13] PATERSON et al[14] gave one such drug, triethylene melamine, in enteric-coated tablets, and found that its action, unlike that of most antileukæmic agents, was strongest against chronic lymphatic leukæmia Hæmopoietic tissue is, however, very sensitive to triethylene melamine, which must never be used without proper hæmatological control The latest of these antileukæmic drugs that can be given orally is 'Myleran,' accounts of which were given in our issue of Jan 31 by Professor HADDOW and Mr TIMMIS, and by Dr GALTON Myleran is especially interesting because chemically it is quite different from the nitrogen mustards, it is 1 4 dimethanesulphonyloxybutane It is effective only in chronic myeloid leukæmia, in therapeutic doses it depresses granulocyte formation in the bone-marrow without affecting the other elements But, like its predecessors, it is a powerful antihæmopoietic drug that in large doses can cause thrombocytopenia or even pancytopenia Folic-acid antagonists have been used in attempts to control acute leukæmias Some temporary remissions have been obtained with 'Aminopterin,' but the toxic effects can be severe and the results are capricious[15 16] In acute leukæmia A C T H and cortisone have also been extensively tested In a group of 40 cases treated, only 2 had lengthy remissions, 7 more had remissions only during treatment[17] STURGIS points out that the favourable responses that have been recorded were mostly in children

All this activity shows that a great effort is being made to meet the challenge of increasing leukæmia *All the methods hitherto developed need close control,* and the patient's only hope of even temporary relief depends on his attending a centre equipped to deal with the disease

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[11] Lawrence J H Low Beer, B V A, Carpender, J W J *Ibid* 1949 140, 585

[12] Paterson E Haddow A, ApThomas I Watkinson J M *Lancet*, 1946 ii, 677

[13] See *Ibid*, 1951, i, 1111

[14] Paterson E Kunkler P B, Walpole A L *Brit med J* Jan. 10 1953, p 59

[15] Dacie J V Dresner E Mollin D L White, J C *Ibid* 1950 i, 1447

[16] Wilkinson, J F Gardikas C *Lancet*, 1951 i, 325

[17] Medical Research Council *Brit med J* 1952, i, 1261

Pneumothorax Therapy

ENTHUSIASM for pneumothorax therapy in pulmonary tuberculosis seems to be waning[1], but this method of treatment is unlikely to be discarded It is a relatively *simple alternative to surgical* measures which few centres can provide for all cases Many clinicians have a certain affection for this method which they can apply at their own discretion without seeking a surgical opinion or transferring the patient elsewhere, pneumothorax may yet prove to deserve in its own right a limited place in treatment Meanwhile, the problem of when to terminate a pneumothorax is still with us

In an attempt to solve this problem HARRIS et al[2] analysed the records at the Edgware and Harrow chest clinics of 279 cases in which a pneumothorax had been abandoned, not because it was unsatisfactory, *but because the* clinician concluded that the disease had been effectively controlled The results, therefore, reflect, not the general value of pneumothorax therapy, but its effectiveness in a selected group of patients in whom things had gone well for several years The investigation showed that no firm criteria had prompted the decision to abandon the pneumothorax There was no correlation between the severity of the initial disease and the duration of relaxation, and whereas some lungs which initially showed only infiltration were kept collapsed for five or more years, others with cavitating lesions were allowed to re-expand in less than three years Some *physicians terminated a pneumothorax only* when refills became too difficult, others when the pneumothorax had been present for five years, and still others on radiological evidence Many clinicians took part in maintaining the pneumothoraces, and no common plan of action could be detected A surprisingly high proportion (46 6%) were badly maintained, and with these the end-results were only *half* as good as with *those* which were *well maintained,* although the efficiency of maintenance was unrelated to subsequent breakdown

HARRIS et al correctly associate faulty maintenance with the staffing of chest clinics, and point out the necessity to keep down the number of patients at refill sessions, in order to give enough time to each patient Another important finding is the disastrous effect of change in personnel among the clinicians Such changes are bad enough when one skilled operator is replaced by another, but they are much worse when an inexperienced locum tenens takes over—which is what commonly happens in clinics at times of holidays or sickness This particular hazard of pneumothorax therapy is seldom recognised It certainly deserves attention, for the results were good in no less than 83 3% where *the pneumothorax was well maintained* YOUNG,[3] also has shown that better results are achieved by a constant operator A system of staffing chest clinics with registrars who are continually changing, often with intervals necessitating the employment of a locum tenens, is clearly not desirable

The investigation emphasises the need for a rational policy with regard to the duration of pneumothorax best avoided, and certainly should not be given to out-patients. Where intramuscular therapy was employed, an initial dose of 20 mg. was given and the blood-pressure was recorded every ten minutes, with the patient sitting up in bed. The dose was then slowly increased until a satisfactory fall in blood-pressure was obtained. The dose thus determined was usually given every three or four hours, provided the blood-pressure was 140/90 mm. Hg or higher. This precaution avoided periods of hypotension. The blood-pressure was recorded hourly by day and two-hourly by night.

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[1] Simmonds, F A H, Laird, R, Macdonald, N *Lancet* 1952 ii, 347

[2] Harris, W C Poles F C, Anderson, A W *Quart J Med* 1952, 21 447

[3] Young F H *Proc R Soc Med* 1949, 42, 244

Although all but 1 of the 10 patients showed a fall in blood-pressure, this fall never lasted longer than three or four hours and it varied considerably from case to case and from time to time, as has been found in non-pregnant patients (Wĕrko et al. 1951). To maintain a relatively stable blood-pressure was therefore more or less impossible. In most cases resistance to hexamethonium developed very rapidly, often over a period of days; but even when it ceased to lower the blood-pressure, the drug still caused the same degree of pupillary paralysis. This suggested that the autonomic blockade was still in force, but that the hypertension was now being sustained by the increased action of a humoral pressor mechanism.

Effect on the Disease

In the vast majority of cases of pre-eclampsia and essential hypertension, rest in bed and sedation are followed by satisfactory regression of signs and symptoms. Though we were usually able, with hexamethonium, to lower the blood-pressure, it is very doubtful whether this materially altered the ultimate course of the illness. No patient actively deteriorated and none developed eclampsia, accidental hæmorrhage, or gross renal damage, and it is therefore possible that the hypotensive treatment was of some value; but there was certainly very little evidence that the prognosis for the fœtus was improved. In some cases treatment may have been started too late, when extensive placental damage had already taken place; but the vascular changes that occur at the uteroplacental site in pre-eclampsia still remain obscure,

CASE-HISTORIES—*continued*

Description of case	Maturity at start of hexamethonium	Dose and route	Effect on B.P.	Duration of treatment	Delivery	Fœtus	Hexamethonium estimations
6. Primigravida aged 23. B.P. at 16 weeks 120/70. Admitted at 31 weeks with B.P. 150/80 and œdema. No albuminuria. Marked deterioration at 33 weeks. B.P. 170/110, albuminuria, and increasing œdema	33 weeks	100 mg. intramuscularly 4–6 hrly., increased to 250 mg. 3-hrly. (Also given ion exchange resins)	Good initial response. Resistance developed rapidly. Increased dose gave reasonable control. B.P. 140/90–160/100	19 days. Last injection 20 hours before delivery	Lower-segment cæsarean section at 36 weeks	5 lb. 14 oz. Vigorous at birth. Developed abdominal distension and general peritonitis. Died on 8th day. P.M.: peritonitis and distension of intestines with no obvious primary cause	At delivery: maternal blood, a trace; cord blood, none detected; amniotic fluid 5·7 µg./ml. Colostrum: none deetcted
7. Primigravida aged 38. B.P. at 20 weeks 160/100. Admitted at 30 weeks with B.P. 160/105. No œdema or albuminuria. Marked deterioration; B.P. rose to 190/120, with albuminuria	32 weeks	80 mg. intramuscularly 3-hrly., increased to 250 mg. 3-hrly.	No response	48 hours	Lower-segment cæsarean section at 32 weeks	3 lb. 3 oz. Treated in premature-baby unit. Normal progress	Not performed
8. Multigravida aged 28; premature stillborn deliveries in 1946 and 1947. B.P. at 14 weeks 150/90. Admitted at 28 weeks with B.P. 196/130 and albuminuria. No œdema. No response to rest and sedation	29 weeks	60 mg. intramuscularly 3-hrly., increased to 200 mg. 3-hrly.*	Resistance developed rapidly. Moderate response only to increased dose	22 days. Fœtal heart not heard after 18 days' treatment	Spontaneous at 32 weeks	Macerated. Placenta extensively infarcted. P.M.: evidence of intrauterine asphyxia	Not performed
9. Multigravida aged 33; three stillborn infants, with pre-eclampsia. B.P. at 12 weeks 160/90. Admitted at 29 weeks with twin pregnancy; B.P. 190/110 and albuminuria. No œdema. No response to rest and sedation	30 weeks	100 mg. intramuscularly 3-hrly.	Moderate response only	7 days. Fœtal heart not heard after 3 days' treatment	Spontaneous at 31 weeks	Both twins macerated. Infarction of placenta not sufficient to account for fœtal deaths	Not performed
10. Primigravida aged 28. Admitted at 30 weeks with B.P. 140/90–150/95. No albuminuria or œdema. Anencephalic fœtus with hydramnios	32 weeks	20 mg. intramuscularly 6-hrly., increased to 30 mg. 6-hrly.	Good response	14 days	Spontaneous after artificial rupture of membranes at 34 weeks	4 lb. 5 oz. Stillborn anencephalic	See note †

* *Case 8.*—After 2 days' treatment with hexamethonium bromide an extensive erythematous rash developed. This disappeared when the bitartrate was substituted for the bromide.

† *Case 10.*—Hexamethonium was given mainly to determine the rate of accumulation in the liquor:
After 2 days' treatment 30 oz. of amniotic fluid withdrawn, C6 content 0·5 µg./ml.
,, 8 ,, ,, 86 oz. ,, ,, ,, ,, ,, ,, 0·5 µg./ml.
3 days after stopping treatment 20 oz. of amniotic fluid withdrawn, C6 content 4·0 µg./ml
7 ,, ,, ,, ,, 54 oz. ,, ,, ,, ,, ,, ,, nil.

economical to avoid operation and to provide surgical shoes" Each year roughly 40,000 pairs of surgical footwear are provided through the National Health Service, a considerable number of these must be for the broad foot with hallux valgus, so there still seems to be good cause for research into its origin and treatment

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Annotations

FOG AND FALLACY

Of our trilogy of reports on the recent London fog (concluded with Dr Logan's paper on p 336) one was from Dr John Fry, who on Jan 31 described the effect of the fog on his Beckenham practice In our correspondence columns this week a Durham colleague, Dr Frank Cort, expresses surprise at the relatively small number of extra visits Dr Fry was called upon to make, compared with his own experience during "a similar occurrence' two or three years ago From this he goes on to point out that the number of visits and attendances per patient per annum is about three times higher in his own practice than it is in Dr Fry's, and that his remuneration per item of service is accordingly about three times less We are glad to print this letter, together with a rejoinder from Dr Fry, because it gives us an opportunity to say, most emphatically, that the value of a practitioner's work cannot and must not be judged by counting his items of service To think in terms of *quantity* is the ever-present temptation of the administrator, but doctors should know better

The truth is that there are many different ways of conducting a general practice efficiently, and practitioners vary widely in their opinion about the frequency with which they need to see their patients Dr Fry's figures suggest that the people on his list are seen by him a little less frequently than the average Dr Cort, on the other hand, prefers to give his Northern patients more than twice as many items of service as are nationally usual But such variations are almost no indication of a practitioner's usefulness to the community indeed they can be interpreted in either direction, according to taste One doctor, by giving his patients ample time when he does see them, by instructing them in simple health and preventive measures, by encouraging their self-reliance, and by discouraging frivolous calls, may keep down the number of items of service asked of him while still providing care that fully satisfies those in his charge Another may find that he likes to give, and that his patients expect and prefer, much more frequent attention Additional factors that may play their part include the differing morbidity in different types of area, and the geographical features and social custom of the district (both of which profoundly affect the frequency of attendance, and the ratio between visits and surgery attendances)

The importance of Dr Fry's figures for the fog lies not in their comparison with other practices but in the variations they reveal in his own practice Dr Fry has achieved a certain pattern of practice which satisfies him and his patients (for he has built and holds a large practice in an area where the average practice is not large) With the figures he has carefully kept, he is able to predict the calls his patients are likely to make on him at different seasons of the year Here in a particular week he finds that he was called upon to give much more than double the number of attendances to patients suffering from respiratory disorders, and affections of the upper respiratory tract, than were needed for the patients of the same practice a fortnight earlier, before the fog descended He has reported this significant fact Similar valuable information, often known to general practitioners but rarely recorded, may well come to light if the College of General Practitioners pursues one of its declared aims—"the encouragement of accurate observation, investigation, and recording of results by general practitioners"

HYALURONIDASE AND URINARY STONES

Last year [1] we remarked on the promising possibility of hyaluronidase as a means of preventing or at least curbing the formation of urinary calculi there is now more news of this interesting subject The story really began in 1950 when Butt [2] observed that subcutaneous injections of hyaluronidase mixed with isotonic saline solution could produce a much clearer urine in patients who had previously been passing a turbid urine containing much sediment The hyaluronidase worked, it was suggested, by increasing the colloid content of the urine and so preventing crystals from forming and growing Indeed, Butt and Hauser [3] were able to give visual proof that an injection of hyaluronidase was followed by the release of protective colloid in the urine, which not only dispersed crystals already there but inhibited the formation and growth of new ones But the addition of hyaluronidase to urine after it had been passed did not increase its colloid content, so the suggestion was made [4] that hyaluronidase acted indirectly by releasing hyaluronate at the site of injection and that hyaluronate was excreted in the urine during the period of restoration of hyaluronate at the site of injection Butt and his colleagues have since shown that potassium hyaluronate is a powerful dispersing agent the evidence suggests, then, that a hyaluronidase substrate is a part of normal urine and that it has much to do with regulating the colloid-crystalloid balance, some disturbance in this balance has for long been blamed rather vaguely for the formation of urinary calculi

Butt et al [5] have now carried their clinical experiments a stage further Before giving hyaluronidase to a patient troubled by recurrent stones, they determined the level of protective colloids in his urine by ultramicroscopic examination and photography, by measurements of surface tension, or by sediment and turbidity tests They then found that in most patients with uninfected urine an injection of 150–300 turbidity reducing units (T R U) of hyaluronidase every 24 or 48 hours produced a considerable increase in protective urinary colloids In the presence of infection much larger doses were needed—often between 300 and 900 T R U and occasionally as much as 2400 T R U daily In this way they were able to suggest a suitable dose for each patient and to control the treatment as it proceeded Indeed, the one discouraging feature of this work is the need to estimate rather carefully the adequate dose for a particular patient, for if too small a dose is given, the colloid crystalloid balance may be tipped the wrong way by sensitisation, and crystal may be deposited rather than dispersed Butt et al do not sound completely happy about this important point, and they are hard at work trying to get to the bottom of it, but if the results they have achieved so far are anything to go by, this question of estimating dosage is not going to prove very troublesome, and moreover, there is no need to worry about giving too much, for large doses of hyaluronidase have no ill effects

Twenty-four patients, who had been forming stones with depressing regularity and for no clear metabolic reason, have been under treatment for from 11 to 21 months All other attempts to subdue the calculi had failed but in nineteen of these patients no new stones have formed and there was no evidence of extracellular multiplication of the parasites under these conditions, although multiplication and liberation of parasites continued in leucocytes introduced with the infecting inoculum from the mouse.

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[1] *Lancet* 1952 i, 1198

[2] Butt, A J *J Florida med Ass* 1951 37, 711 *J Urol* 1952 67 450

[3] Butt A J Hauser F A *Science*, 1952, 115 305, *New Engl J Med* 1952 246 601

[4] Butt A J Hauser E A Seifter J, Perry J Q *Sth med J* 1952 45 351

[5] Butt A J Hauser E A Seifter J *J Amer med Ass* 1952 150 1096

These experiments were made in the Wellcome Laboratories of Tropical Medicine, London, and I am grateful to the director, Brigadier J. S. K. Boyd, F.R.S., for permission to publish the results.

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Hypotension during Anæsthesia

ON Feb. 4 the society's section of surgery met under the chairmanship of Prof. F. A. R. STAMMERS, president of the section, to discuss Hypotension During Anæsthesia.

Dr. J. B. WYMAN put the anæsthetist's case for temporarily lowering the surgical subject's blood-pressure by autonomic ganglionic block with a pentamethonium salt. He based his remarks on experience of 1000 major operations, including 157 thyroidectomies and 135 mastectomies; the majority of patients were middle-aged, but 82 were over 70, and 22 under 20.

There were two advantages. Blood-loss was enormously reduced, and this gave the surgeon a clear, almost dry, operating field and shortened his operating time; and pentamethonium seemed to protect the patient against surgical shock. It was known that sympathectomised dogs could not be shocked irreversibly, and autonomic chemical blockade apparently offered similar protection. It was striking how patients remained in a good steady state throughout operations and were in fine form afterwards. He cited 2 cases of hæmatemesis in elderly people where blood-transfusion failed to raise the blood-pressure or relieve shock, but an injection of pentamethonium produced immediate improvement. One of these patients was a man of 80 with an undetectable systolic pressure when his emergency partial gastrectomy was decided on. After 100 mg. pentamethonium his blood-pressure was unchanged but his condition became better; he was discharged from hospital 14 days after the operation. Established shock was clearly not an absolute contra-indication to controlled hypotension, as had at first been believed.

Two risks with pentamethonium everyone had in mind were that it might provoke a vascular accident, or that it might cause a failure of adequate blood-supply to an important organ—which was why asphyxia from any cause was another contra-indication. It seemed, however, that the rate of linear blood-flow through an organ was more important to it than the volume of flow, and was not necessarily altered by hypotension. When coronary flow dropped, so did the work the heart had to do; and the worst that had been noted was a transient depression of the ST segment in some electrocardiographic leads. 114 patients with systolic pressures over 200 mm. Hg, of whom 11 had auricular fibrillation and 1 was in cardiac failure, seemed to do better on pentamethonium than with conventional anæsthesia. There was 1 case of cerebral thrombosis in the series, and there were 3 cases of pulmonary embolism occurring from 10 days to 3 weeks after operation. In general such sequelæ seemed to be unrelated to the hypotension.

Severe renal disease was a contra-indication to the use of pentamethonium, because the drug's excretion might be thereby delayed. The normal kidney went on secreting urine even when the systolic pressure dropped to 60 mm. Hg (as shown by ureteric catheterisation during operation); but there was sometimes transient postoperative oliguria for 24 hours or so, and in such cases intravenous saline would speed up recovery.

Methylamphetamine hydrochloride was usually used as antagonist to pentamethonium; but it was unsatisfactory, because as a cerebral stimulant, it made patients restless, it was easy to overdo the dose, and at the same time its effects might wear off too quickly and it might lead to unnoticed hypotension later. Morphine could be safely used postoperatively even if the blood-pressure was still low.

In this series of 1000 cases 5 deaths occurred—2 from disease, and 3 from faulty technique—before it was realised how heavy were the penalties for the slightest infraction of the anæsthetic routine.

Mr. ROBERT COX said that the surgeon did not realise how much blood a patient might lose in an ordinary operation. By soaking all used swabs and towels in a known volume of water, adding the contents of the sucker bottle, and measuring the final hæmoglobin level for comparison with the patient's preoperative hæmoglobin level, he had been able to calculate this loss. In a thyroidectomy the loss might be 250 ml., in a radical mastectomy nearly 700 ml., in a prostatectomy 550 ml.: if pentamethonium was used the loss dropped to 30 ml. only. Fewer patients needed a postoperative blood-transfusion. After prostatectomies the urine became clear sooner, and in 44 cases he had only 1 with clot retention.

In longer operations lasting up to 6 hours, such as thoracotomies for œsophageal obstruction, he was impressed by the strikingly fit state of the patient at the end of the ordeal. Orthopædic, plastic, and thoracic surgeons among his colleagues also praised the effects of pentamethonium, which helped to speed operations. The risks of postoperative reactionary hæmorrhage and hæmatoma disappeared as soon as the surgeon became accustomed to tying even small bleeding-points. He had found no increase in thrombosis or in renal or liver failure. In the ward after operation patients were nursed in the head-down position until the blood-pressure, recorded half-hourly, began to recover; then they were gradually brought horizontal and then upright. Oxygen had to be available and could settle the restless patient. He had found that phenylephrine was a better antagonist than methylamphetamine.

Controlled hypotension was obviously valuable in increasing the surgeon's view, particularly in operations such as fenestration for otosclerosis where there was usually considerable bleeding. But he felt that the ability of pentamethonium to shield the patient from shock was even more valuable and made its use of very wide application.

Dr. JOHN GILLIES was a proponent of high spinal block—the oldest method of inducing controlled hypotension, and still the most certain one. He pointed out that motor paralysis, sensory block, and hypotension were all obtained with a single injection, which left the breathing largely unaffected and therefore indicative of the state of the medulla. In contrast, intravenous hexamethonium bromide was less certain and its effects were complex. Dr. H. W. C. Griffiths and he had used high subarachnoid block in 802 cases, including 51 partial gastrectomies, 63 urological cases, 341 thoracolumbar splanchnicectomies, and 222 lumbar-sympathectomies. The majority suffered from cardiovascular disease and were poor risks. There had been 7 deaths: 2 on the table, early in the series; 4 from cerebrovascular accidents in patients who had had preoperative episodes; and 1 following reactionary hæmorrhage. 1 patient who developed a coronary occlusion during induction made a good recovery. 3 patients suffered postoperative oliguria, and 7 had transient ischæmia of limbs already affected by vascular disease. He ascribed the latter to an almost complete genicity of the hæmolytic streptococcus Be that as it may, the epidemic illustrates the difficulty of effectively controlling the spread of streptococcal infection while continuing to admit patients Undoubtedly one reason is that the causal organism remains viable in dust for a long time and may defy disinfection with formaldehyde or other chemicals Dust is likely to be especially dangerous if it is being continuously reinfected from a reservoir of streptococci, and the work of Hamburger and others [1] [2] has shown that often a heavy nasal carrier of β-hæmolytic streptococci can be found, and that fresh cases cease when this reservoir is removed Meanwhile, Dr Gibson and Dr Calman are right to warn those responsible for maternity units against the possibility of similar severe puerperal infections

LIVING WITH CANCER

Mrs Edna Kaehele, who has had inoperable cancer for six years, has written a remarkable little book about living with this disease [3] The dust-jacket asserts plainly that the title " does not mean that you can survive for longer than you thought when you have cancer but that, in spite of having cancer, you can live life abundantly " Mrs Kaehele herself, however, has survived for longer than she thought, and believes it has been, in some part at least, a spiritual victory Her story has a special interest, because it may throw some fresh light on the natural history of this disease Most patients who are beyond successful treatment die, as it were, before they have time to rally Mrs Kaehele failed to die at the appointed time, and she has rallied Perhaps her cancer would have regressed in any case, as a few do, but she certainly passed and survived a point at which most patients would have died, and that in itself is interesting

The growth was beyond operation when diagnosed in July, 1946, and by Dec 3 she had received " fifty six X ray treatments, the radium operation, radon implants, as well as biweekly injections of liver extract and countless shots of vitamins to replace the ones destroyed by radiation " She did not feel as though she had profited from this exhausting course of treatment—though it may, in fact, have slowed the *rate of growth of the tumour, and given her body time to manœuvre* Her weight had gone down from well over 10 st to less than 7 st and she had much pain, and hardly strength enough to stand She was given a blood transfusion and sent home on the understanding that she would be dead before the New Year That she did not fulfil this engagement she attributes largely to the determination of her family, and especially of one sister On Jan 17, 1947, as she was still alive, a course of radium chloride therapy was begun "It was tasteless and painless, and when the series was finished seemed to have been useless as well " However, if not gaining she was losing ground more slowly, and in February she was given another transfusion, and received two more in the course of the following months In July, a year from the date of diagnosis, she began a second course of radium chloride treatment, and after that her doctors were at the *end of their resources*

So much for the medical delaying tactics, she does not underrate their value " I beg you," she says to her readers with cancer, "to search out the best cancer specialist you can find and to make full use of the most advanced resources available "

Nevertheless *for a long time after* her treatment ended she remained very ill, and her weight, though she had stopped losing it, remained at 6–7 st She considers she was greatly supported, however, by the general determination that she should live and by her own strong religious faith She was bedridden for a long time, and for several months food "was not only unwelcome but became unbearable " Her family kept her going by adding gelatin to her coffee, and by persuading, bullying, and nagging Then came a turning point, surely of much clinical interest, when she began to eat ravenously, as though the body so recently rebelling against food was now " crying out in starved desperation." Her weight began to rise, and by the autumn of 1947 she was beginning to come " back to life " By Christmas she was going out again and doing her own shopping It was an emotional as well as a physical reorientation, and she naturally writes of it with emotion

She has put on 2 st in weight, and is now engaged in breeding dogs She needs hardly any medication for pain, which is much less insistent To others with cancer she offers two useful pieces of advice have faith in " your doctor, your God, yourself—faith in *something* ", and eat well, " stuff the body with protein to rebuild the ravaged tissues and saturate it with vitamins to revitalise it " On the subject of pain she is reassuring " I must have suffered just about all that one suffers from death by cancer, and I wish to shout it from the housetop *that my greatest* agony was in waiting expectantly twenty-four hours a day for the unbearable pain I confidently expected to begin any minute "

Her message to doctors is probably equally well chosen. If we kill the patient's hope stone dead by inviting him to die at a given time, die he probably will, at the appointed moment, out of a combination of despair and good manners *She also writes feelingly of the American* patient who delays coming for treatment until too late solely because of the expense The National Health Service has surely done a good thing in removing this cause of death from our statistics

STUDENT HEALTH SERVICES

In fact and tradition, students seldom have the means or indeed the inclination to provide themselves with good food and lodgings, and for one reason or another they are often slow to seek medical advice Theoretically, the National Health Service has overcome the student's difficulty *of finding the money to meet* ill health, but, as the Social and Preventive Medicine Committee of the Royal College of Physicians points out in a progress report on Student Health Services published last month this solution does not always work out in practice A student is often not registered with a doctor in the university town because his home is elsewhere, and the National Health Service does not provide for the regular examinations which the committee recommended in 1946 [1] and which are now required by many universities *and colleges To overcome these difficulties, the* committee would like to see more general practitioners fitted into the organisation of student health services, not only to help the student when he is ill in his " digs " but to take on the wider rôle of adviser in health

Looking back on the development of student health services since 1946 the committee finds that the position in the universities outside London, with the notable exception of Oxford, is now largely in agreement with their earlier recommendations in the matters of medical and nursing care, *lodgings, and food* In Oxford certain colleges have their own arrangements, which in some cases amount to an organised health service, but the university recently set aside a proposal for a service covering the student population as a whole The situation in London is unsatisfactory, particularly for the non medical students Nearly all the medical schools insist on regular X-ray examinations, and students can always obtain advice and treatment from members of the hospital staff, but their colleagues in other faculties are often poorly provided *for* True, University College has an excellent scheme run by its student health association, to which the Royal Veterinary College and the London School of Hygiene and Tropical Medicine are affiliated, and Imperial College is also well equipped to look after its students But the other non medical schools and colleges, with a student population of 6000, have done little to follow the committee's advice Most of them delay diuresis but to increase the total volume of fluid excreted. This was not a blood-pressure effect since it was not abolished by hexamethonium.

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[1] Hamburger M jun Hamburger, V G *J infect Dis* 1945 77 68 96

[2] Cook G T Munro Ashman D *Brit med J* 1949 i 345

[3] Living with Cancer. London Gollancz 1953 Pp 160 8s 6d

[1] See *Lancet*, 1946 i 241

Discussing the effects of lesions of the hypothalamus on appetite, Dr. C. G. KENNEDY reviewed the knowledge of Fröhlich's syndrome. It was now realised that the obesity, sexual infantilism, and increased appetite did not originate directly from the pituitary tumour itself but from its effects on the hypothalamus. In animals lesions had been made in the hypothalamus by a route which rendered it possible to avoid injuring the pituitary at the same time. Within twenty-four hours the experimental lesion led to an increase in appetite, so that the animal ate twice as much as its littermate control. This was accompanied by the development of marked adiposity. The limit was reached in about fifty days when the total fat of the animal amounted to 70% of its body-weight. If the animal was then starved, the increased appetite returned when it was again offered food. If the food was diluted with inert material, the animal ate enough additional food to make up for the diluent. Small lesions produced experimentally in a site lateral to the hypothalamus could produce the opposite effect on appetite even in rats made obese by an operation on the hypothalamus. Discussing a tentative scheme to explain the observed facts, Dr. Kennedy suggested that the cells of the hypothalamus might be sensitive to chemical rather than to thermal influences, that the feeling of satiety might be conditioned by the cerebral cortex and that hunger might be represented at a lower level than the hypothalamus.

In closing the meeting Professor KNIGHT revealed that the topic for discussion had been suggested by members interested in domestic science who wanted some help with their problem of making certain articles of food more acceptable to children. The outcome of their suggestion was doubtless different from what they expected but he hoped that they were not wholly disappointed.

MANCHESTER MEDICAL SOCIETY

Ulcerative Colitis

ADDRESSING the society's sections of medicine and pathology on Jan. 14, Prof. L. J. WITTS said that although ulcerative colitis had been described by Wilks and Moxon in 1875, modern interest in the disease started from the end of the 1914–18 war. The ætiology of the disease was still unknown, but it was a severe inflammatory disorder of the colon which produced damage akin in degree to a 3rd-degree burn. In about half the cases the illness was chronic and protracted, and few patients went for ten years without a second attack. About 20% of patients died in the first year of the disease, and nearly a third were dead by the end of five years. Complications were numerous and troublesome, and there was evidence of a high incidence of carcinoma after an incubation period of ten to fifteen years.

Medical treatment consisted essentially in rest, a high-protein low-residue diet, and measures to correct malnutrition, anæmia, and depletion of body-fluids and electrolytes. Remarkable effects were claimed for psychotherapy, though this did not as a rule cause resolution of the anatomical changes in the colon. Surgical treatment had become increasingly more radical, and permanent ileostomy together with removal of the colon and rectum was now favoured. It was logical to try A.C.T.H. and cortisone, because of their euphoric effect and their non-specific beneficial influence on inflammation. There was evidence that they might produce symptomatic amelioration, including gain in weight and decrease in diarrhœa; but they likewise did not seem to produce objective improvement in the colon. Professor Witts referred to a Medical Research Council trial of cortisone in which five regions were coöperating, and which should eventually reveal whether the advantages of cortisone outweighed its disadvantages.

Reviews of Books

Text-book of Surgery

Editor: H. F. MOSELEY, M.A., D.M., M.CH. Oxfd, F.A.C.S., F.R.C.S., assistant professor of surgery, McGill University. London: Henry Kimpton. 1952. Pp. 896. 110s.

A great effort has been made in this book to meet the requirements of the modern student. Written by the younger members of McGill University, it has freshness of outlook and vitality. Otorhinolaryngology and gynæcology, as specialties, are omitted, but otherwise it contains all the undergraduate should know. The facts are presented in an attractive fashion by experts in their several departments, and the illustrations are enlivening. Emphasis is laid on the newer developments of surgery—vascular, thoracic, neurological—and this is done to some extent at the expense of the older aspects. Thus, while nothing could be better than the review of the surgical treatment of portal hypertension, which occupies 5½ pages, the very common and still unsolved problem of enlarged prostate is dismissed in a single page. But the whole book is so good that such occasional failures to reach its general high standard can be condoned in a first edition. It will be as popular in this country as it is bound to be in Canada.

Vesalius on the Human Brain

Translated by CHARLES SINGER. London: Oxford University Press. 1952. Pp. 151. 21s.

THIS is the first book to contain a translation into English of any substantial part of the text of that landmark in history, the *Fabrica*, printed in 1543. Before Vesalius, there had been several ineffective attempts to introduce figures into anatomical narrative. But, omitting Leonardo (who failed to publish his researches) no-one had relied on visual impressions for the exposition of a series of investigations. It does not detract from his achievement that Vesalius was not his own draughtsman; for his was the mind that conceived the plan, his the hand that made the preparations, his the voice that directed the artist, his the drive and energy that carried this excessively intricate and difficult research to a triumphant end. Yet this great work has never been widely read. Its text has always been largely inaccessible, even to the learned, and still eludes all but a few: for it is vast, verbose, repetitious, a very torrent of words; its idiom is awkward and conspicuously unsuited to its subject; its format is extremely inconvenient for the student's desk. We can but regret that Vesalius's literary skill did not equal the artistry of some, at least, of his draughtsmen. Dr. Singer in this translation has not attempted to be literal and has avoided many of the repetitions. He selected the section on the brain because it is short and self-contained and clearly shows the state of physiology before the time of Harvey: it is probably the maturest part of the work and makes fascinating reading. He provides an admirable introduction and an instructive series of notes, while the text is illustrated with the *Fabrica's* original figures. The Wellcome Trustees and Foundation must be thanked for making this book available.

Side Effects of Drugs

L. MEYLER, consulting physician, Groningen, Netherlands. Translated by Ph. VUIJSJE and W. MULHALL CORBETT. Amsterdam and London: Elsevier Publishing Co. 1952. Pp. 268. 30s.

Dr. Meyler rightly observes that more and more drugs with possible untoward side-effects are becoming available, and that the doctor should ask himself whether the condition he is treating justifies the risk entailed in prescribing the drug. There is certainly room for a book on this subject, particularly for reference when the prescription of an unfamiliar drug is being considered.

Side-effects which are mild and disappear immediately after cessation of the drug matter little. The side-effects

Public Health

MORTALITY IN THE LONDON FOG INCIDENT, 1952

W. P D LOGAN
M D Glasg , Ph D Lond
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The Meuse Valley fog episode in 1930 caused 64 deaths, and the Donora (Pennsylvania) episode in 1948 caused 20 deaths In December, 1952, a four-day fog in London caused about 4000 deaths This paper gives a short account of when and where these deaths occurred, the age-distribution, and the reported medical causes No attempt is made here to present detailed meteorological data or to discuss clinical aspects, these and other features of the incident, including additional details about mortality, will no doubt be discussed in a report which, it is understood, will be made to the Minister of Health when investigations have been completed Two papers have already been published concerning the effects of the fog on hospital admissions [1] and on general practice [2]

TABLE I—DEATHS REGISTERED IN GREATER LONDON FROM WEEK ENDED NOV 15, 1952, TO JAN 10, 1953, COMPARED WITH THE ANNUAL AVERAGE FOR CORRESPONDING WEEKS OF THE FIVE PREVIOUS YEARS, 1947–52

Year	Deaths in week ended								
	Nov 15	Nov 22	Nov 29	Dec 6	Dec 13	Dec 20	Dec 27	Jan 3	Jan 10
1952	1565	1699	1902	2062	4703	3138	2234	2977	2634
1947–52 (av)	1747	1708	1809	1805	1852	1914	1923	2303	2213

The figures given here are from the Registrar-General's weekly returns, with additional data, and indicate that the incident was a catastrophe of the first magnitude in which, for a few days, death-rates attained a level that has been exceeded only rarely during the past hundred years—for example, at the height of the cholera epidemic of 1854 and of the influenza epidemic of 1918–19

INCREASE IN DEATHS

Unusually dense fog developed over practically the whole of the Greater London area early in the morning of Friday, Dec 5, 1952, and continued until early in the morning of Tuesday, Dec 9 In relation to the periods for which the numbers of deaths registered are published in the weekly returns, the fog began toward the close of the week ended Saturday, Dec 6, and continued into the first half of the week ended Saturday Dec 13, and it was in the latter week that the majority of the deaths due to the fog were registered Table I shows numbers of deaths registered in the Greater London area (population about $8^1/_2$ million) from the week ended Nov 15, 1952, to the week ended Jan 10 1953, compared with the annual averages in corresponding weeks of the five previous years Deaths registered increased from 2062 in the week ended Dec 6 to 4703 in the week ended Dec 13 and 3138 in the week ended Dec 20 In the next week (week ended Dec 27) the number of registrations fell to 2234—less than 200 more than in the week before the fog incident It is possible, therefore, that by that time the effect of the fog had more or less come to an end and was not responsible for the subsequent rise in mortality during the weeks ended Jan 3 and 10 On the other hand, part of the decline in registrations in the week ended Dec 27 may have been due to the intervention of the Christmas holidays, during which some registrations may have been postponed It is not possible to be sure, therefore, that all the deaths brought about by the fog had been registered within the two weeks ended Dec 13 and 20 Assuming that they were, the number of deaths so caused can be estimated to lie between 3717 (the excess in the weeks ended Dec 13 and 20 over the week ended Dec 6, 1952) and 4075 (the excess in the weeks ended Dec 13 and 20, 1952, over the corresponding average for 1947–51) Having regard to the opposing considerations that all of the excess deaths in weeks ended Dec 13 and 20 were not necessarily due to fog, and on the other hand that all of the fog deaths had not necessarily been registered within these two weeks, it is reasonable to estimate that in Greater London approximately 4000 deaths were brought about by the fog incident

TABLE III—DEATHS REGISTERED IN LONDON ADMINISTRATIVE COUNTY, BY AGE WEEKS ENDED DEC 6 AND 13, 1952

—	Age							
	All ages	Under 4 weeks	4 weeks–1 year	1–14	15–44	45–64	65–74	75 and over
Dec 6	945	16	12	10	61	237	254	355
Dec 13	2484	28	26	13	99	652	717	942
Ratio of week ended Dec 13 to week ended Dec 6	2 6	1 8	2 2	1 3	1 6	2 8	2 8	[illegible]

TABLE IV—PERCENTAGE AGE DISTRIBUTION OF DEATHS REGISTERED IN LONDON ADMINISTRATIVE COUNTY, WEEK ENDED NOV 29, 1952, TO JAN 3, 1953

Age (years)	Week ended					
	Nov 29	Dec 6	Dec 13	Dec 20	Dec 27	Jan 3
Under 1	3	3	2	2	2	[illegible]
1–44	5	8	5	5	6	[illegible]
45–64	25	25	26	23	24	[illegible]
65 and over	67	64	67	70	65	[illegible]
All ages	100	100	100	100	100	100
Total number	*853*	*945*	*2484*	*1523*	*1029*	*13*

Table II gives numbers of deaths in the weeks ended Dec 6, 13, and 20 in Greater London, divided into London administrative county and the outer ring, with the latter also subdivided by county areas and in the 160 great towns of England and Wales minus Greater London Although a certain amount of dense fog was reported in other areas it is evident that it was only

TABLE II—DEATHS REGISTERED IN LONDON ADMINISTRATIVE COUNTY AND THE OUTER RING (BY COUNTY AREAS) AND IN THE 160 GREAT TOWNS OF ENGLAND AND WALES WEEKS ENDED NOV 29, 1952, TO JAN 10, 1953

Area	Deaths in week ended							Ratio of week ended Dec 13 to Dec 6
	Nov 29	Dec 6	Dec 13	Dec 20	Dec 27	Jan 3	Jan 10	
London A C	853	945	2484	1523	1029	1372	1216	2 6
Outer ring	1049	1117	2219	1615	1205	1605	1418	2 0
Middlesex		*499*	*942*	*725*				*1 9*
Surrey		*293*	*664*	*390*				*1 9*
Kent		*103*	*174*	*104*				*1 7*
Herts		*21*	*45*	*33*				*2 1*
Essex		*201*	*494*	*360*				*2 5*
160 great towns	6042	6647	9452	7701	6472	7842	7617	1 4
Great towns minus Greater London	4140	4385	4749	4563	4238	4865	4983	1 04

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1 Abercrombie G F *Lancet*, Jan 31, 1953, p 234
2 Fry, J *Ibid*, p 235

THE LANCET

LONDON: SATURDAY, FEB. 14, 1953

Leukæmia

LEUKÆMIA, like cancer of the lung, is steadily rising in the table of the causes of death, but—unlike cancer of the lung—it affects all ages, particularly children in the first decade of life and adults after the age of 50. SACKS and SEEMAN [1] point out that the crude death-rate from leukæmia in the U.S.A. rose from 1·0 per 100,000 population in 1900 to 4·3 in 1944, the rate of increase being greatest in the last 14 years of this period. In the U.S.A. in 1942 more people died from leukæmia than from smallpox, meningococcal meningitis, scarlet fever, poliomyelitis, malaria, typhoid fever, and diphtheria combined; each year since 1940 more than 5000 persons have died from this cause. The increase is of peculiar interest to radiologists, since MARCH [2] has shown that, over a 20-year period, this disease is nine times more prevalent in these workers than in the general population. The choice by C. C. STURGIS [3] of the leukæmia problem as the subject of his Minot memorial lecture was therefore timely.

FURTH,[4] who has had as much experience as anyone of animal leukæmia, regards this as a neoplastic disease. "The essential change in leukæmia," he says, "resides in the leukæmic cell and consists of an acquired inability of immature leucocytes to respond to forces normally regulating their proliferation and maturation. This change is essentially that termed neoplastic; the end result is a new type of cell with a wide range of fixed abnormalities as concerns behaviour and appearance." So far as fowl and rodent leukæmias are concerned, there seems to be no doubt about these conclusions. But clinicians are not so sure about the disease in man, and their hesitation has been reinforced by experimental work with human leukæmia: for example, ISRAËLS,[5] whose findings were confirmed by HOOGSTRATEN,[6] showed that human leukæmic cells had not necessarily a fixed behaviour and could mature; and attempts to transmit leukæmia in man have failed. STURGIS remarks that most clinicians have reached two conclusions: firstly, that the ætiology of leukæmia is still uncertain; and secondly, that the balance of evidence at present favours the neoplastic theory. In practice treatment and prognosis are based on this theory.

One feature that has emerged from the animal work is the importance of heredity; susceptibility to "take" a transmitted leukæmia is definitely inherited, and highly susceptible families of mice have been bred. The present view is that the time of appearance and the type of leukæmia depend on interactions of genetic and extrinsic factors. At one time viruses seemed to be responsible for the transmission of leukæmia, but in mice, according to KIRSCHBAUM,[7] virus is not an ætiological agent; it is harboured by the cells of some leukæmic strains and causes an illness which hastens death from leukæmia, and it may alter the antigenicity of the leukæmic cells or the immune reactions of the host. In man familial prevalence is rare; but VIDEBAEK's records from Denmark suggest that there may be some leukæmic families.[8] Another important observation is that of the effect of ionising radiations, such as X rays or those from atomic disintegration. It is well known that leukæmia can be induced in animals by exposure to X rays; we have already mentioned the increased incidence among radiologists; and STURGIS recalls that in people exposed to the atom-bomb explosions in Japan leukæmia developed ten to twenty times as commonly as among the general population.

These findings have not taken us far towards understanding the ætiology of leukæmia. Our ignorance is reflected in the multiplicity of treatments. These are, at present, blood-transfusions, antibiotics, arsenic, X rays, radioactive phosphorus (P^{32}), urethane, the nitrogen-mustard group, folic-acid antagonists, and corticotropin (A.C.T.H.) and cortisone. Blood-transfusion is still much used, especially for temporarily rescuing the patient so that other treatments can be given. Exsanguination followed by replacement-transfusion was tried, but has been dropped; the results were not noticeably better than with a series of ordinary transfusions. Antibiotics have been very useful in controlling infections, especially of the mouth, but they are thought to have no other action. Arsenic, Fowler's solution, was the first of the cellular poisons used against leukæmia, but is now rarely given. Many workers prefer X rays to other forms of treatment; and STURGIS believes that they are still the best remedy for chronic lymphatic leukæmia. It is uncertain whether the radiation should be applied locally to the enlarged spleen or lymph-glands or to the whole body by the so-called "spray" technique. OSGOOD's [9] results suggest that the spray method is preferable. STURGIS prefers localised application for lymphatic leukæmia. He agrees that for myeloid leukæmia the spray technique is the better; but he holds that for chronic myeloid leukæmia radiation by radiophosphorus is the best treatment. LAWRENCE and his co-workers [10] found that in myeloid leukæmia radiophosphorus prolonged freedom from discomfort, but it did not

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[1] Sacks, M. S., Seeman, I. *Blood*, 1947, 2, 1.

[2] March, H. C. *Amer. J. med. Sci.* 1950, 220, 282.

[3] Sturgis, C. C. *J. Amer. med. Ass.* 1952, 150, 1551.

[4] Furth, J. *Blood*, 1951, 6, 964.

[5] Israëls, M. C. G. *J. Path. Bact.* 1940, 51, 235.

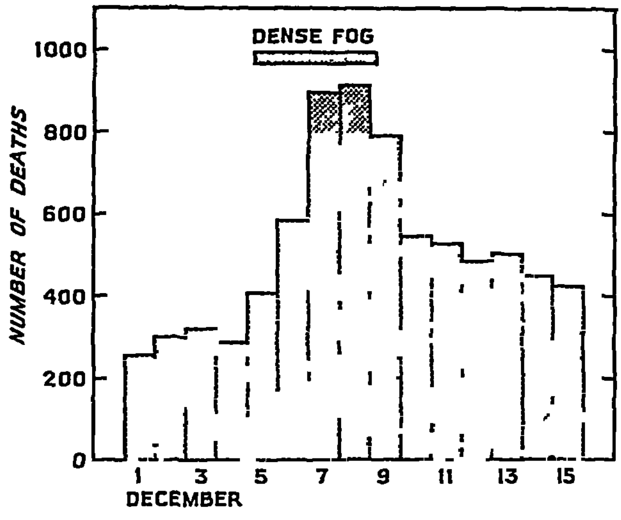
[6] Hoogstraten, J. Cited by L. E. H. Whitby and C. J. C. Britton. Disorders of the Blood. London, 1950; p. 455.

[7] Kirschbaum, A. *Cancer Res.* 1951, 11, 741.

[8] See *Lancet*, 1951, i, 1309.

[9] Osgood, E. E. *Arch. intern. Med.* 1951, 87, 329.

[10] Lawrence, J. H., Dobson, R. L., Low-Beer, B. V. A., Brown, B. R. *J. Amer. med. Ass.* 1948, 136, 672.



Deaths in Greater London each day from Dec 1 to 15, 1952

some light on the mechanism whereby the deaths occurred As table VII shows, there was a very large increase in the week ended Dec 13 in the number of cases certified by coroners and in the number of post-mortem examinations In relation to the increased numbers of deaths, however, the proportions of coroners' cases and post-mortem examinations were slightly reduced Cases certified by coroners include only those where referral to a coroner resulted in an inquest or post-mortem examination, the total number of referrals is not known

Number of Deaths Each Day

One of the most striking features of the incident was the rapidity at which deaths started to increase Table VIII shows the number of deaths *occurring* each day (not numbers of registrations as in other tables) Even on Dec 5, the first day of the fog, there was an obvious increase in the number of deaths, and the daily totals mounted rapidly to their highest levels on Dec 7 and 8, the third and fourth days of the fog There was some decline on Dec 9, and a still greater decline on Dec 10, but even on Dec 15 the daily total was almost twice as high as before the fog began (see figure)

PREVIOUS INCIDENTS

The 1952 incident is not the first in which dense fog in London has caused a sudden increase in deaths, as recently as 1948 a continuous but less dense five-day fog was responsible for some 300 deaths in the London administrative county[3] But so far as can be ascertained from a rapid search through the weekly returns, such events have been very rare, and only three others have been traced in which an association between dense fog and suddenly increased mortality has been clear cut In table IX mortality is related to these three incidents and to those in 1948 and 1952 It is evident that the increase in mortality in the 1952 incident was very much greater than on previous occasions

TABLE IX—INSTANCES OF SUDDEN INCREASES IN MORTALITY IN THE LONDON COUNTY AREA ASSOCIATED WITH DENSE FOG

Year	Dates of dense fog	Deaths				
		Weekly totals				Ratio of deaths in week of suddenly increased mortality to deaths in previous week
1873	Dec 9–11	*Dec 13* 1759	*Dec 20* 2415	*Dec 27* 1540	*Jan 3* 1842	1 4
1880	Jan 26–29	*Jan 31* 2200	*Feb 7* 3376	*Feb 14* 2495	*Feb 21* 2016	1 5
1892	Dec 28–30	*Dec 31* 1830	*Jan 7* 2509	*Jan 14* 2503	*Jan 21* 2101	1 4
1948	Nov 26–Dec 1	*Nov 27* 779	*Dec 4* 1019	*Dec 11* 944	*Dec 18* 891	1 3
1952	Dec 5–9	*Dec 6* 945	*Dec 13* 2484	*Dec 20* 1523	*Dec 27* 1029	2 6

There is reason to believe that the fog incident in December, 1952, caused deaths in London on a scale possibly never experienced before from this cause It is to be hoped that such an event will never recur—or be allowed to recur

SUMMARY

The dense four-day fog in Greater London in December, 1952, was responsible for some 4000 deaths during the two following weeks

The increased mortality affected persons of all ages, but particularly those aged 45 and over

Deaths assigned to bronchitis and pneumonia increased eight times and three times respectively in one week

A considerable increase in numbers of deaths occurred even on the first day of the fog

Four previous London fogs resulting in a sudden increase in deaths have been noted, but the 1952 incident caused by far the largest increase

THE FLOODS AND THE HEALTH SERVICES

On Saturday night, Jan 31, a severe gale combined with an unusually high tide to produce one of the worst floods ever recorded in the flat lands bordering the North Sea England, Holland, and Belgium have all suffered severe loss of life and damage to great tracts of land and property Holland has suffered most, the low islands of Zeeland and the mouth of the Scheldt have been almost entirely devastate a tragic
death-roll which at the time of writi gthen
ing The east coast of England from
Yorkshire to Kent with a force u obably
since the begi the 18th r 2
people lost t ore req t
injury or exp of tho de
homeless, s re flo t
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therapy; by pruning out those cases where refills are being maintained unnecessarily long, needless hazards can be avoided, and more time can be devoted to the remainder. Harris et al. suggest that nothing is to be gained by maintaining an artificial pneumothorax for more than three years. This positive statement in a field where the weeds of evasiveness have flourished abundantly for too long can at least be tested by therapeutic trial. Their estimate, which agrees broadly with the findings of Mitchell[4] in his series of 557 cases, seems unlikely to be far wide of the mark. If it were accepted, refill sessions could be reduced not only in numbers but in difficulty, since the difficult refills are commonly those in pneumothoraces of long standing; pricking of the lung, traumatic pneumothorax, and air embolism would thus become less frequent, and there would be less risk of residual respiratory disability from thickened pleura; and the patient would be saved both working time and travelling time. The results would before long indicate whether such a restriction on the duration of pneumothoraces was justified.

Hallux Valgus

Hallux valgus is in the news again; several workers have been making further attempts to eludicate the ætiology of the condition and to assess the value of various operations. There have long been two chief contenders for the causative crown: tight, wrongly shaped shoes, and metatarsus primus varus. Undoubtedly, however, hallux valgus is found occasionally in people who have never worn shoes, and quite often in people who have always worn "sensible" shoes; and as to metatarsus primus varus, Hardy and Clapham[5] conclude from an extensive survey of children aged 4–15 that "the deformity of hallux valgus *precedes* widening of the first intermetatarsal angle. A congenital widening of the first intermetatarsal angle may not be as important in hallux valgus formation as had been thought." Hardy and Clapham also make interesting observations on the lateral displacement of the distal phalanx on the proximal phalanx, which might be of primary importance in initiating the deformity; and they suggest also that there is need to investigate the function of the abductor hallucis—which makes one wonder how many of us (or our children) can actively abduct our big toes from the remainder. Surveys of peoples who go barefoot may throw further light on the problem; but meanwhile there is commonly no apparent cause whatever for hallux valgus.

Conservative measures do little or nothing to halt this progressive condition, and eventually many patients undergo operations the results of which are far from satisfactory to the discriminating surgeon. Bonney and Macnab[6] have made a critical survey of the results of operation for hallux valgus and hallux rigidus at the Royal National Orthopædic Hospital. As usual the patients were predominantly women; and, like Cleveland and Winant,[7] these workers think that this is partly explained by the greater willingness of men to wear suitable shoes. They show that in patients with a family history of this trouble symptoms appear earlier than in others. Most of their patients had increased intermetatarsal angles, and they assume that this is a primary defect. In the adolescent osteo-arthritis of the joint is not a major factor; and the various arthroplasties, all of which leave the toe somewhat weakened, are obviously far from ideal. The solution might seem to be to do an osteotomy at the base of the first metatarsal; but Bonney and Macnab list many causes of failure. It is remarkable that "in 34 of the 54 feet operated upon the metatarsus primus varus returned to its original state or to a larger angle than before operation after intervals varying between one day and three months after operation." The main technical difficulty after osteotomy is to maintain the correction, and in some cases a screw was passed through the neck of the first metatarsal into that of the second, to maintain the position. (Bonney and Macnab do not mention the simple and satisfactory method by which a suture is passed around the two metatarsal necks.) Even theoretically, however, a metatarsal osteotomy is not fully satisfactory; it would seem that one should either correct the hallux valgus itself at the same time by the appropriate soft-part operation, or, accepting the deformity at the joint as permanent and best for future joint function, do a double osteotomy—one at the base to correct the metatarsus varus, and one at the neck angled in the reverse direction to correct the hallux valgus. A double osteotomy can in fact give very satisfactory results. In adults the theoretical advantages of the single osteotomy have not been confirmed in practice; and Bonney and Macnab point out that this operation "involves placing the articular surface of the first phalanx in relation to an area of the metatarsal head which through long continued subluxation is usually denuded of cartilage"—which is of course the reason for doing a double osteotomy. They conclude that with the single osteotomy the results had been unsatisfactory because of imperfect technique and inadequate selection of patients. Like others, they found that the arthroplasties of Keller and Mayo often gave a good result; but sometimes it was unsatisfactory, and they investigated possible causes of this—including selection of cases, operative technique, and after-treatment—without finding any clear lead. They confirm Lloyd's[8] finding that the functional result was equally good with either form of arthroplasty.

There are of course other procedures, and Ross Smith[9] commends arthrodesis of the first metatarso-phalangeal joint in 30° of dorsiflexion. Immobilisation must, however, be continued for a long time; and his results are no better than those in the best arthroplasty series. No matter what method is used there is still an unpleasantly high proportion of failures either from recurrent deformity and pain, or from interference with the function of the foot as a whole causing metatarsalgia or other troubles. Bonney and Macnab rather gloomily remark that no operation on the hallux valgus will enable the patient with a very broad foot to wear ordinary shoes; "in such a case it is probably wiser and more

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4. Mitchell, R. S. *Amer. Rev. Tuberc.* 1951, 64, 151.
5. Hardy, R. H., Clapham, J. C. R. *Lancet*, 1952, i, 1180.
6. Bonney, G., Macnab, I. *J. Bone Jt Surg.* 1952, 34B, 366.
7. Cleveland, M., Winant, E. M. *Ibid*, 1950, 32A, 163.
8. Lloyd, E. I. *Brit. J. Surg.* 1936, 24, 341.
9. Ross Smith, N. *Lancet*, 1952, ii, 1385.

Special Articles

RESEARCH AND MENTAL HEALTH

LAST WEEK'S CONFERENCE IN LONDON

NOWADAYS in our society the child often finds himself rare, precious, and in the way Dr MILDRED CREAK (physician to the department for psychological medicine, at the Hospital for Sick Children, Great Ormond Street) drew attention to this juvenile predicament at the annual conference of the National Association for Mental Health, held on Feb 5 and 6, with Prof C FRASER BROCKINGTON presiding

Recent Advances in Theories of Child Care

The small family, the small house, and the multiplication of ageing adults, Dr CREAK said, bring new problems in interpersonal relationships In some ways the child is getting a better start than he did earlier in the century She mentioned the change which is coming over the conduct of confinement in hospitals At one period, especially in the United States, there was a strong move to separate the mother and the child, and to substitute artificial feeds, prepared to a precise formula, for breast-feeding The accoucheur and the nurse were the prima-donnas of the performance, and when the mother was allowed to take her baby home she hardly knew how to bath him Opinion has now swung over, and in one American clinic the baby sleeps by his mother, and is fed when he demands it Similar research is also going on in London—with one group of babies fed according to the clock, and another group fed on demand—to determine which babies do better, and which method throws more strain on the mother Dr Creak recalled the observations of Bowlby on the stunting of emotional growth of infants produced by deprivation of the mother, and the persistence later in such children of infantile characteristics they are apt to lack initiative, and to concentrate poorly, their interest being of a superficial flitting kind She discussed the new move to allow more visiting by parents when children are in hospital, and mentioned the film[1] made by Dr René Spitz which shows the damaging effects of long term deprivation on infants in residential care Of nursery schools and day nurseries (now likely to be cut down) she said that, while experts are sure his own home is the best place for the young child, mothers are equally sure they need day-nurseries and nursery schools—largely, she believes, because homes are nowadays so small The maternity and child welfare centres, which greatly help the mother of the pre school child, are nowadays reinforcing their staffs, in some places, with a psychiatrist and a psychiatric social worker, and child-study centres in London and Leeds are studying the normal child The difficulty is that the various bodies giving the mother advice are apt to have various outlooks The maternity and child-welfare clinic, the nursery school, the primary school, and the child-guidance clinic are all differently oriented towards the child, and even the Government departments responsible for children—the Ministry of Health, the Ministry of Education, and the Home Office—*do not* necessarily speak with one united voice She spoke with feeling of the "creeping crushing emergency" of growing lists of psychiatric patients at our hospitals and clinics, and mentioned the debt psychiatry owes to psycho analytic theory, which has drawn attention to the significance of early parent child relationships Many new lines of research are converging on mental health If they are to be brought cooperatively to bear on it, the keynote must be successful communication among researchers

Miss A M SCORRER (chief inspector in the children's department of the Home Office), speaking of children under residential care, mentioned the problems created by rising numbers, old buildings, and the need to find ways of preventing children from coming into care, and of restoring them as soon as possible to their families Hearing the many opinions nowadays voiced on child care, she remarked, made her grateful for the resilience of children She noted that whereas in 1948 at the time of the Children's Act, we were all talking of "deprived" children, we are now more inclined to talk of children "in care," which suggests at least that we are paying more attention to the need for care, and the circumstances which put children in the position of needing it At a recent date there were 63,000 children in the care of local authorities in the country, and during the year preceding this date 36,000 came into care and 33,000 went out of care Over half of them were under five, and 46% of the girls and 39% of the boys were boarded out—nearly a quarter of them in family group homes She reminded the conference that not every deprived child will develop a pathological state later, or *needs to be brought up in the expectation that it will It is not possible to provide a complete substitute for a normal home life, or to prevent serious emotional effects in some cases, but it is possible to provide, for many children, effectual substitutes for home life* Thus in residential nurseries there is now a system of arranging that nursery mothers shall be personally responsible for three or four children Adoption is arranged when possible and there are more adopters than children to be adopted Boarding out with ordinary families is also widely used, and "home groups" are formed, made up of children of various ages and both sexes, who live in an ordinary house with a "home" mother and father, and go out to the ordinary school and join in ordinary neighbourhood pursuits This often works well, but when the child grows up and leaves he is unlike other young people in that he no longer has the family home behind him to return to at a time of stress He is therefore encouraged to make friends in the neighbourhood while he is still in care, and often these friends take the place of uncles and aunts, or other relatives

Miss E N BARTLETT (psychologist to the Essex Education Committee), discussing the application of recent theories to the education of children at school, mentioned the lag between the acceptance of a theory by experts and its application in practice by ordinary teachers Most teachers (like most psychologists), she said, are ordinary and their practice is limited by external conditions in the form of administrators, architects, and epidemics When half the children are away with measles she has often noticed the improvement—the release and optimism—in the affected class A teacher dealing with 55 eight year olds in a classroom meant for 40 is rightly sceptical of the intelligence of those who advocate such things as more personal attention, coaching for the backward in small groups, and special and sensitive handling of the maladjusted child The most effective thing for the psychologist to do in these circumstances is to try to establish among teachers a climate in which new ideas and attitudes will flourish, and in fact the climate is slowly changing to one favourable to such ideas Many things hamper the change Thus the young teacher, fresh from college, and full of ideas of treating children as persons, may be so poor a hand at managing a class that she does not give the children confidence she may excite hostility, and respond with hostility, and even become permanently hostile, and she will find plenty of tired colleagues to point the moral Again, she may understand the new ideas imperfectly—for emotional as well as intellectual reasons The good young teacher, with good luck, may develop into the good experienced teacher, with bad during the hyaluronidase period, and in four of them existing stones have become smaller and less dense radiologically. At least some of the five failures, it seems, may have been caused by incorrect administration of the drug. During the experiment no other form of treatment was used. Most patients had an injection every 24–48 hours; and Butt et al. point out that the site of injection should be changed so that the same area is not injected more often than once in 4 days. Frequent injections are clearly a drawback; but if they can really help a patient threatened by recurrent stones, then he will accept the irksome routine as cheerfully as most diabetics do.

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[1] See *Lancet* 1948 ii 106

TREATMENT OF SLEEP PARALYSIS

SLEEP paralysis is a rather rare disorder of the normal change of consciousness from waking to sleeping or sleeping to waking. It seems to be rather commoner on waking than on falling asleep, although the so-called night-nurse's paralysis may possibly be predormitial sleep paralysis. Those who experience this disorder say that they are quite conscious and their sensory powers are complete, but they are unable to move or speak. This rather frightening state may last for as long as ten minutes. Sometimes sleep paralysis is associated with narcolepsy.[1]

Our understanding of sleep itself makes little headway. Some attribute sleep to general cortical processes, and others to the special action of a localised area of the posterior hypothalamus which is variously regarded as a waking centre, a sleep centre, or even a combination of these two. Narcolepsy and hypersomnia arise in association with many different organic conditions of the brain, but structural involvement of the hypothalamic region is generally regarded as the commonest cause. This does not necessarily prove, however, that we owe ordinary sleep to the hypothalamus: for the sleep of narcolepsy and of hypersomnia may differ from the physiological form.

Weitzner,[2] who has successfully treated sleep paralysis by insulin hypoglycæmia, obviously has no doubt that it is the hypothalamus—be it sleep or waking centre—that is involved in this syndrome; he asserts that insulin hypoglycæmia increases the power of the hypothalamus to regulate sleep, and he recalls that usually one of the first benefits that patients with rheumatoid arthritis derive from treatment by insulin hypoglycæmia is a relaxed and uninterrupted night's sleep. Weitzner's ideas will perhaps not be accepted by all; but his findings may form a useful basis for further observations.

A SUBSTITUTE FOR LYSOL

OF the disinfectant compounds derived from the distillation of coal-tar at rising temperatures, phenol has the lowest boiling-point and is most highly destructive to tissue. It is followed by the cresols, which are much more bactericidal and rather less toxic; being less soluble, they are put up in solution in soap. Lysol, which is a 50% solution of cresols, has a wide range of activity on bacteria and fungi, and has long been popular as an economical disinfectant for general use. It has the disadvantage, however, that its bactericidal value varies with the different oils and fatty acids which may be used in its preparation. Furthermore, it has an irritant or even necrotic action on the skin. Leonard Colebrook, who observed this with concentrations necessary to destroy the hæmolytic streptococcus, condemned lysol for midwifery and suggested that chloroxylenols should be used; these, however, have only a limited action on staphylococci and *Pseudomonas pyocyanea*, and they lose much of their value when organic matter is present.

The skin irritation from lysol is due to the cresols contained in it; and refractionation of the higher phenolic homologues will yield a fraction or "cut" which contains no cresols but is close enough to them to give, when formulated, a disinfectant with most of the desirable qualities of lysol and, in effective concentrations, no damaging action on the skin. The properties of a material of this sort, marketed as 'Sudol,' have been investigated by Finch.[1] It contains 50% of phenols, and a blend of vegetable fatty oils is used as the basis of the soap. It forms a clear solution with distilled water and gives a slight opalescence without scum in tap-water. Its activity against seven representative bacterial species—mainly pyogenic and intestinal organisms—was compared with that of carbolic acid in Rideal-Walker and Chick-Martin tests, and with lysol and the solution of chloroxylenol *B.P.* in modified tests with and without organic matter.

We have already noted the serious limitations of these tests.[2] The comparative figures reported by Finch seem, however, to show clearly the greater bactericidal effect of the lysol substitute, and its greater activity against non-sporing organisms in the presence of organic matter, especially when compared with chloroxylenol solution. In working concentrations, and even for a few minutes undiluted, it does not burn the hands. Further work will no doubt be done to assess its value as a skin disinfectant, and, diluted with equal parts of water, for such purposes as the sterilisation of instruments and baths. The fraction has no doubt been carefully selected to exclude the known carcinogenic components of the distillates. This precaution has to be kept clearly in mind in the search for better disinfectants among the higher "cuts."

THE RESURGENT STREPTOCCCCUS

IN the past two decades the outstanding successes of chemotherapy against bacterial infections have perhaps lulled us into a false sense of security. On an earlier page of this issue will be found an account by Dr. Gibson and Dr. Calman of an outbreak which shows us that the hæmolytic streptococcus has not lost its sting.

Between Nov. 1, 1952, and Jan. 3, 1953, the laboratory at Queen Charlotte's Hospital received 38 swabs from which group-A β-hæmolytic streptococcus was isolated. It was found that 26 of the strains isolated belonged to serological type 13 (3/B3264): of these, 1 came from a throat-swab and 13 from vaginal swabs of patients, 11 were from throat-swabs of nurses and orderlies, and 1 was from ward dust. The first recognised case of streptococcal infection was in November, 1952, when a nurse complained of sore throat. She was sent off duty until her "throat was clear." A fortnight later a baby developed erysipelas, and although this baby was immediately transferred to another hospital streptococcal infection appeared sporadically in patients and staff. At first all the cases were in one ward, but later cases occurred in wards on other floors. By last month it was evident that the epidemic type of β-hæmolytic streptococcus (type 13) had become well established. In 11 out of 14 infected patients the illness was mild; the other 3, however, were acutely and seriously ill with temperatures of up to 105°F with rigors. Of 3 later cases 1 was mild, 1 was the most severe genital-tract infection of the whole outbreak, and 1 was a streptococcal meningitis in an infant who was critically ill.

Dr. Gibson and Dr. Calman emphasise that "this outbreak of puerperal infection was far larger than anything experienced in recent years." They give reasons for thinking that it was not due either to relaxation of antiseptic methods (which have not been changed in the last five years), or to an increased infection-rate in the surrounding population. They are inclined to think that the great increase in the number of cases and the severity of some of them may herald an increase in the patho-

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[1] Levin, M. *J. Neurol. Psychopath.* 1933, 14, 1.

[2] Weitzner, H. A. *Arch. Neurol. Psychiat.* 1952, 68, 835.

[1] Finch, W. E. *Pharm. J.* 1953, 170, 59.

[2] *Lancet*, 1951, ii, 575.

CORPORAL PUNISHMENT

HOWARD LEAGUE MEETING

A PUBLIC meeting was held at the Caxton Hall on Feb 3, under the auspices of the Howard League for Penal Reform, to protest against the reintroduction of corporal punishment which is proposed, as an amendment to the Criminal Justice Act of 1948, by a Private Member's Bill due for its second reading on Feb 13

Mr KENNETH YOUNGER, M P, who was in the chair, said that he regretted the proposal to reverse so soon a measure of penal reform which had been the subject of most controversy during the passage of the Act of 1948 Indeed, this clause had been responsible for the only division of the House on the Act, and it had been referred back to the Commons by the Lords—chiefly at the instigation of judicial and ecclesiastical peers

Mr GERALD GARDINER, Q C, who spoke on Corporal Punishment as a Deterrent, reminded the meeting that one of the two main objects of the Howard League was to reduce crime He could only speak as a lawyer, and say how he thought this could best be achieved At first sight the case for corporal punishment might appear incontrovertible there was an increase in crimes of violence and we all felt sorry for the victims and wanted to stop the crime wave, if corporal punishment would do this, let us have it back It had been found in the past, however, that legislation passed in haste in response to popular agitation, such as that stirred up by the current press campaign, was often proved later to be wrong There was some exaggeration by opponents of corporal punishment about the effects of the "cat", when administered under strict medical supervision only about 2% of the men flogged had to be admitted to hospital On the other hand, the protagonists of corporal punishment tended to minimise the effects of birching

The only thing to do, Mr Gardiner said, was to examine the facts, and he had yet to meet a supporter of corporal punishment who had taken the trouble to study the relevant documents—carefully collected by the Cadogan Committee in 1938 This committee had come to the conclusion that flogging and birching differed very little in the pain they inflicted, and they had examined the history of punishment, studying its effects during the preceding thirty years They had also considered the history of all offenders convicted of robbery with violence (practically speaking, the only offence for which flogging could be awarded), and they had found that the subsequent history of men who had been flogged was worse than that of men who had not been flogged This could not be explained on the grounds that only hardened offenders had been flogged, for the same applied to men flogged for a first offence More of the men awarded corporal punishment committed further offences, and more than twice as many committed robbery with violence again The committee had also examined the claims that corporal punishment had put a stop to garrotting in London in the 1860s and to the other outbreaks of crime In none of these instances, often quoted by supporters of flogging, was this claim substantiated Experience in Scotland, where flogging was stopped in the 1860s, also refuted the argument that corporal punishment had a deterrent value, for the decline in crime in that country had been greater than in England, where flogging was retained until 1948 No civilised country in the world outside the British Commonwealth retained flogging as a penal measure, except the States of Delaware and Maryland in the U S A

The efficacy of corporal punishment as a strong deterrent had always been strenuously maintained by judges, but Mr Gardiner felt that judges were in no way qualified to form a valid opinion The people who were deterred from committing crimes never came into court What deterred the average citizen was his own conscience and sense of moral values, at the other extreme, there were people so antisocial that nothing would deter them The wobbler in between might or might not commit crime, depending on his awareness of a deterrent or its lack For such people, he was convinced, the probability of detection constituted a far more cogent deterrent than the nature of the punishment It was much to be regretted that our police force was now 10,000 under strength, and that the rate of conviction, which before the late war was 75%, was now just under 50%

One class of criminal, the aggressive psychopath, tended to commit the most brutal crimes because of his callousness and lack of conscience, and the "short sharp punishment" of flogging combined with, say, six months in gaol would mean that such a man was returned to the community in the same state within a very short space of time For such cases we needed something between a prison and a Broadmoor, but the longer sentence of preventive detention provided for under the 1948 Act was not being given a chance to prove itself, because of shortages in prison staff and buildings

The Rev DONALD SOPER, PH D, speaking on the Ethics of Corporal Punishment, said that in this country, professedly Christian, the ethics of any punishment should be Christian ones He was not one who disregarded the doctrine of sin and human responsibility, he did not subscribe to modern ideas which attributed all crime to disordered glands, difficult circumstances, or bad government So long as there were sinners, there would be crime, and crime had to be punished The aim of punishment from a Christian viewpoint must be reformative It was often said in favour of corporal punishment for crimes of violence that it was making the punishment fit the crime, he would say rather that it was making the punishment resemble the crime—and psychologists would say repeat the crime

The Christian regarded the criminal as one of the children of God, and therefore of immeasurable worth as a human being Lack of consideration for his individual value was on the road to the totalitarian outlook In his experience of more than twenty years as a prison chaplain, Dr Soper had not come across one criminal whom he had found unworthy of consideration as an individual He thought there was no evidence that corporal punishment reformed a man, it might harden him or cow his spirit, it was the exemplification of the doctrine "an eye for an eye ," expressly repudiated by Our Lord Moreover, it was a topic that invariably aroused strong emotions Why did everyone get in a fever when they discussed it? Surely because it was so closely bound up with the sexual element, the sadism and the masochism latent in all of us He had seen men flogged, and he remembered a man who undoubtedly got erotic satisfaction out of being flogged, and moreover he had heard flogged men talking of this afterwards Similar ignoble emotions were stimulated in the officials who had to administer the flogging It was a form of punishment which degraded both the recipient and the administrator

The argument was sometimes used that some criminals could only be got at by physical pain To do so, Dr Soper thought, was merely to confirm the criminal in the methods of violence he had himself used People like Craig and Bentley were products of a pagan world in which the individual felt lonely and unwanted and sought his satisfaction in power and excitement To reclaim such individuals we needed a form of punishment which had love as its motive—not sloppy sentimentality but the realisation that these individuals were frustrated and lost and needed to be brought back into the family of the community where they would find a place and feel wanted and valued for themselves Corporal punishment belonged to our modern world which had given itself over to violence, and unless we were prepared for sacrifices, such as spending money on our prisons, and for a make use of mass-radiography units, and some have part-time nurses, but other provisions are scanty or non-existent. The colleges which seem reluctant to act justify this situation by saying that there is no demand from the students themselves for anything better or that there is no need for any arrangement outside the National Health Service. One reason for this inactivity has certainly been the absence of any financial provision for student health in the previous five-yearly estimates, and the committee hopes that allowance has been made in the 1952–57 estimates. Moreover, the lack of progress in London may be partly due to the separation of the medical schools from the other schools and colleges: as the committee points out, where this separation is slight—at University College—the students have a first-class health service.

The extension of student health services has also been urged in the past by the Goodenough Committee, by the several conferences on student health held since the war by the Nuffield Provincial Hospitals Trust, and by the students themselves through the National Union of Students and the British Medical Students Association and in other ways. And clearly much has been done in response. But it is surprising that in so many of the London colleges these authoritative opinions have been largely disregarded. If the reason is financial, the answer is that it is false economy to save money at the expense of health; if it is one of principle—based on the claim that a responsibility no longer exists—then the committee of the Royal College of Physicians has pointed clearly to the fallacy.

SUBACUTE INCLUSION ENCEPHALITIS

CONSIDERABLE progress has been made in the differentiation of a number of types of virus encephalitis, which, both clinically and pathologically, falls into fairly well-defined groups. Apart from those following vaccination and infections such as measles, influenza, and mumps, Greenfield [1] recognised four main divisions:

(1) Acute polioclastic encephalitis, where an acute inflammation affects mainly the grey matter.

(2) Acute hæmorrhagic leuco-encephalitis, where lesions are primarily in the white matter.

(3) Subacute sclerosing encephalitis.

(4) Subacute inclusion-body encephalitis.

To these may be added acute encephalitis due to infection by the herpes simplex virus and those rare cases of encephalitis associated with generalised cytomegalic inclusion disease of children.

Subacute inclusion encephalitis was first described in 1933 when Dawson [2] recorded the case of a 16-year-old boy who died after 7 weeks' illness characterised by involuntary jerking movements and finally by lead-pipe rigidity of the limbs, loss of self-control, and hallucinations. At necropsy eosinophilic inclusion bodies were found in both the nuclei and cytoplasm of degenerate nerve-cells and astrocytes in areas of the brain showing the usual histological picture of encephalitis. He called the disease "inclusion encephalitis" and suggested that a virus was responsible, though none could be isolated. So far 16 similar cases have been recorded, 9 of them in this country [3] [4]; and from them a clinical pattern can be made out. All the patients were between the ages of 4 and 17, and only 2 were over 11. The majority of fatal cases ran a course of from 3 to 9 months, although some survived for as long as 21 months. Brain et al.,[3] who described the first 4 cases in this country, emphasised that the disease got steadily worse over a number of weeks. Psychological changes were usually the first to be noted; deterioration of school work, apathy, forgetfulness, lack of emotion, indifference, and intellectual impairment were commonly found in the early stages. Less often the children showed from the start more definite signs, such as muscular twitching, limping, or a tendency to stumble. Sooner or later, persistent or intermittent muscular spasms appeared, and progressive paralysis followed, leading to severe quadriplegia associated with complete dementia and cachexia. The cerebrospinal fluid either remained normal throughout or showed a Lange reaction of paretic type. Campbell et al.[4] consider that the clinical picture is so striking that it is unlikely to have been missed by neurologists in the past, and they therefore believe that it represents a new clinical entity. They observed 2 children who had the clinical features of subacute encephalitis but who later recovered, and they believe that, as the condition becomes more widely recognised, the prognosis may prove to be more hopeful.

The inclusion bodies accompanying the inflammatory changes in the brain are commonest in nerve-cells, although neuroglial cells may be affected to a less degree. Intranuclear inclusions are usually single and large, and stain with eosin and phloxine; they often fill the nucleus leaving only a few granules of chromatin on the nuclear membrane. The single intranuclear inclusions are probably formed by the coalescence of a number of smaller bodies, for multiple inclusions are sometimes found in the nuclei of less degenerate cells. The cytoplasmic inclusions are multiple, and they are smaller and more strongly eosinophilic than those within the nuclei, but these too may fuse to form a single body sometimes replacing the entire cytoplasm. Ultimately the cell degenerates and shrinks, and is finally represented by a mass of inclusion material. These cells are easily distinguished from the inclusion cells of both herpes-simplex encephalitis and cytomegalic inclusion disease.

Perivascular infiltration with inflammatory cells and gliosis are widespread in the grey matter of the cerebral cortex, basal ganglia, and brain-stem, and may even extend into the dorsal and ventral horns of the cervical cord. The changes in the white matter seem to be secondary to damage to the nerve-cells or to local extension of the inflammation into the subcortical tissue. Virological examinations have been performed in 8 cases, but no virus has yet been isolated. The same applies to cytomegalic inclusion disease, which is almost certainly due to a species-specific virus; and it is probable that the virus responsible for subacute inclusion encephalitis is pathogenic to man only.

A condition with the same clinical picture as that found in subacute inclusion encephalitis was described in 1945 by van Bogaert.[5] In both his cases the brain showed extensive focal inflammation affecting the grey and white matter at least equally. There was partial demyelination, diffuse infiltration with plasma cells, scattered fat-granule cells, and mobilisation of microglia. The most conspicuous feature was a disproportionate neuroglial proliferation in the white matter and in the cerebral cortex. There was less evidence of damage to nerve-cells than in subacute inclusion encephalitis, and no cells containing inclusion bodies were seen. van Bogaert called the condition "subacute sclerosing leuco-encephalitis." Although Brain and his colleagues considered that this leuco-encephalitis was distinct from Dawson's encephalitis, Greenfield pointed out that the two diseases differ only in degree, and that the more thoroughly the brain is examined the more cases of subacute encephalitis will prove to be of inclusion type.

Sir HOLBURT WARING, consulting surgeon to St. Bartholomew's Hospital, and formerly president of the Royal College of Surgeons and vice-chancellor of the University of London, died on Feb. 10, at the age of 86.

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1. Greenfield, J. G. *Brain*, 1950, 73, 141.
2. Dawson, J. R. *Amer. J. Path.* 1933, 9, 7.
3. Brain, W. R., Greenfield, J. G., Russell, D. S. *Brain*, 1948, 71, 365.
4. Campbell, A. M. G., Guy, J., Walter, W. G. *Arch. Dis. Childh.*, 1952, 27, 507.
5. van Bogaert, L. *J. Neurol. Psychiat.* 1945, 10, 61.

no easy matter in a packed day A minute or so before I am due, I cross the frontier and advance briskly down the long corridor In the distance I can see two sisters standing at attention in the open doorway I bow to each, the sisters about turn, I take my place between them, and the three of us march in step along the deserted labyrinth At the bedside we converse for the first—and last—time, finally agreeing on the most appropriate number of aspirins The procession re-forms and the sisters see me to the door, once more standing at attention until I am safely outside the three-mile limit

This ritual, so orderly and dignified, needs only a few touches to rival more famous ones, such as the ceremony of the keys or the admission of a bishop to his cathedral With these in mind, I have proposed certain amendments to the management committee According to my suggested protocol, the physician wears the scarlet gown of a doctor of medicine Three smart taps with a wooden stethoscope on the home door initiate the following dialogue "Who knocks there?" "The doctor" "Whose doctor?" "The nurses' doctor" "Come in, doctor!" The doctor raises his velvet hat thrice, the sisters curtseying each time in reply To round things off, the patient makes a show of resistance (as well she might) when the procession enters her room These proposals incorporate all that is best in our public life, and with the committee's approval I shall seek a *fiat* from the Court of Claims After all, everything has to begin some time, and the sooner this does the better

* * *

H M C Secretary answering a question about a proposed new nurses' home "The committee will be glad to know that the nurses' home at hospital is in the pipe-line at the Regional Board"

* * *

Sometimes we wonder whether the good old days of the last century were a better proposition than the days of 1953 and whether we really work as hard today as did our forefathers I thought I did and expected at least a modicum of sympathy when I remarked last evening in what I hoped was a casual tone that 20 to 30 visits a day did seem a trifle much even for January But my elderly uncle's reply rather shook me He had often wondered, he said, what I considered a heavy visiting-list 70 or 80 used to be his quota for a day and sometimes it was up to 100 And he examined his cases But of course when he was a G P doctors started their visits before breakfast, going on steadily (stopping, I suppose, though he did not mention it, for meals, surgeries, and such-like luxuries) till nightfall Truly those giants of yesterday were tougher than the puny medicos of today But, if he is right, the N H S patient of today is better trained than his grandfather When I put up my feet and relax at what I hope is the end of a busy day I can thank God and the health service that I haven't 70 to 80 patients still awaiting my arrival Perhaps that thought will help me when I am wakened at 3 A M by the phone to hear an old body telling me that her bed is full of ants and will the doctor do something about it But somehow I don't think it will

* * *

MRS BUNDLE

You felt you'd like an overhaul
Rather than trouble me to call
You'd come to me instead
When half way here you wondered ought
You ever to have come and thought
Of going back to bed.

But, though it might be tempting fate,
You struggled on and got here (late)
And talked an awful lot
You never dreamt that I would ask
You to undress—an endless task—
You like to wrap up hot

What you had doffed you had to don
I found with half my morning gone—
Precisely nothing wrong
When next you need an overhaul
Please stay in bed and let me call—
It won't take half so long

Letters to the Editor

REGISTRATION OF FEVER NURSES

SIR,—As an administrator and clinician connected with an isolation hospital which since 1938 has enjoyed the approval of the General Nursing Council as a training school for fever nurses, I should like to draw attention to the recent regrettable decision by that body t enforce, as soon as possible, the ban on the training o student nurses for the Fever Register

The requirement of the General Nursing Council in respect of hospitals to be approved as training schools for nurses was originally a minimum of 100 beds, but this standard was raised in 1947 to a minimum daily average occupation of 100 beds, except in fever hospitals where it was found that owing to the decline in the number of cases of infectious disease the requirement could not everywhere be implemented In 1949 the General Nursing Council first expressed the wish that entries to training for admission to the Register for Fever Nurses should cease as soon as possible, although no inquiries were then made regarding those fever hospitals which could attain the required minimum daily occupation of 100 beds

In the particular hospital with which I am associated the daily average occupation of beds has risen from 66 in 1938 to 112 in 1952 and the total annual admissions from 700 to 1264 Yet the management committee has been informed that student nurses must not be accepted after the end of 1953, and that training of student nurses for the Fever Register must be terminated four years thereafter As far as I am aware, the General Nursing Council has taken this final step without consulting those concerned in the fever hospitals recognised as training schools, and apparently without a sense of the irreparable harm which might be done to the nursing and hospital services of the country It has been suggested that the nursing experience available in infectious-disease hospitals should be used to enrich the training of student nurses from general hospitals In the hospital group to which I am attached this has been the practice for two years, the student nurse serving for one period of three months in the infectious disease wards as part of their general training, but in no way can this be considered equivalent to the longer training of the fever nurse It has only been possible to carry on the fever hospital by having a large staff of student nurses in training for the Fever Register, and the staffing problem of the isolation hospital cannot be solved by this short period of fever nursing included in the general training of nurses The position might be easier if the General Nursing Council were to decide that fever training should be a compulsory component of the syllabus of training for general nursing, but this decision is not likely to be made There is no suggestion that fever training and registration might continue as a postgraduate accomplishment of the general trained nurse—a course which might also help to solve the problem, and would be much more acceptable and fruitful than the suggested inclusion of fever nursing in a scheme of training for assistant nurses

This attitude to the training of students in a branch of nursing which has a technique all its own would imply that there is something inferior in the fever trained nurse In the opinion of many clinicians and hospital matrons the fever trained nurse is a highly valued member of the profession Fever training i essential for the ward sister in charge of a ward for infectious diseases and for the senior nursing staff of an infectious disease hospital It is an extremely valuable asset to sisters in charge of tuberculosis and children's wards, and it should be essential for the health visitor engaged in making epidemiological inquiries and giving in Greater London that there was an appreciable increase in mortality in the week ended Dec. 13. In the remainder of the great towns (aggregate population 14 million) the increase amounted to only 164 deaths, compared with an increase of 2641 in Greater London. Incidentally the fact that the subsequent rise in numbers of registrations in the weeks ended Jan. 3 and 10, already noted for Greater London, was paralleled in the remainder of the great towns supports the suggestion that this later increase in mortality was independent of the fog.

Within the Greater London area the abrupt increase for the week ended Dec. 13 occurred both in the central area (administrative county) and in the outer ring; as the right-hand column of table II shows, the weekly mortality in the central area almost trebled (ratio 2·6) and in the outer ring it doubled (ratio 2·0). The breakdown of the outer ring into towns within the constituent county areas indicates that mortality increased most sharply in the Essex section (ratio 2·5) and least in Kent (ratio 1·7). But clearly no large section of the Greater London area escaped. As examples of what happened in some districts, deaths registered in Stepney increased from 29 to 119 (ratio 4·1), and in East Ham from 16 to 62 (ratio 3·9).

TABLE V—NUMBERS OF DEATHS ASSIGNED TO VARIOUS CAUSES, LONDON ADMINISTRATIVE COUNTY: WEEKS ENDED NOV. 29, 1952, TO JAN. 3, 1953

Cause of death	Week ended Nov. 29	Dec. 6	Dec. 13	Dec. 20	Dec. 27	Jan. 3
Respiratory tuberculosis ..	19	14	77	37	21	24
Cancer of lung ..	27	45	69	32	36	48
Vascular lesions of C.N.S. ..	98	102	128	119	91	131
Coronary disease ..	131	118	281	152	109	150
Myocardial degeneration ..	79	88	244	131	108	136
Influenza	7	2	24	9	6	4
Pneumonia *	28	45	168	125	91	104
Bronchitis	73	76	704	396	184	215
Other respiratory diseases ..	8	9	52	21	13	10
Motor-vehicle accidents ..	1	8	4	10	4	5
Suicide	5	10	10	7	5	12
Total (all causes)	853	945	2484	1523	1029	1372

* Excluding deaths at ages under 4 weeks.

ANALYSIS OF DEATHS

Age-distribution

Table III compares the age-distribution of deaths registered in the London administrative county in the weeks ended Dec. 6 and 13. Although the increase in mortality was greater at older than at younger ages it was slightly less at ages 75 and over (ratio 2·7) than at ages 45–74 (ratio 2·8). The mortality of newborn infants almost doubled, and that of infants aged 1–12 months more than doubled. Deaths of children rose by a third (from 10 to 13) and of young adults by close on two-thirds (from 61 to 99). It is clear, therefore, that all ages shared to some extent in the increased mortality, and that it was by no means confined to the very young or the very old. Altogether there was relatively little disturbance of the usual age-distribution of deaths, as is shown in table IV which gives the percentage of deaths at various ages during several successive weeks.

TABLE VI—DEATHS FROM BRONCHITIS AND FROM PNEUMONIA BY AGE, LONDON ADMINISTRATIVE COUNTY: WEEKS ENDED DEC. 6, 13, AND 20, 1952

Age (years)	Bronchitis			Pneumonia (at ages over 4 weeks)		
	Dec. 6	Dec. 13	Dec. 20	Dec. 6	Dec. 13	Dec. 20
Under 1 ..	2	6	1	5	9	7
1–44	—	11	4	2	4	6
45–64	21	193	95	11	31	16
65 and over ..	53	494	296	27	124	96
All ages ..	76	704	396	45	168	125

Causes of Deaths

Deaths registered in the London administrative county increased by about 1500 in the week ended Dec. 13, and the about half of the increase was attributed to bronchitis or pneumonia. Deaths from bronchitis increased by over eight times (from 76 to 704) and deaths from pneumonia by almost three times (from 45 to 168) (table V). In the next week—the week ended Dec. 20—deaths from bronchitis totalled 396, still a very high figure, and deaths from pneumonia numbered 125. Other causes of death that increased greatly in the week ended Dec. 13 were respiratory tuberculosis (from 14 to 77), cancer of lung (from 45 to 69), coronary disease (from 118 to 281), myocardial degeneration (from 88 to 244), and "other respiratory diseases" (from 9 to 52). 24 deaths were certified as due to influenza compared with 2 in the previous week. There was no increase in deaths from motor-vehicle accidents—possibly because fewer vehicles were on the roads—and there was no increase in deaths by suicide.

The age-distribution of deaths from bronchitis and from pneumonia are shown in table VI. As for deaths from all causes combined, the increases were greatest at advanced ages, but young persons by no means escaped. Deaths from bronchitis at ages under 45 rose from 2 in the week ended Dec. 6 to 17 in the next week, and deaths from pneumonia almost doubled (from 7 to 13).

TABLE VII—NUMBERS OF DEATHS CERTIFIED BY CORONER OR CERTIFIED AFTER POST-MORTEM EXAMINATION, GREATER LONDON: WEEKS ENDED DEC. 6, 13, AND 20, 1952

Week ended	Total deaths	No. certified by coroner	No. certified after post-mortem examination		
			Coroners'	Others	Total
Dec. 6 ..	2062	458 (*22%*)	452	169	621 (*30%*)
Dec. 13 ..	4703	962 (*20%*)	960	267	1227 (*26%*)
Dec. 20 ..	3138	680 (*22%*)	680	203	883 (*28%*)

Deaths Certified by Coroners

One of the results of the sudden increase in mortality was to double the work of coroners and coroners' pathologists. Their reports will provide valuable information about the pathological changes found and may throw

TABLE VIII—DEATHS IN GREATER LONDON AND CONSTITUENT AREAS BY DATE OF OCCURRENCE, DEC. 1–15, 1952 (EXCLUDING ANY DEATHS OCCURRING WITHIN THESE DATES BUT NOT REGISTERED BY DEC. 20). ATMOSPHERIC POLLUTION READINGS AT KEW OBSERVATORY, RICHMOND (SOUTH-WEST LONDON)

Area	Deaths on Dec. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Greater London	259	301	321	288	406	581	894	910	792	543	528	484	501	449	425
London A.C.	112	140	143	120	196	294	513	518	430	274	255	236	256	222	213
Outer ring	147	161	178	168	210	287	381	392	362	269	273	248	245	227	212
Atmospheric pollution (mg. per c.m.), max. reading ..	*0·30*	*0·95*	*0·30*	*0·95*	*2·55*	*2·56*	*1·70*	*1·95*	*1·45*	*0·30*	*0·30*	*0·45*	*0·45*	*0·95*	*0·30*

5 *Disorders of muscular rhythm and of gait, and trick movements* are related to the defects of muscle power, over action of antagonists, myogenic contractures, and the influence of extrinsic forces, including gravity and peripheral fixation of limbs The variations in muscular torque in response to gravity, acceleration, and deceleration, the association of the paradoxical effects of peripheral fixations, and synergic inhibitions—these together form a problem of the utmost complexity in the diffuse and often incomplete palsies of poliomyelitis

There are other function structure derangements

(a) *Pseudo arthritis*, as described by Poynton and others

(b) *Vascular disorders* of whole regions, which are well known to contribute to limb shortening and defects in skin, and which presumably contribute to the muscular defects already noted

(c) The combined effect of *extrinsic forces and intrinsic defects*, causing secondary distortions in bone and derangements of articular tissues

These problems do need further study, but special poliomyelitis centres are not required Cooperation by teams including a physiologist, neurologist, physiotherapist, and nurse with the orthopædic surgeon in existing orthopædic centres is the ideal approach, which could be readily achieved

Exeter NORMAN CAPENER

MORE FOOD

SIR,—In his letter (Jan 24) Dr Bender says that he finds it difficult to imagine any reward sufficient to attract a farmer to marginal land But I know a hard-working farmer for whom there is more than one a marginal farm can be made to pay financially (though it may not be easy), but far more rewarding is seeing the improvement in land, crops, and head of stock which can be carried, and hearing neighbours and visitors remark on this improvement Oil lamps are still used, but the enjoyment and satisfaction of doing a worthwhile task well is, in this case at least, a great part of the reward, and the amenities of a civilised life are not necessarily those found in cities

Edinburgh J A WATT.

ŒSOPHAGEAL CONTRACTION AND CARDIAC PAIN

SIR,—Your issue of Dec 6 contained the St Cyres lecture delivered by Dr William Evans a few months previously

Having attended his lecture and disagreed profoundly with his statements, I have since carried out investigations into the frequency of reflux of barium within the œsophagus, as my own conviction was that this was not pathological and was, in fact, common

The first three young subjects examined at a barium-meal session showed reflux within the œsophagus, this appears to occur when the diaphragm in inspiration occludes the lower end of the œsophagus, and when that occlusion is more powerful than œsophageal peristalsis The reflux, in fact, occurs by relaxation of the œsophagus, and there is never at any time any suggestion of retrograde peristalsis

In the course of an investigation being carried out to elucidate the earliest signs of hiatus hernia, the "œsophageal arrhythmia" described by Dr Evans has been observed in a very large number of patients, it seems to take place in at least 50% of normal subjects There can be no doubt that this feature is entirely physiological and in no instance so far encountered has it been associated with "cardiac like" pain

The reflux is found most usually in patients with a demonstrable phrenic ampulla, and this latter appearance seems also to be related to the efficiency with which the diaphragm occludes the lower end of the œsophagus

Diagnostic Radiology Department,
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London E C 1

R A KEMP HARPER

PRACTICAL PENICILLIN

SIR,—As one of the general practitioners in whose practice Mr Cohen carried out part of his investigations, I was interested to read his report (Jan 24) and the letter from Dr Ryle (Jan 31)

The regimen introduced by Mr Cohen has been continued here in this practice, and my partners and I can vouch for the efficacy of a large single dose of 'Distaquaine Suspension' in many of the cases of sep encountered in our daily work In addition, there is no doubt that this method simplifies treatment and saves time and trouble to our patients and to us

Mr Cohen is obviously the best man to reply to Dr Ryle's several points, and I have no doubt that he will, but as he is now permanently resident in Suva Fiji, there will probably be some delay

Liverpool J SITNER

BOVINE TUBERCULOSIS AND HUMAN TUBERCULOSIS

SIR,—Dr Bradshaw (Jan 31) refers to the mistakes in my figures (which have been corrected), and says that they call in question the accuracy of the remaining data I should like to say that a copy of the *Veterinary Record* which contained these data was sent on Aug 17, 1951 to each of the medical officers of health who had supplied me with figures, none of them reported any inaccuracy or disagreed with my deductions I hope that medical officers who have followed this correspondence will say so if I am wrong

Dr Bradshaw says that "immunity to tuberculosis can be produced by certain types of living mycobacterium" Will he give me evidence of this and explain why it is not generally applied? He adds "dead organisms or bacterial products have never been shown to produce immunity" What does he think about London, where practically all of the milk is heat treated and comes mainly from non designated sources and where, on the whole, tuberculosis is much less serious a problem than it is in the counties of Scotland with a very high proportion of cattle attested?

Dr Anderson (Feb 7) says that I have made "the mistake of estimating the incidence of pulmonary tuberculosis from notifications statistics"

I have said that the eradication of tuberculosis from cattle leads to an increase in pulmonary tuberculosis in human beings for, taking Scotland as a pattern, out of 11 counties with a high proportion of cattle free from tuberculosis, 10 show such an increase—some a very big increase Out of 11 counties with few uninfected cattle, 10 show a very considerable reduction in human notifications This broad average seems to confirm my view

Dr Anderson mentions county health authorities as advising attestation of dairy herds I think he is confusing "attested" with "tuberculin tested," for local authorities play no part in the formation of attested herds The granting of a "tuberculin tested" licence is certainly the province of the local authority, but an "attested herd" certificate is granted by the Ministry of Agriculture An attested herd is a herd in which all the animals have given a negative result to 3 consecutive tuberculin tests After 1954, only milk from attested cattle may be designated as tuberculin tested

Turning to "the uncertain remote benefits of drinking tuberculous milk," tuberculosis of the udder, and so of the milk, is an extremely rare condition in cows By contrast, the milk of cattle free from tuberculosis contains none of the antibody substance, and the drinking of it makes human beings highly susceptible to the human bacillus and to pulmonary tuberculosis Incidentally, non pulmonary tuberculosis is commoner in English counties with a high proportion of attested cattle Finally, the risk of a milk borne infection (which can be eliminated by heat treatment) is much less than that of a certain increase in notifications of pulmonary disease where the cattle are free from tuberculosis

High Wycombe L PITCHFF

nd interference with, water-supplies: a limited mains pply of chlorinated water has been provided for mestic and washing use and a ration of about a gallon pure water a day a head brought into the island for inking and cooking purposes. Elsewhere there has en little or no interference with main water-supplies, ough many have been chlorinated as a precaution, it surface wells have been affected by flooded sewers nd people have been advised locally to boil all water. s most of the flood water is brackish, contaminated pplies are usually unpalatable.

At Kings Lynn the Isolation Hospital was flooded, nd evacuated just in time. The other hospitals in the wn were affected, but were able to keep going. Except r the railway Tilbury Hospital has been completely olated by the floods; but it has not been evacuated nd has continued to serve the population round the ocks. Long Reach Hospital, Dartford, was flooded; is the main smallpox hospital for the London area nd was empty: alternative arrangements have been ade to deal with any cases that might arise. Two onvalescent homes and one small hospital in other gions were put out of action. Otherwise the hospitals caped lightly and could deal with the patients brought them suffering from injury, shock, or exposure, as ell as a number of old people normally cared for at ome but too frail for rest centres. Arrangements were de for transfer of casualties to other hospitals inland necessary, but happily little use had to be made of is precaution.

Local general practitioners worked hard and well to aintain services, and many offers of help were received om other areas. Instructions have been given to those oncerned that spectacles and dentures lost or damaged n the disaster are to be replaced as speedily as possible, ee of charge.

The great problem, however, has been a welfare one —the care of the homeless. Rest centres were opened n all the affected areas and many thousands passed hrough them. Voluntary workers and officials have ombined to smooth out the immense difficulties of handling such great numbers of cold, wet, frightened people, of warming, feeding, and identifying them, and f passing them on to friends, relations, or voluntary billets. Known cases of open tuberculosis have been taken out of the rest centres and admitted to sanatoria. The central reserve stores have contributed blankets, mattresses, camp-beds, heating stoves, crockery, towels, nappies, and all the many things needed over and above the great stream of clothing which is flowing so swiftly and steadily from all parts of the country.

At the time of writing, a week after the disaster, the [illegible] changing. Most of the homeless have [illegible] but in certain areas there is still a sub- [illegible] number awaiting accommodation. The flood waters are receding and the problem of cleansing houses of mud, often sewage-contaminated, has to be faced. There is no reason at present to fear an outbreak of enteric, but the possibility of odd cases, even of small outbreaks, of this or other sewage-borne infections cannot be entirely excluded in areas where contamination with sewage has occurred. Meanwhile influenza is complicating some of the work but not so far seriously. The critical emergency is over for the moment (though another high tide is due at the end of this week) and those concerned are looking forward to the long and difficult task of restoring normality.

Statistics for 1921–30

Part III[1] of the Registrar-General's Decennial Supplement series for 1931 has now been issued. This volume groups the data for England and Wales on population, births, marriages, and deaths previously published in the annual statistical reviews for the ten years 1921–30.

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[1] Registrar-General's Decennial Supplement, 1931, Part III. H.M. Stationery Office. Pp. 574. £3 10s.

Influenza

The indications, reported last week, of an increased incidence of influenza in London and Southern England have been followed by a distinct increase in the number of deaths from this cause. In the 160 great towns such deaths totalled 313 in the week ended Jan. 31, compared with 29, 51, 72, and 132 in the four preceding weeks from Jan. 3 to 24. In London and the south eastern region there were 219 deaths, while in Greater London alone there were 170 deaths. Elsewhere, only in East Anglia has there been any considerable relative increase in deaths—to 25 in the week ended Jan. 31, compared with 3 in the previous week. Other regions of England and Wales remain free from any widespread outbreak of the disease.

In the week ended Jan. 31 the 313 deaths in the great towns were distributed by age as follows: under 1 year, 1; 1–5, 3; 5–15, 1; 15–25, 3; 25–35, 4; 35–45, 9; 45–55, 9; 55–65, 46; 65–75, 104; 75 and over, 133.

Laboratory reports confirm that the majority of the cases are due to the "Scandinavian" strain of A-prime virus, though virus B has been reported to be present in certain areas.

Emergency Bed Service.—A red warning was replaced on Feb. 3 by a yellow warning, which was withdrawn on Feb. 4 but reimposed on Feb. 10.

Weekly Claims to Sickness Benefit.—The weekly claims on the Ministry of National Insurance (including Scotland) for sickness benefit since the start of this year, with comparable figures for 1952, have been as follows:

Week ended	*Claims* *1953*	*1952, corresponding week*
Jan. 6	199,063	188,164
Jan. 13	208,168	166,409
Jan. 20	201,721	155,292
Jan. 27	239,091	162,522
Feb. 3	276,883	175,552

Fluoridation of Water-supplies

Six years ago the civic authorities of Marshall, Texas, agreed to the addition of fluoride to the town's water-supply. It is now reported[1] that six-year-old children in Marshall have less than half the number of dental cavities found in children of the same age living in neighbouring towns. It is said that more than 35% of Marshall children have no dental caries, compared with 13% in nearby Jacksonville.

The Third Quarter in Eire

In Eire during the September quarter of 1952,[2] the birth-rate was 21·5 per 1000 population, and the death-rate 9·9. The death-rate for tuberculosis was 0·4 per 1000 population (respiratory 0·3 and other forms 0·1), compared with 0·6 (0·4 and 0·2) in the corresponding quarter of 1951. The maternal-mortality rate was 1·6 per 1000 births registered (0·9 in the corresponding quarter of 1951). The infant-mortality rate was 36, and the neonatal death-rate 20, per 1000 births registered.

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[1] *Times*, Jan. 29, 1953.

[2] Quarterly return of the Marriages, Births, and Deaths registered during the September quarter, 1952. Obtainable from the Government Publications Sale Office, G.P.O. Arcade, Dublin. Pp. 47. 6*d*.

Infectious Diseases in England and Wales

Disease	Week ended Jan. 3	10	17	24	31*
Diphtheria	25	22	12	19	24
Dysentery	262	214	312	419	435
Encephalitis:					
Infective	5	1	3	4	2
Postinfectious	1	3	5	3	6
Food-poisoning	47	72	46	62	60
Measles, excluding rubella	30,499	24,738	21,385	21,882	26,460
Meningococcal infection	55	43	45	38	45
Ophthalmia neonatorum	32	33	40	28	32
Paratyphoid fever	..	2	8	8	7
Pneumonia, primary or influenzal	1423	1169	1205	1349	2029
Poliomyelitis:					
Paralytic	27	23	25	15	22
Non-paralytic	10	11	6	9	7
Puerperal pyrexia	220	258	212	265	282
Scarlet fever	1716	1238	1589	1832	1850
Smallpox	..	..	..	..	..
Typhoid fever	1	..	1	3	1
Whooping-cough	2165	2060	2170	2792	2799

* Not including late returns.

affecting the patients, and (2) the practitioner and the way in which he conducts his work—a personal and individual matter which each G P will work out for himself

"Dr Cort is surprised at the relatively small amount of work which my practice entails In turn I am astounded at the figures which he quotes for his practice In my practice over the past-four years the average attendance rate per patient per year has been 3 5 This compares with figures of 4 1 from a semirural practice,[2] 5 7 from a rural practice,[3] and 5 from the Social Survey unit[4] Prof Bradford Hill[5] also quotes a figure of 5 for National Health Insurance patients in 1938, while the Ministry of Health at an inquiry in 1937 gave a figure of 3 66 Thus the average number of attendances per patient per year seems to be between 4 and 5 Yet Dr Cort, with 30,600 attendances for 2600 patients, gives a yearly attendance rate of 12

"Assuming that Dr Cort works six days a week in a year, it can be seen that he does an average of 40 visits a day and sees some 60 persons in his surgery If he works rapidly, at a rate of five minutes for each surgery consultation and ten minutes for each visit, this volume of work will necessitate some twelve hours' work daily He says that two or three years ago he attended 45% of his entire list (2600 units) in a week This means that in one week he attended to 1170 of his patients at a rate of 167 a day for seven days a week, necessitating some nineteen and a half hours' work a day (excluding meals and other personal essentials)"

An editorial comment will be found on p 332 —Ed L

ACROMEGALY AND NEUROFIBROMATOSIS IN SISTERS

Sir,—The following is a record of two sisters, one of whom suffered from acromegaly and the other from neurofibromatosis (von Recklinghausen's syndrome)

A woman, aged 65, was admitted to Bootle Hospital with symptoms of intestinal obstruction and with dysuria In addition she had advanced acromegaly with prominent jaw, large tongue, big hands and feet, and hirsuties Her general condition was poor and she was emaciated A large mass was detected in the pelvic colon, and there was gross pyuria Other preliminary investigations showed a blood sugar level of 300 mg per 100 ml (but no glycosuria) and a blood non-protein nitrogen level of 36 mg per 100 ml Radiography of one hand showed typical acromegalic changes, but the pituitary fossa was within normal limits

Her sister, aged 61, with whom she lived, was noticed to have extensive neurofibromatosis involving the face, neck, and arms (and probably elsewhere) in association with areas of pigmentation This sister was feeble minded and extremely apprehensive She would not allow detailed clinical examination, and permission to take photographs of either of them was refused

While investigation of the acromegalic sister was proceeding she suddenly vomited, appeared to aspirate most of the vomit, became cyanosed, and died in asphyxia Necropsy showed a large adenocarcinoma of the descending colon, pyelonephritis, and cystic degeneration of the anterior pituitary

The coincidence of acromegaly and neurofibromatosis is well known Sternberg[6] in his early monograph on acromegaly states "Mollusca fibrosa of various sizes especially on the face and eyelids is frequent," and he cites nine reported instances More recently the association of these two disorders has been described by Ormond,[7] de Castro,[8] Barber and Shaw,[9] and others Although in both syndromes a familial tendency is recognised, this is, so far as I can ascertain, the first time that acromegaly and neurofibromatosis have been recorded in siblings

Liverpool

D Blair Macaulay

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[2] Watts, C A H Personal communication
[3] McGregor R M Edinb med J 1950 57 453
[4] Stocks P Sickness in the Population of England and Wales in 1944–47 Studies on Medical and Population Subjects no 2 General Register Office London
[5] Hill A B J R Statist Soc 1951 114, 1
[6] Sternberg J Acromegaly London, 1899
[7] Ormond, A W Proc R Soc Med 1919, 13, Sect Derm 124
[8] de Castro A Rev neurol 1934 1, 39
[9] Barber H W Shaw M Proc R Soc Med 1922 15, Sect Derm 30

ISOSPORA BELLI (WENYON) FROM DUODENAL INTUBATION

Sir,—Despite the fact that we have encountered numerous cases of coccidiosis in man[1] the site of infection remains unknown The condition seems to be self limiting and has not, in our hands, come to necropsy, so the exact source of the oocysts we observe in the stools remains in doubt

Recently we had a patient with nephritis who was passing in the stool an exceptionally large number of oocysts of *Isospora belli* and had passed a solitary *I hominis*

A duodenal tube was passed on two occasions, and the stomach and duodenal contents submitted to zinc sulphate flotation On the first occasion oocysts of *I belli* were found in both the duodenal juice and the somewhat bile stained gastric contents The tube was passed on a second occasion and this time the first specimen of gastric juice contained no oocysts that we could find The duodenal fluid, and a second suction of gastric contents—this time bile stained—both showed oocysts of *I belli*

The finding of the parasites in duodenal fluid suggests that the site of infection may be the duodenum or bile tract A large proportion of the oocysts seen were in the two sporoblast stage—a fact difficult to reconcile with our usual experience with *I belli* in which, in contradistinction to *I hominis*, the parasites are immature on arrival in the stool There may be some development in the deeper tissues, such as occurs with *I bigemina*

Our thanks are due to Dr J C Thomas, Provincial pathologist, Natal Provincial Administration, for laboratory facilities, and to Dr N R Pooler and Dr A L Brown for access to the case

South
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R Elsdon Dew
G G Roach
L Freedman

"GOLF BACK" AND THE NEW SWING

Sir,—Is the modern golf swing liable to produce lame back?

The movement is essentially a long swing with a braced left arm, the left wrist being "locked" by showing three or four knuckles It employs the fullest body shoulder pivot with the trunk held much more erect than in the traditional method, from which, essentially, all wrist-rolling action is deleted

No less an authority than Mr *Henry Cotton* alleges that the new swing contributes to a growing number of players with injured backs,[2] and he regards its teaching as a bad discipline In America, where this technique is most widely used, a number of top ranking professional golfers have been disabled by what is popularly described as "slipped disc," while in this country there have been similar examples of "golf back"—notably the case of Mr Harry Weetman The questions therefore are whether the modern swing is unphysiological, and whether golf back is in fact more prevalent today among those who use it

Having recently acquired this technique at the hand of Mr Max Faulkner, who is perhaps its leading exponent in this country, I regard the movement as no more and no less unnatural than the traditional swing And I think we should be very cautious about accepting the contention that it is more liable to cause disability Lame back has always been recognised as an affliction of golfers, though usually a transitory one And while the nature of this disability has defied precise analysis it is probably fair to say that the popular notion that most examples are due to "discs" is incorrect Any golfer in middle life (or for that matter any athlete of like age) who suddenly changes the execution of a luck, she may not. But at all events the state of the child's emotions has been recognised as an essential factor in education: the intelligence cannot function rightly unless all is well with the feelings. Every gain in knowledge and skill is steadying and releasing, enabling the child to go on towards maturity. In addition to his bread-and-butter tasks the child needs as she put it, experience of pungency and excellence. Nothing but commonplace experiences makes a commonplace person. The right kind of books should fall in his way at the right time. She mentioned *The Kon-Tiki Expedition* and *The Worst Journey in the World* as offering pungency; and any subject can give the child experience of excellence. The woodwork master and the games master share a particular claim to success here because they can demonstrate skill. The child under eight needs the opportunity to enter into group projects; but he expects a school to be a school and not a child-guidance clinic, and within those limits should be able, she said, to get the emotional nurturing he needs from the teacher. Round about eight he reaches a crisis in which the need to excel in some direction or another is very strong, and the success of others can produce a sense of inferiority. The character of the emotional nurture provided by the teacher should change from mothering to friendliness and interest, and the group projects should have more objective and real ends. Aggression needs some outlets other than surreptitious sulks, or semi-hysterical laughter at the unexpected gift of a joke from the rostrum. Even an explosion from the teacher, used skilfully, has its advantages. Adolescents need individual contact and respond well to the tutorial system; a transference situation is almost necessary for successful teaching at this age, and it is the experience of universities that an undergraduate may discover it was the schoolmaster, not the subject, that he liked. The sullen wooden school-child who is unable to learn often speaks of the teacher as "she," and the rest of the class as "they," because he feels out of it. Affection and interest may decide whether he is able to keep going or not. How much of all this can be got across to the ordinary teacher? Directly, Miss Bartlett thought, relatively little; indirectly much. A course of lectures on the backward child will attract every teacher within reach, whereas one with the same content but entitled "Mental Health" will hardly bring in one.

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[1] Elsdon Dew R Freedman L S Afr J clin Sci 1950 1 182 Elsdon Dew R Freedman L Trans R Soc trop Med Hyg (in the press)
[2] *News of the World* Dec 7, 1952

In the ensuing discussion a school-teacher urged that the principles of mental hygiene should be taught to girls in secondary schools, since they would be having to put them into practice on their own children in a few years' time. Another speaker defended the day-nurseries, which she said often prevented children coming into care by giving the harassed mother just the relief she needed, and by providing for the child what was in essence an extension of the home.

Recent Research into Mental Illness

At another session, Dr. DENIS HILL (physician for psychological medicine, King's College Hospital) said the factors which may prevent an individual from adapting himself to his environment are constitutional and environmental, and the interplay between them. The danger-signal is anxiety. In the infant emotional development is hindered when normal gratification is reduced (for instance, by separation from the mother); or rationed (by a too strict feeding régime, or other evidence of hostility); or impossible (perhaps because the father is too powerful a rival). Psycho-analytic theory has not shown why one person responds to stress by neurosis and another does not; but differences of genetic endowment must play some part. Studies of twins have shown that there is a single-factor type of inheritance for schizophrenia. If one of a pair of identical twins has schizophrenia there is an 86% chance that the other will develop it. With ordinary brothers and sisters and non-identical twins the chance is only 14%, and in half-brothers only 7%. Conditions reducing the stability of the body-weight reduce the resistance to schizophrenia in those predisposed to it. There is also evidence that a tendency to neurosis is inherited, but here multiple genes are involved. Stresses and resistances vary: thus one form of stress may break down a weak resistance in a person vulnerable to almost any stress; but may also find the Achilles heel in a person who would resist other kinds of stress. Some physical evidence of liability to schizophrenia may be offered by the type of skin capillary loops visible in the nailbeds. Possibly in this disease these are immature in type, and it may become possible to think in terms of capillary age much as we think in terms of bone age. Modern techniques, such as the use of the electro-encephalograph, the electron microscope, the behaviour of radioactive substances in the brain, the response to anoxia, glucose starvation, and various drugs, are beginning to provide us with new evidence. It has been shown that schizophrenic patients are unable to maintain a constant level in almost all physiological functions. The adrenal cortex pours over 90 secretions into the blood; and in America the adrenal cortex has been removed in some cases, and substitution therapy given. The results cannot yet be assessed. Many epileptics have a hyperexcitable area in the temporal lobes; in some cases this can be removed surgically, with benefit to the patient. Electrical stimulation of small areas of the temporal cortex, during the operation, has caused these patients to recall vividly some event or events in their past lives—so vividly that as far as they are concerned they relive the scenes. Yet when these areas are removed they can still recall these events, and can remember that the surgeon was able to stimulate recall in this way.

Dr. R. STRÖM-OLSEN (physician-superintendent of Runwell Hospital), speaking of the influence of recent advances in the prevention and treatment of mental illness, remarked that there is as yet no agreement on standards of mental normality. He reviewed briefly the many methods of prevention and treatment now in use. Child guidance, he said, is reducing the incidence of adult neurosis, Darby and Joan clubs are reducing the danger of mental breakdown in old age, and youth clubs, vocational guidance, and marriage guidance are all useful forms of preventive work. We have a growing knowledge of the effect of drugs for narcosis, for abreaction, and in neurophysiological research. The multidimensional approach in neurosis is giving results, and day hospitals, and psychiatric social clubs are valuable in the treatment of patients getting back to work, or suffering from the loneliness so common among the mentally sick. These are the more valuable in that long inpatient treatment of neurotics has never been very successful. Psychodrama, drawing, painting, and sculpture are also proving effective means of expression. In America they have tried putting two psychiatrists, one more senior, on to the same case; they treat him jointly, and it is said that the transference is more easily dissolved in these circumstances. Outpatient methods are developing. Disulfiram ('Antabus') has provided a new and successful means of dealing with those alcoholics who will tolerate the treatment. Œstrogen therapy has been of great service in reducing hypersexuality in males, and in particular has given relief to homosexuals. The value of male sex hormone in the treatment of frigidity in women has not yet been substantiated. In the field of neurosurgery the standard prefrontal leucotomy operation has given place to open operation and the more exact techniques of topectomy and cortical undercutting, but no final opinion on results can be given as yet.

tuberculosis, and the steps taken to combat that disease had frequently been described With the greatly reduced tuberculosis mortality in 1951, the latest year for which detailed figures were available, the female death rate fell below the male rate

Replying to further questions, Commander Galbraith said the death rate from respiratory tuberculosis among women between 15 and 35 years of age in Scotland had fallen from 149 per 100,000 in 1948 to 56 in 1951 The corresponding rates for England and Wales were 68 and 28 The precise reasons for the continuing disparity between the two countries were not known, but he saw no reason why the measures taken in recent years to combat the disease should not result in this disparity being further reduced in the near future

Mental Hospitals' Staff

Replying to a question, Miss M P Hornsby Smith stated that the deficiency of nursing staff in mental hospitals was now about 3500 men and 7600 women In 1947, the first year for which figures are available, the deficiency was 2300 men and 7000 women The numbers employed had increased since 1947 by 1200 men and 3800 women (counting part timers as a half), but the needs had increased at a greater rate

Registration of Opticians

Replying to a question, Mr Iain Macleod said that in conjunction with the Secretary of State for Scotland he proposed discussing the findings of the Interdepartmental Committee on the Statutory Registration of Opticians with the bodies concerned, with a view to preparing proposals to be laid in due course before the House of Commons It should not be inferred that the Government accepted all the detailed recommendations of the committee

Atmospheric Pollution

Replying to Mr. Somerville Hastings, Mr Harold Macmillan said that as far as was known there was no reduction in the amount of sulphur dioxide emitted to the atmosphere when coal and coal products were burnt in slow combustion stoves, but probably a little less smoke was formed from coal

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Obituary

ALAN STUART WHITEHEAD

M D , M Rad Lpool, D M R D

Dr A S Whitehead, consultant radiologist to the Eastern Hospital management group of the Liverpool Regional Hospital Board, died on Feb 2 at the age of 36

He was educated at King George V School, Southport, and the University of Liverpool, where he graduated M B in 1941 and was awarded the clinical exhibition in medicine He acted as house-surgeon and house-physician at the Emergency Hospital, Southport, during 1941–42 and later he served in the R A M C He spent a short time in general practice before taking the postgraduate course in radiology at the University of Liverpool in 1947 In 1948 he was appointed registrar in the Royal Liverpool United Hospitals and later senior registrar at Broadgreen General Hospital and Mill Road Maternity Hospital In 1949 he took the D M R D and the M RAD Two years later he became assistant radiologist to the Eastern Hospital group and last October consultant radiologist to Mill Road Maternity Hospital Newsham Hospital and Bootle General Hospital He graduated M D last year His published work included papers on Congenital Toxoplasmosis, Radiological Double Contour Effect, and Placentography

P H W writes "Whitehead's advice was continually sought by his colleagues and they thought highly of his opinions which were so willingly given Since his work was of such a specialised nature we invited him to help us with the postgraduate course in radiology he freely gave his time to the teaching of the students and we could always rely on him to help with additional work He will be greatly missed by all his colleagues in hospital and by the students It is tragic that so young a life should be cut short at the beginning of a promising career"

Dr Whitehead leaves a widow and two children

EDWARD EDMONDSON PAGET-TOMLINSON

M D Camb

Dr Paget-Tomlinson, who died at Ulverston, Lancs on Jan 20, at the age of 70, came of a Westmorland family He was the son of W S Paget Tomlinson F R C P , who had retired from his Liverpool practice in 1890 on succeeding to the Tomlinson estates at Kirkby Lonsdale

Edward Paget-Tomlinson qualified from the London Hospital in 1909, and after holding house appointments there he took his M B Camb the following year Fo some time he practised at Malton, Yorks, later moving to Horncastle, Lincs, where he was appointed surgeon to the Horncastle War Memorial Hospital He was also in practice for some years at Kirkby Lonsdale before he retired to Ulverston During the late war he interrupted his retirement to act as medical officer to the A R P service there, and he was a willing and valuable temporary helper in any local war-time emergency

P M -B writes "P -T , as he was popularly called in my early days at the London Hospital, represented the type of sportsman who sprang from Cambridge University—beautifully proportioned, clean in mind and clean in body, and an adept at every form of field athletics, excelling especially in the jumps and hurdles, but he was as keen on his work as on games To him life was a series of grand and exciting experiences, for he delighted in all forms of plant and animal life The picture of his cheerful, handsome face and his sincere manner has always remained with me Equally charming and considerate to everyone in all walks of life, it is small wonder that his name became a household word wherever he practised"

JOSIAH OLDFIELD

M A , D C L Oxfd, M R C S

Dr Oldfield, who died on Feb 2 within a fortnight of his 90th birthday, brought into our own times the breadth and liveliness of interest of a Victorian amateur of reform

He was born at Shrewsbury, the son of David Oldfield and educated at Newport, Salop, Grammar School and Oxford University, where he took a second class in the honours schools of theology and law Called to the bar at Lincoln's Inn in 1892, he practised in the Oxford circuit before beginning to study medicine at St Bartholomew's Hospital, where he qualified in 1897 Shortly afterwards he founded, in the New Kent Road, the Humanitarian Hospital of St Francis, of which he was for some time chairman and senior physician

But medicine remained only one of his interest In 1901 he was awarded the D C L of Oxford University for his thesis on capital punishment, and in the same year he founded the Society for the Abolition of Capital Punishment Though many thought his interests as a reformer were too diffuse, he went to great pains to collect first-hand information about the reforms he advocated and in the winter of 1901 he visited India to study, in his own words, "the effect of the English Government on the people," and to try to discover "the reality of their grievances and at the same time to learn the cause of the modified success of the Christian Missions" there

He had been partly drawn to medicine by his interest in dietetics, and in 1903 he became warden and senior physician to the Lady Margaret Fruitarian Hospital at Sittingbourne, Kent He also practised as a consultant in digestive diseases He had himself adopted the fruitarian diet while at Oxford and he strenuously advocated its adoption "by the higher classes for æsthetic and humane reasons" He supported his theories by the practical method of planting fruit trees and by writing many popular books, including *Diet in Rheumatism*, *Diet in Digestion*, *Fasting for Health and Life*, and *Eat and Keep Well*, and he wrote many vigorous letters to the newspapers

During the 1914–18 war he raised and commanded a field ambulance, and he held the rank of lieut -colonel in the R A M C Soon after the war he continued the study of the effect of British government on subject peoples, which he had begun in India, by a tour of the West Indies, and during this visit he was admitted to the Jamaican Bar revolutionary change in our moral outlook, violence would become our master.

The meeting passed unanimously a resolution calling on the Government to reject the proposed Bill.

Medicine and the Law

The Nurse and the Tea-tray

After the perils of hot-water bottles in hospitals and nursing-homes[1] we have now the perils of the hot-water jug on the tea-tray. In Trew *v.* Middlesex Hospital[2] it appeared that a nurse placed a tea-tray on the lap of a private patient sitting up in bed. The tray tilted and hot water from the jug was spilt and burnt him. The plaintiff's allegations of negligence were that the hospital ought to have provided a bed-table, or that the nurse should have set the tray in a safe position or should have ensured that he had control of it. The patient had one leg in a sling and the other on a pillow; he had been sitting as upright as he comfortably could. There was perhaps not much room on the bed for a horizontal position for the tray. The evidence of the nurse was that the patient was somewhat impatient; she said she had asked him if the tray was all right and he had assured her it was. The defence also emphasised that the patient had immediately received an apology and had said "Accidents will happen." It was suggested, moreover, that the injury was not very serious.

Mr. Justice Gerrard said that the nurse was a small, brisk woman who, according to the plaintiff, was in a hurry. Generalising perhaps a little speculatively, he said he could well imagine, and he thought it was a fact, that the nurse "breezed into the room, put down the tray and went out, giving the patient no time to protest." He gave judgment for the plaintiff for £100 with costs.

Medical Practice a "Business"

If the judges have occasionally seemed to transcend the rules of common sense in their interpretation of words, no-one will quarrel with the decision of Mr. Justice Danckwerts[3] that, in the circumstances of the case before him, a medical practice could be a "business." A father bequeathed a substantial part of his residuary estate upon trust so that money might be available for his son at the age of 35 "for the purpose of starting . . . in business or for the advancement of any business with which he may be concerned." The son had not qualified as a doctor at the date of the execution of the will. He qualified at the age of 34. After he was 35 the trustees asked the court whether they could lawfully apply the money for buying him a house to be used partly as his residence and partly as his surgery.

The learned judge said the clause should not be narrowly construed. Its object was to assist the son to maintain himself in a gainful occupation. Both the dictionaries and the reported decisions suggested that the word "business" was capable of including a profession. His lordship took note of the fact that the old method of buying a practice had now been altered; but he found evidence that it was often a condition of success that a doctor could take over a residence. Plainly his chances must be affected by his ability to acquire premises for his surgery and for consultation. He held that the trustees might buy a house in which the son could reside, but it must not be merely a family residence; it must be purchased with a view to advancing his prospects in the medical profession.

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[1] See *Lancet*, 1952, ii, 1077, 1078.

[2] *Times*, Jan. 31, 1953.

[3] *Ibid*, Feb. 7, 1953.

In England Now

A Running Commentary by Peripatetic Correspondents

What struck me most at Canvey Island was how well all those concerned with rescue work or resuscitation had stood up to a long period of stress, anxiety, and lack of sleep. Their capacity for grappling with problems and for paying minute attention to detail seemed to be enhanced rather than diminished. The only sign of impaired efficiency I noticed was a tendency to loss of memory for recent events. For example, one very tired worker asked a doctor at least six times in a quarter of an hour if he was short of a particular article. But the prevailing mood inclined to elation, and unwarranted laughter was a common sign of strain. Appetites seemed to be bigger, and, not surprising to anyone who has served with the Armed Forces, enormous quantities of tea were consumed.

The psychological picture of the victims of this disaster was not unlike that of victims of the blitz. But their apathy was striking. Whether this was due to exposure and cold, a reaction to a state in which past and future are momentarily lacking in impact on the mind, or to some factor inherent in the flood experience itself, is a matter for conjecture. Some showed a tendency towards dissociation, and fastened an effect on to an emotionally indifferent object instead of the real source of grief. One mother, for instance, whose child had been killed bemoaned the loss of a new wireless set. A brittle brightness was quite usual, and I only saw one case of frank hysteria—a young man who quickly responded to sedation. It seems, however, that some of these people may need some form of abreaction. The disaster bore heavily upon the extremes of life, and I have carried away a vivid picture of the effect of a large bundle of comics and sweets being given to some children. The improvement in their general state was dramatic.

But one thing Canvey Island has done for me is to change completely my views about general practice. The work of the local doctors was impressive in its competence though many of them had worked non-stop without sleep for 48 hours. And their devotion to their patients was equalled by the confidence in which their patients held them. The therapeutic value of the very presence of these men, known and trusted, familiar faces in an unfamiliar world, was something which mere technical ability could not equal. This was not the time for bottles of medicine, letters to outpatient departments, nor applied psychology, but a striking reminder that, at any rate in some circumstances, and probably in more than most of us like to think, the man is more important than his methods.

* * *

So the longest and least loved month of the year has ended and no-one is sorry. December we tolerate because of Christmas and the few days snatched from our youth which it brings us. February we endure because it is short and, even more, because it is the forerunner of spring. But January has nothing. As one of my patients from her wisdom of 96 years remarked: "It seems longer than it is because we tack on the last few days of December to its beginning." And come to think of it we do. There are the carols and turkeys and all the festivities of Christmas Day, followed by the distended tummies and thank-you letters of Boxing Day. Then after a brief hiatus the shops reopen, all signs of Christmas gone and their windows full of their January sales. We think of our income-tax, our telephone and gas bills. We replenish the coal cellar, put anti-freeze in the radiator, and generally gird up our loins and prepare for the worst. When the New Year at last appears Christmas seems months away, and in our own minds we are well on with the winter. Then comes the snag: January has still 31 more days to run. We realise once again that figures lie and that whatever the calendar says the first month of the year is as ever twice as long as any of its fellows.

* * *

A professional call at the nurses' home is a formal affair. When I am wanted, a duly authorised person notifies my office. Plenipotentiaries then negotiate until they agree on a mutually convenient quarter of an hour—

Royal College of Surgeons of England

Prof Reynaldo dos Santos (Lisbon) has been elected to the honorary fellowship

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Feb 2, with Dr Andrew Allison, the president, in the chair, A H Edwards was admitted a fellow (qua surgeon)

C M F /M E F Physicians' Reunion Dinner

This dinner will be held on Saturday, March 28, at Simpson's in the Strand, with Dr D Evan Bedford in the chair Further information can be had from the hon secretary, Dr A Willcox, 59, Harley Street, London, W 1

Colyer Prize

An award of this prize will be made this year It is offered for the best original work in dental science by a dental surgeon educated at a dental school in Great Britain or Northern Ireland who has not been qualified more than five years Applications should be sent to the prize committee of the Royal Society of Medicine, 1, Wimpole Street, London, W 1, not later than Sept 21

The Horder Club

This club was formed about six years ago to honour Lord Horder and his work on the rheumatic diseases It is comprised of a group representing many of the facets of the study of the rheumatic diseases and includes general physicians and, physicians interested in rheumatology and physical medicine, together with orthopædists and radiologists It is hoped soon *to add one or more men primarily interested in the basic* sciences The club met on Jan 29 and discussed a film shown by Dr Campbell Golding, illustrating some features in the radiographic study of rheumatoid arthritis The hon secretary is Dr Ernest Fletcher, 41, Harley Street, London, W 1

St Bartholomew's Hospital, London

On Feb 5 the Court of Common Council approved a prop to build an extension to Barts which will contain 120 be

Biological Reagents for Skin Testing

Coccidioidin, histoplasmin, and *blastomycosis* antige diagnostic skin tests may now be obtained from the departr *of pathology, St John's Hospital* for Diseases of the S Lisle Street, London, W C 2 (tel Gerrard 8383, ext 22) not from the London School of Hygiene and Tropical Medi as previously

Society for General Microbiology

The first Marjory Stephenson memorial lecture will be gi to this society by Mr D D Woods, F R S, at the Ro Institution, Albemarle Street, London, W 1, at 6 P M Monday, April 13 He is to speak on the *Integration* Research on the Nutrition and Metabolism of Micro organ

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CORRIGENDUM *Function of the Hospital Outpatient Dep ment*—At the joint discussion on this subject held by sections of medicine and general practice of the Royal Soc of Medicine (*Lancet*, Feb 7, 1953, p 275) the chair taken by Sir Alun Rowlands, president of the section medicine Dr E P Scott, president of the section of gen practice, attended the meeting but was not in the chair

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EMERGENCY BED SERVICE—In the week ended last Mond applications for general acute cases numbered 1992 The proporti admitted was 79 58% A yellow warning, withdrawn on Feb was reimposed last Tuesday

The verbatim transactions of the third Commonwealth Hea and Tuberculosis Conference, which was held in London last Ju have now been published Copies (21s) may be had from t N A P T Tavistock House North London W C 1

Diary of the Week

FEB 15 TO 21

Tuesday, 17th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (*London School of Hygiene and Tropical Medicine*, Keppel Street W C 1) Dr J C White Human Hæmoglobins and Derived Pigments

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
8 P M *Section of Pathology* Dr A Neuberger, F R S, Prof C Rimington, Dr W M Davidson Prof C H Gray, Dr J O Houston Hæmoglobin Metabolism

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street, W C 2
5 30 P M Dr W J O'Donovan Hysteria Cutis

WEST END HOSPITAL FOR NERVOUS DISEASES 40, Marylebone Lane, W 1
5 30 P M Dr D Gordon Neuroradiological demonstration

MIDDLESEX COUNTY MEDICAL SOCIETY
3 P M (North Middlesex Hospital, Silver Street Edmonton, N 18) Cases
4 45 P M Dr E C O Jewesbury Narcolepsy

SOCIETY FOR THE S [illegible]
5 P M (Westmin [illegible] chool Horseferry Road S W 1) P [illegible] W H O) International Aspects of [illegible]

Wednesday, 18th

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medicine) Sir Henry *Dale*, O M *Future of Pharmacy and Pharmacology*

ROYAL SOCIETY OF MEDICINE
5 P M *Section of Comparative Medicine* Dr E G C Clarke PH D Mr John Hickman M R C V S Dr D H Collins, Dr J T Scales Metals and Synthetic Materials in Relation to Tissues
8 15 P M *Section of General Practice* Dr L V Gimson Hypertension

INSTITUTE OF DERMATOLOGY
5 30 P M Dr J A Dudgeon *Virus Diseases*

INSTITUTE OF UROLOGY St Paul's Hospital Endell Street W C 2
5 P M Mr D I Williams Spina Bifida and Incontinence

EUGENICS SOCIETY
5 P M (26 Portland Place W 1) *Prof* T H Marshall M A Social Selection in the Welfare State (Galton lecture)

HARVEIAN SOCIETY OF LONDON
5 30 P M (St Mary's Hospital, Paddington W 2) Clinical meeting

UNIVERSITY OF OXFORD
5 P M (Radcliffe Infirmary) *Prof* Dugald Baird Epidemiological Aspects of Obstetrics (*Litchfield lecture*)

Thursday, 19th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields, W C 2
5 P M Mr J F Richardson Early Renal Symptoms of Parathyroid Tumour

UNIVERSITY COLLEGE Gower Street W C 1
4 45 P M Prof V B Wigglesworth F R S Chemical Aspects of Insect Physiology

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicin Sir Alan Drury F R S Uses and Applications of Hum Blood plasma Fractions

INSTITUTE OF CHILD HEALTH The Hospital for Sick Childr Great Ormond Street, W C 1
5 P M Dr D V Hubble The Thin Child

ST GEORGE'S [illegible] Hyde Park Corner S W
5 P M Dr [illegible] *urological demonstratio*

BRITISH INSTI [illegible] 'elbeck Street, W 1
8 P M Pro [illegible] diotherapeutic Techniq in Breast Carcinoma

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE Mans House, 26, Portland Place, W 1
7 30 P M Dr M A C Dowling Malaria Eradication Experime in Mauritius

LONDON [illegible] IETY
8 30 [illegible] Mr Sol M Cohen *Pla*

LIVERP [illegible] ount Pleasant Liverpool
8 P M Dr J Berkson Oxygen, the Premature Baby and Retrolental Fibroplasia Mr A Sutcliffe Kerr Unilater Proptosis

UNIVERS [illegible]
5 P M [illegible] Wynd, Dundee) Prof J Crighto [illegible] l Heart

Friday, 20th

UNIVERSITY COLLEGE
5 30 P M Dr T S Work Biosynthesis of Proteins (Second o two lectures)

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE
5 30 P M Dr D P Cuthbertson Problems of Quality a Quantity of Protein

ROYAL SOCIETY OF MEDICINE
4 30 P M *Section of Epidemiology and Preventive Medicine* Dr [illegible] Dr John Taylor, Mr Reginald Lovell D Sc [illegible] McCall Epidemiology of Sal [illegible] and Animals with Special Refe [illegible]
8 15 P M *Section of Radiology* Dr I [illegible] nique of Simulated Rotation [illegible] Carcinoma of the Bronchus Dr Mary Douglas [illegible] formity of Dosage in Carcinoma of the Bladder Dr Cha [illegible] I Lewis Treatment of the Meningeal System [illegible] *Radioactive Isotope and Wedge Filters* Dr J Walter Radioactive Gold in Malignant Effusions

FACULTY OF RADIOLOGISTS
4 P M (Royal College of Surgeons) Prof B W Windeyer Radiotherapist's Impressions of a Visit to Canada

INSTITUTE OF DERMATOLOGY
5 30 P M Dr R T Brain Common Skin Diseases *in Childre*

NORTH WESTERN TUBERCULOSIS SOCIETY
5 P M (Liverpool Medical Institution) Dr G S *Erwin* ar [illegible] gynæcologist Tuberculosis and Pregnancy

Saturday 21st

BIOCHEMICAL SOCIETY
11 A M (London School of Hygiene and Tropical Medicine) Biological Transformations of Starch and Cellulos

advice on the domestic care of the infectious diseases commonly nursed at home.

Although there is little difference in the health conditions north and south of the Border, it seems that the Scottish General Nursing Council intends to continue the registration of fever-trained nurses. It may be that the future gaps in the English nursing service will have to be filled by the importation of fever-trained nurses from Scotland, or alternatively that nurses from England will have to travel northwards to secure acknowledgment of this valuable branch of nursing experience.

Although the common infectious diseases are in a period of decline, the threat of their renewed prevalence must always remain. The ever-present possibility of smallpox or typhoid fever in widely spread epidemics, the potential renewal of virulence in some of the common infectious diseases, and the present prevalence of virus infections such as poliomyelitis call for many nurses trained in handling infectious diseases. In a very few years the reserve of such nurses will be seriously depleted—a position which should cause the utmost concern to all those responsible for the health of the people.

JAMES GRANT
Medical Officer of Health and Medical
Superintendent, Sheriff Hill
Infectious Diseases Hospital.

Gateshead.

SIMULTANEOUS AORTIC AND AXILLARY EMBOLISM

SIR,—Mr. Hardy and Mr. Noon are to be congratulated on their skilful management of their quite remarkable case of aortic and axillary embolism. Their discussion of the case (Jan. 24) will be of great interest to any surgeon who may be called on to undertake this operation. I should like to endorse all their points and also to venture one or two comments based on experience of 11 cases of peripheral embolism, including 4 cases of aortic embolectomy in 2 of which the patient recovered from the operation.

Certainly extreme care and gentleness is essential in handling and sewing vessels smaller than the aorta. Although extrusion of the embolus and clot by milking is to be preferred to endarterial manœuvres, there are occasions when clot remote from the exposed vessel requires removal by suction. I found my ball-ended needle more effective than a catheter for this purpose,[1] and it has since been valuable on several occasions. In aortic embolectomy it is an advantage when possible to have one assistant in control of the aorta and another standing between the abducted legs in control of the common iliac vessels.

I believe it is very important during the first three to four postoperative days to use all proved methods of relaxing vascular spasm and increasing the collateral circulation. In addition to those mentioned by Mr. Hardy and Mr. Noon, including the valuable technique advised by Mr. Kinmonth,[2] I believe that lumbar sympathetic block should be done twice daily and also an intra-aortic injection of papaverine given in saline. This injection can easily be carried out at the same time as the left paravertebral injection.

This treatment results in noticeable improvement in the limb circulation, and has been used in 2 cases of femoral embolectomy in the last two months. In the late case of femoral embolism these and other measures, such as the oxygen tent, may contribute to the saving of a limb.

One last point of interest is that I have injected at laparotomy 5 ml. of 10% phenol along the lumbar sympathetic chains through the posterior peritoneum in some elderly patients who have also been suffering from the effects of senile obliterative arteritis of the lower limbs. This simple procedure has given effective sympathetic release, and it may therefore be worth while in cases of aortic embolectomy.

Whipps Cross Hospital,
London, E.11.

D. LANG STEVENSON.

POLIOMYELITIS

SIR,—I agree with Professor Trueta in his comments (Jan. 31) on your abstract (Jan. 10) of Dr. Ritchie Russell's book. I am interested in Dr. Ritchie Russell's views on the defects of prolonged hospital treatment, but feel that he is not just in his assessment of orthopædic practice.

Anterior poliomyelitis remains an enigmatic disease despite the work done during the past half-century. Ritchie Russell has emphasised the need for fresh and unbiased inquiry into all its aspects. While the approach with an open and inquiring mind is valuable, weight should be given to the experience of those who have been concerned with the long-term treatment of the disease for many years. A certain school of orthopædics has unjustly been blamed for advocating rigid splintage, but it is certainly true that in the past, for a reason that no longer applies, the older orthopædic teachers did prolong immobilisation unnecessarily when the acute illness was past. This practice derived largely from the view that if structure was preserved functional restoration would be facilitated. Certainly by these means they prevented the ghastly deformities which developed in the absence of any treatment.

This conflict between the claims of structure and of function has lasted for at least two centuries since John Hunter (quoted by Wood Jones) stated that " it is a vain quest to attempt to solve any of the problems connected with living organisms by studying only one of the twin factors that constitute the basis of life." If we could only regard function as, so to speak, the fourth dimension of structure many therapeutic problems would be easier.

The following are some of the disturbances which cause disability in poliomyelitis. I find it impossible to distinguish the precise contribution of each to structural or to functional disability, because they are inseparable. The most important feature is that which Steindler calls myogenic contracture, and to this the following contribute:

1. *Muscular disuse and reciprocal over-action.*—The weakness of affected muscles and the over-action of antagonists as a cause of deformity is less often seen nowadays, except in untreated poliomyelitis. It probably is less important than other factors.

2. *Muscle spasm.*—This is a transitory phenomenon, the cause of which is not clear. It has been found in partly paralysed muscles as well as those relatively unaffected, but is absent in totally flaccid muscles. It has been ascribed to local irritability of muscle tissue, a myositic element, or various types of neuroanatomical disturbance.

3. *Muscular atrophy and fibrous replacement.*—These changes that follow denervation appear to be the same as those in the later stages of badly treated peripheral-nerve injury. In poliomyelitis such degenerative changes are diffuse and variable in intensity. They would seem to be due to changes in elasticity, which normally is a quality of the non-muscular connective-tissue elements of muscle.

4. *Osteomyotatic aplasia.*—This factor operates only in childhood. The term is, perhaps, cumbersome. By it I mean the failure of the normal stimulus to muscle-fibre growth. According to the work of Wheeler Haines, the length of muscle-fibres is determined by the extending force of growing bone. Such an influence on deformity is, I think, evident in calf-muscle paralysis, where the absence of an upward distracting influence by the os calcis prevents the growth of the plantar muscles. Relative shortening or aplasia of this type in functioning muscles may contribute to talipes calcaneus and paralytic scoliosis. This is not a question of muscular over-action but of failure to grow in length.

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[1] Stevenson, D. L. *Lancet*, 1938, i, 723.
[2] Kinmonth, J. B. *Brit. med. J.* 1952, i, 59.

TABLE II—SODIUM AND POTASSIUM CONCENTRATIONS AND RATIOS IN ALIMENTARY SECRETIONS AND IN STOOLS

Material	No of samples	Average [Na] m eq/l or m eq / kg	Average [K] m eq /l or m eq / kg	Na/K ratio
Gastric juice	76	56	12.6	4.5/1
Bile	48	151	5.2	29.0/1
Gastric secretion	64	113	4.6	25.0/1
Intestinal suction	12	121	9.6	13.0/1
Ileal fistula	12	132	6.2	21.0/1
Gastro enteritis in infants				
(a) Watery stools	11	68	42.0	1.6/1
(b) Formed stools	6	25	56.0	1.0/2.2
Normal infant stools*		1.3	3.8	1.0/2.9
Normal adult stools*		5.0	12.0	1.0/2.4

*Milli equivalent per day

The analytical results are from these sources
Alimentary secretions Lans, Stein, and Meyer (1952)
Stools in gastro enteritis Darrow (1946)
Normal stools Shohl (1939)

tion of sodium usually fall, but the potassium increases in concentration and amount (Annis and Alexander 1952). Although much of the potassium in stools may be bacterial and unavailable for reabsorption, the experiments with urine suggest that the colon can absorb sodium, but not potassium. This must operate in favour of enhancing potassium loss, and diminishing sodium loss, although there is ample evidence that in really copious diarrhœa sodium conservation by the colon is overborne. Quite apart from these local factors making for a higher potassium loss relative to sodium than would be predicted from analysis of isolated secretions, there are general factors which make the body more vulnerable to potassium than to sodium depletion, in the sense that any given external deprivation of potassium will produce a greater intrinsic depletion than would the corresponding external deprivation of sodium. Notable among these is the relative inefficiency of the kidneys in conserving potassium in response to depletion (Tarail and Elkinton 1949). There is no doubt that the kidney can conserve potassium by excreting a urine of lower potassium concentration than plasma (Mateer et al. 1949, Fourman 1952), and the progressive renal conservation of potassium is quite clearly seen in normal subjects on a very low potassium intake (Black and Milne 1952). As a rule, however, in clinical potassium depletion the urinary excretion of potassium remains considerable, although not so high as in the normal person. The occasional competence of the kidney to conserve potassium suggests that its usual failure to do so may be largely conditioned by extrarenal factors. These include glycolysis, protein breakdown, and acidosis, all of which make potassium from cells available for excretion. Acidosis may have a more direct action on the kidney itself, in that potassium may be drawn on as a base for excretion with fixed acid. The extent to which the adrenal cortex is overactive in disease states is still a matter of considerable controversy; an increased output of cortical hormones would increase renal excretion of potassium and diminish that of sodium, and to that extent might be operative in equalising sodium and potassium deficits even when the extrarenal loss of sodium was greater.

Loss of Potassium in the Urine

Although gastro-intestinal disease, including steatorrhœa (Harrison et al. 1943), was the earliest recognised cause of clinical potassium depletion, and remains the most frequent, potassium depletion has been demonstrated in other types of disease, the common factor being an abnormal loss of potassium in the urine. As with sodium, diminished intake of potassium plays only a subordinate part as compared with abnormal loss. The precise part played by the kidney itself in these abnormal urinary losses of potassium varies. Sometimes it is responding normally to a shift of potassium from cells into the extracellular fluid (E.C.F.); at other times it seems to be more directly "at fault," in that it excretes potassium from an extracellular fluid which is apparently normal in respect of that ion, or even depleted. This may happen under the influence of hormones or foreign substances, or because of intrinsic renal disease.

The distinction between what we may call "metabolic" and "renal" loss of potassium in the urine may not be easy to make; for one thing, the kidneys are part of the body, and the tubule cells are subject to the same hormonal stimuli as the other body cells. Also, a primary renal loss of potassium will induce a secondary transfer of potassium from cells to extracellular fluid, and conversely metabolic release of potassium soon involves renal mechanisms of increased excretion. Even in a condition so ostensibly "metabolic" as diabetic keto the loss of potassium from the body is only partly related to release of potassium from the cells due to acidosis, glycogen depletion, and protein breakdown; it is certainly augmented by the renal effects of acidosis and osmotic diuresis (Brodsky and Rapoport 1951), and also possibly by increased adrenocortical activity (Stowers 1951). In spite of such difficulties, it is still possible to find examples of potassium depletion which are predominantly "metabolic" in origin, and others which are "renal." In the first group we may include the potassium depletion associated with tissue breakdown (Howard and Carey 1949), primary water depletion (Black, McCance, and Young 1944, Elkinton and Winkler 1944), and mobilisation of glycogen stores (Fenn 1939). The potassium depletion induced by saline infusion (Coller et al. 1945), or observed postoperatively (Pearson and Eliel 1949) is probably of mixed metabolic and renal origin, like that in diabetic coma. The excretion of potassium by normal kidneys is increased by deoxycortone or by natural adrenal cortical hormones, as in Cushing's syndrome; potassium excretion is also increased by *p*-aminosalicylic acid (Cayley 1950), by liquorice (Strong 1951), and by mercurial diuretics (Blumgart et al. 1934). In primary renal failure, potassium wastage is uncommon, although paralysis related to potassium depletion has been described (Brown et al. 1944). Usually potassium excretion remains adequate to keep the serum-potassium normal, in spite of the greatly reduced glomerular filtration of this ion; secretion of potassium by the tubules can sometimes be inferred from an excess of excreted over filtered potassium (Platt 1950). Potassium depletion of renal origin, in the absence of uræmia, has been reported in renal tubular acidosis and the de Toni Fanconi syndrome (Milne, Stanbury, and Thomson 1952), and in the "early diuretic phase" of recovery from anuria (Bull, Jockes, and Lowe 1950). Potassium depletion observed in association with chronic alkalosis may also be of renal origin (Stanbury and Thomson 1952).

Recognition of Potassium Depletion

Knowledge of the various mechanisms which can lead to potassium depletion is of considerable importance, since the clinical picture is neither obtrusive nor well defined, except for paralysis which is by no means a constant finding. Moreover, the biochemical demonstration of potassium depletion may be far from easy in the individual patient; for the serum level of potassium may be within the rather wide normal range of 3.5–5.6 m eq per litre (Wootton et al. 1951) or may even be raised, when concurrent sodium depletion has reduced the E.C.F. volume at a time when potassium is streaming out of the cells (Danowski et al. 1949). On the other hand, the serum-potassium may be low in the absence of a general body deficit of potassium owing to an excessive uptake of potassium into cells. This may happen spontaneously, in periodic paralysis (Danowski et al. 1948), or secondarily

AUGMENTED RESPIRATION

SIR,—Dr. O'Brien, in his letter (Jan. 31), questions the value of our method of treating atelectasis neonatorum on the ground that other "less ingenious" methods of artificial respiration have persistently failed. This is not good logic, and he can hardly advocate the abandonment of further attempts to meet this most serious emergency.

Experimental work by Day et al., to which he refers, has shown that full-term fœtal atelectatic lung can be satisfactorily inflated; and Dr. O'Brien misrepresents the purport of this important article. They failed, however, in the case of gross structural immaturity. In the case of hyaline membrane Potter could not re-expand affected lung post mortem with air, nor do we yet know whether this condition is reversible in the living subject.

Recently Dr. O'Brien and Dr. Roberts[1] described resuscitation of the newborn by intermittent positive endotracheal inflation. The usefulness of this method in the immediate treatment of asphyxia in full-term infants has long been generally accepted since Gibberd and Blaikley first introduced it. Nevertheless the danger of overdistension of the alveolar ducts likewise applies. As described by O'Brien and Roberts, however, oxygen, delivered at $1\frac{1}{2}$ litres per minute, is intermittently supplied at an empirical rate which bears no relation to the child's requirements or spontaneous efforts, if any, and at pressures which are neither accurately determined nor controlled.

Dr. O'Brien suggests that our treatment not only fails to assist a baby in breathing but even accelerates the development of factors responsible for atelectasis. This criticism is no more than conjectural and is not based on observations comparable to our own with the servo respirator in action. He alludes to the possible fate of normally aspirated liquor amnii, but if a baby can be kept alive and breathing it has a chance of dealing with this in the physiological manner. Our use of negative pressures is also likely to improve circulation by encouraging rather than opposing venous return to the heart.

We believe that it often takes several hours of treatment to overcome atelectasis by gradually assisted expansion; and we have, in the past, from time to time failed to save the child by stopping treatment too soon after witnessing clinical improvement. Since our article appeared, two further severely affected cases, in which the prognosis appeared very grave, have been successfully treated in the servo respirator and are doing well.

We did not state, as represented by Dr. O'Brien, that atelectasis found at necropsy is unrelated to the ante-mortem state; but we produced instances to show that, in some cases, total non-aeration of the lungs may be found post mortem where evidence of at least some degree of aeration has been present before death—an observation already made by Potter.

Our trip spirometer is calibrated on each occasion it is used by means of pumping air into it with a well-lubricated 10 ml. syringe, using the same non-return valves. Mask leaks are tested for by gently compressing the sides and observing pen deflection. The alginate seal, when used, forms a far more natural and complete seal than any inflated cuff; and, provided it is not being subjected to pressures, it permits the minimum of leakage. For many months now we have taken the precaution of switching off the respirator pressures for the taking of recordings.

We do not claim the accuracy of a physiological experiment and have already listed the limitations of the method, many of which are due to the mechanics of the writing pens; but plans to improve these defects are already well under way. As it is, the method, though rough and ready, is simple, can be operated by a nursing sister, and causes the minimum of disturbance to a sick child.

Basal conditions are not applicable in the face of respiratory distress, and maximal respiratory capacity is more indicative of the child's ability to survive. It would be wanton to forgo any contributory information, thus available, in making a clinical assessment; and Dr. O'Brien's objections ignore the practical needs of the case.

Let us not widen the existing gap between scientific experiment and clinical reality.

Institute of Obstetrics and
Gynæcology, Postgraduate Medical
School of London, W.12.

IAN DONALD
JOSEPHINE LORD.

TUBERCULIN SENSITIVITY

SIR,—Having been ill for some time, I have only now been able to study the intriguing paper by Dr. Edwards and Dr. Palmer (Jan. 10). They claim that "low-grade" tuberculin sensitivity is non-specific, and they repeat this postulate so clearly in their article that there is no doubt they mean it is *always* non-specific. Prior to discussion of this surprising postulate, there is one question which I think they should answer.

Do they believe that, after a first tuberculous infection, specific skin allergy will invariably remain at what they term a high level throughout life, regardless of whether the focus heals or not, and even if the individual never undergoes a further infection? If they believe this, what are the grounds for their belief? To put it more directly, do they disbelieve that after a first tuberculous infection, and in the absence of further infection, specific cutaneous allergy may through the months and years gradually wane to a very low level? For if it does so wane, surely it must pass through a stage of reacting only to high doses of tuberculin and so constitute "low-grade" sensitivity within their definition.

Tuberculosis Research Unit,
M.R.C. Laboratories,
Holly Hill, London, N.W.3.

MARC DANIELS.

EFFECTS OF A SEVERE FOG ON A GENERAL PRACTICE

SIR,—I was interested to read Dr. Fry's article in your issue of Jan. 31. The figures given by him concerning the increase in the volume of work surprised me in more ways than one.

Firstly, an increase of 50 cases a week in a practice of 4500 indicates that only slightly more than 1% were affected as a result of the fog. This is a comparatively trivial figure compared with a similar occurrence in my practice two or three years ago when the volume of work increased to such an extent that I attended 45% of my entire list (2600) in a week.

Secondly, I am surprised at the relatively small amount of work indicated as normal for the practice concerned. Dr. Fry's figures show his yearly items of service as approximately: visits 3900, attendances 13,000; total 16,900. My own figures for a practice of 2600 people show the following: visits 11,900, attendances 18,700; total 30,600. In other words Dr. Fry's rate of remuneration per item of service is approximately three times mine. Can you, Sir, offer any suggestions as to how this great disparity arises?

Whitburn, co. Durham.

FRANK CORT.

*** This letter has been shown to Dr. Fry, who replies as follows:

"The main purpose of my short report on the effects of the severe London fog was to show what type of *clinical material* was encountered during the period. It was *not my intention* to show how much or how little work my practice entailed during a year. This has been discussed in a previous report.[1]

"It is, I believe, quite impossible to judge the worth and quality of a practitioner by the volume of work that he does. Obviously this volume will depend on very many factors, such as (1) the type of practice and the nature of the diseases

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[1] O'Brien, D., Roberts, H. *Brit. med. J.* 1952, ii, 963.

[1] Fry, J. *Brit. med. J.* 1952, ii, 249.

TABLE II—SODIUM AND POTASSIUM CONCENTRATIONS AND RATIOS IN ALIMENTARY SECRETIONS AND IN STOOLS

Material	No of samples	Average [Na] m eq/l or m eq / kg	Average [K] m eq /l or m eq / kg	Na/K ratio
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Bile	48	151	5 2	29 0/1
Gastric secretion	64	113	4 6	25 0/1
Intestinal suction	12	121	9 6	13 0/1
Ileal fistula	12	132	6 2	21 0/1
Gastro enteritis in infants				
(a) Watery stools	11	68	42 0	1 6/1
(b) Formed stools	6	25	56 0	1 0/2 2
Normal infant stools*		1 3	3 8	1 0/2 9
Normal adult stools*		5 0	12 0	1 0/2 4

*Milli equivalent per day

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Alimentary secretions Lans, Stein, and Meyer (1952)
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tion of sodium usually fall, but the potassium increases in concentration and amount (Annis and Alexander 1952) Although much of the potassium in stools may be bacterial and unavailable for reabsorption, the experiments with urine suggest that the colon can absorb sodium, but not potassium This must operate in favour of enhancing potassium loss, and diminishing sodium loss, although there is ample evidence that in really copious diarrhœa sodium conservation by the colon is overborne Quite apart from these local factors making for a higher potassium loss relative to sodium than would be predicted from analysis of isolated secretions, there are general factors which make the body more vulnerable to potassium than to sodium depletion, in the sense that any given external deprivation of potassium will produce a greater intrinsic depletion than would the corresponding external deprivation of sodium Notable among these is the relative inefficiency of the kidneys in conserving potassium in response to depletion (Tarail and Elkinton 1949) There is no doubt that the kidney can conserve potassium by excreting a urine of lower potassium concentration than plasma (Mateer et al 1949, Fourman 1952), and the progressive renal conservation of potassium is quite clearly seen in normal subjects on a very low potassium intake (Black and Milne 1952) As a rule, however, in clinical potassium depletion the urinary excretion of potassium remains considerable, although not so high as in the normal person The occasional competence of the kidney to conserve potassium suggests that its usual failure to do so may be largely conditioned by extrarenal factors These include glycolysis, protein breakdown, and acidosis, all of which make potassium from cells available for excretion Acidosis may have a more direct action on the kidney itself, in that potassium may be drawn on as a base for excretion with fixed acid The extent to which the adrenal cortex is overactive in disease states is still a matter of considerable controversy an increased output of cortical hormones would increase renal excretion of potassium and diminish that of sodium, and to that extent might be operative in equalising sodium and potassium deficits even when the extrarenal loss of sodium was greater

Loss of Potassium in the Urine

Although gastro-intestinal disease, including steatorrhœa (Harrison et al 1943), was the earliest recognised cause of clinical potassium depletion, and remains the most frequent, potassium depletion has been demonstrated in other types of disease, the common factor being an abnormal loss of potassium in the urine As with sodium, diminished intake of potassium plays only a subordinate part as compared with abnormal loss The precise part played by the kidney itself in these abnormal urinary losses of potassium varies. Sometimes it is responding normally to a shift of potassium from ce into the extracellular fluid (E C F), at other times seems to be more directly "at fault," in that it excret potassium from an extracellular fluid which is apparent normal in respect of that ion, or even depleted This m happen under the influence of hormones or foreig substances, or because of intrinsic renal disease

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Recognition of Potassium Depletion

Knowledge of the various mechanisms which can lead to potassium depletion is of considerable importance, since the clinical picture is neither obtrusive nor well defined, except for paralysis which is by no means a constant finding Moreover, the biochemical demonstration of potassium depletion may be far from easy in the individual patient, for the serum level of potassium may be within the rather wide normal range of 3 5–5 6 m eq per litre (Wootton et al 1951), or may even be raised, when concurrent sodium depletion has reduced the E C F volume at a time when potassium is streaming out of the cells (Danowski et al 1949) On the other hand, the serum potassium may be low in the absence of a general body deficit of potassium, owing to an excessive uptake of potassium into cells This may happen spontaneously, in periodic paralysis (Danowski et al 1948), or secondarily certain movement, thereby pressing into activity unhabituated muscle groups, is probably being imprudent and facing risk. Accepting this proviso, there seems to be no good reason why the new swing should not be practised, since it is a pleasure to execute and gives the golfer more power and control.

In view of the new provisions for promoting golfing prowess in the young, it would be useful to know how far (if at all) the objections to the new swing are well founded.

London, W.1. MICHAEL ALBURY.

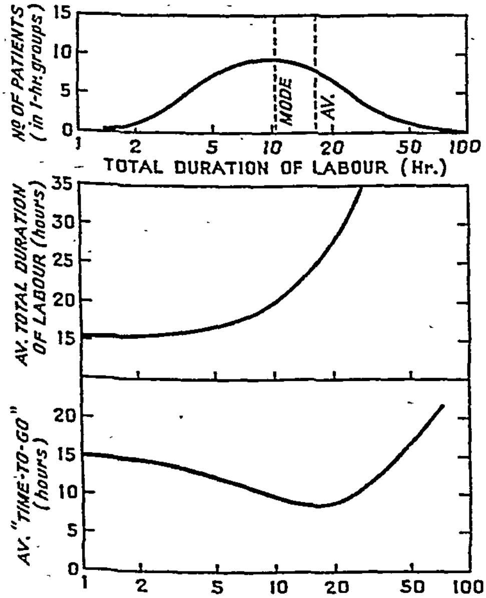
EXPECTATION OF FURTHER DURATION OF LABOUR

SIR,—In deciding on treatment in cases where labour is proving to be slow, it would be helpful to know the average further duration of labours in like circumstances. Averages must take account of such factors as the strength and frequency of uterine contractions, the rate of dilatation of the cervix, minor degrees of disproportion, and unusual presentations. Data are still insufficient for full sets of figures; and, moreover, the values are probably specific for a given location and epoch. Values can, however, be prepared for various parities, and the curve reproduced in the accompanying figure is for primiparæ.

Curve 1 shows the number of patients delivered after labours lasting for various times. The figures were collected from a group of 370 normal deliveries by counting the patients in each 1-hour group. The modal value is 10 hours, but the average value is higher than this (16 hours) owing to the inclusion of long pathological labours. This curve is similar to those published by Busby.[1]

Curve 2 shows for various times the average length of labour of all patients still undelivered at a given time. It commences at 16 hours and rises to 28 hours' total labour for all patients undelivered after 20 hours.

Curve 3 shows the average "time-to-go." It is obtained by subtracting the time already spent in labour from the figures of curve 2. Time-to-go has an average at the start of labour of 16 hours; after 10 hours the further expectation has fallen to 10 hours; there is a minimum expectation at 16 hours of a further 8 hours; and after this the curve rises steeply owing to the large percentage of pathological cases in the remaining patients.



A, number of primigravidæ, in a group of 370, delivered after different times. B, average total length of labour in primigravidæ, according to time already in labour. C, average further duration of labour in primigravidæ, according to time already in labour.

This graph emphasises the need for early action to prevent long labours. A primigravida who is still in the first stage of labour after having regular contractions for 16 hours needs to have her case carefully reviewed.

Obstetric Hospital,
University College Hospital,
London, W.C.1. C. N. SMYTH.

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[1] Busby, T. *Amer. J. Obstet. Gynec.* 1948, 55, 846.

THE MEDICAL SERVICES IN THE KOREAN WAR

SIR,—The letter from General Sir Neil Cantlie last week adds little to the report by your correspondent on Jan. 17. Your correspondent stated: "Our own units have continued to use plasma as the chief means of replacing colloids and electrolytes in initial treatment." He also added: "The Americans have depended more on fresh blood."

In my previous letter (Jan. 24) I pointed out that during the late war, when ample supplies of blood and plasma were available, experienced workers in the forward areas used more than twice as much blood as plasma. Apparently this is also the practice of the American medical services today. It is difficult to understand why it is not also the practice of the Commonwealth medical services, and, in the absence of any explanation, one is regretfully forced to the conclusion that blood is not as readily available to the Commonwealth medical units in Korea as it should be.

Hove. REX BINNING.

Parliament

Hospital Endowments (Scotland) Bill

IN the House of Lords on Feb. 5 Earl FORTESCUE, on behalf of the Earl of HOME, Minister of State, Scottish Office, introduced this Bill, which provides for the constitution of a Scottish hospital endowments research trust. It also empowers the Hospital Endowments Commission to transfer endowments to the trust. The Bill is based on the recommendations of the Hospital Endowments Commission,[1] set out in a white-paper last August.

QUESTION TIME

Industrial Dermatitis Appeals

Mr. J. T. PRICE asked the Minister of National Insurance if, in cases of industrial dermatitis referred to medical appeal tribunals, the medical members appointed to adjudicate were in all cases qualified dermatologists.—Mr. R. H. TURTON replied: I could not accept the suggestion that medical appeal tribunals should always include specialists in the particular condition from which an appellant may be suffering. But in a case of dermatitis the evidence before the tribunal always includes a report by a dermatologist.

Mr. PRICE: Would the Minister not agree that it is considered by people well qualified to judge that in discussing or adjudicating upon these difficult cases the presence of general physicians who have no dermatological qualifications is quite useless, because these cases involve questions not only of disease but of medicolegal fact which has a bearing on the decisions made? Is the Minister aware that there is a good deal of disquiet about the manner in which these cases are being disposed of at the moment?—Mr. TURTON: The Ministry have not had such indications. There is general satisfaction with the decisions of the medical appeal tribunals, which consist of physicians of very great eminence. The adoption of any suggestion such as that made by the hon. member would involve a great delay in the treatment of these cases.

Tuberculosis among Women in Scotland

Replying to a question, Commander T. G. D. GALBRAITH, joint under-secretary of State for Scotland, said he was aware that for the 15–35 age-group in Scotland, contrary to the usual experience elsewhere in Europe, the female death-rate was higher than the male death-rate in the years 1948–50. This was due to the excess of female deaths from respiratory was replaced by hydrogen ions, giving a combined acidosis and potassium deficiency A further important difference between the two studies was that with actual ingestion of the resin Fourman was able to withdraw some potassium directly from the body, and also in his subjects urinary excretion of potassium remained high, presumably because of the acidosis, whereas in our subjects actual potassium loss was almost entirely urinary, and became rapidly curtailed For these reasons, his potassium deficit became much greater

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[1] See *Lancet*, 1952, ii, 251.

Experimental Depletion

The detailed results of our experiments have already been published (Black and Milne 1952), and here I shall only summarise the main findings, and discuss one or two conclusions which I think can be drawn from them and are of some general interest Two normal subjects were put on a diet containing less than 10 m eq of potassium daily, in contrast to a normal dietary intake in the preliminary periods of 140 m eq daily In spite of the low intake, both subjects continued at first to excrete sizable amounts of potassium in the urine, and the cumulative loss of potassium was 268 and 289 m eq in the two subjects The rapid initial loss of potassium soon diminished, and by the sixth day both subjects were very little removed from balance, even with the low intake used The low urinary excretion of potassium continued into the after-period, in which a high potassium intake was given, under these conditions, potassium was retained to an amount considerably greater than the pre existing deficit The serum potassium fell progressively as the potassium depletion increased, and under our experimental conditions the serum-potassium level was negatively correlated with the cumulative negative potassium balance ($r = -0\ 762$, $P < 0\ 01$) This relationship is of course commonly departed from in clinical conditions where potassium depletion is complicated by a diminished E C F and plasma volume, the results of concurrent sodium depletion

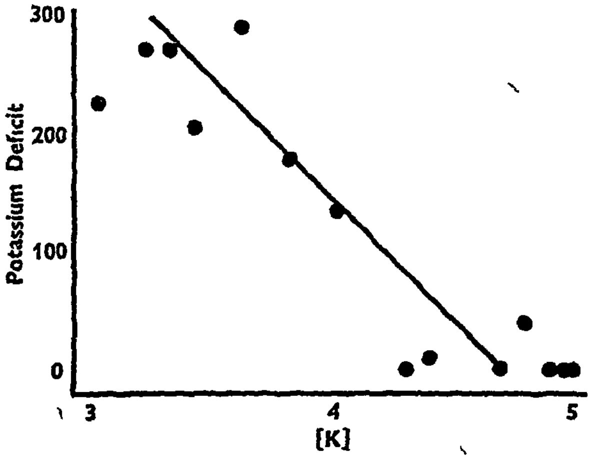

Fig 4—Relation between body potassium deficit and serum-potassium concentration

The fall in serum-potassium coincided with a rise in serum-bicarbonate, and there was a negative correlation between them ($r = -0\ 89$, $P < 0\ 01$), the possible significance of this finding will be discussed later Serum levels of sodium and chloride showed small changes, diverging sufficiently to accommodate the increment in bicarbonate The urine became less acid during the resin periods, and the output of ammonia and titratable acidity fell, these urinary changes are at least in part related to a diminished intake of chloride during the resin period, during which sodium was supplied from the resin, and not in combination with chloride, as in the preliminary and after periods There was during the resin period a large retention of sodium, and even of chloride, although the chloride intake was lower during the resin period than beforehand When the potassium depletion was repaired, there was a corresponding sodium and chloride diuresis The balances showed no significant loss of calcium or magnesium, but during the resin period there were small losses of nitrogen and phosphorus The losses of both these substances were much smaller than would have been observed had potassium, nitrogen, and phosphorus been lost together in the proportions found in tissue cells There was no loss in weight during the period of potassium depletion

Some interesting comparisons can be made between our experience of potassium depletion and that of Fourman, in relation to the clinical question "Does moderate potassium depletion per se cause any notable symptoms?" In our experiments, there were no dramatic symptoms, except when one of us took 3 g of ammonium chloride, and felt rather ill after it Otherwise we were able to perform our normal tasks, it may be with diminished efficiency Our daily portion of 3 litres of sweetened milk was no more distasteful when we were short of potassium We had no muscular weakness, although the serum-potassium fell on one occasion to 2 6 m eq per litre The harmful effect of ammonium chloride tallies rather well with Fourman's more fully documented experience in this respect, and also with clinical observation During the resin period, when Fourman's subjects were both acidotic and potassium-depleted, they "felt and looked very ill, took their diet with extreme difficulty, and became absent minded and then confused" During the recovery period of his experiments, the acidosis receded within a few days, and the plasma-bicarbonate rose above control values, there was still considerable potassium depletion, but at this stage symptoms were not dramatic, although "the subjects were morose apathetic, and tired easily" One subject drove to North Wales and did some hill-walking, with a deficit of 600 m eq of potassium The experimental evidence may be summarised in the statement that moderate potassium depletion does not in itself cause severe symptoms, but it may do so when associated with acidosis

The relevance of these experimental findings to clinical medicine obviously depends on there being no great quantitative divergence between the experimental and the clinical deficits of potassium This criterion of relevance is satisfied, at least so far as acute clinical potassium depletion is concerned The actual potassium deficit in patients is unknown, but can be gauged from the retention of potassium observed during recovery Two such studies on patients recovering from diabetic coma give retentions ranging in one series from 130 to 450 m eq, with an average of 290 m eq (Danowski et al 1949), in another from 147 to 385 m eq with an average of 279 m eq (Nabarro et al 1952a) The observed retention of potassium in our two subjects was 415 and 348 m eq, and in Fourman's subjects there were deficits of 338, 674, and 839 m eq The experimental potassium deficits are therefore somewhat greater than those observed in acute clinical potassium depletion, but appreciably higher retentions, up to 1000 m eq, have been recorded in chronic potassium depletion associated with loss of gastro intestinal secretions (Martin et al 1951)

Acidosis and Potassium Depletion

How are we to explain the undoubted occurrence of symptoms related to potassium depletion in a proportion of patients recovering from diabetic coma, when experimental depletion of similar or greater magnitude causes no such symptoms? It may be that the acidosis which is still present into recovery is potentiating the low serum potassium as a cause of symptoms, acidosis seemed to have this action in both the experimental studies just quoted I have seen profound apathy and muscular

Even when he was in his 80's his work as a writer went on, and his books the *Mystery of Birth* and the *Mystery of Marriage*, were published in 1948 and 1949. During these last years he had made his home at St. Margaret's Hospital, and his impressive appearance and personality made him an object of veneration and awe to the local population of Doddington. He continued his consulting practice, and patients came to him from all over the country. He remained physically and mentally alert, and in 1951 he was in private correspondence with us on the implications of the Cassidy case and the Denning judgment, arguing very wisely that medical members of hospital staffs must be accorded full responsibility for their professional acts.

ARTHUR FREDERICK GOLDSMITH

M.R.C.S.

Dr. Goldsmith died on Jan. 27, at the age of 82, in Bedford, where he had been in practice for many years. His family had a long record of service in the town: for his father, Dr. G. P. Goldsmith, practised there for forty years and his elder brother, Dr. G. Harvey Goldsmith, was consulting ophthalmological surgeon to the Bedford County Hospital.

Dr. "Fred," after he qualified from St. George's Hospital in 1874, joined his father's practice. Much of his work lay among the poor, and his old patients still talk of his skill and never-failing generosity. When his father retired in 1904 he succeeded him as district medical officer under the board of guardians, and he was also appointed public vaccinator. Dr. Goldsmith was an enthusiastic church worker, and he was for many years a churchwarden at St. Paul's Church. After he retired in 1932 he and his wife at first lived in Cornwall, but some years ago he returned to Biddenham, near Bedford, where he died.

Births, Marriages, and Deaths

BIRTHS

ALEXANDER.—On Feb. 6, at Ellerburn, Nunburnholme Avenue, North Ferriby, East Yorks, to June Alexander, M.B. (née Tyson), wife of Gordon Alexander, M.B., D.PATH.—a son.

THOMPSON.—On Jan. 29, at Newcastle upon Tyne, to Dr. Margaret Thompson (née Swinburne), wife of Dr. R. B. Thompson, M.R.C.P.—a son.

Appointments

CANN, A. M. R., M.D. Lond., D.C.H.: senior M.O. (school health service), Kingston upon Hull.

CULLINGTON, D. E., M.A., M.B. Camb., D.C.H., D.P.H.: M.O.H., Barking, Essex.

EARLE, J. H. O., M.D. Lond.: consultant asst. pathologist, Royal Cancer Hospital, London.

FLEMING, A. CHALMERS, M.B. Durh.: deputy medical superintendent, Hortham Hospital, Almondsbury, near Bristol.

HILL, T. W., M.D. Glasg., D.P.H.: asst. school M.O., Middlesbrough.

JARRATT, GEORGE, M.B. Lond., M.RAD. Lpool, D.M.R.T.: asst. radiotherapist, Hogarth radiotherapeutic centre, Nottingham General Hospital.

LOVE, S. H. S., M.B. Belf., D.A.: consultant anæsthetist, Belfast H.M.C. group.

MINTO, C. N., M.B. Aberd., D.P.H.: M.O.H., Caithness, and district hospital officer, Northern Regional Hospital Board for Caithness.

O'REILLY, J. T. J., M.B. N.U.I., F.R.C.S.I.: surgeon, County Hospital, Waterford.

OWEN, R. G., M.R.C.S.: appointed factory doctor, Penygroes, Caernarvonshire.

SAVILLE, STEPHANIE, M.B. Dubl.: anæsthetic registrar, Bath group of hospitals.

WARRACK, A. J. N., M.B.E., M.D. Lond., D.T.M.&H.: consultant pathologist, City General Hospital Laboratory, Sheffield.

Colonial Service:

BOULGER, L. R., M.B. Manc.: pathologist, Nigeria.

DAVIES, [illegible] C., M.R.C.S., D.P.H.: A.D.M.S., Tanganyika.

GOTTLIEB, [illegible]RYSTYNA, M.B., Polish School of Medicine, Edinburgh: schools M.O., Northern Rhodesia.

GREEN, BARBARA, M.B., D.T.M.&H.: senior M.O., Nigeria.

HARDY, J. M. H. R., L.R.C.P.E.: police M.O., Mauritius.

ROMBEJKO, EDWARD, MED.DIP. Warsaw: M.O., St. Helena.

Newcastle upon Tyne Regional Hospital Board:

LEGGAT, P. O., M.D. Aberd., M.R.C.P.: consultant chest physician (asst.), Newcastle (East) tuberculosis administrative area.

LYALL, D. J., M.B. Aberd., D.A.: consultant anæsthetist (asst.), Tees-side H.M.C. group.

MCDONALD, ROBERT, M.B. Aberd., D.P.H., D.P.M.: consultant psychiatrist, St. George's Hospital, Morpeth, Northumberland.

Notes and News

THE APPEARANCE OF ANIMALS

SWIFTLY reviewing the different shapes, patterns, and colours of various forms of animal life, Professor Portmann[1] lays emphasis on the facts that: (1) the external appearance is no guide to the internal (external symmetry often hides internal asymmetry); (2) the shape of many animals is based (as any zoological schoolboy knows) on a repetition of similar segments (metamerism); (3) there are many odd resemblances between animal and vegetable shapes; and (4) as the brain increases with the evolution of higher forms of animals, so the decoration of the head, or alternatively of the caudal end of the body, increases, especially after the descent of the testes to an extra-abdominal position.

The author's main contention seems to be that decoration of the body increases with the evolving importance of eyesight and is then intended to enable members of a species to recognise one another visually. "In all these cases," he says, "we are presented with optical structures, organs to be looked at, the total appearance of which has a meaning only when it is appreciated as being directed towards a beholding eye." Later he speaks of "morphological elements which are correlated with a beholding eye in the same way as transmitters are with a receiving set which is tuned in to them."

Other colours and patterns help their owners as warning colours and as camouflage, and in molluscs and radiolarians (which cannot see one another) colours and patterns can be produced "without any relation to visibility." But Professor Portmann does not attempt to explain this, although he seems to recognise that some colours and patterns arise without any utilitarian import. This takes us back half a century to Hans Gadow, who pointed out that neither natural selection nor sexual selection could produce colours and patterns but could only determine which colours and patterns already produced would survive. Indeed Professor Portmann makes a similar statement. Mysticism, however, creeps in when he declares that those colours and patterns which have a visual use constitute a special organ whose function is to produce a visible effect.

DATE OF BIRTH

A FILM with this title has been made by the National Film Board of Canada and is being sponsored in this country by the Ministry of Labour and National Service. The film tells of the economic and social problems associated with the provision of employment for older men and women. It runs for 18 minutes, and copies may be hired from the Central Film Library, Government Building, Bromyard Avenue, Acton, London, W.3, or from the affiliated libraries in Scotland and Wales.

University of Oxford

At a convocation to be held on July 1 in connection with the Rhodes centenary it is proposed to confer the honorary degree of D.C.L. on Dr. W. G. Penfield, O.M., F.R.S., director of Montreal Neurological Institute and professor of neurosurgery in McGill University.

Royal College of Physicians of London

The following, having satisfied the censors' board, were elected to the membership on Jan. 29:

E. M. McLachlan, M.B. N.Z., R. J. Marshall, M.D. Belf., J. Q. Matthias, M.B. Lond., G. W. Scott, M.D. Lond., H. M. Sinclair, D.M. Oxfd, W. H. J. Summerskill, B.M. Oxfd, J. L. G. Thomson, M.B. Lond., Joan M. Wagner, M.B. Witwatersrand, M. H. Watson, M.B. N.Z., J. L. Whitby, M.B. Camb., J. C. Woodrow, M.B. Leeds.

These names should have been included in the list published last week.

Royal College of Physicians of Edinburgh

At a meeting of the college held on Feb. 3, with Dr. W. A. Alexander, the president, in the chair, the following were elected to the membership:

D. G. McIntosh, D. G. C. Whyte, M. P. Goel, L. S. C. Mendis, G. M. Baird, B. Bevan, D. P. Gupta, J. B. Gibson, A. D. Muldoon, F. C. [illegible] W. Frain-Bell, J. Paul, Go[illegible]n, J. M. Neilson, R. H. [illegible] I. H. Pullon, M. Dan, Z. H. El Massry, S. Sing, J. A. Chunn, J. L. Potter, S. J. Irani, P. Sobti.

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[1] Animal Forms and Patterns: A Study of the Appearance of Animals. By ADOLF PORTMANN. Translated by HELLA CZECH. London: Faber & Faber. 1952. 25s.

in the depletion period, and this was only partially compensated by change in excretion, so the dietary change must have contributed to the extracellular alkalosis In subject 2, on the other hand, who had part of the sodium supplement as bicarbonate, the excretory change more than compensated for the dietary change, and the extracellular alkalosis cannot be attributed in any degree to the increased alkalinising action of the diet

These deductions from the (fixed base minus chloride) in diet and excretion are perhaps more simply arrived at from comparison of the sodium and potassium balance In subject 1 the positive balance of sodium was greater than the negative balance of potassium, indicating an increase in the total fixed base On the other hand, in subject 2 potassium was lost to a greater extent than sodium was retained, so that the fixed base content of the body decreased The extracellular alkalosis in subject 1 may thus have been partly caused by inadequate renal response to an alkalinising diet, but in subject 2 this explanation seems inadmissible, and we are faced with an alkalosis in extracellular fluid, but with an actual fall in the body content of sodium and potassium of the order of 60 m eq This would seem to require that the extracellular alkalosis be balanced by an intracellular acidosis, a possibility which we must now discuss

EXTRACELLULAR ALKALOSIS WITH INTRACELLULAR ACIDOSIS

The classical study of Darrow et al (1948) showed that in potassium-depleted rats the rise in serum-bicarbonate was closely correlated with changes in intracellular composition, notably the entry of sodium into the cells Further work by his group (Cooke et al 1952) has now shown that this replacement of intracellular potassium loss by entry of sodium is incomplete, only about two-thirds of the potassium deficit being made good by sodium Cooke et al suggest that hydrogen ions pass from the extracellular fluid to within the cells during potassium depletion, leaving an extracellular alkalosis This concept of an intracellular acidosis, caused by entry of hydrogen ions from the E C F, is supported by the observations of Gardner (1952) on the muscles of potassium-deficient rats He found that when the extracellular bicarbonate was increased there was at the same time a fall in intracellular bicarbonate and carbon dioxide tension, and the calculated intracellular pH fell from a control value of 6 98±0 08 to 6 42±0 05

Our own experiments did not include muscle biopsy, and so we can offer no proof of intracellular acidosis comparable in elegance to these results on animals However, it is difficult to see what other mechanism could explain the extracellular alkalosis in the subject who showed a net loss of base from the body, with no shrinkage in total body fluid In both subjects the amount of sodium which left the cells during recovery was substantially less than the amount of potassium which went in, suggesting that during depletion there was a " K–Na gap " of the type which would favour, or even necessitate, a hydrogen-ion shift The much greater loss of potassium than of phosphate from the cells would also suggest a fall in phosphate valency, such as would be promoted by the entry of hydrogen ions into the cells All these points are consistent with the mechanism proposed, but do not of course prove it

Therapeutic Implications

The evidence which I have so far presented suggests that acidosis increases the " penetration " of hypokalæmia as a cause of symptoms, and also that potassium depletion may be associated with an over-all acidosis even in the presence of a raised serum-bicarbonate If these submissions are accepted, it would appear logical to treat clinical potassium depletion by potassium in combination with anions which are oxidised in the body, such as lactate, citrate, or acetate These potassium salts are alkalinising in their effect Leonsins (1951) has suggested a mixture containing potassium bicarbonate, acetate, and citrate, 1 g of each to 8 ml of water (2 teaspoonfuls) I have had both personal and clinical experience of this mixture, it is much less nauseating than a comparable amount of potassium chloride, and the slightly alkaline taste can be disguised in fruit juice Given four times a day, it supplies 116 m eq of potassium When direct administration of potassium is contraindicated by a high serum level, as in the early treatment of diabetic coma, the acidosis should still be treated with sodium lactate, as advocated, among others, by Nabarro et al (1952b)

Potassium Depletion and Body-fluid

Let us now consider the alterations in body fluid accompanying experimental depletion of potassium

During the resin period, both subjects lost potassium, retained sodium and chloride, and showed no significant change in weight Most of the potassium must have come from the cells, for the potassium loss was several times greater than the estimated initial extracellular potassium, moreover, the concentration of extracellular potassium never fell below half the initial value Some of the sodium may have gone into cells, but it is unlikely that chloride did so Calculation of change in extracellular fluid volume from the chloride balance (Danowski et al 1951) indicated increases of 3 0 and 1 9 litres in the two subjects A fall in the hæmatocrit percentage, which was observed in both subjects, gives evidence of E C F expansion, independent of balance calculations In the recovery period, there was a considerable urinary loss of water and sodium, suggesting that the excess of E C F was then being excreted, at this time the hæmatocrit percentage rose again The loss of cell fluid, which had been masked during potassium depletion by expansion of E C F, then became apparent by weight losses of 4 0 and 2 6 kg in the two subjects The changes in body-fluid distribution in one subject, calculated from the chloride and water balance, are shown in fig 6 It is of interest that one of Fourman's subjects developed actual œdema of the legs and face, and œdema in association with potassium depletion has been observed clinically (Eliel et al 1950)

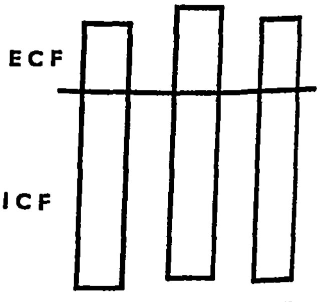

Fig 6—Changes in amount and distribution of body fluid in subject I

The calculated diminutions in intracellular fluid volume in our subjects agree fairly well with the amount of potassium known to be lost, and there is no evidence of a fall in the potassium concentration in the remaining I C F The absence of any notable change in serum sodium may be further evidence that the osmolarity of body-fluid, as opposed to its distribution, was not grossly altered On the other hand, with the more severe depletion associated with acidosis, Fourman and Ainley Walker (1952) found a loss of potassium which greatly exceeded the calculable volume change in I C F, and the concentration of potassium inside cells must have fallen Severe potassium depletion in animals is likewise associated with a fall in the potassium concentration of muscle I C F (Darrow et al 1948, Cotlove et al. 1952) The rather limited data available suggest that with potassium, as with sodium, the first effect of depletion on body-fluid is a shrinkage of the relevant compartment of body fluid, followed later by a fall in concentration, but we cannot exclude the possibility that the rather

BODY-FLUID DEPLETION*

D. A. K. BLACK
M.D., B.Sc. St. And., F.R.C.P.
LECTURER IN MEDICINE IN THE UNIVERSITY OF MANCHESTER

THERE is some truth in the statement that potassium stands in a relation to intracellular fluid similar to that which sodium bears to extracellular fluid. The great deposit of potassium lies within the cells, and the extracellular moiety of potassium is even smaller than the amount of intracellular sodium. Moreover, I hope to show later that potassium depletion, even of quite moderate degree, is attended by a diminution in volume of intracellular fluid (I.C.F.), and that with more advanced depletion the concentration of potassium in I.C.F. falls—quite a close functional analogy to what happens in sodium depletion to the volume and sodium concentration of extracellular fluid. There are, however, important differences, both quantitative and qualitative, between sodium and potassium in their respective phases of body-fluid. As we have seen, sodium accounts for over 90% of the base of extracellular fluid; but the predominance of potassium in intracellular fluid is less striking, for it forms at most two-thirds of the total base, the remainder being largely magnesium. Sodium is somewhat inert pharmacologically, so much so that in America it has been dubbed "osmotic stuffing"; but no-one has cared to take similar verbal liberties with potassium, in view of its well-known actions on neural transmission and muscular contraction. Even in a presentation mainly concerned with the relation of potassium to body-fluid, these pharmacological effects of the potassium ion demand some attention; but I cannot discuss them in the detail they deserve, and would refer you for this to the well-known review by Fenn (1940).

Physiologists have known for decades that lack of potassium in the surrounding medium will impair muscular contraction. The clinical counterpart to this is found in familial periodic palsy, whose centenary in description we may celebrate this year (Cavaré 1853). This relationship was first clearly established by Aitken et al. (1937), although with the spurious wisdom of hindsight we could commend Sir Farquhar Buzzard on his acumen in giving potassium tartrate to his patients in 1901. While these exciting discoveries were being made about extracellular potassium, the great mass of body-potassium lay neglected inside the cells, remote from direct analysis and untroubled by isotopes. Admittedly, balance studies commonly included potassium, as a measure of changes in intracellular fluid (Gamble, Ross, and Tisdall 1923); but the existence of potassium depletion involving mainly the cells was not established and shown to be clinically significant until the work of Darrow (1945). Darrow (1946) himself cites many examples in the literature, from as far back as Schmidt (1850), of diarrhœa associated with notable potassium loss. The observed losses often exceeded the total extracellular potassium, and must therefore have come in part from the cells; but the view that cell membranes were virtually impermeable to cations held sway, and inhibited any serious consideration of potassium depletion being predominantly an intracellular affair. By 1945, a dynamic approach to the problems of cell electrolyte composition had largely replaced the static schema centred on membrane permeability; and also by that time escape of potassium from cells had been demonstrated experimentally in several different contexts. For example, frog muscle in vitro lost potassium to the medium when this was made more acid or of lower potassium concentration (Fenn and Cobb 1934). Muscular contraction had been shown to be associated with loss of potassium (Fenn and Cobb 1936). Breakdown of glycogen or of tissue protein was known to be associated with discharge of potassium from the cells (Fenn 1940). Darrow's discovery of a large intracellular potassium deficit in infants with diarrhœa could therefore be readily accommodated in current theory—perhaps a necessary condition for the acceptance of all except the very greatest advances in knowledge.

By observing the retention of nitrogen and potassium during recovery, Darrow (1946) was able to show that potassium was retained in considerable excess of the amount which could be accounted for by tissue protein repair, as estimated from the positive nitrogen balance—a state of affairs which is often summarised in the phrase "retention of potassium in excess of nitrogen." Of the 6 infants studied, 2 had retention of potassium equivalent to 19% and 23% of the estimated normal potassium content of the body; the other 4 had retentions around 10% of the estimated total. Analysis of muscle from infants who had died from gastro-enteritis showed a potassium content up to 40% less than the normal. The inference that potassium deficits of this order should be treated by replacement therapy is supported by the findings of Govan and Darrow (1946). Of 53 infants treated by "conventional therapy" 17 died, whereas of 50 treated with potassium chloride in addition to the standard treatment, only 3 died.

Potassium Loss in Gastro-intestinal Disease

It was appropriate that the first clear demonstration of gross potassium depletion should have been made on gastro-intestinal disease; for the commonest mechanism for the loss of potassium, as indeed of sodium, from the body is escape of gastro-intestinal secretions, associated as a rule with interference with food intake. For example, Martin et al. (1951) found that 81% of patients suffering from potassium depletion had disease of the gastro-intestinal tract. Lans, Stein, and Meyer (1952) found a similar preponderance of gastro-intestinal disease in their series; they report analyses of different secretions, showing that the potassium concentration is usually distinctly higher than that of plasma (table II). From these analyses, and from the volumes of the various gastro-intestinal secretions given by Gamble (1947), the total daily secretion of potassium into the alimentary tract is of the order of 66 m.eq., or 2·6 g.—about as much as is found in a mixed diet. Reabsorption of this potassium may be impeded by ion-exchange resins in the hydrogen cycle given by mouth; these have on occasion led to significant potassium depletion (Dock and Frank 1950).

Although gastro-intestinal secretions usually contain more potassium that is found in plasma, they contain much less potassium than they do sodium, and it is not altogether easy to see why gastro-intestinal disease can cause deficits of potassium quite comparable in absolute magnitude to those of sodium. However, other factors come in to modify the expectation that more sodium would be lost than potassium. When gastric juice contributes largely to the total loss, the relatively low Na/K ratio in this particular secretion will be reflected in a relatively high potassium loss. When on the other hand the main loss is by diarrhœa, the ratio of K/Na in the stools is much higher than in pure gastro-intestinal secretions. In the 6 infants studied by Darrow (1946), the loss of sodium in the stools often exceeded that of potassium when the stools were watery, but when the water content of the stools dwindled the loss of potassium exceeded that of sodium. Normal stools contain more than twice as much potassium as sodium (Shohl 1939); and when urine is introduced into the colon, and retained for three hours, the amount and concentrapotassium depletion could be worked out on these lines, but the normal and the diurnal variability of potassium excretion, and the effect of concurrent sodium depletion, present obvious difficulties If these can be surmounted, such a test would be of value in the difficult group of patients with potassium depletion and a normal serum level of potassium

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* The second Goulstonian lecture for 1953, delivered before the Royal College of Physicians on Jan. 15.

The Pragmatic Sanction

As the sands run out towards the end of my attempt to portray body-fluid depletion, I enjoy a drowning man's vision of many sins of omission I have scarcely mentioned the influence of hormones on electrolyte distribution, the effect of metabolic activity in promoting electrolyte shifts, and the special problems of infancy yet all these are matters of the greatest importance My extenuation must be that in covering so vast a field I have been driven to a base empiricism, in that I have had to set therapeutic recommendations on a rickety foundation of half-truths My consolation is that the practical application of these methods, however insecurely founded they may be in theory, has often produced good results This pragmatic sanction, if one may call it so, is no justification for complacency, for the therapeutic successes are considerably overshadowed, not indeed by utter failures, but by unsolved and challenging problems, such as the low-salt syndrome associated with œdema, or the effects of potassium loss on cellular function

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Symptoms Caused by Potassium Depletion

Muscular weakness and paralysis seem to be generally related to the serum-potassium level rather than to "global" potassium depletion; this is most clearly seen in periodic paralysis, in which a shift of potassium into the cells brings on an attack, without any net loss of potassium from the body (Danowski et al. 1948). Even here, however, the relationship is not strict, for Allott and McArdle (1938) point out that paralysis may be absent at levels of serum-potassium lower than those associated with attacks in other patients. The electrocardiographic changes seem also to be related to the serum-potassium level rather than to the total potassium deficiency in the body (Darrow and Pratt 1950). On the other hand, complete or partial atony of the smooth muscle of the bowel has been attributed to depletion of intracellular potassium, and this has even been adduced as a cause of paralytic ileus (Streeten and Ward-McQuaid 1952). The argument here does not seem completely rigid, at least in the experimental work quoted (Streeten and Vaughan Williams 1952); for the method used to deplete intracellular potassium would be associated with entry of sodium into the cells, and this might be the more important change. It has been shown that various enzyme actions are inhibited by sodium and potentiated by potassium (Cannon 1952), making it difficult to assign special importance to either ion when there is a reciprocal shift of both. Besides, the low intracellular potassium observed could be a sequel rather than a cause of paralytic ileus. Eliel, Pearson, and Rawson (1950), in patients after operation, have demonstrated potassium depletion, and they describe in association with this a formidable list of symptoms—"apathy, lethargy, nervousness and irritability, muscular weakness, abdominal distension and occasional ileus, occasional confusion, disorientation, delirium, muscular twitching and tetany, electrocardiographic changes and occasional arrhythmias and œdema." Other workers have made similar claims in other clinical contexts, but the account given by Eliel et al. may be taken as representative.

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Apart from these general limitations of the experimental method, its application to potassium depletion has been beset by the special difficulty that almost all natural foods are rich in potassium, and a really "low-potassium" diet must also be a rather strange one. For small animals, synthetic diets can and have been used to provide a balanced food intake; but the quantities needed for man would be very costly. An electrolyte-free diet of good calorie content is indeed available in the glucose/arachis-oil mixture devised for the maintenance of patients with anuria; but this diet is also protein-free, a disadvantage when tissue breakdown is to be avoided as far as possible. The introduction of exchange resins has made it possible to remove potassium from foods or from the alimentary tract; this method has been used in two recent experimental studies (Black and Milne 1952, Fourman and Ainley-Walker 1952). Milne and I used a resin in the sodium cycle, and passed 3 litres of milk through it each day, giving us a diet adequate in calories and protein, very low in potassium, and rather high in sodium. Fourman used a resin in the hydrogen cycle, so that the potassium withdrawn from the body

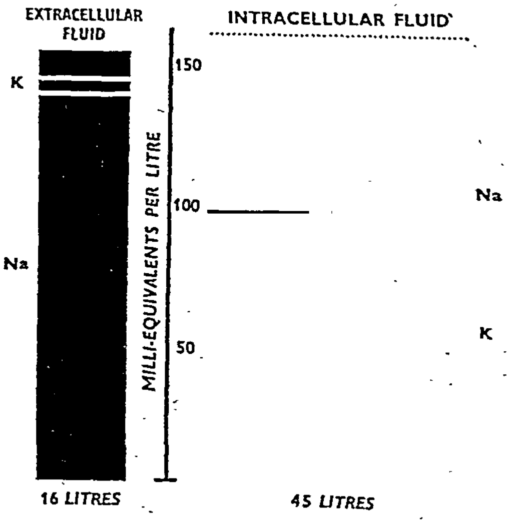

Fig. 3—Distribution of sodium and potassium in extracellular and intracellular fluid. Concentrations of electrolyte on the ordinate, volumes of the respective compartments on the abscissa, so that areas represent total amounts of electrolyte.

TABLE II—FOLLOW-UP CASES REINFECTED, RELAPSING, AND FAILURES

Case no	Follow up	Sensitivity of infecting organisms (µg per ml)					Second antibiotic chosen	Dosage 6 hrly (mg)	Mean assay value of urine (µg per ml)	Clinical result of urinary condition	Bacteriolo ical result of urinary condition
		P	S	C	A	T				After 2nd course	
2	New infection atypical *B coli*	1 25	2 0	2 5	100	50	Chloramphenicol	112	10	Cure	Sterile
4	New infection entero cocci	2	> 20	3 5	> 25	50	Penicillin, chloramphenicol	6 75	10	Cure of infection	Sterile
5	New infection *B coli*										
7	Persistence of staphylo cocci	25	20	30	0 5	2 5	Aureomycin	4	2	Asymptomatic	Sterile
9	New infection staphylococci	0 3	20	4 0	> 250	5 0	Penicillin	0 2	<1 0	Cure	Sterile
10	Persistence	0 3	20	4 0	> 250	5 0	Penicillin, streptomycin, aureomycin	0 035 17 5 1 0	Not calculable	Symptomatic relief, diabetes controlled	Modification
12	Recurrence		0 5	7 5	25	25	Streptomycin	1 0	1 5	Cure	Sterile
15	New infection proteus		0 6	4 0	100	50	Streptomycin	2 0	3 5	Asymptomatic	Sterile

A, aureomycin, C, chloramphenicol, P, penicillin, S, streptomycin T, terramycin

have to be attacked is usually not clear, but the criteria of infection and cure are definite and the same in all cases—namely, the presence or absence of clinical symptoms and signs, and the presence or absence of exudate and micro-organisms in the urine

Of the 17 patients treated (tables I and II) 15 were females The ages ranged from 17 to 72 (average 49)

Each case was considered individually when the sensitivity of the organism was known, and the antibiotic thought to be most suitable was administered six-hourly The five-day period adopted at first was found to be unnecessarily long in some cases, and administration of the antibiotic was cut short twenty-four hours after a specimen of urine was apparently sterile

Terramycin, chloramphenicol, and aureomycin were given by mouth, and penicillin and streptomycin by injection

Bacteriological Examination of Urine

Catheter specimens of urine were examined in all the women, and mid-stream specimens in the men The urine was examined at least twice before treatment was started (In a few cases a longer period of observation without treatment was possible) The urine was examined six hours after the first dose and daily thereafter Follow-up specimens were examined fifteen days after therapy and again some months later

Bacteriological examination of each specimen included microscopy of wet and stained preparations from the centrifuged deposit All the specimens were examined microscopically and culturally within twenty minutes of sampling, and the number of organisms present was estimated by a plate-count of the fresh uncentrifuged specimen (Dick and Marwick 1953)

The effect of treatment on the number of organisms present in the urine and on the amount of exudate is shown in table III

Determination of Sensitivity and Assay

The centrifuged deposit was used to inoculate plates for a screen sensitivity determination (Gould and Bowie 1952, Bowie and Gould 1952), and diagnostic plates were incubated aerobically and anaerobically It was usually possible to identify the species of bacteria, and to determine their sensitivity to the antibiotics, within twenty-four hours, in most cases their sensitivity could be determined satisfactorily enough for calculation of the dose (see below) On subculture further biological identification was made if necessary, and confirmatory sensitivity tests were made with uniform standard inocula The sensitivity of each organism to all the antibiotics used was determined at each isolation so as to discover whether there was any change of sensitivity to the antibiotic in use or to any of the others

The supernatant urine was used for assay where appropriate In all the cases the agar diffusion method (Heatley 1944) was carried out in parallel with the serial tube dilution method using both a standard test organism and the infecting pathogen of the particular case under examination (Mackie and McCartney 1950) In cases where the dosage of antibiotic was very small and the expected concentrations in the urine were about 1 0 µg per ml or less, a turbidimetric method of assay was also employed (McMahan 1944)

Calculation of Dose of Antibiotic

The excretion-rates of the different antibiotics vary widely Almost all the penicillin administered can be recovered in the urine, whereas only a small percentage of biologically active chloramphenicol is recoverable (Glazko et al 1950) Previous estimates of these excretion-rates have been made by different methods, and it seemed advisable to carry out a pilot experiment on a series of people to ascertain what proportion of the antibiotics we intended to use would be found in the urine with our particular methods of assay

A group of students and a group of patients, with healthy renal tracts, were selected and given various amounts of antibiotics by different routes, the body weight and the intake and output of water were measured

TABLE III—EFFECT OF ANTIBIOTIC ON NUMBERS OF BACTERIA AND PRESENCE OF EXUDATE IN URINE

Case no	No of organisms per ml					Exudate	
	Before therapy	From start of therapy (hr)				Before first course	After first course
		6	30	78	126		
1	10^7	10^3	10^7	10^5	0	+++	−
2	10^7	10^6	10^4	0	0	+++	±
3	10^8	10^6	0	0	0	++	−
4	5×10^6	10^4	0	0	0	+++	±
5	10^4	0	0	0		+	−
6	5×10^5	10^6	0	0	0	+	−
7	10^8	10^5	10^5	10^4	0	+++	∓
8	5×10^6	10^5	10^3	0	0	++	−
9	5×10^4	5×10^5	10^4	5×10^5	0	+++	+
10	5×10^6	10^6	5×10^4	10^5	10^5	+	+++
11	5×10^7	0	0	0		+	−
12	5×10^7		10^5	0	0	++	−
13	10^5	10^3	10^2			+	−
14	5×10^4	10^2	0	0	0	+	−
15	10^6	5×10^3	0	10^4	10^7	+	++
16	2×10^6	10^5	0	0	0	+	−
17	10^8	0	0	0	0	++	−

to rapid deposition of glycogen when insulin and glucose are given (Keys 1938). Retention of potassium is easily demonstrable during recovery from potassium depletion (Nabarro et al. 1952a), but does not of course afford a rapid assessment of the severity of depletion. Determination of the potassium content of muscle obtained at biopsy (Mudge and Vislocky 1949) likewise gives information of value but not of immediate clinical applicability. The potassium content of red blood-cells may not always be representative of that of tissue cells (Eliel et al. 1950); in moderate experimental potassium depletion, the potassium concentration in erythrocytes did not change appreciably (Black and Milne 1952). Determination of exchangeable potassium in the body with K^{42} may become the basis of a clinical test for potassium depletion, but the method has not yet been sufficiently explored. There is some evidence that the urinary output of potassium after a standard oral dose of potassium salts is related to the existing potassium household, and may thus be used as a clinical measure of potassium depletion. In the meantime, I would draw your attention to the more fundamental problem of assessing to what extent the multifarious clinical symptoms which have been described in association with potassium depletion can in fact be fairly ascribed to this particular biochemical distortion.

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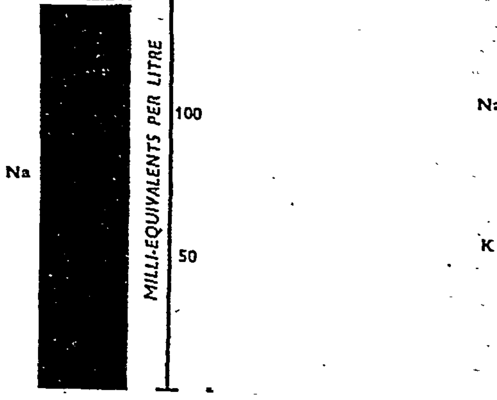

Fig. 3—Distribution of sodium and potassium in extracellular and intracellular fluid. Concentrations of electrolyte on the ordinate, volumes of the respective compartments on the abscissa, so that areas represent total amounts of electrolyte.

After the start of therapy the number of viable bacteria present in the urine decreased rapidly in most cases, especially those treated with streptomycin This decrease was accompanied by disappearance or considerable reduction in the amount of exudate (table III)

DISCUSSION

Bacteriological sterilisation of the urine was effected in most of the cases in the present series by a concentration of antibiotic in vivo approximating to that required to inhibit the infecting species in vitro The removal of the pathogens and the cessation of exudation were as rapid as would be expected if the usual therapeutic doses of antibiotic had been exhibited (Gould 1951), and the clinical response of the patients was at least as favourable (Cameron 1951)

The exhibition of antibiotics in a rational manner as described here has advantages which may be gained by the application of data obtained from the in-vitro tests at present made as a routine in hospital laboratories The most suitable antibiotic available against a particular pathogen may be given in a dosage which will cause no toxic effects in the patient and no side effects, such as gross upset of oral and intestinal flora Except for chloramphenicol, this rational dose is very low indeed. It may be possible to prevent the development of resistance to antibiotics by exposing the organisms to in-vivo concentrations closely related to their in vitro sensitivities

Certain species and groups of micro-organisms appear particularly liable to become resistant to antibiotics, and those possessing the rapid one-step streptomycin pattern of resistance constitute a definite clinical problem

All the individuals in a bacterial population are sensitive not to one particular concentration of a drug but rather to a range of concentration, which may be narrow or wide according to the antibiotic and species concerned If this range of concentration is X–Y, only 1% of the bacterial population may be killed at X (bacteriostatic level) but 99 9% at Y (bactericidal level) It is the latter value which is generally given in sensitivity reports Probably the potential resistant variants are to be found among the individuals which persist at this concentration, but these cells will not become resistant and dominant until a higher and critical concentration of antibiotic is reached The aim in therapy should therefore be to subject the organism to a concentration that is related as closely as possible to Y, which is the in-vitro bactericidal level This was the aim in the cases treated in the present series

The organisms isolated before treatment, when grown in vitro, all showed a well-defined zone X–Y but could be induced to form resistant variants by exposure to concentrations of antibiotic greater than Y in each case This was readily done by using streptomycin, it is well known that this antibiotic will induce resistant variants in culture and in the body during treatment We think it highly significant that in the present series no antibiotic resistant organisms were isolated either during or after treatment, although exposure lasted at least five days, sometimes longer

We gained the impression that, when used in rational doses, streptomycin is no more likely to induce resistance than is any other antibiotic, and further that it is the most valuable antibiotic in most urinary-tract infections

The principle behind the exhibition of antibiotics in this rational manner may well be applicable to the treatment of infection in other parts of the body Advance along these lines will depend on further knowledge of the antibiotic levels attained in individual tissues under any particular scheme of dosage

SUMMARY

The in-vitro sensitivity has been used in calculating a rational dosage of antibiotic in cases of infection of the urinary tract

17 cases were treated with satisfactory clinical and bacteriological results

No development of resistance to any of the antibiotics resulted from this therapy, and the number of resistant replacement strains encountered was less than when "standard" doses of antibiotics are exhibited

If the dosage of antibiotic is based on the in vitro sensitivity of the infecting micro organism, it will often be much lower than the "standard" dosage There is reason to suppose that if no more than the lowest effective dose is used, the infecting organism is unlikely to become resistant to the antibiotic

We have pleasure in thanking Prof T J Mackie, Dr W D D Small, and Dr E C Fahmy for their encouragement and guidance throughout this work, Mr K Marwick and Mr K. D Mackenzie for their untiring technical assistance, and Sister E A Hunter, Sister I Fraser, Sister C Hodgson, Staff nurse M Brown, and the nurses of wards 28, 29, and 49 of the Royal Infirmary, Edinburgh, for their enthusiastic coöperation.

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AN ANATOMICAL APPROACH TO POLIOMYELITIS

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FROM time to time theories of the pathology of poliomyelitis have been brought forward based on the conception that the pathways of the cerebrospinal fluid (C S F) are intimately concerned in the transmission of the virus Thus Burrows (1931) has carefully correlated the symptoms of poliomyelitis with the post mortem appearances in a large number of cases As a result of his findings he has regarded the perivascular spaces of the central nervous system as akin to the lymphatic vessels elsewhere in the body, and has suggested that their involvement in poliomyelitis is the direct cause of the damage to the nerve cells

Field and Brierley (1948a) have shown that the behaviour of particles introduced into the cranial subarachnoid space of animals may be similar to that of the virus of poliomyelitis in man Theories as to the pathology of poliomyelitis based on this type of experimental work must of necessity assume that the virus behaves as an inert particle similar in all respects to the particles injected experimentally This assumption is obviously a large one and must constantly be borne in mind before any conclusions about the pathology of nervous disease are based on the behaviour of injected particles In the presence, however, of the great difficulties that beset the study of the artificially induced disease, there appears to be a place for this method of investigation in the search for a rational pathology and therapy for poliomyelitis

The observations made in the present investigation were based on the fate of particles introduced into the subarachnoid space of the newborn rat, which animal has weakness in a patient recovering from diabetic coma whose serum-potassium was 3·1 m.eq. per litre, but whose bicarbonate was only 20·2 m*M*. per litre. Potassium chloride was given by mouth, and the apathy and weakness disappeared in an hour or two: the serum-potassium rose to 5·6 m.eq., but the mild acidosis remained uncorrected. By contrast, I have seen a patient with pyloric stenosis, whose serum-potassium was only 2·1 m.eq. per litre, but he was alkalotic with a bicarbonate of 38·2 m*M*. per litre; there was no demonstrable muscular weakness. Allott and McArdle (1938) have already noted the absence of paralysis in a patient with pyloric stenosis, and a serum-potassium of only 2·0 m.eq. In further and more general support of my contention that potassium depletion is more likely to cause symptoms when associated with acidosis, perhaps I may quote the independent clinical experience of Smart (1952), who says: "It is unusual to see paralysis in cases of potassium deficiency, but when it does occur it is usually seen in patients who are recovering from diabetic coma, in subjects with renal lesions such as chronic nephritis, or so-called calcinosis, or, much more rarely, in subjects with sprue and in patients with Addison's disease who have received too much DOCA." All these are conditions likely to be associated with acidosis, with the apparent exception of treated Addison's disease. I hope that what I have later to say on the so-called "hypochloræmic alkalosis" of potassium depletion may explain this solitary departure from the predicted association of symptoms with acidosis. Although there are obvious risks in transferring in-vitro evidence to a clinical situation, it is perhaps pertinent to mention here that the effects of a low environmental concentration of potassium on neuromuscular irritability are increased by making the surrounding fluid more acid (Gellhorn 1928, Lehmann 1937).

The Rise in Bicarbonate

May I now invite your attention to the rise in serum-bicarbonate which accompanied potassium depletion in both our subjects, and disappeared when the depletion was repaired. Raised serum-bicarbonate in association with potassium depletion has been described clinically, in Cushing's syndrome (McQuarrie et al. 1937), and also after surgical operations (Eliel et al. 1950); with potassium therapy, the serum-bicarbonate level falls (Kepler et al. 1948). This raised bicarbonate has often been described as a "hypokalæmic metabolic alkalosis," but it is difficult to see why loss of a base from the body should lead to alkalosis. When a similar rise in serum-bicarbonate occurred in experimental potassium depletion, there was an obvious opportunity of analysing its mechanism against the background of available balance results. We can distinguish four mechanisms, not mutually exclusive, by which the rise in serum-bicarbonate could be produced:

(1) Respiratory acidosis.
(2) Renal conservation of base.
(3) Change in the acid-base composition of the diet.
(4) Transfer of base from cells to extracellular fluid, with replacement by hydrogen ions.

RESPIRATORY ACIDOSIS

In clinical potassium depletion, irregularity of respiration, with inadequate ventilation, has been described (Denton et al. 1951). Hypopnœa could in theory lead to a raised serum-bicarbonate, in which event the alveolar carbon-dioxide tension (pCO_2) would also be raised. This sequence was an unlikely one in our subjects, in view of the absence of general clinical symptoms, and we were able to show in one subject that the alveolar pCO_2 remained unchanged at the height of depletion. This indicates a calculated rise of plasma pH from 7·48 to 7·58, and establishes the presence of an alkalosis in extracellular fluid.

RENAL CONSERVATION OF BASE

Berliner et al. (1951) have shown that potassium and hydrogen ions compete for some component of the ion-exchange mechanism in the distal renal tubule, so that a diminished secretion of potassium might favour the elimination of hydrogen ions in the urine. The secretion over a period of a urine too acid for the body's metabolic needs would cause alkalosis, and they propose this as a mechanism for the "alkalosis" associated with clinical potassium depletion. There was in fact some evidence in our subjects that hydrogen-ion secretion was being favoured by diminished potassium secretion; for the output of (ammonia + titratable acidity) was negatively correlated with the potassium output, increasing even in the presence of E.C.F. alkalosis, which would be expected to decrease renal output of acid. This apparently disadvantageous change in renal behaviour was not, however, the main cause of the observed alkalosis, though it may have enhanced it in a minor degree; for the urine in the depletion periods was considerably less acid than in the control periods. It might still be argued that although the urine became less acid, it might nevertheless be prevented by the Berliner mechanism from becoming as alkaline as the changed metabolic needs of the body would dictate. We must now examine this possibility quantitatively.

CHANGE IN ACID-BASE COMPOSITION OF DIET

The conditions of the experiment introduce a complication into our treatment of this subject. Since potassium was almost entirely replaced by sodium in the depletion periods, we were forced to give supplements of sodium salts in the preliminary and after periods, if the sodium intake was to be constant. We did this with chloride alone in the first experiment, so that the chloride intake was considerably higher in the control and after periods than in the depletion period. In the second experiment, we modified this by giving chloride and bicarbonate in the proportions found in E.C.F., believing that such a mixture would be "biologically neutral." There was still, however, a substantial excess of chloride in the diet, in the control and after periods, so that in both experiments in the depletion period less fixed base (sodium plus potassium) was "covered" in the diet by chloride, and this might well favour alkalosis.

To examine this matter further, we have calculated the fixed base and chloride intake and output in the various periods. As the fixed acids other than chloride did not change in the diet, the difference between dietary fixed base and chloride is a measure of the alkalinising tendency of the diet, while the difference between output of fixed base and chloride indicates the extent to which the dietary change has been compensated by change in excretion. In subject 1, who had the sodium supplements entirely in the form of chloride, there was a very considerable excess of (fixed base minus chloride)

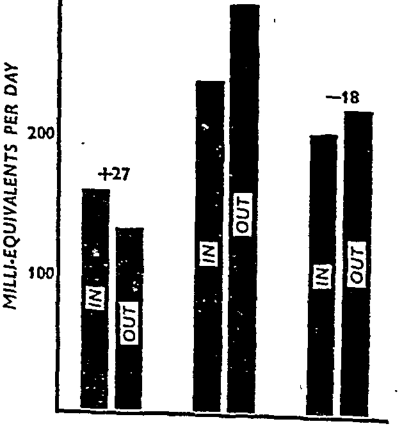

Fig. 5—Comparison of intake and output of "alkali" in preliminary, resin, and after-periods in subject 2. "Alkali" under the conditions of the experiment is given by Na + K – Cl.

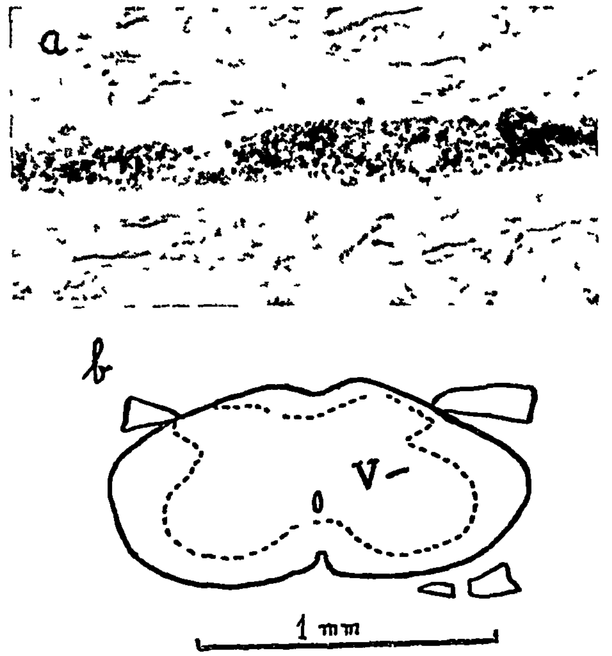

Fig 3—Transverse section of spinal cord of rat aged 21 days : *a*, carbon particles in perivascular space round small blood vessel (× 1250) , *b*, position of blood vessel (V) illustrated in *a*

the finding of Brierley (1950) that, under physiological conditions, particles can penetrate into the perivascular spaces To the perivascular spaces has been ascribed, by those workers who postulate a centrifugal direction of flow, the function of production or at least augmentation of the C S F More rarely the opposite view is taken that absorption takes place along these channels The results of the present experiments lend support to the view that these channels represent anatomical cul-de-sacs similar to those surrounding the emerging nerve-roots—backwaters in which there is a gentle eddy in both directions rather than a constant flow in one Their main function may be to act as fluid cushions intervening between the nerve cells and the contracting and expanding blood vessels of the brain and spinal cord

Burrows (1931) has regarded the pressure of the exudate in the perivascular spaces as the cause of the injury to and ultimate destruction of the anterior-horn cells in poliomyelitis The presence of such an exudate may lower the cushioning properties of the perivascular spaces and thus expose the nerve cells to the pressure changes produced by the passage of blood through the vessels That the presence of an abnormal substance in the perivascular spaces round the vessels in the region of the anterior horn may damage the anterior horn cells is shown by the work of Davis et al (1930), who found that iodised oil injected through the cisterna magna into the subarachnoid space of dogs eventually destroyed the anterior-horn cells The vulnerability of the anterior horn may be related to the rich vascularity of this region, for the greater the vascularity of a region of the cord the greater, presumably, is the area occupied by the perivascular spaces

The various situations in which particles injected into the subarachnoid space can be found may have some bearing on the stages of poliomyelitis in man The abdominal upset which often ushers in the illness may be due to the presence of the virus in the abdominal lymph glands, whether it reaches these from the intestines or from some other locus of infection The " meningitic " phase may be due to the presence of the virus in the subarachnoid space which it could reach along the pathway from lymph gland to subarachnoid cul de sac These subarachnoid cul de sacs occur along both cranial and spinal nerves and may collect exudate in poliomyelitis in the same way as they collected particles in the experiments on rats The presence of an exudate in this situation might be responsible for the occurrence, in this phase of symptoms such as neck rigidity and root pains due to irritation of the appropriate cranial and spinal nerves

The third or " paralytic " stage is, as is well known, associated with the presence of exudate in the perivascular spaces of the spinal cord It is interesting to note that particles injected into the subarachnoid space of rats were found within the subarachnoid cul de sacs round the emerging nerve roots a few minutes later, but their appearance within the perivascular spaces was delayed until 24–48 hours after the initial injection (Brierley 1950) It is tempting to conclude that the filling of the perivascular spaces depends on the blockage of the pathway of escape of the particles from the C S F via the subarachnoid cul de sacs into the prevertebral lymph glands The bearing which such a possibility has on this phase of the poliomyelitis cycle is self evident

THERAPY OF POLIOMYELITIS

The anatomical observations outlined here suggest that three stages can be distinguished in the fate of particles injected into the subarachnoid space of newborn rats (1) the formation of subarachnoid cuffs round the emerging nerve roots , (2) the filling of the prevertebral lymph glands , and (3) the appearance of particles in the perivascular spaces of the cord These stages appear to be so closely related to the phases of invasion by the virus in man that the question arises whether this fact can be used in treating poliomyelitis

The cellular exudate found in the perivascular spaces of the spinal cord in poliomyelitis may be (1) a simple exudate from the blood vessels, (2) due to a reaction in the perivascular spaces, or (3) an accumulation of cells derived from a generalised process in the subarachnoid space If, as Burrows (1931) has suggested, the destruction of the anterior horn cells is primarily due to mischief occurring in the perivascular spaces, then, irrespective of the origin of the exudate, the adequate drainage of the perivascular spaces appears to be of fundamental importance to the treatment of poliomyelitis

It is perhaps significant in relation to this proposition that repeated lumbar puncture has been widely advocated as a method of treatment The removal of C S F by lumbar puncture is one of the three methods by which it is possible to achieve a circulation of the fluid in the perivascular spaces The other methods by which a flow of the fluid in these spaces can be promoted are extreme exsanguination and the intravenous administration of hypertonic solutions Whereas extreme exsanguination is clearly impracticable, perhaps a method of treatment based upon the intravenous administration of hypertonic solutions has potentialities which have yet to be realised

The intravenous administration of a hypertonic solution promotes the circulation of the C S F in the perivascular spaces Hence the combination of this technique with the intrathecal injection of a therapeutic agent would enable that agent to reach the perivascular spaces

Whichever theory concerning the transmission of the virus of poliomyelitis is held, it is clear that such a method of administration must bring a therapeutic agent into closer contact with the virus, whether it be in the neurone or in the perivascular spaces, than any of the methods of therapy which depend on the agent reaching the virus via the blood-stream

The combination of the intravenous injection of hypertonic solutions with the intrathecal administration of antibiotic substances appears therefore to be high sodium intake of our experiments may have contributed to E.C.F. expansion and I.C.F. shrinkage. Our own experience would suggest that the clinical effects of an isosmotic reduction of I.C.F. are negligible, in interesting contrast to the great thirst and the definite malaise evoked by a comparable reduction in I.C.F. volume caused by primary water depletion, and so associated with hypertonicity (Black, McCance, and Young 1944).

Making Good the Deficit

It has to be emphasised that the potassium depletion induced in our experiments was moderate, and the clinical deductions which can be drawn directly from them are correspondingly limited. They suggest rather strongly, however, that potassium depletion of the order of 250–300 m.eq. is not likely to be a direct cause of symptoms, except when associated with acidosis. This conclusion cannot necessarily be extrapolated to depletions of the order of 1000 m.eq., such as arise from large and sustained losses of alimentary secretions; but a short note by Aikawa and Felts (1952) claims that in cortisone-induced potassium depletion "reduction of less than 30% in exchangeable potassium was not accompanied by clinical symptoms or signs of deficiency." On the other hand, large deficits of an important intracellular base would be expected to influence cell function unfavourably, and there is evidence from work on animals that potassium depletion may interfere with enzyme activity (Boyer et al. 1942), with glycogenesis (Gardner et al. 1950), and with the utilisation of dietary protein (Cannon et al. 1952). Cardiac and renal lesions have been found in potassium-depleted rats (Follis et al. 1942, Darrow 1944), and similar lesions have been reported in patients (Keye 1952). The abnormal electrocardiogram associated with potassium depletion on the basis of experiments on animals has often been demonstrated in patients, together with irregularities of cardiac action; and there is some evidence that potassium depletion increases cardiac susceptibility to the action of digitalis (Lown et al. 1952).

Perhaps the most convincing evidence of the actual clinical value of repairing a potassium deficit is the study of Govan and Darrow (1946), quoted previously, in which mortality in the same outbreak of gastro-enteritis was much less in the infants given potassium supplements. The balance of evidence seems to me quite clearly to favour the giving of potassium whenever there is good clinical and biochemical evidence of potassium deficiency. There is no real difficulty when the patient can take potassium salts by mouth, and a good case can be made out for giving potassium by this route to any patient with adequate renal function who is losing potassium in stools or urine, and who is not vomiting. Unfortunately, many patients with potassium depletion are unable to take or retain oral potassium, and in them the risks of potassium depletion must be balanced against the risks of parenteral potassium administration. There seems little doubt that a large deficiency of potassium can cause unpleasant symptoms, and even contribute to a fatal issue, but a moderate potassium depletion can probably be disregarded until potassium salts can be given by mouth. The risk of parenteral potassium administration is quite definite, and the danger of cardiac arrest depends on the serum level of potassium; a rise to 10 m.eq. per litre may be fatal. How is it to be avoided?

A potassium depletion must always have been actually demonstrated in the individual patient before potassium infusion is even considered; it is not right to give potassium infusions to patients after operation, for example, just because other postoperative patients have been judged to have a potassium depletion. Not only is a demonstrable potassium deficiency the only valid reason for giving parenteral potassium; it also lessens the toxicity of potassium. Potassium-depleted rats show increased resistance to potassium poisoning (Miller and Darrow 1940, Muntwyler 1950). Human evidence on this point is difficult to obtain, but the increase in serum-potassium after an oral dose of potassium is less in a potassium-depleted subject than in the same subject when normal (Black and Milne 1952). I have heard of one patient with a severe potassium depletion who had a pint of 2% potassium chloride (270 m.eq. per litre) given intravenously in less than three hours, without ill effect. I can only say that if anyone wanted to do this to me, I should insist on a severe potassium depletion beforehand.

Sodium and potassium depletion occur more often together than separately, and the coexistence of sodium depletion adds to the risks of giving potassium parenterally. With sodium depletion, the serum level of potassium is often high, in spite of a cellular potassium deficit, and the patient is that much nearer to a toxic serum level. Moreover, the renal excretion of potassium is interfered with in these patients, and the E.C.F. volume is smaller, so that added potassium will cause a greater concentration change. Perhaps I may repeat the suggestion made in the first lecture, that sodium replacement should be carried to the point of restoring circulatory and renal efficiency, before potassium is given parenterally. In more practical terms, the blood-pressure should be normal, "shock" or peripheral circulatory failure should have been corrected, and the urine volume should be adequate.

Since potassium toxicity is a matter of extracellular fluid concentration, the rate of infusion and the potassium concentration of the infused fluid are of first importance. Potassium solutions, either chloride, phosphate, or lactate, for general use should not contain more than 40 m.eq. of potassium per litre, and should not be given more rapidly than a litre in three hours. I am aware that more concentrated solutions have been given more rapidly without mishap by physicians and surgeons specially interested in potassium metabolism; but they know the hazards, and the night-nurse in a general ward does not. My conservatism in this matter is dictated by the belief that potassium therapy, if necessary intravenously, can be of great value in selected cases; and I do not want to see it discredited by accidents in the "routine administration" of potassium to patients who are not materially depleted of potassium. Just as with sodium, treatment which is appropriate to one patient may be mischievous and even dangerous in another.

In the first lecture, I discussed the evidence needed to establish the presence of sodium depletion. The position with regard to potassium is more difficult, in that we cannot determine practicably the concentration of potassium in the main body-reservoir of potassium, the I.C.F., as we can do so easily with sodium in plasma, which represents extracellular fluid. We have therefore to rely more on indirect evidence, such as a history of potassium loss, or more precisely of some condition likely to cause potassium loss; muscle weakness and electrocardiographic changes; and indirect biochemical evidence. A low serum level of potassium almost always implies a general potassium depletion, especially in the fasting patient; but a normal serum-potassium does not exclude potassium deficiency. An unexplained rise in the alkali reserve should make one consider potassium depletion.

When the serum level of potassium is normal, but potassium loss is likely from the history, a decision on potassium depletion is difficult. One approach is to correct sodium depletion, and repeat the serum-potassium estimation, giving potassium if the level has fallen. Black and Milne (1952) found that the urinary excretion of potassium after a standard dose was related to the initial deficit of potassium in the body. Some preliminary observations on normal people suggest that a test for

TABLE III—COMPARISON OF VITAMIN E AND CONTROL GROUPS ACCORDING TO PATIENT'S ASSESSMENT OF RESULT OF TREATMENT

Result	Vitamin E	Control	Total
Improved	8	6	14
No change	12	14	26
Deteriorated	0	1	1
Total	20	21	41

patient's individual average number of circuits was calculated The means of these individual averages were then computed in the two groups, and they are shown in table I to be quite close Similarly, for each patient the average duration of pain after stopping exercise was determined The mean value was shorter in the vitamin-E group but not significantly so The two groups do, however, differ significantly in the average time taken per circuit The vitamin-E group take, on the average, 5·6 seconds per circuit, against 6·5 seconds for the control group, the difference of 0·9 has a standard error of 0·3, and such a difference, or a larger one, would be expected to occur purely by chance only about once in fifty times Thus the random allocation has led to rather more of the initially brisker walkers being chosen for the vitamin-E than for the arachis oil treatment This means that any apparently marked effect of treatment in favour of vitamin E must be examined carefully to see whether it may have resulted from the initial disparity in walking speeds between the groups

The distribution of cases, as classified by the method of Boyd et al (1949), is shown in table II There is no conspicuous difference between the groups, but again the vitamin-E group contains a slightly higher proportion (55%) of grade-II (less severe) cases than the control group (43%)

TABLE IV—INCREASE IN AVERAGE NUMBER OF CIRCUITS DURING WHOLE TREATMENT PERIOD COMPARED WITH PRE TREATMENT PERIOD

Group	No of cases	Average no of circuits		Mean increase ± standard error
		Pre treatment	During treatment	
Vitamin E	20	19·02	20·66	1·64 ± 0·86
Control	21	18·12	19·04	0·92 ± 0·84
			Difference	0·72 ± 1·20

RESULTS OF TREATMENT

Various measures of the improvement shown by the two groups during or after the period of treatment are summarised in tables III–VII The patients' own assessments of the effect of treatment are tabulated in table III There is clearly no appreciable difference between the two groups These subjective assessments of the patients are more optimistic than the objective ones presented in the following tables Throughout the period of treatment the observers could not distinguish between patients given vitamin E and those given arachis oil either by the patients' statements or by clinical examination

For each patient the average number of circuits walked in the pre treatment period (the measure used in table I) was subtracted from the average number walked during the whole of the treatment period This difference provides a measure of the patient's improvement in exercise tolerance during the treatment period Table IV shows the mean increase that took place in each of the groups, with its standard error It will be seen that in neither group was there any substantial improvement in performance The vitamin-E group shows a slightly greater increase (0·72 circuits) compared with the control group, but the difference is not significant

Very similar results are shown in table V, where the pre-treatment averages are contrasted with those prevailing during the last month of treatment The vitamin E group again shows a slight, but non significant, improvement over the control group The control group here was reduced to 19 patients because 2 of the 21 did not visit the clinic during this part of the treatment period

The possibility that the treatment took effect after the conclusion of the three months' treatment is examined in table VI Here, for each patient, the pre treatment average number of circuits is subtracted from the average number achieved during the three months following the end of treatment The post treatment visits were rather irregular, but all the patients except 1 in each group had at least one visit during this period Once again the effect shown is small, and there is no significant difference between the groups

TABLE V—INCREASE IN AVERAGE NUMBER OF CIRCUITS DURING LAST MONTH OF TREATMENT COMPARED WITH PRE TREATMENT PERIOD

Group	No of cases	Average no of circuits		Mean increase ± standard error
		Pre treatment	Last month of treatment	
Vitamin E	20	19·02	20·86	1·84 ± 0·96
Control	19	17·81	19·03	1·22 ± 0·99
			Difference	0·62 ± 1·38

The duration of pain that was experienced by each patient after his exercise tolerance test is analysed in table VII The average duration experienced by the patient in the pre-treatment period (as used in table I) was subtracted from the corresponding average observed during the treatment period The difference between these two values was then expressed as a percentage of the pre treatment values to reveal the relative improvement (or deterioration) in the patient For instance, in the pre-treatment period a patient may, on the average of his observations, have experienced pain for 40 seconds During treatment his average duration may have become 30 seconds, and this is represented by an improvement of 10 seconds in 40 (25%) The means, over the two groups of these individual percentage changes are given in table VII In the whole period of treatment the vitamin E group shows a small and non significant reduction of 9·7% in duration of pain, while the control group shows a small and non-significant increase of 8·3% The difference between these two values (18%) has a standard error of 7·0% and is therefore technically significant

It is essential to determine whether this significant result in favour of the vitamin-E group is due merely to the disparity between the groups which has been noted earlier Analysis within the two groups shows that it was patients who took the longest time over a circuit in the pre treatment period who tended also, on the average, to show subsequently the least improvement

TABLE VI—INCREASE IN AVERAGE NUMBER OF CIRCUITS DURING FIRST THREE MONTHS AFTER TREATMENT COMPARED WITH PRE TREATMENT PERIOD

Group	No of cases	Average no of circuits		Mean increase ± standard error
		Pre treatment	First three months after treatment	
Vitamin E	19	18·88	19·85	0·97 ± 1·01
Control	20	18·32	19·82	1·50 ± 0·99
			Difference	−0·53 ± 1·41

DOSAGE OF ANTIBIOTICS

RELATION BETWEEN THE IN-VITRO AND IN-VIVO CONCENTRATIONS EFFECTIVE IN URINARY-TRACT INFECTIONS

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The in-vitro bacteriostatic or bactericidal concentration of an antibiotic for any bacterial species can be readily ascertained in the laboratory. But, though the results are of recognised value in selecting the most suitable antibiotic for treatment, they are not used in deciding the dosage. This is largely because little is known about the concentration of the various antibiotics in the different tissues of the body during treatment. Reliance is placed instead on "standard" serum levels, and, according to these levels "standard" dosage schedules have been devised with reference to excretion-rates. The infecting micro-organisms are classified as sensitive or otherwise in relation to the expected serum levels of antibiotic resulting from these "standard" doses.

No attempt has yet been made to effect in vivo exactly the same concentration as is known to inhibit the micro-organism in vitro.

This paper records an attempt to correlate the therapeutic dosage of antibiotics, and the resulting in-vivo concentrations, with the results of in-vitro sensitivity estimations.

METHODS

Selection of Cases and Administration of Antibiotics

Infections of the urinary tract were selected for the trials because they are common, the collection of satisfactory specimens is relatively easy, and the cases are generally amenable to treatment. In uncomplicated cases the invading micro-organisms seem to be relatively accessible to antibiotics given systemically; and, compared with infections such as endocarditis, therapeutic results are more closely related to in-vitro sensitivity. The particular site at which the micro-organisms

TABLE I—ANALYSIS OF CASES

Case no.	Age (yr.)	Diagnosis	Infecting organism	Sensitivity of infecting organisms (µg. per ml.)					Antibiotic chosen	Dosage 6-hrly. (mg.)	Mean assay value of urine (µg. per ml.)	Clinical result of urinary condition	Bacteriological result of urinary condition
				P	S	C	A	T				After 1st course of antibiotic	
1	17	Pyelonephritis, mitral stenosis	*Bact. coli*	3	0·2	4·5	250	50	Streptomycin	1·0	0·33	Cure	Sterile
2	72	Pyelonephritis	*Bact. coli*	2·25	0·5	3·0	200	50	Chloramphenicol	60	2·5	Cure	Sterile
3	66	Pyelonephritis, respiratory infection	*Bact. coli*	30	0·3	4·5	250	25	Chloramphenicol	100	15	Cure	Sterile
4	71	Renal calculus, pleural effusion	*Bact. coli*	30	1·0	1·5	0·5	3	Streptomycin	7	2	Cure	Sterile
5	25	Acute pyelonephritis	Enterococcus, staphylococcus	3·0 0·05	7·5 0·05	4·0	0·25	3·5	Penicillin, streptomycin	4 0·2	8	Cure	Sterile
6	66	Prostatic obstruction, hypertrophic cystitis	Enterococcus	0·1	0·2	2·5	0·2	1·0	Penicillin	0·12	0·25	Cure of infection; referred for surgical treatment	Sterile
7	64	Malabsorption syndrome, pneumoconiosis, cystitis	Coliforms, enterococcus, *Staph. aureus*	3 3	0·5 125	8 13	250 250	50 50	Streptomycin, chloramphenicol	4 750	55	Cure	Removal of enterococci and all 3 coliforms; *Staph. aureus* persisted
8	52	Acute cystitis	*Bact. coli*	30	2·5	8·5	200	25	Streptomycin	12	6	Cure	Sterile
9	50	Pyelonephritis, congestive cardiac failure, hemiplegia	Streptococcus	30	·25	6	0·04	1·25	Aureomycin	0·8	1	Symptomatic improvement	Sterile
10	59	Pyelonephritis, diabetes mellitus	Coliforms, enterococcus, actinomycete	3 3 0·012	5 25 0·02	8 5 1	7·5 0·25 1·25	2·5 1·25 50	Chloramphenicol	100	12	Symptomatic relief	Modified
11	56	Pyelonephritis, diverticulitis	*Bact. coli*	4	0·3	7·5	20	6	Streptomycin	22·5	3	Cure	Sterile
12	31	Pregnancy, pyelonephritis	*Bact. coli*	8	0·5	6	30	20	Streptomycin	3·13	2	Symptomatic cure	Sterile
13	25	Chronic pyelonephritis, renal failure	*Bact. coli*	30	25	3·0	200	25	Chloramphenicol, aureomycin	..	..	Urine clear, continuing renal failure	Sterile
14	30	Pyelonephritis	*Bact. coli*	3	0·6	1·0	0·25	1·25	Streptomycin	4	1·5	Cure	Sterile
15	62	Pyelonephritis	Enterococcus	0·05	6·0	1·0	0·2	0·125	Terramycin	2·4	2·5	Cure	Removal
16	25	Pregnancy, pyelonephritis	Enterococcus	1·5	17·5	12·0	0·5	2·0	Aureomycin	0·75	0·5	Cure	Sterile
17	64	Chronic pyelonephritis	*Bact. coli*	11	0·15	2·5	200	6	Streptomycin	16	1·5	Cure	Sterile

A, aureomycin; C, chloramphenicol; P, penicillin; S, streptomycin; T, terramycin.

in the duration of pain in spite of the greater effort (Hamilton and Wilson 1952) If the treatment were beneficial, a definite *improvement in the vitamin-E* group over the controls should have been revealed by this method of performing exercise-tolerance tests

Patients with intermittent claudication of all degrees of severity have been studied, though Boyd (1951) has stated that only the less seriously affected (his grades I and II) respond to vitamin E With the more severe exercise of walking over steps the pain, once developed, persists in all patients, and with this test none fall into Boyd's grade I Our grades II and III thus include several cases that would have fallen into lower groups if the tests had been performed by walking on the level There is *thus* no doubt that the series contained in both control and treated groups many of the milder cases reputed to respond to vitamin E

These observations and considerations indicate clearly that vitamin E is of no appreciable benefit to patients with intermittent claudication The previous favourable reports have not included details of any adequate control studies In investigations of intermittent claudication reliance has always to be placed on an end-point determined by the patient's assessment of his pain It has previously been demonstrated that this may be modified by any action involving therapeutic suggestion In these circumstances the trial of any drug must be most rigorously controlled Frequent exercise-tolerance tests are essential before, during, and after the period of treatment, preferably at fortnightly intervals Finally, the trial should be conducted on the "double blind" principle, and before any drug is claimed to be effective it must be shown to be so when both patient and observer are unaware of the nature of the treatment

SUMMARY

The effect of natural vitamin E in intermittent claudication was investigated in 41 patients, divided at random into control and treatment groups The controls received capsules containing arachis oil, and the treatment group received capsules identical in appearance but containing vitamin E The daily dose was 450 I U, the equivalent of 450 mg of tocopherol, and was continued for twelve weeks

Until the whole trial was completed the clinical observers (and the patients) were unaware of the treatment given in any particular case The assessment of the effect of therapy was based on the patient's opinion, the clinical examination, and the results of exercise tolerance tests

No appreciable difference was found between the response of the two groups

It is concluded that vitamin E is of no value in the treatment of intermittent claudication

This investigation was made at the suggestion of the Medical Research Council, who arranged the supplies of vitamin E We should like to thank Prof G W Pickering and Prof E J Wayne for helpful advice and criticism We are grateful to them and to the physicians and surgeons of St Mary's Hospital, London, and the Royal Infirmary, Sheffield, for access to patients under their care We should also like to thank Dr A M Adelstein for assistance in the statistical analysis

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AUTOMATIC FRACTIONAL ANALYSIS OF EXPIRED AIR AS A CLINICAL TEST

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Roelsen (1939) demonstrated that in emphysematous patients, more than in normal people, the composition of the expired air varied with the volume expired His findings have been confirmed by Marshall, Bates, and Christie (1952), who interpret them as evidence of poor spatial correlation between ventilation and perfusion in emphysematous lungs The possibility thus arises of using fractional analysis of expired air as a clinical test for emphysema However, because of the labour entailed by the analysis of multiple samples of gas, the methods of the previous workers are hardly suitable for routine clinical use

We describe here the use of a commercial analyser for continuous recording of the carbon dioxide content of respired air The abnormal pattern is easily recognised and, since repeated observations are conveniently made, the method lends itself to a study of the influence of relevant factors A somewhat similar procedure, using a specially constructed instrument, was described by Dubois et al (1952) who were, however, concerned with normal rather than pathological respiration

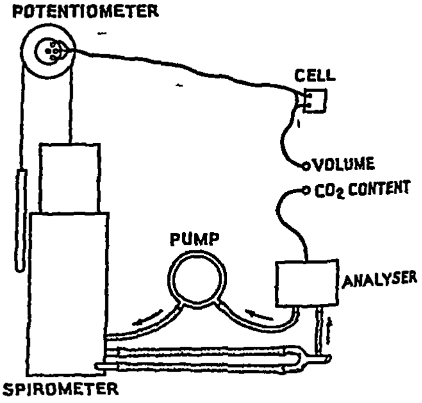

Fig 1—Arrangement of spirometer and carbon dioxide analyser

METHODS

The patient breathes into a Benedict spirometer fitted with a carbon dioxide absorber Attached to the wheel of the spirometer is a potentiometer which gives an electrical record of the amount of air in the bell at any moment A side tube to the mouthpiece is connected by a short length of rubber tubing to the analyser* Air is drawn, at a rate of about 30 ml per second, from the mouthpiece through the analyser by a small electric pump and is then returned to the spirometer bell In this way the respired gases are continuously sampled without disturbing the registration of their volume (fig 1)

The analyser's electrical system uses amplitude modulation of a 6 cycle-per sec carrier, rectified and smoothed to give a response time of several seconds As a much quicker response was required, the unrectified signal was taken out and rectified, without smoothing, by an external circuit With this arrangement the response to sudden changes of gas mixture is complete in about one third of a second

Sometimes, in addition, intrathoracic pressure and trunk expansion were recorded by the method of Dornhorst and Leathart (1952) and the concentration of the antibiotic in the serum and urine was estimated six hours after administration. The results (table IV) gave us a six-hourly percentage recovery-rate for each antibiotic. (The possible cumulative effect of repeated doses was ignored at this stage.) Since the in-vitro sensitivity was determined in each case by the same technique and with the same material, excretion-rates and expressions of sensitivity are correlated as far as possible. In calculating the dose of antibiotic for each patient we aimed at a *mean antibiotic level in the urine* equivalent to the level which inhibited the infecting organism in vitro. In view of the known variation in the excretion of antibiotics, confirmed by these experiments, and the known experimental error of our in-vitro tests (+25%), we decided to use a "dose-enhancing factor" to cover all variables, in the hope that this would ensure an antibiotic level in the urine at least as great as the in-vitro bactericidal concentration. The dose was calculated by multiplying the sensitivity expressed in µg. per ml. (table I) by the average six-hourly volume of urine passed during the period of observation; the product was multiplied by the reciprocal of the six-hourly excretion-rate of the antibiotic (table IV) to allow for the proportion of antibiotic not excreted in the urine. Finally this value was multiplied by our dose-enhancing factor.

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* Infra Red Development Co Ltd Type S C

The calculation of the dose of streptomycin in case 1 (table I) is given as an example. The sensitivity of the coliform organism in this case was 0·2 µg. per ml., the urinary output was 200 ml. in six hours, the excretion-rate of streptomycin was 20% (table IV), and the dose-enhancing factor adopted in this case was 5. The six-hourly dose of antibiotic was therefore

$$\left(0{\cdot}2 \times 200 \times \frac{100 \times 5}{20}\right) \mu\text{g.} = 1000\,\mu\text{g. or } 1\text{ mg.}$$

TABLE IV—6-HOURLY EXCRETION OF ANTIBIOTIC

Antibiotic	Recovery of oral dose (%)		
	Students	Patients	Mean
Penicillin	66–92	70–84	80
Streptomycin ..	18–24	16–25	20
Chloramphenicol ..	2·6–4·6	1·2–4·8	3·4
Aureomycin ..	22–33	20–25	27
Terramycin ..	4·4–10·5	1·5–5·3	7·5

Table V shows the dose-enhancing factor used, and the factor actually obtained experimentally, in each case. The latter value was about half the estimate in most cases; hence the factor might well be reduced to 2·5.

RESULTS

The immediate result of treatment in 14 of the 17 cases (table I) was sterilisation of the urine. Of the remaining 3 patients case 7 had a staphylococcus originally present in small numbers, which remained after the first course of aureomycin; case 10's infection was of multiple species and long standing, in the presence of gross bladder disease making modification of the infection all that could be hoped for; and case 15 became infected with proteus during therapy, after removal of the original infecting species.

Of the 14 patients in whom the infection was cleared by the first course of antibiotic 5 became infected after therapy had stopped (table II), 4 with new infecting species and 1 with the original pathogen. Of these 5 patients 4 were successfully treated with a subsequent course of antibiotic, and the 5th passed out of our hands before completing a second course. The over-all result was that the urine in 14 of the original cases became sterile and remained sterile during the follow-up period, which varied from one to six months.

We think it of profound significance that in no case did antibiotic resistance develop in any of the original species either during therapy or after therapy, even when this was prolonged, as in case 12. Some species causing new infections did, however, show resistance to the antibiotic first exhibited.

TABLE V—RATIO OF URINE CONCENTRATION TO IN-VITRO INHIBITORY CONCENTRATION

Case no.	Calculated maximum ratio (dose-enhancement factor)	Experimental ratio
	1st course of antibiotic	
1	5	1·6
2	5	2·5
3	5	3
4	5	2
5	5	2·5
6	5	2·5
7	5	4
8	5	2·5
9	5	5
10	3·5	2
11	15	10
12	5	4
13	..	..
14	5	2·5
15	5	15
16	1	1
17	15	10
	2nd course of antibiotic	
2	10	4
4	5	3
7	5	3·5
9	5	Not calculable
10	5	Not calculable
12	10	4
15	10	6

Subcultures of every organism isolated in this series of cases were kept for various investigations, such as fuller biological identification, at a later date. Those organisms isolated on the first bacteriological examination in each case, and several isolated during treatment, have all proved capable of developing resistance in vitro to the antibiotic to which they had been exposed in vivo. Further, resistance to the antibiotics exhibited did develop in 3 of the cases in this series when the usually accepted "standard" doses were given outside these trials (table VI).

In the cases infected with a single bacterial species the use of a single antibiotic was effective in sterilising the urine. This was accompanied by clinical improvement or cure (cases 1, 3, 6, 8, 11, 13, 14, 16, and 17).

The use of two or more antibiotics simultaneously is indicated and is effective in urinary infections where more than one species of micro-organism is present and in-vitro tests indicate that no single agent will cover all the pathogens. A combination is also indicated and is effective when two antibiotics are observed to act synergically in vitro against a single bacterial species, and the use of the combination allows appreciably smaller quantities of one or both antibiotics to be exhibited. In case 13 it was found possible to use a twentieth of the usual dose of chloramphenicol by combining it with a very small dose of aureomycin.

TABLE VI—EFFECT OF STANDARD DOSES OF ANTIBIOTICS IN RAISING THE RESISTANCE OF ORGANISMS IN URINE OF PATIENTS IN THIS SERIES

Case no.	Sensitivity before antibiotic (µg. per ml.)					Therapy	Sensitivity after antibiotic (µg. per ml.)				
	P	S	C	A	T		P	S	C	A	T
4	30	1	1·5	0·5	3	Aureomycin 15 g., chloramphenicol 3 g.	30	1·0	15	250	50
13	30	1·3	3	50	25	Streptomycin 13 g., followed by chloramphenicol 13 g.	30	1000	2·5 20	25	25
19	30	1·5	2·5	10	10	Streptomycin, sulphonamide	30	100	2·5	10	10

A, aureomycin; C, chloramphenicol; P, penicillin; S, streptomycin; T, terramycin.

about 0 5% during a forced expiration of 1–2 litres (fig 2). in ten patients, considered on other grounds to have emphysema, the climb ranged from 2 to 4%, although the greatest volume expired was usually curtailed (fig 3) The continuous records bring out further differences Normally, as was also found by Dubois et al (1952), the rate of climb is virtually independent of the rate of expiration , hence during a long expiration the record is straight and gently sloping Moreover, the carbon dioxide content of the expired air is almost independent of its volume, though of course inversely related to the size of preceding breaths In the emphysematous patient the rate of climb is directly related to the rate of expiration and, as this is usually decreasing, the record is curved, while, since the carbon dioxide content increases with the volume expired, a larger expiration carries the content well above that of adjoining breaths One can appreciate how the patient's expired air will, during moderate ventilation, be far from representative of his mean aveolar air, and how an abnormally large discrepancy between the gas tensions in the expired air and in the arterial blood can develop

Normal patterns were obtained from a patient, aged 73, with early hypertensive cardiac failure, and from two young patients with uncomplicated asthma The latter finding agrees with the conclusions of Bates (1952) that ventilation-perfusion relationships were as a rule normal in asthma

Patients with gross chest disease (bronchiectasis, &c) but without overt emphysema gave patterns of intermediate climb (1–1 5%) The significance of these must await further experience

The effect of a bronchodilator spray (1% isopropyl-adrenaline) was examined in all the patients Many claimed easing of breathing, and in two cases bronchodilatation was demonstrated by changes in the intrathoracic pressure-record *In no instance was improvement in the abnormal carbon dioxide pattern produced* indeed the climb was sometimes increased, probably because the patient emptied his chest further after the spray In three cases parenteral adrenaline was also without effect on the pattern

One patient with asthma and early emphysema was studied during and after a period of exacerbation of his asthma Although the intrathoracic pressure records showed a great difference in the state of the bronchioles, there was little change in his abnormal carbon dioxide pattern (fig 4)

DISCUSSION

The procedure described is easy to apply with little disturbance even to severely dyspnœic patients It yields evidence that is sometimes unequivocal, since patterns such as that shown in fig 3 must imply disturbed ventilation-perfusion relationships It is still uncertain if this type of disturbance occurs with significant frequency with normal expired air patterns Although this is in principle possible if all regions are emptied simultaneously, some sequential emptying is very likely on mechanical grounds Further experience is therefore needed before it can be asserted that the test can exclude as well as demonstrate the presence of emphysema

The stability of the pattern in face of spontaneous and induced changes in bronchiolar resistance is unexpected on current views of the mechanism of its production However, its comparative stability enhances confidence in its diagnostic significance

SUMMARY

A method of automatic registration of volume and fractional analysis of carbon dioxide content of expired air is described

The occurrence of an abnormal pattern of expired-air composition with emphysema is confirmed

The abnormal pattern persists with induced or spontaneous changes in bronchiolar constriction

The procedure forms a practical clinical test for the presence of one important form of pulmonary dysfunction

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AN OUTBREAK OF BENIGN MENINGO-ENCEPHALITIS

ISOLATION OF COXSACKIE VIRUS

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During the summer of 1951 an unusual number of patients with symptoms and signs of mild neurotropic illness were admitted to a Coventry hospital with a diagnosis of "meningitis" or of non-paralytic poliomyelitis The admission to hospital during the same period of a few patients with paralytic poliomyelitis, the high incidence of this infection in recent years, and the knowledge that not all cases develop paralysis had induced a bias in favour of the diagnosis of non paralytic poliomyelitis Later the high proportion of non paralytic patients raised doubts about the rôle of poliomyelitis virus, and virus investigations were undertaken

Wallgren (1925) described an apparently identical condition, which he called acute epidemic aseptic meningitis, considering it to be distinct from poliomyelitis because not all the reported outbreaks were associated with poliomyelitis As a result of investigations since then it is now recognised that this clinical syndrome may occur in other known and suspected virus infections, including benign lymphocytic choriomeningitis, mumps and glandular fever, and in leptospiral infection (MacCallum 1949) Epidemiological studies by Thomson (1952) showed that in 1950 the first year in which the notification of poliomyelitis required separate returns of paralytic and non-paralytic cases, the proportion of non-paralytic cases was remarkably constant (20–40%) By contrast in 1951, between the 24th and 37th weeks there was a sudden rise to over 50% in the notifications of non-paralytic forms of poliomyelitis, the increase being greatest in the Midlands

The rôle of the Coxsackie group of viruses in the causation of this syndrome has been uncertain Several workers (Melnick et al 1949, Silverthorne et al 1951) have reported the isolation of Coxsackie viruses from patients diagnosed as having non paralytic poliomyelitis, but Smadel (1951), on the basis of serological studies, concluded that the Coxsackie viruses seemed to be of little importance in his group of patients

We describe here the cases seen by us in 1951 and the results of virus investigations

EPIDEMIOLOGY

In 1950 and 1951 (in contrast to 1947–49) the number of cases diagnosed in this hospital as non paralytic poliomyelitis showed a marked preponderance over those with paralysis (*table* I)

Non-paralytic poliomyelitis was diagnosed in the presence of fever, meningeal or meningo encephalitic symptoms, and an abnormal cell count in the cerebrospinal fluid (C S F), with or without an increase of protein, all occurring in the absence of paralysis or of not previously been used in an investigation of this kind. A suspension of particles can be introduced into the cranial subarachnoid space of the newborn rat with remarkable ease and little or no danger to its life. This has made possible for the first time the daily injection of an indicator into the cranial subarachnoid space of a laboratory animal over a long period, and consequently the introduction of a large amount of indicator relative to the size of the subarachnoid space.

MATERIALS AND METHODS

Newborn rats were anæsthetised with a mixture of chloroform and ether. After indian ink, colloidal silver, and colloidal silver iodide had been tried, 'Dag' colloidal carbon (Acheson Colloids) was found to be the most satisfactory indicator. On the day after birth each young rat was given an injection of 0·1 ml. of the indicator into the cranial subarachnoid space. After the injection the rat was returned to its mother. The injection was repeated daily, and the rats were killed at intervals up to three weeks.

The study of the pathways followed by the injected particles was facilitated by the dissection of the spinal cord and membranes under a binocular microscope, and by the preparation of whole cleared specimens and of sections of the rats stained by a variation of the Bielschowsky method and with hæmatoxylin and Van Gieson's stains.

OBSERVATIONS

In the region of the spinal canal the colloidal carbon collected in three main situations: (1) in the prevertebral lymph-glands, (2) in cuffs round the emerging nerve-roots, and (3) in the perivascular spaces of the spinal cord.

Prevertebral Lymph-glands

The lymph-glands on the posterior wall of the thorax and abdomen were clearly visible as black masses laden with colloidal carbon (fig. 1). This appearance was visible macroscopically within half an hour of the subarachnoid injection. In the thorax of rats allowed to survive for a while fine vessels, outlined by colloidal carbon, were seen running from the region of the nerve-roots to the lymph-glands.

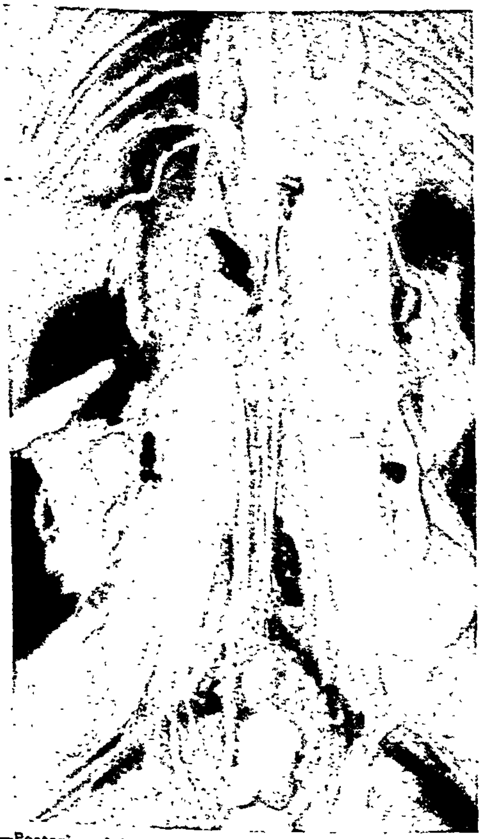

Fig. 1—Posterior abdominal wall of rat aged 21 days showing carbon particles in prevertebral lymph-glands.

Cuffs Round Nerve-roots

These were clearly outlined by large deposits of colloidal carbon (fig. 2). Both the cranial and spinal nerves presented these *Tuschenmanchetten* (Ivanow 1927). The subarachnoid cuffs were especially well filled round the nerve-roots contributing to the brachial and lumbosacral plexuses. Accumulations of carbon particles also outlined the vessels on the surface of the spinal cord.

Perivascular Spaces of Spinal Cord

These contained large amounts of carbon particles (fig. 3), especially in the perivascular spaces surrounding the vessels supplying the anterior horn.

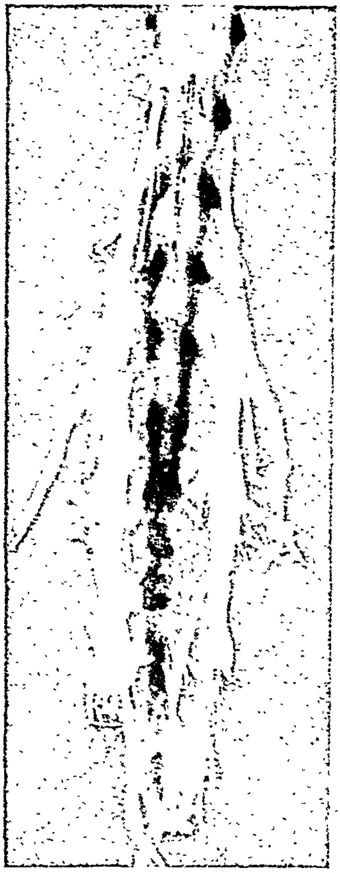

Fig. 2—Lower end of spinal cord of rat aged 21 days showing subarachnoid cul-de-sacs round anterior nerve-roots.

Summary

The path of particles introduced into the cranial subarachnoid space of the rat seems to be as follows. The particles pass rapidly down the subarachnoid space to the lower end of the spinal cord, being distributed freely through the C.S.F. They congregate in the subarachnoid cul-de-sacs surrounding the emerging nerve-roots and pass from these to the regional lymph-glands of the posterior abdominal wall. Later they tend to pass centripetally into the perivascular spaces of the spinal cord.

DISCUSSION

The experimental results briefly outlined above indicate that particles greater than the poliomyelitis virus can pass freely from the abdominal lymph-glands to the perivascular spaces of the spinal cord in intimate relation to the anterior-horn cells. Field and Brierley (1948b) have shown that the prevertebral glands are connected both with the lymphatics of the intestines and with the subarachnoid cul-de-sacs round the emerging nerve-roots. It therefore seems reasonable to infer that, in certain circumstances, ingested particles, especially if they are very small, might make their way from the intestines to the C.S.F. via the subarachnoid cul-de-sacs and thence to perivascular spaces of the spinal cord.

The nature and function of the perivascular spaces of the spinal cord are therefore matters of considerable importance. The flow of fluid in the perivascular spaces has been held by some workers to be from within outwards (Weed 1914, Schaltenbrand and Bailey 1927) and by others to be in the opposite direction (Mott 1910). The results obtained in the present investigation confirm

TABLE III—SUMMARY OF ABNORMAL C S F CELL COUNTS

Cells per c mm	No of cases	Polymorphs (P) predominant	Lymphocytes (L) predominant	P & L about equal
Up to 10	8	3	3	2
10–100	45	9	29	7
100–200	19	2	15	2
200–1000	16	5	10	1
1000–1500	2	1	1	0
Total	90	20	58	12

at the first lumbar puncture could be held responsible for these abnormalities That any significant quantity of air entered the theca during lumbar puncture appeared unlikely, and bloodstaining seldom accompanied the *taking of first specimens* Further, the mixture of normal and widely varying abnormal findings in the second specimens matched the findings in first specimens Therefore it was felt that the abnormalities on second testing were on the whole attributable to the illness

The 13 cases in which there were no abnormalities of the C S F, or were not present at the time of sampling, recall experience in poliomyelitis where normal C S F findings may occur even in the nervous phase (Paul 1951), indeed a wide range of C S F findings from normal to a lymphocytic or high polymorph pleocytosis—much as in this meningo-encephalitic series—has been reported (Martin and Elkington 1950)

The abnormal C S F cell-counts are summarised in table III

CASES IN WHICH VIRUS INVESTIGATIONS WERE MADE

CASE 1—Female, aged 15, admitted on seventh day of disease

C S F 10 polymorphs and 10 lymphocytes per c mm
Protein 40
Sugar 61 } mg per 100 ml
Chlorides 740

CASE 2—Male, aged 14, admitted on second day of disease

C S F 30 polymorphs, 34 lymphocytes and 160 red cells per c mm
Protein 60
Sugar 65 } mg per 100 ml
Chlorides 740

CASE 3—Female, aged 14, admitted on fifth day of disease

C S F *10 polymorphs and 30 lymphocytes per c mm*
Protein 40
Sugar 62 } mg per 100 ml
Chlorides 720

CASE 4—Male, aged 25, admitted on fourth day of disease

C S F (2 occasions) normal findings

CASE 5—*Female, aged 7,* admitted on fifth day of disease

C S F 250 polymorphs and 20 lymphocytes per c mm
Protein 40
Sugar 54 } mg per 100 ml
Chlorides 800

CASE 6—Male, aged 4, admitted on fourth day of disease; *a typical case of paralytic poliomyelitis*

CASE 7—Male, aged 12, admitted on third day of disease

C S F 60 polymorphs and 700 lymphocytes per c mm
Protein 40
Sugar 56 } *mg per 100 ml*
Chlorides 740

CASE 8—Male, aged 10, admitted with scarlet fever, four days after admission he had pyrexia 101°F, frontal headache, and neck rigidity

C S F 20 polymorphs and 70 lymphocytes per c mm
Protein 40
Sugar 50 } mg per 100 ml
Chlorides 720

This was possibly a mild case of postinfective encephalitis, not included in the totals of meningo encephalitis cases

VIRUS INVESTIGATIONS

Specimens of serum obtained in the acute and convalescent stages of the illness, and specimens of stools obtained on about the same day as the first samples of serum, were received from the 8 patients already described Details of the days, relative to the onset of illness, on which the sera were obtained are given in table IV The methods used in the preparation of stool suspensions for virus isolation and in making the neutralisation tests in suckling mice have been previously described (Kenyon et al 1952) The dilutions of serum refer to the initial dilutions before the addition of virus suspension

Isolation of Coxsackie Virus

A strain of one of the Coxsackie group of viruses was isolated from 1 (case 1) of the 8 stools investigated The stool had been obtained nine days after the onset of illness Histologically the newly isolated strain of virus caused lesions in the fat pads and brain of suckling mice and belonged to the B group of viruses By neutralisation tests it was found to be similar to the strain of virus isolated from the outbreak in a children's home in Coventry in 1951 (Kenyon et al 1952), but complete identification was not achieved

Isolation of Poliomyelitis Virus

As there was a possibility that the clinical condition resulted from infection by poliomyelitis virus, attempts at isolation were made by inoculation into rhesus *monkeys of individual or pooled stool suspensions* previously used in suckling mice Each monkey was given, under anæsthesia, 0 6 ml of suspension intracerebrally and 1 ml intranasally, the intranasal inoculation being repeated next day Daily temperature records were kept for three weeks after inoculation

TABLE IV—HUMAN SERUM NEUTRALISATION TESTS

Case no	Age (yr)	*Days* after onset of illness	Serum dilutions					Saline control
			1/1	1/10	1/50	1/250	1/1250	
1	15	9	(1) 0/6	5/5	—	—	—	10/10
		23	0/7	0/5	1/10	8/8	—	19/23
2	14	3	0/4	2/5	7/8	—	—	12/12
		21	0/5	1/4	9/12	—	—	13/14
3	14	7	1/7	0/6	7/7	—	—	12/12
		20	2/7	0/7	0/6	3/6	7/7	17/18
4	25	3	6/6	—	—	—	—	6/6
		21	7/7	—	—	—	—	6/6
5	7	1	1/7	2/5	6/7	—	—	16/16
		19	0/7	3/5	1/7	0/10	3/4	20/21
6	4	2	3/13	5/5	—	—	—	8/12
		18	4/13	5/5	—	—	—	
7	12	3	4/12	0/7	7/7	—	—	17/17
		19	0/12	2/6	2/7	2/10	4/4	23/24
8	10	5	5/12	7/7	—	—	—	12/12
		21	3/11	0/6	6/6	—	—	8/8

(1) This indicates the number of mice which died as a result of *inoculation over the number of mice inoculated* Surviving mice were those alive when 3–4 weeks old
The figures given represent accumulated inoculations

No 1 monkey, which received a pool of equal volumes of stool suspensions *from cases 1 and 2, had a pyrexial* reaction on the sixth and seventh days after inoculation, without the development of paralysis Histological examination of the spinal cord removed twenty eight days after inoculation showed *no* evidence of poliomyelitis

No 2 monkey, which received stool suspensions from case 6, had a pyrexial reaction on the eighth and ninth days *after* inoculation, with paralysis on the tenth day, when the spinal cord was removed Histological examination confirmed the diagnosis of poliomyelitis

No 3 monkey, which *received a pool* of equal volumes of *stool suspensions* from cases 3, 5, and 7, showed no pyrexial reaction or evidence of infection Histological examination *of the spinal cord* removed twenty one days after inoculation showed no evidence of poliomyelitis

No 4 monkey, which received *stool* suspensions from case 6 showed no pyrexial reaction or evidence of infection No *histological* examination was *made*

The stool suspension from case 4 was not investigated in monkeys

The *stool suspension* from *case* 6 was inoculated intracerebrally into adult mice No paralysis was observed after two passages, each of *thirty days' duration* worthy of trial in the treatment of experimentally induced poliomyelitis.

SUMMARY

A new experimental technique has been used for studying the fate of particles injected into the subarachnoid space of newborn rats.

The implications which the results of these experiments have on the pathology and therapy of poliomyelitis are discussed.

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THE TREATMENT OF INTERMITTENT CLAUDICATION WITH VITAMIN E

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THE suggestion that administration of vitamin E is beneficial in peripheral arterial disease was originally made by Shute et al. (1948). Its use has been advised in the treatment both of angina pectoris and of intermittent claudication. In angina the earlier favourable claims (Vogelsang and Shute 1946, Vogelsang et al. 1947) were not confirmed by the more carefully controlled studies of later observers (Makinson et al. 1948, Donegan et al. 1949, Ravin and Katz 1949). On the other hand the administration of synthetic vitamin E in cases of intermittent claudication of moderate severity has been strongly advocated by Boyd et al. (1949), Ratcliffe (1949), and Boyd (1951), and as a result this drug is now widely prescribed.

If vitamin E acts by expediting the recanalisation of occluded arteries or the development of collateral arteries in cases of intermittent claudication, it is difficult to understand why it should not be equally effective in angina pectoris when this is due to occlusive coronary arterial disease. In a small series of cases of intermittent claudication Hamilton and Wilson (1952) found that synthetic vitamin E had no effect on exercise tolerance, which was measured at short intervals throughout the period of treatment.

In view of this conflict of evidence the action of vitamin E in intermittent claudication has been further investigated in a larger series of cases. On this occasion the natural product, as recommended by Shute et al. (1948), rather than the synthetic preparation, has been used.

TABLE I—SIMILARITY OF VITAMIN-E AND CONTROL GROUPS

(Table shows mean values with their standard errors for each group)

—	Vitamin E (20 cases). Mean ± S.E.	Control (21 cases). Mean ± S.E.
Age (years)	54·8 ± 1·8	55·9 ± 1·8
Duration of illness (years) ..	3·6 ± 0·5	3·3 ± 0·5
Exercise-tolerance tests:		
Average number of circuits ..	19·0 ± 1·6	18·1 ± 1·6
Average duration of pain after exercise (sec.)	42·0 ± 5·9	55·7 ± 5·8
Average time per circuit (sec.)	5·6 ± 0·2	6·5 ± 0·2

METHODS

41 patients have been studied. All had typical intermittent claudication of the calf muscles due to occlusive arterial disease. In only 1 patient was the arterial disease the result of thrombo-angiitis obliterans. In the remaining 40 cases the arterial lesion was assumed to be atheromatous. None of the patients had diabetes. Exercise-tolerance tests were made, so far as possible, at fortnightly intervals by walking over steps (Hamilton and Wilson 1952). The patient halted as soon as the pain in the legs developed. The number of circuits over the steps and the duration of the exercise were recorded, and the rate of walking was calculated. The duration of the pain after stopping was also measured. A full clinical examination was made before and after the course of treatment, and the patient's opinion about any change in his capacity to walk was ascertained.

Natural vitamin E was dispensed in gelatin-coated capsules, the specification for their preparation being that " the d. alpha tocopheryl acetate shall be prepared from vegetable oils and each capsule shall contain Type VI concentrate, equivalent to 75 mgm. d.l. tocopheryl acetate." Similar capsules were filled with arachis oil, and these control preparations were identical in size and colour with the vitamin-E capsules so that they could not be distinguished in any respect by either the investigators or the patients. During the twelve-week period of treatment two capsules were taken thrice daily. The dose of vitamin E was accordingly 450 I.U. per day.

Numbered sets of bottles containing either vitamin E or arachis oil were prepared in the Statistical Research Unit of the Medical Research Council; the order of administration of the two treatments was based upon a list randomly constructed in the unit and held there. After a preliminary period of observation of at least a month, the patient was allotted a number and took the similarly numbered capsules continuously for twelve weeks. The investigations were continued for a further month after the period of treatment. The nature of the treatment in individual cases was not revealed to the investigators until after the whole trial was completed.

COMPARABILITY OF GROUPS BEFORE TREATMENT

As the treatment allocated to each patient was determined randomly, a careful comparison of those receiving vitamin E and those receiving arachis oil is essential. This has been based on the observations made before treatment, and the results are shown in table I. The mean age and the mean duration of the illness are similar in both groups. For each patient the number of circuits walked before the onset of pain was recorded at each visit before treatment, and from these observations the

TABLE II—SIMILARITY OF VITAMIN-E AND CONTROL GROUPS BY BOYD CLASSIFICATIONS

Grade	Vitamin E	Control	Total
II	11	9	20
III	9	12	21
Total ..	20	21	41

have caused a proportion of the benign meningo-encephalitic illnesses described

We are indebted to Dr F O MacCallum for advice and helpful criticism, and Dr A Beck, Lieut Colonel H J Bensted, Dr C L Greenbury, Dr R E Jones, and Dr W McC Wilson for help in various stages of the investigations

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AN UNUSUAL TYPE OF HERNIA

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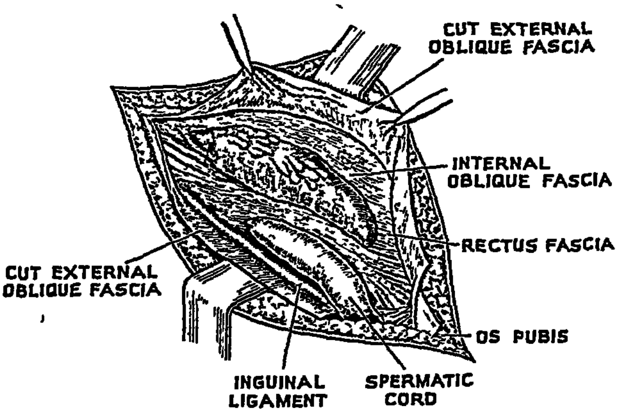
THE hernia described below was, to me at least, unique, for in a long experience of operative surgery I have seen nothing similar Clinically it so much resembled the common type of indirect inguinal hernia that the routine procedure was adopted, and the exact relationships of the sac were not recognised until the area had been fully dissected

A man, aged 42, gave a six months' history of a swelling in his right groin This was said to be getting slightly larger and causing aching or dragging pain He had had no previous operations

On examination he was well built and muscular In his right inguinal canal was a well defined fusiform swelling which transmitted an expansile impulse on coughing and extended as far as the external ring It was easily reducible



The hernia fully exposed at operation

An indirect inguinal hernia was diagnosed and the patient was in due course admitted to hospital for operation

Operation —When the inguinal canal was opened through a routine incision over it, the spermatic cord was seen to be normal No sac was connected with the cord The external ring was normal, the cremaster muscle was well developed, and the testis was normal There was no sign of a direct hernia This was puzzling in view of the clinical signs, which had been so clear at the first examination and had been confirmed by the surgical registrar when the patient was admitted The external oblique muscle was therefore incised a little further, and retraction of the upper flap of the aponeurosis exposed a long thin process of fat lying above the cord, parallel with it and about $^1/_2$ in from it (see figure) To trace this pad of fat back to its origin, the incision in the external oblique was extended another inch laterally, whereupon it was evident the process was issuing through a gap in the internal oblique muscle at a point about $1^1/_4$ in lateral to and $^3/_4$ in above, the internal ring The fatty process was then dissected and was found to contain a well established peritoneal sac about 3 in long and $^1/_2$ in in diameter at its widest point The opening in the internal oblique muscle was oval, about $^1/_2 \times ^1/_4$ in , with fibrosed and thickened edges The sac contained omentum Repair was effected by removal of the sac, freshening the edges of the gap in the internal oblique muscle, and suturing with floss silk Further reinforcement was obtained by overlapping the aponeurosis of the external oblique muscle The result of the repair has so far (twenty months after operation) been good

It is a little difficult to determine why such a hernia should appear, unless it were due to a congenital defect in the internal oblique muscle , but, if this were so it is also difficult to understand why no hernia should have developed until after more than forty years of life There was no history of sudden strain or violence which might have torn fibres of the internal oblique muscle The only other suggestion I offer is that it was a traction hernia caused by a pad of properitoneal fat which insinuated itself between the muscle-fibres and pulled a process of peritoneum after it

This hernia must really be classed as an interstitial hernia (Noonan 1950), but it is surely unusual for an interstitial hernia to present in the inguinal canal in such a way as to simulate an indirect inguinal hernia The diagnosis of interstitial hernia is always difficult, particularly when it is immediately properitoneal—i e , deep to the transversalis muscle—and, in fact, strangulation takes place in many cases before the diagnosis is evident

It would be interesting to know whether any similar case has been observed

REFERENCE

Noonan, T J (1950) *Lancet*, ii 849

New Inventions

A PROTECTIVE HOOD FOR LABORATORY BURNERS

THIS device is designed to prevent the scattering of infective material from wire loops when these are flamed It consists of three detachable parts, and can be made in a moderately well-equipped workshop

It was found, during experiments with different designs, that the main problem was to allow adequate ventilation without permitting the escape of infective material If insufficient air were admitted, the enclosed bunsen flame would lose its normal size and shape, and, unless the alternative exit were large enough, hot air would escape through the slit cut for insertion of the loop, burning the operator's hand Both these difficulties were overcome by baffled ventilation holes in the top and base as illustrated

The base, which is supported by a tripod, consists of a rimmed metal disc with a ring of small holes at the periphery To prevent any escape through them of infective material, they are guarded above by a flat baffle ring A central hole admits the burner and fits

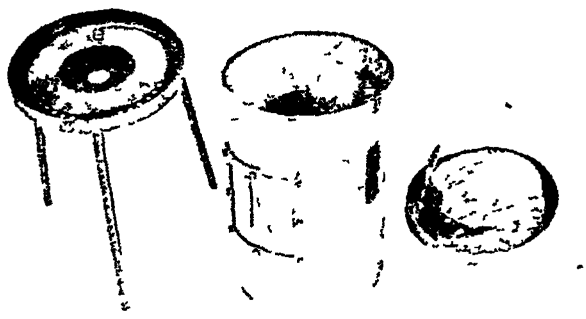


Fig 1

in their duration of pain—i.e., comparing the pre-treatment and treatment periods. Thus, for each extra second in the original time that a patient took per circuit there was, on the average, a 6·7% increase in the duration of pain observed during treatment (the regression coefficient of 6·7 has a S.E. of 3·2 and is therefore significant at the 0·05 level). It has already been shown (table I) that the vitamin-E group has a mean time per circuit of 5·6 seconds, compared with 6·5 seconds for the controls. This difference, which to two decimal places is 0·85 seconds, would alone be expected to cause a subsequent difference between the two groups in the percentage change in duration of pain—i.e., (0·85) (6·7) = 5·7%. The observed difference of 18·0% in table VII should therefore be reduced by 5·7 to give the correct value, 12·3%. This corrected value still favours the vitamin-E group, but it has a standard error of 7·2% and is thus not technically significant, although it is sufficiently nearly so to require further consideration.

These observed changes in the duration of pain during the course of treatment were also analysed in relation to the treatment schedule. Table VII shows that the relative improvement of the vitamin-E group, compared with the deterioration of the control group, was slightly more distinct in the first two months' treatment than later. The corrected difference of 15·5% just reaches significance at the 0·05 level. In the third month of treatment and in the post-treatment period the differences, on the other hand, are not significant. In both groups in the post-treatment period the changes from the pre-treatment level are quite small and unimpressive.

The rather small numbers of patients available in this trial may have led to moderate effects of vitamin-E treatment not being detected, owing to the considerable variability between patients. It is therefore of some interest to record the probable upper and lower limits to the effects of vitamin-E treatment as revealed by these controlled observations. These points are "95% confidence limits," between which the true mean effect is likely to lie. They are obtained by taking the observed differences in means given in tables IV–VII, and adding to, or subtracting from, them "t" times the standard error. (The factor t is the 0·05 level of the t-distribution on N-2 degrees of freedom, where N is the total number of patients used in the comparison. For a comparison using all the patients, as in table IV, N = 41 and t = 2·02.) The odds are 19 to 1 that the two limits include the true mean value for the type of patient used in this trial. The limits are given in table VIII. Those for increases in exercise tolerance probably exaggerate the possible beneficial effect of vitamin E, owing to the original disparity of the groups. In the calculation of limits for the percentage change in duration of pain the corrected value of table VII has been used.

TABLE VII—CHANGE IN AVERAGE DURATION OF PAIN DURING AND AFTER TREATMENT AS PERCENTAGE OF PRE-TREATMENT AVERAGE

Period	No. of cases	Mean ± standard error	After correction for time/circuit	Regression of percentage increase in pain on time/circuit
0–12 weeks' treatment	20	Vit. E −9·7 ±5·0		
	21	Control +8·3 ±4·9		
		Difference −18·0 ±7·0	−12·3 ±7·2	6·7 ±3·1
0–8 weeks' treatment	20	Vit. E −10·2 ±5·4		
	21	Control +11·7 ±5·3		
		Difference −21·9 ±7·5	−15·5 ±7·7	7·5 ±3·3
8–12 weeks' treatment	20	Vit. E. −10·0 ±5·0		
	19	Control +4·9 ±5·1		
		Difference −14·9 ±7·1	−11·4 ±7·6	4·4 ±3·5
Post-treatment period	19	Vit. E −8·5 ±6·5		
	20	Control +5·2 ±6·3		
		Difference −13·7 ±9·1	−12·0 ±9·9	1·9 ±4·3

TABLE VIII—95% CONFIDENCE LIMITS FOR MEAN EFFECTS OF VITAMIN E IN COMPARISON WITH CONTROLS

Comparison	Limits
Table IV—Average increase in circuits during treatment	− 1·7 to + 3·1 circuits
Table V—Average increase in circuits during last month of treatment ..	− 2·2 to + 3·4 circuits
Table VI—Average increase in circuits after treatment	− 3·4 to + 2·3 circuits
Table VII—Average change in duration of pain, as percentage of pre-treatment level	− 26·8% to + 2·3%

DISCUSSION

In determining the results of treatment reliance has been placed on the statements of the patients, the clinical examination of the lower limbs, and the performance of exercise-tolerance tests. Neither of the first two indicated that vitamin E was in any way superior to arachis oil. In the exercise-tolerance tests treatment produced no marked or technically significant difference between the two groups as regards the distance that could be walked before the onset of pain. The only difference of any substance found between the two groups was in the duration of pain after exercise. During the whole period of treatment this increased by + 8·3%, on the average, in the controls and decreased by − 9·7% in the vitamin-E group. The difference between the two figures was shown to be significant. The statistical analysis of the results also showed that the duration of pain after exercise tended to become significantly greater in the slow walkers in both treatment groups as the trial proceeded. These slow walkers were initially rather more numerous in the control group; and, if a correction is made for this discrepancy, the difference between the two groups is no longer technically significant, though it continues to favour slightly the patients on vitamin E.

From the clinical point of view, however, too much importance should not be attached to these results, because the assessment of the duration of a pain that gradually fades away is notoriously difficult, and there was considerable variability in these measurements even in the same patient. It will be noted that the changes from the pre-treatment values are small in each of the two groups, and they are of significance only because they are in opposite directions. A more detailed analysis of the results showed that the difference between the two groups was greatest during the first two months' treatment but was non-significant during the third month and the period immediately after treatment. This is the reverse of what might be expected if the changes were the result of vitamin-E therapy.

The results of this investigation have shown that the beneficial effect of vitamin E in the treatment of these cases of intermittent claudication was not appreciably greater than that of arachis oil, and the earlier favourable reports of Boyd et al. (1949) have not been confirmed. Our failure to demonstrate improvement could be due (1) to the methods of assessement being insufficiently exact, with the result that a real improvement was overlooked, or (2) to the wrong type of patient being treated. In our exercise-tolerance tests the patients walked over steps, whereas in Boyd's series they walked on the level, either along hospital corridors or on a moving platform. The two methods, however, are fundamentally similar because they both measure the amount of exercise required to produce pain. A true improvement is reflected in an increase in the amount of exercise that can be taken before the onset of pain and in a decrease

Alcohol, Culture, and Society

CLARENCE H PATRICK, professor of sociology, Wake Forest College, North Carolina Durham, N C Duke University Press London Cambridge University Press 1952 Pp 176 22*s* 6*d*

THE sociologist is concerned with human culture in so far as it provides the means by which man, even in the most primitive societies, creates around himself a secondary world where he can look for the satisfaction of his biological needs even the Bushman is not wholly dependent on his natural environment, as the animals are From prehistoric times, alcohol has supplied a human cultural need, and it is with the use of alcohol, the underlying purposes of this, and the effects on both the individual and society, that Professor Patrick is dealing in this compact study

From time immemorial alcohol has been a problem potent for good and ill Greek and early Roman moralists disapproved of its use, but the Indo Aryan tribes of India about 1000 B C believed that their god, Indra, was only capable of heroic deeds when intoxicated England in the 17th and 18th centuries was notoriously intemperate, landlords of gin houses used to hang signs out offering the customer enough gin to get dead drunk for twopence, and free straw to lie on The Pilgrim Fathers were by no means teetotal, and from the 18th century onwards a taste for distilled liquors (obtainable from the West Indies as rum) rather than for wines and beer (obtainable only from the Old World) was making itself felt Present day drinking habits in the United States vary according to social class, in the working class and the upper class men and women drink together, whereas in the middle classes this is frowned upon

The great influence of social *mores* on drinking patterns is discussed, and also the attempts being made by the U S liquor trade to influence these by skilful advertising campaigns

Störungen der Fettresorption im frühen Säuglingsalter

FRITZ HAUSER, Privat Dozent in the University of Basle Basle and New York S Karger 1953 Pp 108 Sw fr 14

THIS treatise from the pædiatric clinic of Basle University is obviously strongly influenced by the teachings of Verzár After a discussion of the theories of fat absorption the author comes down heavily on the side of complete hydrolysis of triglycerides with subsequent resynthesis in the intestinal mucosal cell Frazer's opposing theory of partial hydrolysis and of predominantly particulate absorption of unsplit fat is summarily rejected It is a pity that Dr Hauser gives us no references to what he describes as Verzár's recent unanswerable counterarguments, and that he has followed Frazer's publications only up to 1946 an acquaintance with the more recent work would have prevented him from misinterpreting Frazer's ideas on the fate of long-chain fatty acids The main part of the text deals with disturbances of fat absorption due to disease, but in many of the 21 cases described fat absorption was not studied at all, and their inclusion is puzzling The last chapter contains some interesting points on the management of disturbed fat absorption in premature infants

Wounds of the Extremities in Military Surgery

OSCAR P HAMPTON, JUN, M D, F A C S, instructor in clinical orthopedic surgery, Washington University London Henry Kimpton 1951 Pp 434 70*s*

DR Hampton's distinguished service with the American Army in the Mediterranean theatre of war forms the basis of his beautifully produced book His first four chapters deal with such things as first-aid, the initial surgery of wounds in forward areas, and reparative surgery at base hospitals He then discusses special injuries of bones, vessels, nerves, and joints, as well as amputations, burns, and regional injuries There is a certain amount of overlapping, but the arrangement makes for easy reference

With the main themes of Dr Hampton's teaching his colleagues in the British Army would agree, but there are some points on which they may differ Having admitted the advantages of the open flap method for amputations in the forward area, and made a strong case for it, he advocates guillotine amputations He advises the hip spica for the transport of fractured femurs—though of all the awkward, bedsore making pieces of apparatus for loading into and out of ambulances, the hip spica takes first prize Fortunately he gives a full page of diagrams showing the application of the Tobruk splint, which, though it may not hold the fragments quite still, permits of traction and of comparative comfort during transport, and does not necessitate the patient being turned sideways to get him through a door The three pages on burns seem unduly brief for injuries which often present an exceedingly difficult problem

Wounds of the limbs exceed in number all other wounds, and this lavishly illustrated book would be a good companion for any surgeon who had to return to war surgery Moreover, the principles of traumatic surgery do not vary whether wounds are inflicted by design or accident, and many an industrial or road accident would be better handled if all surgeons had read this book

The Measurement of Hearing

IRA J HIRSH, Central Institute for the Deaf and Washington University, St Louis, Missouri New York and London McGraw Hill 1952 Pp 364 51*s*

THIS book is one of a large series of publications on psychological problems, and has been written for such diverse professional persons as the experimental psychologist, the clinical otologist, acoustic and communication engineers, and the physicist interested in sound The lucid explanations of the principles of sound production and electro-acoustic equipment are helpful for the understanding of the various clinical procedures adopted in most clinics and laboratories today Similes are used well to simplify technical points, and the meaning of such terms as difference limen, discrimination loss, recruitment, and social adequacy index is made clear The psychological aspects are so practical and physiologically rational that they will appeal to both otologists and laymen Mention might have been made, however, of such subjects as tone deafness, the appreciation of music, and the relative intelligibility of different languages to people with different degrees of deafness The book should certainly be read by all those interested in acoustics Many otologists would benefit from the clear and logical explanation of the science of audiology

Rheumatic Diseases

Diagnosis and Treatment EUGENE F TRAUT, M D, F A C P, associate (Rush) clinical professor of medicine University of Illinois London Henry Kimpton 1952 Pp 942 150*s*

DR Traut says that in the United States 7½ million persons have "rheumatism," and 30 million have a deep personal concern in joint disease of these, 1½ million have degenerative joint disease He has accordingly attempted to assemble material on this subject which is accepted as factual by current authorities He has tried "not to display unjustified enthusiasm and devote too much space to discussions of the exciting new endocrinologic therapy of rheumatic diseases", and the rather disappointing result is that only half a dozen pages in this very large book are devoted to the actual treatment of rheumatoid arthritis with cortisone and A C T H He advocates the use of a stock vaccine made from a greening streptococcus of low virulence, which he regards as an indispensable part of his armamentarium Of gold therapy he says "it is questionable whether chrysotherapy for arthritis deserves extensive consideration"—an opinion that would not be generally accepted on this side of the Atlantic The chapter on physical medicine follows current practice, and includes a number of simple and valuable exercises for the daily use of the patient, and the interesting chapter on the ocular manifestations of rheumatic disease is a welcome innovation In the chapter on fibrositis Dr Traut pays tribute to the pioneer contributions of the British, though the only British reference given is to a book published in 1919 Indeed, there are very few references to papers of non-American origin, which is a considerable weakness This well-produced but expensive volume gives an interesting review of the beliefs of the author and his colleagues in Chicago, but does not present so wide or impartial a view of rheumatic diseases as do "Comroe" and other well-established American books on rheumatology

RESULTS

In all cases the carbon dioxide content of expired air rose abruptly from zero after clearance of the anatomical dead space. In what follows "expired air" will refer to that part of the breath after this abrupt rise has taken place.

Our results confirm those of the previous workers. In six normal persons the carbon dioxide content climbed

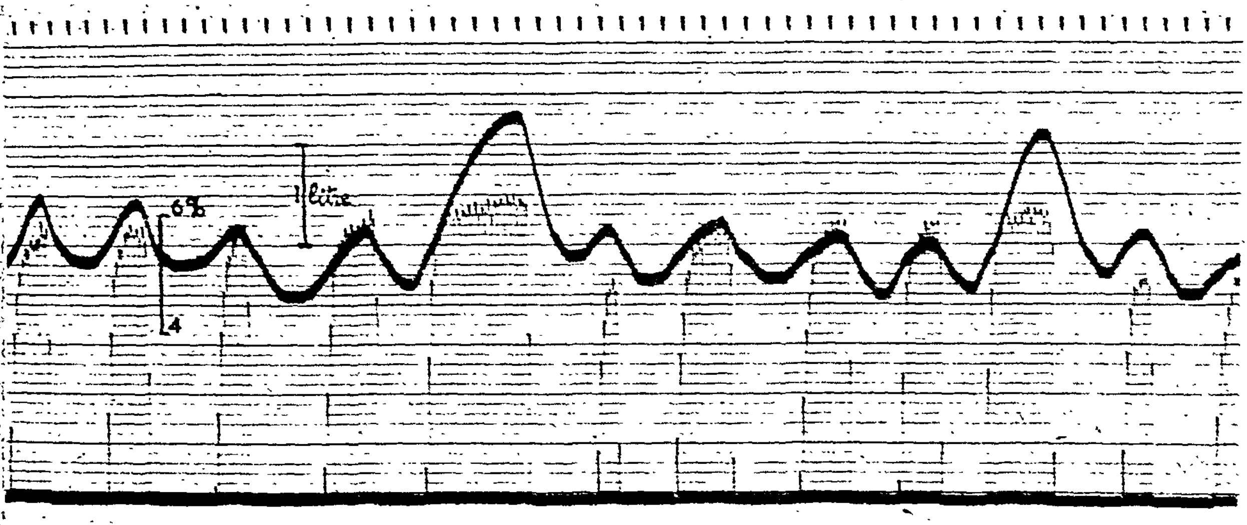


Fig. 2—Normal spirometric and carbon dioxide record: a large expiration does not entail an increase in carbon dioxide content of expired air.

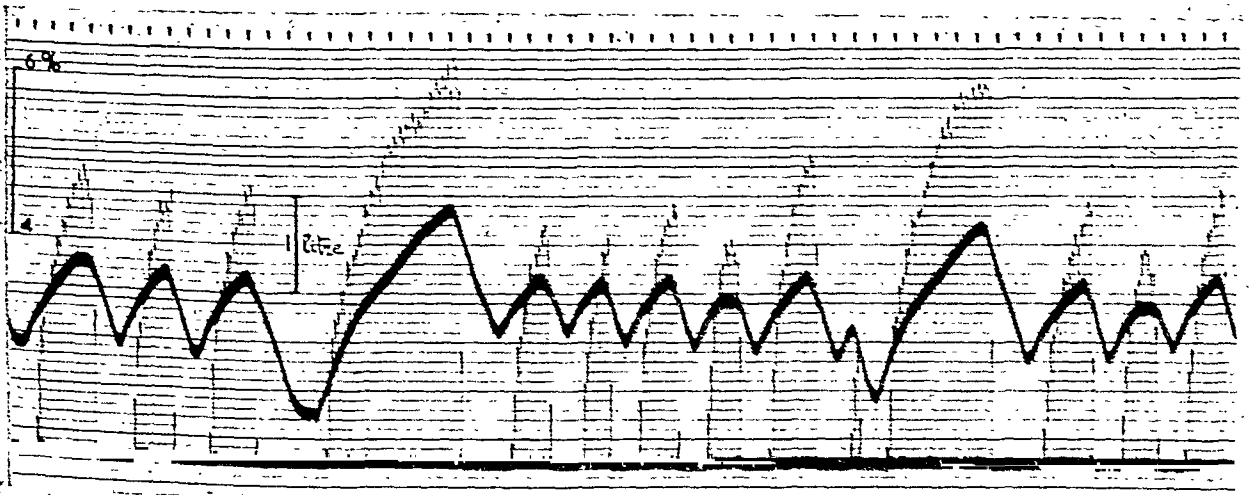
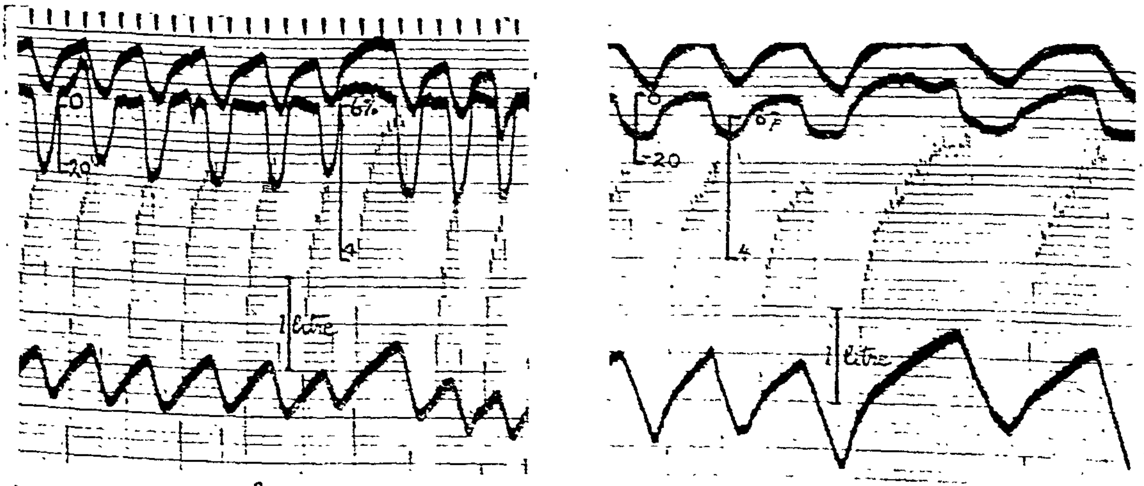


Fig. 3—Spirometric and carbon dioxide record in emphysema: carbon dioxide level varies with volume of expired air.



a b

Fig. 4—Records (from above down) trunk movement, intrathoracic pressure (mm. Hg), carbon dioxide content, and spirometer: *a*, during severe asthma (note large intrathoracic pressure swing); *b*, after spontaneous improvement. (Carbon dioxide record is still abnormal.)

of all the periods spent by the trained staff in teaching, and was distributed, over the week, among all the students working in the ward—who might number anything from 8 to 2. Some sisters said that they made the giving and receiving of reports an occasion for explaining new cases to student nurses, but several said they did not explain new cases to students: they thought the information would probably “ filter through.”

The students receiving this diminutive instruction were doing 74% of all the nursing done in the wards. Nor were they engaged entirely on what the team agreed to call “ basic ” nursing procedures, meaning “ those nursing duties having their origin in the physical needs of the patient ” (they define these further in a list). Students also took some share in “ technical ” nursing, classed here as the care given as a result of the disease from which the patient is suffering; this includes such things as helping the medical staff with technical procedures, giving medicines, taking pulses and temperatures, doing dressings, giving injections, preparing patients for operations, checking drugs, stockmaking, testing urines, and looking after patients returned from operation. In one ward student nurses were responsible for taking blood-pressures. It is noteworthy that 72% of the total time spent on dressings was contributed by students. Students also have to take responsibility when the sister and staff nurse are both out of the ward together—as may happen when one of these seniors is on holiday. On night duty a student nurse is regularly left alone in charge of a ward while her companion is taking a meal. There can be little opportunity, the report says, for trained staff to supervise the work done by student nurses (for instance, in the dressing of wounds) and virtually none for giving practical instruction. No doubt the student is taught the theory of wound dressing by the sister tutor, but on the job she has to pick up her practical technique from her seniors in training. This recalls the monitoring system of the old national schools, where a child who had got his letters taught them to a group of smaller ones. It is a useful makeshift when teachers are scarce, but it cannot be classed as efficient training.

The student nurse is so little of a student and so much of a nurse for the same reason that the ward-sister is so little of a nurse and so much of a clerk. Besides having to attend any doctor at any time, and for whatever purpose, he may choose to visit the ward, the ward-sister also has to do a great amount of form-filling, report-writing, telephoning, and stock counting—all important duties from the administrative standpoint, but emphatically not nursing. In short, as the report says, the end-result of nurse training in the hospital service is not nursing but administration. Only 16% of the time spent on nursing in these wards was contributed by State-registered nurses, and for a considerable part of the day, when the staff nurse was off duty, the sister was usually the only fully trained nurse on the ward, and vice versa.

Matters would be easier to arrange, no doubt, but for the inflexible obstacle of the patient and his needs. He must be wakened, washed, eased, and fed—all, by ancient custom, before the medical staff appear on the ward. The peak period of work in the morning thus occasions an unnaturally early start to the patient's day. This, the team found, begins on an average at 5 A.M. and ends at 10 P.M., and there is little chance for him to sleep undisturbed in between. The amount of work expected of the night nurse, in preparation for the morning peak, is beyond her capacity if the patient is to be wakened at a reasonable hour. The physical needs of patients, the report points out, cannot be altered; so any attempt to eliminate peak periods of work for nurses must depend on the cooperation of the medical staff and other specialist services. The team do not offer any evidence that this has been forthcoming so far, though they politely abstain from criticism.

Their suggestions for a better way of doing things turn on the proposal that nursing should be done by trained nurses, and not merely supervised by them. Basic nursing, they say—and we warmly agree with them—should not be delegated to an auxiliary grade, nor should nursing be thought of predominantly as a matter of exercising special technical skills. Each trained nurse, they suggest, should be responsible for a specified group of patients, “ a nursing unit,” and should have the help of nursing auxiliaries who may be either student nurses, assistant nurses, pupil assistant nurses, or orderlies. Trained nursing skill would thus be conserved for its “ proper ” task, the whole nursing care of the patient. This could be done, they believe, by reallocating many non-bedside tasks, by providing adequate nursing equipment and labour-saving devices, by revising working hours of staff to provide enough hands at peak periods and by having more reliefs. It will be possible only if the status of trained staff in hospitals is made attractive enough to persuade nurses to remain at work there. The ward-sister should, as now, be chief administrator, with complete responsibility for the care of her patients; but she should have as her right-hand woman a personal secretary, like other busy and responsible people. She would thus have time to teach her students, and they would have time to pause and learn. This is one of the experiments which has long deserved a trial, and there are others—such as a shortened course for students—with which it might well be combined. Such experiments have been advocated, on general principles, for a long time. But this report gives the backing of fact which those advocating such experiments have long needed. It does not bring to light much that critics of nursing training have not known or guessed; but their generalisations can no longer be set aside as mere opinion. Here are facts.

Acute Respiratory Insufficiency

Of the many patients now suffering from a seasonal exacerbation of respiratory disease a fair number present a clinical picture familiar yet little discussed and without an agreed name. Around London this winter their number was much increased by the severe fogs. Such a patient is commonly a man in late middle age who has had a cough for some years and has become moderately short-winded. Quite suddenly his condition becomes very much worse, with urgent dyspnœa and severe general upset. His face has a purplish flush; his eyes are bloodshot; his lips and tongue are cyanosed; his hands are warm; and his pulse is rapid and full. The jugular venous pressure may be raised, and if the condition has persisted for

TABLE I—ADMISSIONS OF PARALYTIC AND NON-PARALYTIC CASES 1947–1951

Year	Paralytic cases	Non-paralytic cases	Percentage non-paralytic
1947	21	16	43·2
1948	5	5	50·0
1949	22	14	38·8
1950	27	79	74·5
1951	14	90	86·5

evidence indicating a different ætiology. 90 such cases were admitted in 1951, and 22 clinically similar cases (table II) had normal C.S.F. cell-counts, although 9 of these gave a C.S.F. protein content of 60–80 mg. per 100 ml. In all, 112 patients were admitted to hospital with a similar clinical picture and were drawn from a predominantly urban population living either in, or within ten miles of, Coventry, a city of over 250,000 inhabitants, which itself accounted for 100 of the cases.

The admission-rate rose in May, continued at a high level until the end of July, and then dropped sharply. The fall roughly corresponded with the advent of the local holiday week and of school holidays.

During the peak months 1 case each of tuberculous, pneumococcal, and *Hæmophilus influenzæ* meningitis were seen; on admission they were indistinguishable clinically from the more severe of the meningo-encephalitic cases.

Multiple cases in families were probably not uncommon—e.g., a girl, aged 11 years, admitted in June, had meningeal signs and a C.S.F. cell-count of 140 per c.mm., while about the same time all the four other children in the family, aged 3, 5, 7, and 12 years, were ill but nursed at home.

Children of school age accounted for 55% of cases; the youngest patient was aged 6 months and the oldest 49 years.

Judged by history and pyrexia the duration of illness was 3 days or less in 20%, 4–7 days in 54%, 8–10 days in 18%, and 11–14 days in 8% of cases.

GENERAL CLINICAL DESCRIPTION

The onset of illness was sudden, with pyrexia commonly between 101° and 103°F. In cases lasting three days or less, severe headache and signs of meningeal irritation developed immediately. In cases of longer duration it sometimes seemed possible from the history to distinguish a premeningeal phase with pyrexia and moderate headache, generally lasting one or two days; in such cases a remission of from a half-day to two or three days occurred between the phases.

A mild sore throat was an early symptom in 27 (22)[*] patients; faucial congestion was noted in about the same number but without exudate. Herpes labialis occurred in 5 (4) patients aged from 11 years to 40.

Vomiting (often repeated) occurred in 73 (60) patients but seldom persisted after admission to hospital; 6 (5) others had nausea only.

Backache occurred in 19 (12) patients, and general limb aches in 10 (7) patients. Other sharp ill-localised and intermittent pains, sometimes persisting for a day or two, were recorded as follows: chest and shoulder girdle 6 (5) patients, abdomen and pelvic girdle 13 (9) patients, limb or limbs 5 (4) patients, head and face 3 (2) patients. In all, only 41 (30) of the 112 (90) patients complained of one or other form of these "muscular" aches and pains.

Headache, frontal and occipital or both, was constant and often said by older patients to be the worst they had ever had. Spinal rigidity was also constant, in degrees varying from slight to severe, though never so severe as to cause head retraction or opisthotonos. Neck rigidity sometimes occurred without dorsolumbar rigidity, and less often the converse obtained. Kernig's sign was recorded 50 (38) times, and photophobia 6 (4) times. In 6 (5) cases the knee-jerks or the ankle-jerks were temporarily unobtainable; plantar responses were always flexor. 1 (1) female adult had retention of urine. There were no paræsthesiæ other than history of pins-and-needles at onset in 1 case.

In 26 patients there were, in addition to headache, other cerebral features (sometimes in combination)—irritability or delirium 12 (10) cases, drowsiness or stupor 7 (6) cases, convulsions 6 (6) cases (ages varying from 7 months to 11 years), and diplopia 3 (3) cases. These features and the meagre C.S.F. changes in some cases seemed to justify use of the term meningo-encephalitis for the whole series. The C.S.F. findings in these 26 cases matched those in the more purely meningeal cases. Encephalitic states could be very brief, as in a man who had returned to work during a remission and, feeling nauseated, visited the lavatory only to fall promptly into a stupor, from which he "woke up" about an hour later. Other signs of possible encephalitic origin were flushing and profuse perspiration in 3 (3) cases, and giddiness in 2 (1) cases; vomiting in some cases occurred with the nervous phase. In 21 (14) cases brief nystagmoid movements of doubtful significance were elicited (4 of these patients had mental changes). The 3 cases already mentioned as having diplopia had no other paretic manifestations, and it was felt unlikely that they were poliomyelitis. No strabismus was observed.

Treatment in all the cases was symptomatic only, and recovery was invariably rapid and without, so far as is known, any sequelæ.

C.S.F. FINDINGS

The C.S.F. was usually clear and under moderately increased pressure judged by rate of drip. In at least 1 case it was opalescent (cells 702 per c.mm., mainly lymphocytes). Cell-counts and examination of cell types and of the protein, chloride, and sugar contents were routine; culture was not usually done except where it was felt that tuberculosis had not been excluded, or where the C.S.F. was opalescent or turbid. In all the cases rapid recovery ensued without chemotherapy.

TABLE II—ADMISSIONS OF PARALYTIC AND NON-PARALYTIC CASES 1951

Months in 1951	Paralytic cases	Originally classified non-paralytic cases	Additional non-paralytic cases (normal C.S.F. cell-count)
Jan.–April ..	2	7	1
May–Aug. ..	9	77	18
Sept.–Dec. ..	3	6	3
Total ..	14	90	22

Abnormalities were found in cell-counts (limit of normal taken as 5 lymphocytes per c.mm.) and in protein contents (normal range taken as 20–40 mg. per 100 ml.), but the chloride and sugar values varied within normal limits. Abnormal cell-counts occurred in 90 cases and in all save 3 the cells were a mixture of polymorphs and lymphocytes; the 3 exceptions had counts of only 4 or 5 per c.mm., all the cells being polymorphs. The amount of protein was increased mostly to 50–100 mg. per 100 ml. in 39 cases, in 30 cases accompanying a pleocytosis, and in 9 others a normal cell-count. In 13 cases no abnormality was found, but 2 of these each had a sibling concurrently ill and having a C.S.F. pleocytosis.

In 26 out of 31 cases in which the first sample of C.S.F. gave normal cell and protein findings a second diagnostic lumbar puncture was done at an interval of from two days to about a week. 14 of the second specimens gave abnormal cell-counts ranging from 5 polymorphs per c.mm. to 335 cells per c.mm. (mainly lymphocytes); 4 others had a slight increase of protein (60–80 mg. per 100 ml.); and 8 still gave normal findings. It was queried whether trauma, hæmorrhage, or entry of air sensitivity unimportant The W H O investigators have wisely begun by concentrating on a close study of these skin reactions, and they have used them to determine, among other things, the effect on the vaccine of storage, heat and light, and variations in preparation and concentration, as well as the results of mixing living and dead bacilli and varying the technique of intracutaneous vaccination The results were summarised by PALMER [6] and discussed in these columns [7]

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[*] The figures in parentheses are cases with abnormal C.S.F. cell-counts.

Perhaps one of the most important contributions of the W.H O team is their insistence that tuberculin sensitivity is quantitative and not a simple qualitative phenomenon that may be described as present or absent, positive or negative They produce convincing evidence that the sensitivity of groups of people cannot be adequately described by such inexact and often almost meaningless estimates as the "percentage of positive reactors" The skin reactions must be measured and the level of tuberculin sensitivity expressed in terms of the distribution and mean size of the reactions in the group as a whole In this way it is possible to discriminate differences between groups that might be missed by less precise methods The accurate measurement of the diameter of the indurated area requires skill and practice Even with experienced workers the experimental error is not insignificant,[8] and with those less experienced it may be very large But if the tuberculin skin reaction continues to be looked upon (and described to students) as a rough qualitative test, no-one will trouble to acquire skill in its use Many investigations have shown how valuable the quantitative use of the reaction can be For example, BENTZON [9] demonstrated changes in tuberculin sensitivity during some of the infectious diseases, and MEYER [10] studied the standardisation of tuberculin preparations in man Careful measurement of the reactions during the preliminary skin-testing in the W H O investigation revealed some interesting differences in the patterns of tuberculin sensitivity in the countries concerned [11] These differences could not have been found if the all-or-none method of recording results had been used The frequency-distribution of the reactions to small doses of P P D tuberculin showed that there seemed to be three main kinds of tuberculin sensitivity—high-grade and low-grade sensitivity and relative insensitivity The high-grade sensitivity is thought to be due to infection with *Mycobacterium tuberculosis*, but certain characteristics of the low-grade sensitivity, coupled with earlier and similar observations in the U S A,[12] suggest that this sensitivity is independent of true tuberculous infection Low-grade sensitivity, it seems, has much to do with geographical factors, for example, it was much commoner in India and Egypt than in Denmark and Mexico City, and in the mountainous area around Darjeeling low-grade sensitivity was commoner in the low-lying valleys than in the higher tea plantations [13] This sensitivity, it is suggested, may be due to infection with an organism antigenically related to *Myco tuberculosis* Perhaps this explanation is an over simplification, but the hypothesis, if true, has many important implications For instance, the results of tuberculin surveys expressed in "percentage positive" figures may not be valid measures of the frequency of tuberculosis in a population It may well be that surveys in some countries have overestimated the prevalence of the disease The W H O monograph is concerned only with tuberculin sensitivity, and the authors have avoided accepting the assumption that a large local reaction and a high level of skin-sensitivity indicate immunity and a "successful" vaccination Their work shows that the local reaction and the sensitivity are much influenced, sometimes independently,[14] by many factors in the preparation and administration of the vaccine If local reaction, sensitivity, and immunity run parallel with one another, the immunity produced by the many million vaccinations so far performed must be extremely diverse in both degree and value But there is little evidence at present to justify the belief that the vaccination lesion or the postvaccination sensitivity are necessarily reliable measures of the production of immunity

The past year has brought two new reports of extensive investigations into the results of B C G vaccination DAHLSTROM and DIFS [15] studied the tuberculosis morbidity in over 60,000 conscripts to the Swedish army they found that the incidence of primary tuberculosis in those not vaccinated was approximately five times as high as in those vaccinated, and the incidence of postprimary tuberculosis was about three times as high ARONSON and ARONSON [16] have continued their work among groups of Indians in the U S A and Alaska Their assessment of B C G is based on carefully compiled mortality figures During 15 years' observation the mortality from tuberculosis was six times as high in the non-vaccinated as in the vaccinated Although the method of allocating the children to the groups was unfortunately not up to the highest statistical standards, this report, added to the latest news from Sweden, makes out a strong case in favour of the protective powers of B C G

B C G vaccination is now being carried out on a huge scale throughout the world In this country its use is still limited to certain groups of people thought to be exposed to the greatest risk of infection These favourable reports have prompted further discussion about whether it should be used more widely and to what sections of the population it should next be offered The discussions are always concerned with groups and categories, such as infants, "school leavers," and National Servicemen, little is heard on the question of whether B C G should be made available to individuals At present, a child who is not a "contact" cannot be vaccinated, however much the parents and the general practitioner desire it without reference to a chest physician B C G vaccination in this country has rightly been judged as a matter for planning and strict control, but there now seem good reasons for lessening control, while preserving the general plan of campaign

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[6] Palmer C E *Lancet*, 1952, i, 935

[7] *Ibid*, p 953

[8] Meyer, S N, Hougen, A, Edwards P *Publ Hlth Rep*, *Wash* 1951, 66, 561

[9] Bentzon, J W *Tubercle* 1953 34, 34

[10] Meyer, S N *Amer Rev Tuberc* 1952 66 292

[11] Edwards L B, Palmer C E *Lancet* Jan 10, 1953, p 53

[12] Palmer C E Ferebee S H Stange Peterson, O *Publ Hlth Rep*, *Wash* 1950 65 1111

[13] Bates, L E, Busk, T, Palmer C E *Ibid* 1951, 66 1427

[14] Palmer C E Edwards, P Q *Brit med J* Feb 14, 1953, p 363

[15] Dahlström, G, Difs H *Acta tuberc scand* 1951, 25, suppl 27

[16] Aronson, J Aronson, C F *J Amer med Ass* 1952 149, 334

TABLE V—MONKEY-SERUM NEUTRALISATION TESTS

Monkey no.	Serum	Serum dilutions				Saline control
		1/1	1/10	1/50	1/250	
1	Pre-inoculation ..	(1) 16/16	8/8	—	—	5/5
	28 days post-inoculation	—	0/6	1/9	16/16	15/16
2	Pre-inoculation ..	4/5	—	—	—	3/3
	10 days post-inoculation	4/10	5/5	—	—	6/6
3	Pre-inoculation ..	9/9	—	—	—	8/8
	21 days post-inoculation	11/12	—	—	—	5/6

(1) See table IV.

SEROLOGICAL INVESTIGATIONS

Complement-fixation Tests

The specimens of serum from the 8 patients were negative when tested against lymphocytic choriomeningitis and mumps antigens. The leptospiral agglutination tests were also negative.

Neutralisation Tests

The newly isolated strain of Coxsackie virus was used in these tests as a dilution of mouse-tissue suspension which, after being mixed with an equal volume of serum, contained about 100 L.D.$_{50}$ of virus.

In view of the increase in neutralising antibody titre against a strain of Coxsackie virus, found in sera from 4 patients, similar tests were made with sera from 3 of the inoculated monkeys (table V).

Monkey no. 1, inoculated with the stool suspension (case 1) containing the newly isolated strain of Coxsackie virus, had developed neutralising antibody against this virus. Its excreta were not examined for the presence of the virus. The sera from the 2 other monkeys showed no evidence of the development of a significant amount of neutralising antibody.

DISCUSSION

The admission to hospital of more than 100 patients with meningo-encephalitis, mainly within a comparatively short period during the summer of 1951, was unusual. A tentative diagnosis of non-paralytic poliomyelitis was encouraged by the simultaneous occurrence of cases of paralytic poliomyelitis. Later the disproportionately small number of patients with paralysis made this diagnosis less likely to be correct. In view of the benign nature of the illness it is probable that many more patients were treated at home.

The main features were a sudden onset, with pyrexia of variable duration up to two weeks and a biphasic pattern in some patients. There were severe headache, vomiting, cervical and spinal stiffness, occasional diplopia, and sometimes delirium or stupor. A positive Kernig's sign was not always obtained. The course of illness was uncomplicated, and recovery was complete. The C.S.F. in 90 cases showed a pleocytosis of 10–1000 cells per c.mm., with counts of 10–200 in most patients. Lymphocytes were the preponderant cells, but polymorphs sometimes predominated. Often the protein content was slightly increased. In about 10% of patients changes in the C.S.F. were noted only at the second time of testing, and the other patients, although clinically identical, showed no abnormalities.

Besides poliomyelitis, the clinical picture of mild neurotropic infection could have resulted from other infections—e.g., lymphocytic choriomeningitis, mumps, and leptospirosis—but the occurrence of so many cases distributed over a fairly wide area within a short time and without other distinguishing features rendered these infections unlikely for the group as a whole. Laboratory tests showed that sera from 8 patients were negative for lymphocytic choriomeningitis, mumps, and leptospirosis. Of stools from 7 patients which were investigated, a strain of poliomyelitis virus was isolated only from the patient with paralysis, an experience similar to that of Silverthorne et al. (1951). This has been found to be of the Leon type. A strain of Coxsackie virus was isolated from the stool of 1 patient out of 8 investigated, and it was found to be similar to the strains of Coxsackie virus isolated earlier in 1951 from an outbreak of febrile illness in a children's home near Coventry (Kenyon et al. 1952). In that outbreak strains were isolated from all 5 patients investigated, and in view of those findings the isolation of only one strain was initially thought to be a chance phenomenon unrelated to the illness under investigation. Further, no case of aseptic meningitis was observed during the outbreak in the children's home. Although our knowledge of these viruses is very incomplete, it has been found (Bury and Tobin 1952) that a single strain of Coxsackie virus may give rise to different clinical types of illness. Conversely, immunologically distinct strains of Coxsackie viruses may give rise to a similar clinical type of illness. Whether the excretion of virus differs with different illnesses or whether it occurs intermittently was not investigated. Subsequently it was demonstrated that sera from 7 out of 8 patients had neutralising antibody against this strain of virus, a point in support of its wide distribution throughout the Coventry area. During the course of illness no increase in neutralising antibody was found in 2 patients, 1 of whom had poliomyelitis. A slight increase occurred in case 8, who was admitted to hospital with scarlet fever and subsequently had mild encephalitis. A significant increase in antibody occurred in 4 patients, including case 1, from whom the strain of virus was isolated, and also in monkey no. 1. Sera from monkeys nos. 2 and 3 showed no significant amounts of neutralising antibody against this strain of Coxsackie virus.

In the absence of other known causes, and in accordance with practice, it may be accepted that, as a significant increase in neutralising antibody titre against a strain of Coxsackie virus occurred during the course of illness in 4 patients, this virus was a link in their infection. Of the remaining patients 1 had poliomyelitis and 1 had possibly a mild post-infective encephalitis. In 2 patients, 1 of whom had no changes in the C.S.F., a definite diagnosis was not made, but the possibility of infection by an unidentified organism has not been excluded.

It is hoped that the sera from the 8 patients will ultimately be tested for neutralising antibody against the three types of poliomyelitis virus.

Possibly some of the patients in this widespread occurrence of benign neurotropic illness were infected with a Coxsackie virus, but the problem remains whether or not the illness was, for the most part, provoked by a single ætiological agent, or whether there were several factors involved. Further investigation is essential before the ultimate rôle of the Coxsackie viruses and the part played by the poliomyelitis viruses are decided.

SUMMARY

112 cases admitted to hospital in 1951 with a benign meningeal or meningo-encephalitic illness, of whom 90 cases had an abnormal C.S.F. cell-count, are reviewed.

Virus investigation of specimens from 8 patients was undertaken. A strain of Coxsackie virus was isolated from 1 patient with mild meningo-encephalitis. In this patient and in 3 others increased neutralisation of this virus was observed in samples of serum obtained in the convalescent stage of illness. No increased neutralisation was observed in 3 patients, including 1 with paralysis. A strain of poliomyelitis virus was isolated only from the patient with paralysis.

Serological tests for lymphocytic choriomeningitis, mumps, and leptospirosis were negative.

Although the small number of virological investigations prohibits any general conclusion on the group as a whole, the possibility exists that a Coxsackie virus may

of pharmaceutical chemists first passed the minor examination, but since the introduction of university degrees in pharmacy, graduates have obtained this higher title by way of a greatly modified examination In practice, however, no one outside the profession realised that any distinction or difference existed Recently the Pharmaceutical Society ceased to examine at the "chemist and druggist" level, so the holders of this title now form a dwindling group The Pharmacy Bill, a private member's Bill now before Parliament, seeks to place all pharmacists on the register of pharmaceutical chemists If this becomes law, the present chemists and druggists will receive the title of "pharmaceutical chemist" by way of bonus Perhaps the existing holders of this qualification will feel they have suffered some loss of status and they may wish for a distinctive title as a sign of the standard they have attained

The century-old Act not only prohibited the Pharmaceutical Society from conducting examinations in medicine, surgery, and midwifery, but also debarred members of the medical profession from registering as pharmaceutical chemists, the new Bill will repeal the latter and retain the former provision Certain domestic matters of the society, including the abolition of the limit on the annual retention fee paid by members, are also covered by the Bill The Bill is sponsored by members on both sides of the House and seems to contain little that is controversial Incidentally, there is talk at the moment of establishing an examination in practical pharmacy for unqualified assistants, but it is to be hoped that this will not lead to a repetition of history and a demand for legislation to recognise a new class by statute

MEDICINE AND GEOGRAPHY

ORGANISED scientific collaboration between the different countries of the British Commonwealth is one happy result of the late world war Representatives of the Medical Research Council, Department of Scientific and Industrial Research, Agricultural Research Council, and Commonwealth Agricultural Bureaux have met regularly in London since 1946 with scientific representatives of Canada, Australia, Southern Rhodesia, South Africa, India, New Zealand, the Colonies, and latterly also Pakistan and Ceylon, to see what can be done to improve the exchange of scientific information and of specialist scientists, and how national laboratories can work for the benefit of the whole Commonwealth or share in international research The fruits of this combined approach include an index of English translations of foreign scientific papers, a book listing inter-Commonwealth postgraduate scholarships in science, maps of the prevalence of insect and fungus plant diseases, and the coördination of culture collections of micro organisms two reference laboratories of the Public Health Laboratory Service at Colindale (dysentery and food-poisoning) now work for the whole Commonwealth, with the exception of Canada These and other achievements are recorded in the report, just published,[1] of a special Commonwealth conference held in Australia last year

On the whole this scientific liaison work is for the benefit of official science, and relatively little is of medical import, but geographical anthropometry—the study of the normal physical standards of inhabitants of different countries or of different tribes in a single country—is proposed as suitable for research by collaboration throughout the Commonwealth This not only is essential for defining where disease begins, but may also prove a good test of the value of somatotyping and similar attempts to classify human physiques It seems a pity that the conference turned down a proposal to study geographically the prevalence of dental caries—apparently because this would be better investigated on a fu international scale The Commonwealth is large enoug for useful studies on the geography of many disease- and to wait till, say, the World Health Organisation ha money for international research of this sort and ca persuade its member nations to collaborate may be t wait a very long time The American Geographica Society has already begun to publish maps of th distribution of diseases[2] and how this is changing wit the years, and Sigerist[3] has discussed the kind o useful work to be done Research on this subject ca only be by international collaboration, and the Briti Commonwealth Scientific Conference ought to conside further how it might be promoted—for instance, b coordinating the work of national health department on the notification of disease

RUPTURE OF THE BLADDER

THE early diagnosis of intraperitoneal rupture of th bladder may be difficult Moreover, Negley[4] emphasise its importance by drawing attention to the danger o spread of infection, he found that the operative mortalit within the first twelve hours was 11%, it rose to 22% after twelve hours, and to 43% by the second day Various tests for the earlier diagnosis of this condition have been suggested and tried Recently, Cipolla and his colleagues[5] reported that in dogs a 0 5% solution of fluorescein was not absorbed from an intact bladder, but was readily absorbed from the peritoneal cavity and could be detected later in the blood-stream Similar results were obtained in experiments on human beings The authors suggest that in every case of suspected rupture of the bladder a 10 ml specimen of blood should be taken, and then 100 ml of a 0 5% solution of fluorescein passed through a urethral catheter into the bladder The control serum is compared with three specimens of serum removed at intervals of five minutes, the presence of fluorescein confirms the diagnosis A tear in the bladder may be plugged by omentum and the perforation may not be detected by other tests In dogs, Cipolla et al found that less fluorescein was absorbed when the tear was plugged by omentum than when it was open to the peritoneal cavity, and they suggest that this finding may be used to distinguish between a ruptured bladder which is sealed with omentum and one which is not

DIAGNOSIS OF MYASTHENIA GRAVIS

BEFORE the introduction of neostigmine by Mary Walker in 1935 myasthenia gravis was usually diagnosed by observing the characteristic distribution of the muscles affected—the occular and bulbar muscles and proximal rather than distal limb muscles—and by the history of diurnal fluctuations as well as remissions and relapse over months or years The greatest difficulty arose in patients with an unusual mode of onset, those with no tendency to remission, and those who in an early stage of the disease showed no physical signs and might be diagnosed as hysterical

Neostigmine, with its rapid action, was widely welcomed as a diagnostic agent The patient whose muscular power is not increased by a dose of 1 5 mg intramuscularly or 0 5 mg intravenously has not got myasthenia gravis—though the response varies widely from one patient to another Neostigmine may, however, also cause some temporary improvement in thyrotoxic myopathy[6] [7] and in dysphagia due to early progressive bulbar palsy Moreover, it has to be used with some care, and always with atropine (0 6 mg) because of it-closely round it. The steel cylindrical part has a mica window, so that the loop is visible while being flamed. The metal window-frame is bolted to the cylinder and can easily be removed to allow the mica to be replaced. A slit 1·5 × 4·5 cm. admits the loop for flaming. The top consists of a larger rimmed metal plate enclosing the cylinder, and a smaller one, 2 cm. below, enclosed by it; both have numerous ventilation holes, and the lower plate baffles the holes in the upper. Extending down 4 cm. from the upper plate is a small vertical baffle which helps to prevent the flame from escaping through the slit; when the apparatus is assembled, this baffle lies immediately within the slit, overlapping it slightly.

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[1] British Commonwealth Scientific Conference, Australia 1952 Report of Proceedings H M Stationery Office Pp 74 3s

[2] *Sci Amer* February, 1953, p 22

[3] Sigerist, H E A History of Medicine New York and London 1951, vol 1, p 66

[4] Negley J C *J Urol* 1927, 18 207

[5] Cipolla A F, Khedroo, L G, Casella, P A *Surgery*, 1953, 33 102

[6] Laurent L P E *Lancet*, 1944 i 87

[7] Sheldon J H, Walker, R M *Ibid*, 1946, i, 342

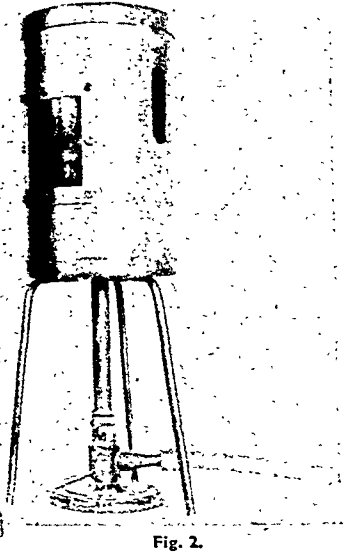

Fig. 2.

The apparatus does not get uncomfortably hot in use if the pilot lever of the burner is turned down whenever the flame is not required. It is quite stable on the bench. The metal used is mild steel.

We are grateful to Mr. E. V. F. Pittock for the photographs.

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Reviews of Books

Rose and Carless' Manual of Surgery

for Students and Practitioners. 18th ed. Editor: Sir Cecil Wakeley, bt., k.b.e., c.b., ll.d., m.ch., d.sc., f.a.c.s., president of the Royal College of Surgeons of England. 2 vols. London: Baillière, Tindall, & Cox. 1952. Pp. 1471. 63*s*.

It is nearly ten years since the last edition of "Rose and Carless" appeared. In all its long history this is perhaps the most notable edition, for the book has been transformed and almost entirely rewritten. In accord with modern trends the special sections on pathology and bacteriology have been discarded, and collaborators have been brought in to deal authoritatively with the various divisions of surgery which have become specialties. The result is a textbook which reflects accurately the best modern English practice. The editor has been happy in his selection of authors. There is an evenness in presentation rarely found in multiple-author books.

One of the greatest difficulties in compiling a textbook for the undergraduate is to decide how much knowledge he can be reasonably expected to acquire: it is very easy for a specialist's judgment to err on the side of demanding more than the average student should be asked to pick up in the crowded years before qualification. This is a large book, and contains a formidable and rather frightening amount of knowledge for the man beginning his clinical work. But the alarm the student may feel when confronted with these two volumes will be lessened when he really dives into them; for the matter is presented well, clearly, and attractively. It is all so exciting to the newcomer to clinical surgery that he will soon find that the task of reading through this large book is very much lighter than at first sight it appears. As the surgery of the special senses and anæsthesia are included the ordinary pass student will need no special books on these subjects. The outlook is completely modern, and the illustrations and general make-up are excellent.

Psychiatry and Medicine

An Introduction to Personalised Medicine. Leslie A. Osborn, m.d., professor of psychiatry and acting director, Wisconsin Psychiatric Institute, University of Wisconsin Medical School; director of mental hygiene, Wisconsin Department of Public Welfare. New York and London: McGraw-Hill. 1952. Pp. 494. 64*s*.

This book sets out "to depict in clinical perspective the close relationship that is developing between psychiatry and medicine. It deals particularly with personal and interpersonal factors as they influence health and illness." Professor Osborn has had experience in the fields of general practice, geriatrics, and psychiatry, but his chief interest has been in clinical teaching on the lines of this book; as head of the department of psychiatry in the University of Buffalo School of Medicine, he had ten years' experience of teaching medical and dental students and social workers. His aim is to make us more aware of the patient as a complete person rather than as an aggregate of tissues and organs, and to inculcate a habit of mind that assesses the individual's constantly changing attitudes to his environment, to society, and to health or illness.

The first part of the book deals with theoretical concepts; the teachings of Freud as modified by Adolf Meyer seem to underlie the author's approach. The second part is concerned with practical applications of theory in clinical study and therapy, and a short concluding section considers preventive psychiatric treatment. An appendix gives some useful outlines of psychiatric and neurological methods of clinical examination, though even here the characteristic warning that no "system" can replace consideration of the individual heads the chapter.

The word "personalised" in the subtitle does not do justice to the sort of medicine which Dr. Osborn evidently practises; nor does it, to British ears, hint at the common sense and warm humanity of these pages.

Cancer in General Practice

Ronald W. Raven, o.b.e., f.r.c.s., surgeon, Royal Cancer Hospital: P. E. Thompson Hancock, f.r.c.p., physician, Royal Cancer Hospital. London: Butterworth. 1952. Pp. 265. 30*s*.

Though this book is intended for, and will be useful to, the general practitioner, its contents scarcely correspond to its title. "Cancer: a synopsis for general practitioners" would be more accurate. The chief physical facts about malignant growths occurring in the organs, systems, and regions of the body—incidence, pathology, spread, early and late symptoms, diagnostic procedures, treatment by surgery and irradiation, prognosis in terms of survival—are set out on an anatomical basis. There are illustrations—clinical, pathological, and radiographic—and a full bibliography, but no complete case-histories. Here and there a rule for investigation is laid down or a régime (in colostomy, for instance) is given in detail; but the outlook throughout is that of the surgeon, physician, or pathologist in a hospital investigating and treating disease processes, not that of the general practitioner essaying the often impossible task of early diagnosis and directing, sustaining, comforting, watching, and relieving the afflicted subject.

The problems raised by cancer in general practice are far more complex, formidable, and heartbreaking than is even hinted here. Some of them can be deduced from the grim facts given in the book, but few are directly faced and it is hard to believe that the authors have them clearly in mind. Perhaps even the implications of the advice given are not always appreciated. "Thus it is a rule to perform sigmoidoscopy on every patient who presents any abnormality of the anus or rectum. . . . No symptom, however trivial, should be overlooked and a complete examination should be made." Does this mean that every pruritus, superficial crack, pile tag, or anal hæmatoma must be sent to hospital for sigmoidoscopy? And if every abnormality *were* so referred would the complete examination indeed be made? Again, a thoughtful practitioner will surely require more evidence than is here adduced before urging a young woman with a stage-I carcinoma of the breast to accept double oöphorectomy as a supplement to mastectomy.

Special Articles

REABLEMENT OF HOUSEWIVES

A Lead from King's College Hospital

WHEN the housewife lays down her tools the effect on her family is much like that of a general strike on the nation at large. Ordinary pursuits are delayed and hampered, and special projects interrupted by the basic requirements of civilised living—meal-getting, house-cleaning, and washing-up. Reablement of men for industry, and of children for the schoolroom, has gone far, but the housewife disabled by rheumatoid arthritis, poliomyelitis, hemiplegia, or other disaster gets, if she is lucky, some physiotherapy and a few cheery words of encouragement. These are good in their way, but seldom fit her to get herself up, washed and dressed in the morning, or to do the vegetables, brush a floor, clean a saucepan, open a tin, or generally keep the home fires burning—even in a literal sense.

It is easy to plan a reablement programme from the wrong end, beginning with what the patient hopes to do in his job rather than with what he can immediately do for himself. Dr F. S. Cooksey, who is in charge of the physical-medicine department at King's College Hospital, points out[1] that though the personal activities of daily living are considered seriously in special centres for the limbless, the paraplegic, and the blind, they are ignored as far as the general run of disabled patients are concerned. His department offers a programme of reablement specially designed for housewives, beginning with the movements needed in dressing, feeding, getting in and out of a bath, using a toilet, and so on, and proceeding to all the skills required in getting a dinner.

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The centre is small for the work it does. Rooms of various sizes have been partitioned off from a central space containing a desk for a secretary. One small room has been set aside for patients who need to practise dressing and undressing, and the walls are hung with a number of encouraging gadgets showing that this task can be greatly simplified. Men as well as women need this kind of help, so the gadgets include cuff-links which, having been put into the shirt in advance, expand on a spring and let the hand slide through the cuff, elastic shoe laces which can be left permanently in the shoes, a long handled shoe-horn which makes it easy to put the shoes on without stooping, and a device for sliding into nylon stockings, again without stooping, and also—which the wearer doubtless thinks even more important—without getting them snagged by the toe-nails. A tie, already neatly tied, is mounted on a spring like a bicycle clip, which can be snapped round the neck with one hand, and members of either sex, using a towel attached to the wall by a spring, can practise the motions needed for drying the back after a bath. Other encouraging exhibits are knives and forks with big handles, easily grasped by a partly paralysed hand, and spoons bent round at an angle so that they can be raised to the mouth by those whose elbows are fixed.

In a neighbouring workshop patients of both sexes are engaged in occupational therapy—but with a difference. They are making objects of use in the hospital (like rubber-covered rockers to be worn with plasters), and the tasks are assigned not on grounds of interest or variety but simply because they benefit a particular joint or group of muscles. Many patients, it seems, prefer sticking at a repetitive job which is benefiting a disabled limb to completing an object in which they have no particular interest. This preference became apparent when patients who attended rigorously at the gymnasium for directed physical training, and also put in strenuous hours doing unsupervised exercises in the department, failed to turn up for occupational therapy. When set to do a repetitive job which exercises the damaged limbs, they will attend regularly, without complaining of monotony.

THE KITCHEN UNIT

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The working bench, with the sink in the middle, is flanked at one end by the oven and hot-plate of the gas cooker (which are separate and side by side) and at the other by a refrigerator (fig. 1). The hot-plate, and the middle shelves of the oven and refrigerator, are all on the same level as the top of the bench, and this is set at a convenient working height for a patient sitting in a wheel chair. The top of a stout trolley is also at the same height, and dishes can thus be slid from the bench to the trolley, and from the trolley to the oven, with no lifting. The trolley top is boxed in with stout wooden planks, partly to prevent things from slipping off it and partly so that

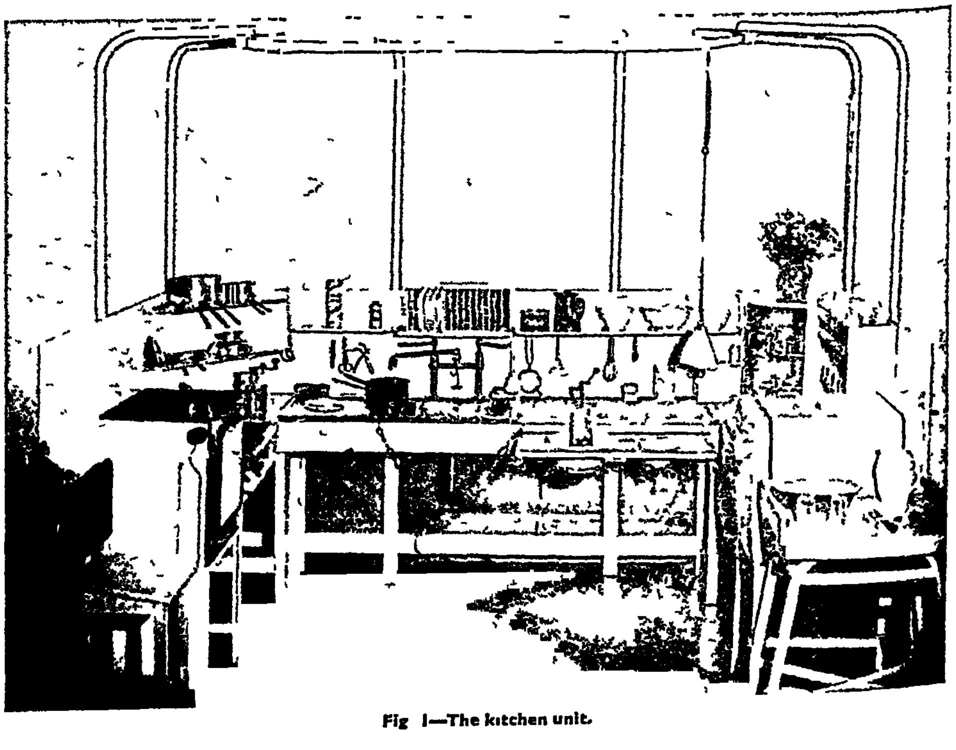

Fig 1—The kitchen unit.

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[1] *Ann phys Med* 1952, 1 120

THE LANCET

LONDON: SATURDAY, FEB. 21, 1953

Facts about Nursing

Miss NIGHTINGALE had some clear notions about the nature of nursing; but without that penetrating mind to guide us we have fallen into confusion. The word "nursing," she said,

> "... has been limited to signify little more than the administration of medicines and the application of poultices. It ought to signify the proper use of fresh air, light, warmth, cleanliness, quiet, and the proper selection and administration of diet—all at the least expense of vital power to the patient ..."

In their welcome and unique report,[1] the Job Analysis Team of the Nuffield Provincial Hospitals Trust say that the modern tendency (clearly revealed in their survey) "is to regard 'the administration of medicines and the application of poultices' as the proper task of the skilled nurse, and to delegate the routine care of patients to less highly trained persons." This team, under the directorship of Mr. H. A. GODDARD, with Mrs. C. COLWELL as administrative assistant, Miss C. M. GRANT GLASS as nursing adviser, and Miss J. M. BLOMFIELD as leader of the field investigators, set out to give an exact and full account of the present duties of nurses in hospitals. The Working Party on the Recruitment and Training of Nurses,[2] it will be remembered, undertook a job analysis of the daily routine of 36 student nurses and 3 pupil midwives, and of a smaller number of sisters, staff nurses, assistant nurses, and nursing assistants, for the purpose of establishing the time spent on domestic duties, the amount of repetitive work in the nurse's training, and the extent of overlapping between various training courses. The Trust's team have approached the task more comprehensively and in a different way, by keeping entire wards under continuous observation over a period of time.

12 general hospitals which were also nurse-training schools were selected, 9 of them former voluntary hospitals and 3 former municipal hospitals. In situation they were scattered over England and Scotland, 4 serving rural, and 8 urban or industrial, populations; and they ranged in size from under 200 to 1500 beds. The block system of training operated in 6, the weekly study day in 1, and the remaining 5 maintained the old pattern which requires the student nurse to interrupt her ward work for lectures, and do her reading after work, in the evenings. Only 3 hospitals had introduced the three-shift system for student nurses: the remainder used the two-shift system with a spell of split duty during the day.

In these 12 hospitals the observers watched 26 wards on a minute-to-minute basis, noting everything that was done in them by all grades of staff (including orderlies, porters, and ward-maids), day or night, over a period of a week.

Two findings seem to us outstanding: almost three-quarters of the time spent on nursing duties in these wards was contributed by student nurses; and in most of these hospitals nursing was being done with inadequate equipment. The first point is perhaps less of a surprise than the second.

A contrast is evident between the medical, and particularly surgical, equipment in our hospitals and the equipment of the wards. Bedpan sterilisers have rarely been installed, which means that student nurses waste time daily in cleaning and disinfecting bedpans; as heated racks for the cleaned pans are equally scarce, students waste time and fuel daily by warming them with hot water before taking them to patients. Trolleys are often so scarce that it is impossible to keep them laid for any special purpose (such as blanket bathing), and time is therefore wasted in laying trolleys afresh for every purpose. The research team saw no bedpan trolleys at all, though in one ward the nurses had improvised them from linen containers. One hospital had provided a wire carrier for urinals. Only one bread-cutting machine was seen on a ward, and it was out of order; the hygienic idea of using sliced wrapped loaves does not seem to have penetrated to our hospitals. Three wards did their sterilising with a fish-kettle on a gas-ring, and two of them had no means of sterilising bowls other than by flaming with methylated spirit. Bedpans and wash-bowls were often exceedingly scarce, some wards having as few as 7 wash-bowls for 37 patients or 5 bedpans for 28 female patients; only three wards had more than 8 screens to a ward, and some had only 4, which meant that screens had often to be dragged or carried the whole length of the ward. None of the wards studied had substituted curtains for screens. A shortage of matches was the cause of many wasteful journeys to and fro with a taper.

It is customary just now to talk about economising our nursing-power: one simple way to do it would be to provide nurses with the tools of their trade in adequate quantity. How is it that matrons—masterful women in other respects—have failed to make themselves felt over this essential preliminary measure? And why have the medical staff—and especially surgeons, who are able campaigners for their own tools—not seen to it that their nursing teams are properly supplied?

Equipment apart, nurses are much hampered by the bad design of wards. A bathroom or sluice room placed at the end of a ward, instead of in the middle, may mean a walk taking 26 seconds each way when a bedpan has to be fetched and removed. Wash-basins may be equally badly placed at one end only of a ward. In one modern hospital studied the sterilising-room had no running water, and jugs had to be brought from the kitchen; and staff cloakrooms may be at a considerable distance from the ward. If bad structural design is a burden that probably must be borne for the time being, there is comparatively little expense in putting extra taps and wash-basins—or even water-closets—in sites where experience has shown them to be most needed.

Nursing is not the only work done in a ward: in fact, only about 60% of the time of the staff is spent on it. Nearly a quarter goes on ward organisation, and about a sixth on domestic work. The observers found that domestic work was done very largely by domestic staff, and that in most cases the student nurse was not required to do an excessive amount of it. Everyone will be glad to know that this perennial blister has been pricked at last. On the other hand the training needs of student nurses were regularly subordinated to administrative necessity, and the amount of time spent on teaching them in the wards, the team say, was negligible. "The highest figure recorded was 11 hours in the week, and the lowest 7 minutes." These figures represent the sum

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[1] The Work of Nurses in Hospital Wards. London: The Nuffield Provincial Hospitals Trust, Nuffield Lodge, Regent's Park, N.W.1. Pp. 218. 6s. Postage 6d.

[2] Report. H.M. Stationery Office, 1947; see *Lancet*, 1947, ii, 392, 401.

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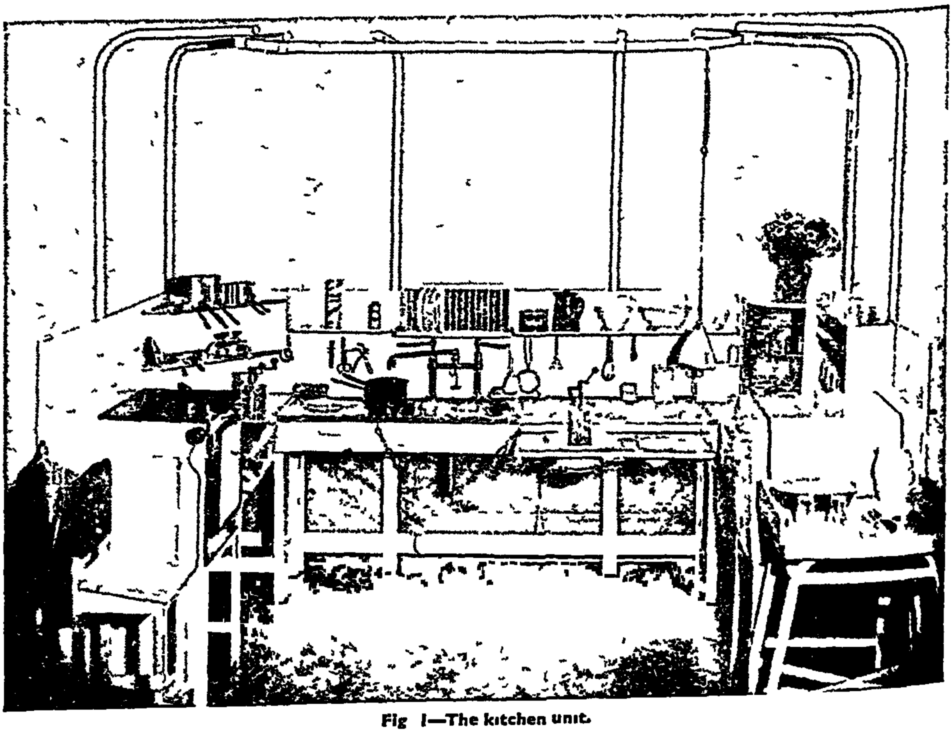

Fig 1—The kitchen unit

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[1] Ann phys Med 1952 1 120

some days œdema may be found. Examination of the chest most commonly reveals restricted movements and suppressed breath-sounds with scattered crepitations and occasionally conspicuous rhonchi. The sputum is purulent, and may have only recently become so. The temperature may be normal or moderately raised. Because of the added sounds in the chest and the manifest severity of the illness bronchopneumonia is often diagnosed; but radiographs seldom show consolidation. The arterial blood sample will have diminished oxygen saturation and raised carbon dioxide content and tension.

The diagnosis of cor pulmonale applies to those patients who have raised jugular pressure or œdema; this is a complication, common but not inevitable, of the disorder common to all—acute respiratory insufficiency. Usually in these patients moderate emphysema or other widespread disorder of pulmonary function has been suddenly aggravated by bronchial infection. How the infection, without necessarily extending into the alveoli, causes this abrupt functional deterioration is unknown. Bronchiolar congestion or constriction increases the work of breathing in some but not all of the patients; the fever is seldom great enough to provoke a large increase in oxygen needs; and one is led to suspect that the infection has in some way disturbed the distribution of pulmonary blood-flow.

The patient appears desperately ill; but, unless he was previously in heart-failure, he will probably recover. Because the spontaneous improvement may be as dramatic as was the onset, it is easy to overvalue any treatment. Morphine, sometimes given under the impression that the patient has left ventricular failure, may prove rapidly lethal. Intravenous digitalis and venesection (tempting because of the bulging veins) are also best avoided. Chemotherapy, however, is indicated, and fortunately penicillin is still usually effective. Isopropyl adrenaline, inhaled in a spray, will often relieve bronchiolar obstruction, and should be tried if the nature of the respiratory efforts suggests increased airway resistance. Arterial anoxæmia—the most serious consequence of the impaired respiratory function—can be corrected by increasing the oxygen content of the inspired air. This is most conveniently done by means of a tent; and by maintaining a good flow it is nearly always possible to restore the arterial saturation to a safe level. At best, however, this leaves unaltered the hypercapnia and respiratory acidosis, which unfortunately may sometimes be aggravated. This is because the more severely affected patients have modified their chemical respiratory drive and have come to rely on anoxia as the main respiratory stimulus. When the anoxia is relieved by breathing oxygen the ventilation falls and carbon dioxide retention is increased; and this can lead to headache, drowsiness, and even coma.[1] The reasonable way to counter this development is to maintain or increase ventilation. BOUTOURLINE-YOUNG and WHITTENBERGER[2] first reported favourably on the use of a respirator; and STONE et al.[3] have described four cases treated by this means: three were treated successfully with a Drinker respirator, and the fourth with an intermittent-pressure device. STONE et al. evidently feel that the respirator was an important factor in the patients' recovery, but most of those who have tried this treatment are likely to remain unconvinced. The Drinker respirator, designed for a paralysed patient, is far from ideal: the patient feels congested and dislikes lying flat; he probably has difficulty with sputum and is much alarmed if head movements are restricted. Because of his mechanical disabilities high pressures must be used to maintain a reasonable tidal air, and these cause uncomfortable movement of the neck seal. Moreover with a restricted tidal air high respiratory rates are needed, and these the standard motor cannot supply. Nor does any commonly available respirator seem much better. Possibly "electrophrenic respiration"[4] or a really effective respiratory-stimulant drug may prove preferable. At present the mechanical augmentation of ventilation in this type of respiratory insufficiency, in contrast to that due to muscular weakness, remains a therapeutic tour-de-force which can be effected if the patient can stand it.

In all this it is important to keep a sense of proportion. Most patients with acute respiratory insufficiency manifestly benefit from oxygen therapy despite some rise in carbon dioxide tension. Only a few patients become comatose or develop other serious troubles, and with these it is always possible to moderate the oxygen therapy to attain the best compromise. All who treat such patients should be aware of the possibility of respiratory depression, but patients must not be allowed to die of anoxia because of an exaggerated fear of carbon dioxide poisoning.

B.C.G.

IN 1922 WEILL-HALLÉ tried to protect children against tuberculosis by giving them the attenuated strain of tubercle bacilli produced by CALMETTE and GUÉRIN. During the next 25 years the vaccine was used extensively in many countries. Much work was done on its preparation and properties, its ability to induce tuberculin skin-sensitivity, and its alleged production of immunity to tuberculosis. But by 1947, when vast campaigns of vaccination were started by the International Tuberculosis Campaign, little precise information about B.C.G. was available, and it soon became clear that scientifically controlled studies were urgently needed. The Tuberculosis Research Office of W.H.O., with the collaboration of the Danish State Serum Institute and the International Tuberculosis Campaign, began a series of investigations into some of the basic problems; and the research office has now produced a monograph[5] which contains not only the reports of the separate investigations, many of which have already been published, but the complete quantitative data on which they are based. It is a valuable record of carefully planned and executed international research. There is no method of detecting or measuring immunity to tuberculosis produced in an individual by B.C.G. vaccination. The local reaction and the induced skin-sensitivity to tuberculin have generally been regarded as guides to the effectiveness of the vaccination, although CALMETTE himself considered

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[1] Davies, C. E., MacKinnon, J. *Lancet*, 1949, ii, 883.

[2] Boutourline-Young, H. J., Whittenberger, J. L. *J. clin. Invest.* 1950, 30, 838.

[3] Stone, D. J., Schwartz, A., Newman, W., Feltman, J. A., Lovelock, J. *Amer. J. Med.* 1953, 14, 14.

[4] Whittenberger, J. L., Sarnoff, S. J., Hardenbergh, E. *J. clin. Invest.* 1949, 28, 124.

[5] Edwards, L. B., Palmer, C. E., Magnus, K. B.C.G. Vaccination. W.H.O. monograph series. Geneva, 1953.

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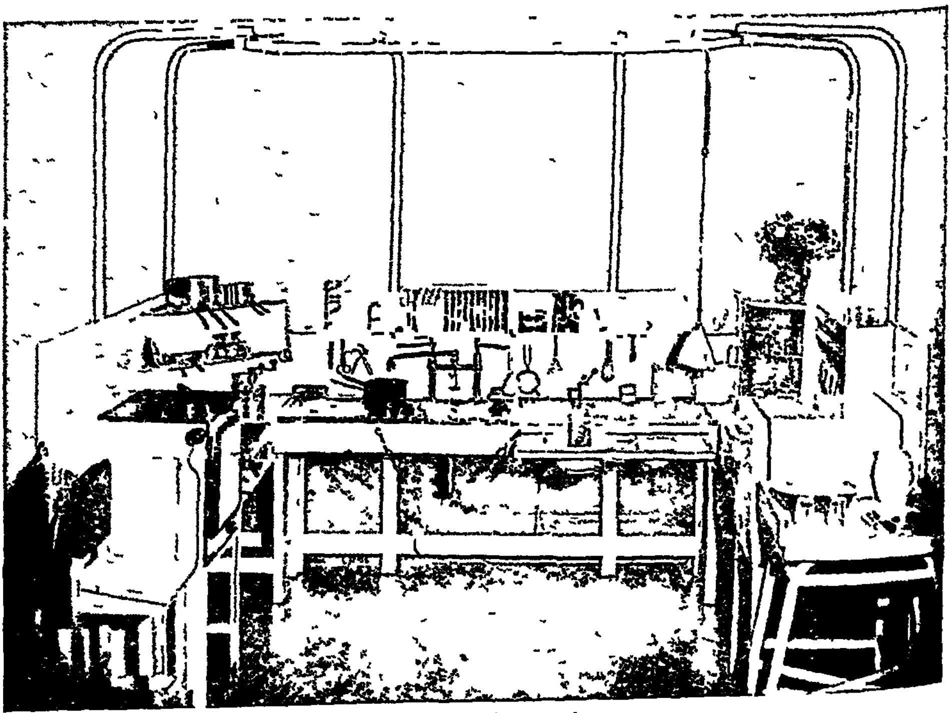

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[1] Ann phys Med 1952 1 120

Annotations

INFLUENZA 1953

Disastrous floods and fogs have made this one of the worst winters for a long time; and influenza, making its biennial attack in this country, has added to our difficulties. But, in general, influenza has so far been mild. On its previous visit, two years ago, the influenza-A virus swept rapidly through the country, and in the first month of that epidemic there were nearly 5000 deaths from influenza. In the present epidemic the deaths from influenza have climbed slowly, and during the same period there were rather less than 600. Once more, deaths have been most numerous in elderly people—about 90% of those who have died were over the age of 55. A curious feature of this year's epidemic is that the incidence of influenza has been very much greater in the south of England than in other parts of the country; but perhaps that is simply a reflection of the higher incidence in the north during the 1950–51 epidemic. Some idea of the size of the epidemic comes from the claims for sickness benefit received by the Ministry of National Insurance; about 100,000 claims in excess of normal were recorded for the week ending Feb. 3, and most of these claims were probably the result of influenza.

At about the same time as the epidemic appeared in this country, sharp outbreaks were reported from France, Germany, and the U.S.A. Slightly earlier there was a severe epidemic in Japan, and lesser outbreaks have since been reported from Scandinavia, Finland, Holland, and Switzerland. Detailed laboratory and epidemiological observations must be completed before the source or sources of this year's influenza can be identified or the method of spread traced. Preliminary laboratory reports indicate, however, that in all the countries involved A-prime viruses have been recovered. Those isolated in this country show an antigenic similarity to strains recovered this year in the U.S.A., Japan, and Denmark, and also to the Scandinavian subtype which was partly responsible for the European epidemic of 1950–51. On the other hand, strains from France and Switzerland seem to resemble the Liverpool subtype which was also prevalent in 1950–51. It seems, therefore, that this year's epidemic had at least two foci of origin.

When the spring has chased these troubles away, the lessons of this year's epidemic will be clearer. In particular, the results of the influenza vaccine trial, organised by the Ministry of Health and the Medical Research Council, and of the epidemiological investigations of the World Health Organisation influenza programme, will be awaited with great interest in the hope that we shall be able to look forward to our next encounter with the virus with greater confidence.

DETERGENTS

The domestic use of detergents has increased enormously, and some of the results are causing concern. Mostly these agents are products of the petroleum industry; they are paraffin-chain salts, their long hydrocarbon chain having an electrolytically dissociated group at or near the end. They thus have strong surface activity which favours the penetration of water into the interstices of fabrics. They also exercise a powerful emulsifying action on greasy dirt; the film on the threads of cloth is rolled into loosely adherent globules which are easily detached by agitation and can be rinsed away.[1] In the home detergents are used, as well as for laundering clothes, to wash dishes and utensils; and in industry they are used for various degreasing processes. They also find a proper use in dermatology as emulsion bases and in antiseptic shampoos and the like. The domestic detergents foam readily and are apt to be judged by this quality. Foam, however, though it breaks up the oil and mechanically assists removal of dirt, is not necessary for detergent action, which may be little reduced by the addition of antifoaming agents.[2]

Detergents prove harsh to some skins, and may even cause dermatitis; they may act as primary irritants or may produce sensitisation. Their action may be partly due to their defatting and drying effect, which may aid the penetration of other irritants or aggravate constitutional skin disease. As Hodgson[3] points out, however, these agents are a valuable aid to the housewife, who soon learns which brand, if any, she must avoid. The commercial firms are aware of the danger, and before marketing their products usually submit them to immersion and patch tests on the human skin.

When the detergent leaves the kitchen sink, other problems arise. At the sewage works it is usual, especially on Tuesdays, to find that the agitation in the aeration tanks has produced a surface layer of foam as much as six feet deep. The narrow service "roads" between the tanks are slippery and dangerous; and huge masses of foam are liable to be whipped off by the wind, perhaps carrying pathogens and certainly a potential danger to car-drivers, on whose windscreens they may alight. In America such masses of foam are believed to have accounted for some "flying saucers." How far detergents interfere with the biological processes of sewage purification is not fully known; but they are not removed by present methods of treatment and therefore reach the effluents and the rivers into which these may discharge. River and harbour boards are concerned about the possible effect of these agents on fish or on the food of fish. Further, if the river should be a source of water-supply, the water undertaking is perturbed about the possible effects of the continued presence of detergents on the purification plant and on consumers.

There is no simple answer to this problem. The use at sewage works of water-sprayers or of chemicals with an anti-foaming action has been suggested. These, however, would increase the cost of sewage treatment and might bring other difficulties in their train. Workers in the U.S.A., who have longer experience of the trouble, have so far not found a solution. Clearly there is urgent need for research, in which we hope that the authorities and scientists interested will have the full coöperation of the manufacturers.

ONE REGISTER FOR PHARMACISTS

Unlike medicine or dentistry, pharmacy has two statutory registers, and consequently the term "registered pharmacist" includes the two groups, "pharmaceutical chemists" and "chemists and druggists." The reasons for this apparent anomaly lie in the history of the profession. The first Pharmacy Act, passed in 1852, sought to prevent ignorant and incompetent persons from assuming the title of, or pretending to be, pharmaceutical chemists or pharmaceutists or members of the Pharmaceutical Society. Accordingly the Act directed that a register of pharmacists and their assistants and apprentices should be established and maintained. Seventeen years later further legislation permitted assistants to become "chemists and druggists," entitled to sell and supply poisons, so that for over eighty years there have been two registers of people with these privileges.

Pharmaceutical chemists form less than one-tenth of the membership of the Pharmaceutical Society (membership of the society has been coextensive with registration as a pharmacist since the Pharmacy and Poisons Act, 1933, became law). They have had no advantages, apart from that of title and the benefits of having reached a higher educational standard. Formerly, the majority help housewives with damaged hearts to find easier ways of doing their work Some general advice on planning the work so as to walk and reach as little, and to sit as much, as possible is followed by photographs and descriptions of a simplified kitchen Tools are hung on hooks, within easy reach of the housewife sitting at the bench, and at the sites where they will be most often used Materials and supplies are placed on shallow shelves in the same vicinity Thus at the "mix centre"—the bit of bench which the housewife uses for pastry making and mixing ingredients—the rolling-pin, spoons, measures, sugar and flour, dried fruits, flavouring agents—are on shelves facing the sitting housewife, all within easy reach, and the pastry bowl is kept on a shelf fixed on the inside of the cupboard door which swings open at her knee. The sink is backed by shelves for detergents, and is flanked by the "vegetable centre," where the day's vegetables are stored in a wire basket at the back of the bench and the necessary knives and parers hang in rows beside the cooking pans This part of the bench is pierced with a large hole closed by a chromium lid which fits flush with the surface When the lid is removed the hole is directly over a tall rubbish-bin standing in the cupboard below, and vegetable parings are dropped straight through into it The can, like the pastry bowl, stands on a shelf on the cupboard door, and when the door is opened the can swings out with it and is easily removed for emptying

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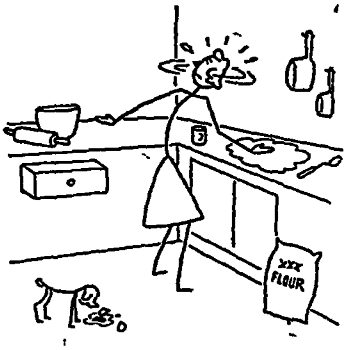
[1] Adam, N. K., Stevenson, D. G. *Endeavour*, January, 1953, p. 25.

[2] Sisley, J. P. B. *Corps gras industr.* 1943, 1, 66.

[3] Hodgson, G. *Practitioner*, 1953, 170, 166.



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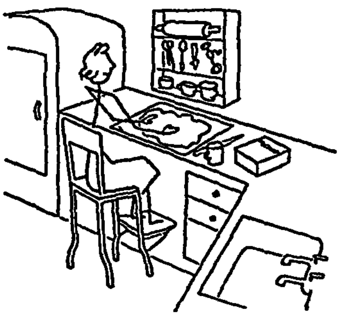

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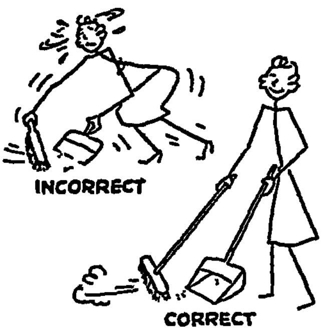
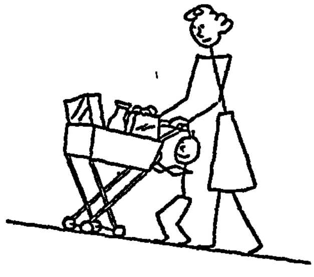


The "heart" housewife, like Dr Cooksey's patients, has a trolley for moving plates and dishes, but a very light one It, too, is the same height as the bench, the oven, and the top of the cooker Some cupboards in this kitchen are partitioned vertically to hold baking tins and other objects often stacked inconveniently in piles Everyday china is stored at the right of the sink in a set of shelves open at both sides, like a hatch, thence it can be transferred to the trolley with little effort Tinned foods and other things used first at the stove (like gravy-browning) are stored, one tin deep, on shallow shelves near the cooker Small pieces of equipment used for many purposes (like measuring spoons) are duplicated and kept in the various sites where they will be needed Long-handled brushes and dustpans save the housewife from stooping, and she uses dusting mittens (not so far current in England) which allow her to dust with both hands Her chair has wheels on the back legs, so that she can push it about like a barrow, and when she goes marketing she uses a shopping cart with a light frame and canvas container to bring home her purchases.



The canvas shopping cart.

AMERICAN PLANNING FOR HEALTH

THE MAGNUSON REPORT

In December, 1951, President Truman announced that he had signed an executive order creating the President's Commission on the Health Needs of the Nation The major objective of the commission would be to make a critical study of total health requirements in the United States, both immediate and long range, and to recommend courses of action to meet those needs

Less than a year later, on Dec 18, 1952, the chairman of the commission, Dr Paul Magnuson, submitted the commission's report and recommendations, and concluded his letter of transmittal with these words "In all humility we think that this report lays the groundwork for men of good will to unite in a common effort to improve the people's health, the backbone of our democratic strength in a free world"

The report is in five volumes, of which the first embodies the commission's principles, major findings, and considerations[1]

To investigate and report on the health needs of 155 million people within twelve months is no light task by any standards, and it is first necessary to inquire as to the qualifications of the people who accomplished it

Dr Paul Magnuson is professor emeritus of bone and joint surgery at Northwestern University, Illinois The vice chairman, Chester I Barnard, is chairman of the National Science Foundation, and the commission includes Dean Clark, Lowell Reed, and John Grant Of the sixteen members, including chairman and vice chairman, six are medically qualified, two were dentists (including the late Ernest G Sloman), one, Marion Sheahan, is a registered nurse, and the remainder are laymen The lay interests are extraordinarily wide, with such people as Walter P Reuther, president, United Automobile Workers, Clarence Poe, president and editor, the *Progressive Farmer*, Elizabeth Magee, secretary, National Consumers' League, the president of the International Association of Machinists, Joseph C Hinsey, PH D, dean of Cornell University Medical College, and the president of Fisk University

METHODS

The commission first assessed, with the help of its technical staff, the total health resources of the country, and then set out to estimate the health needs of the American people Not surprisingly they found this the most difficult of their tasks It was accomplished by means of panel sessions, at which more than four hundred experts appeared (the official record of these panels runs to more than two million words), and by eight regional public hearings "at the grass roots," right across the continent from Philadelphia to San Francisco "The public outpouring at these hearings was so great that a number of them ran two or three hours beyond the scheduled closing time" In addition to individual panels, joint panels, and public hearings, monthly commission meetings were held lasting from two to six days each

Volume 1 of the report deals with all aspects of the subject under investigation—*population*, vital statistics, tendency to cause intestinal colic and, more rarely, vomiting.

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[1] Building America's Health a report to the President by the [illegible] on the Health Needs of the Nation. [illegible] Vol 1 [illegible] Recommendations Washington 1952

Osserman and Kaplan [8] have described their experience with a new antimyasthenic substance as a diagnostic agent. This substance, edrophonium chloride (3-hydroxyphenyldimethylethyl-ammonium chloride) was given intravenously in a 10 mg. dose without atropine. Results comparable to those from 0·5 mg. of neostigmine were seen, with no unpleasant side-effects, in 15 myasthenics. The new drug has a brief action of less than an hour, and will therefore have no place in treatment. In the consulting-room and the outpatient department, however, it should prove useful because of the absence of side-effects and the fact that if a first injection gives a doubtful result a second, larger dose may be injected an hour later. Doses of up to 20 mg. are well tolerated.

HEPATIC BLOOD-FLOW

THERE is as yet no satisfactory simple method of determining the hepatic blood-flow in man. A reliable indirect method would be invaluable to the clinical scientist; direct measurements such as those made in animals are of course out of the question.

The methods now in use are based on the Fick principle, by which the volume of blood passing through an organ can be calculated from the difference in concentration of some arbitrarily chosen substance in the afferent and efferent blood. To make this calculation in the case of the liver, samples of blood must be obtained from the hepatic veins—by no means a simple matter. Several observers,[9] [10] however, have used this method with bromsulphalein as the test substance; and the average hepatic-flow in subjects without hepatic disease was 1 ml. of blood per ml. of liver substance per minute. A further serious drawback to this method has been revealed by having the catheter in different positions in the hepatic vein; this has shown that different areas of the liver differ in their ability to extract the dye. Thus it is almost impossible to obtain a true mixed hepatic-vein sample.

Dobson and Jones[11] have shown that the phagocytic activity of the liver for radioactive particulate matter injected intravenously gives a guide to the hepatic blood-flow; and thus the need for catheterisation of the hepatic vein is obviated. They showed in dogs, rabbits, mice, and rats that over 90% of an appropriate suspension of radioactive chromium phosphate was retained within the liver and spleen. Moreover the liver extracted more than 90% —i.e., hepatic venous blood contained less than 10% of the radioactive material that was present in portal blood. (Since almost all the blood passing through the spleen also flows through the liver, the phagocytic activity of the spleen does not significantly affect the calculation of hepatic blood-flow based on the rate of removal of the radioactive suspension.) It is therefore apparent that, at least in these animals, hepatic blood-flow could be calculated fairly accurately from the rate of removal of the intravenously injected test substance. After the material has been injected intravenously samples are withdrawn at short intervals to estimate the quantity still remaining in the blood-stream. From the time taken for this to fall to 50% of the initial value, the minimal hepatic blood-flow can be readily calculated. This figure is a minimal value because the calculation is based on the supposition that the liver removes 100% of the foreign particulate material brought to it. The correct figure is probably only 90%, and the true hepatic blood-flow is thus 10/9 times that calculated.

Owing to the undesirability of injecting radioactive material, Dobson and Jones have restricted their clinical study to cases in which such injections were given for therapeutic purposes. Three cases of malignant disease with grossly enlarged livers were investigated. Owing to the obviously pathological state of the liver, the values obtained for hepatic blood-flow were probably grossly abnormal; these values ranged from 0·7 to 1·7 volumes of blood per volume of liver per minute. The principle of the test does not, however, depend on radioactivity per se; and there is no reason why non-radioactive inert particulate material should not replace the chromium phosphate used in these experiments. All that is required is some substance that can be easily and accurately estimated in micro quantities. Alternatively a radioactive particulate substance could be used which has a much shorter half-life than 14 days—the half-life of the P^{32} used in the radioactive chromium phosphate. With such material the hepatic blood-flow and the factors influencing it could be safely studied in man.

WEATHER AND POLIOMYELITIS

POLIOMYELITIS keeps cropping up in the winter, but the great majority of cases arise in the summer and autumn. One unexplained exception to this rule, however, has been reported from Melbourne, where the three main poliomyelitis epidemics since 1937–38 have reached their peak between July and October—the coldest and wettest season of the year.[1] In New York State the ratio of summer to winter cases in a series of epidemics was 12 : 1, compared with 2·2 : 1 in Japan during the same period.[2] This suggests that degree of climatic difference between summer and winter may be an important factor in determining the seasonal distribution of cases; but it would be unwise to assume that the endemic poliomyelitis of Japan can be simply compared with the epidemic disease of the U.S.A.

In the United Kingdom the first great epidemic of poliomyelitis was in the summer of 1947, which was hotter than the average; and at the time it was widely believed that this might be a causal factor. Bradley and Richmond [3] have now studied the relation between temperature and humidity readings and the incidence of poliomyelitis in England and Wales during the six years 1947–52. The average weekly dry-bulb and vapour-pressure readings in London, Plymouth, Manchester, and Tynemouth were tabulated against the estimated number of people infected each week. These figures for infection were calculated by dating back the uncorrected weekly notifications by three weeks, in order to bring them as far as possible into line with the meteorological conditions at the time when the patients were likely to have been infected. The results are inconclusive; but they do confirm that poliomyelitis in these six years was definitely seasonal, the season each year extending from the 18th to the 42nd week. The rise in each year did not take place until a certain level of temperature and humidity had been reached; but these alone did not necessarily initiate the rise. The seasonal fall was even more independent of such meteorological factors. Moreover the incidence of poliomyelitis during the season was not clearly related to variations in temperature and humidity. The seasons with the lower average dry-bulb and vapour-pressure readings tended to have the lowest incidences of poliomyelitis; but this could have occurred by chance. It seems clear that other factors besides high temperature and humidity determine whether there shall be an epidemic of poliomyelitis.

DR. HAROLD BALME, consultant adviser on rehabilitation to the Ministry of Health and to the World Health Organisation and a former president of Cheeloo University in China, died on Feb. 13 at the age of 74.

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8. Osserman, K. E., Kaplan, L. I. *J. Amer. med. Ass.* 1952, 150, 265.
9. Bradley, S. E., Ingelfinger, F. J., Bradley, G. P., Curry, J. J. *J. clin. Invest.* 1945, 24, 890.
10. Lavers, G. D., Cole, W. H., Keeton, R. W., Gephardt, M. C., Dyniewicz, J. M. *J. Lab. clin. Med.* 1949, 34, 965.
11. Dobson, E. L., Jones, H. B. *Acta med. scand.* 1952, suppl. 273.

1. Annual Report of Fairfield Hospital, Melbourne, 1952.
2. Paul, J. R. *Amer. J. Hyg.* 1947, 45, 206.
3. Bradley, W. H., Richmond, A. E. *Mon. Bull. Minist. Hlth Lab. Serv.* 1953, 12, 2.

commission's endorsement of the prepayment principle and Federal matching grants to States (on the basis of relative wealth and need), but emphasises the desperate need for prompt action among the rural population of America Dr Hinsey concurred in the financial recommendations only if free choice of health personnel and freedom of type of practice were maintained, and a system of remuneration mutually satisfactory to members of the health professions and the public could be devised

The United States has no unified central health department, and the report reveals some of the reasons for this They include opposition by the Veterans Administration and the Department of Defense, which fear the dangers to their medical services, and "the zealousness of some of its partisans to give this Department a bigger bite than it can possibly chew in its formative years" The recommendation is brief and to the point it is that "the Congress establish a Department of Health and Security" Dr Hinsey again dissented as he considered that the matter required further study Mr Graham and Dr Russel V Lee felt that there should be a Department of Health with cabinet status but had doubts on extending its function beyond health activities

SPECIAL PROBLEMS

The report next turns to special aspects of health service, including the expansion of programmes of disease detection, and especially multiple screening, a bold attack on chronic disease to be promoted by the health departments, and the development of home care services Research into mental illness must be given top priority, and prevention of accidents a high priority Also "less time should be spent on perfunctory annual examinations of school children as they are too often performed today," and more time devoted to careful health screening and follow-up

The report examines the special problems of industrial workers and rural people, including the deplorable conditions of migratory labourers The problems of ageing, the veterans, the rural Negro, and the Indians are all carefully considered and the difficulties of drafting doctors, dentists, and veterinarians into the armed forces (obviously a sore point) are recommended for further study

PROPOSED HEALTH COMMISSION

Finally comes the recommendations that

1 The Congress establish a Federal Health Commission

2 Comparable bodies be established in State and local communities

The Health Commission is to fill the rôle of constant critic and evaluator with an absolutely free hand, while the Federal health department would be primarily an administrative organ of government The health commissioners should receive no salaries, not more than half the members should be professional health workers, and no member should be an officer or employee of either Federal or State government The commission should have the power to hold public hearings, and should make an annual report to the President and the Congress on the health status and health needs of the American people, including recommendations for legislation whenever this is indicated

THE COST

As to the total cost of the recommendations, the Federal government at present spends just over 1000 million dollars each year on civilian health activities The health programme outlined in this report would require an annual Federal expenditure of approximately 1000 million dollars more

Parliament

Prevention of Misuse of Drugs

In the House of Lords on Feb 12 the **Earl of Onslow**, moving the second reading of the Therapeutic Substances (Prevention of Misuse) Bill, said that its main object was to empower the Minister concerned to regulate the use of new drugs This applied particularly to isoniazid, a cheap product, which at the moment did not come within the scope of the 1947 Act, and could, if used for self-medication, do great harm The other purpose of the Bill was to allow the Minister and his colleagues by regulation to permit the use of certain of these drugs particularly at the moment penicillin, in the feeding of pigs and table poultry

Lord **Amulree** thought that if penicillin was to be fed to pigs, it must be supplied by a veterinary surgeon, otherwise people might buy it for themselves He also suggested that the Royal Veterinary College should be consulted about any regulations to be made under the Bill when it became an Act Lord **Haden-Guest** was doubtful whether it was necessary to add the veterinary surgeons to the two well-qualified bodies—the Agricultural Research Council and the Medical Research Council—under whose advice the supervision of the giving of penicillin was to be

Replying to the debate, the **Earl of Onslow** said the A R C and the M R C were satisfied that penicillin fed to pigs in this form could do no harm The quantity was so small that it could not affect the consumers of the pig meat The penicillin would be fed in one of two ways, either in a compound food, where the makers would have to put on the compound a statement of what had been included in it, or in a special mixture—so diluted that it was impossible to extract the penicillin for use in other ways—which the farmer would then be able to mix in his own feeding-stuffs He was quite satisfied with the assurance that there could not be anything harmful in the admixture in the feeding stuffs for either poultry or pigs

QUESTION TIME

Health Services Charges

Mr **Arthur Blenkinsop** asked the Minister of Health the number and cost of prescriptions issued, dental treatment provided, and appliances issued, for which charges were imposed under the National Health Service Act, 1952, for November and December, 1952, compared with the figures for November and December, 1951 —Mr **Iain Macleod** replied The following are the figures for England and Wales

PRESCRIPTIONS

—	Number of prescriptions		Average cost per prescription	Total cost
November 1951	19,034,911	actual	46 02*d*	£3 649,880
December, 1951	17,815 111		46 58*d*	£3,457 607
November, 1952	17 439 000	declared by chemists	Not yet available	
December 1952	20 100 000			

These figures include prescriptions for appliances ordered by [illegible] and dispensed by chemists and prescriptions [illegible] and dispensed by chemists [illegible] number of prescriptions

DENTAL TREATMENT

—	1951		1952	
	Nov	Dec	Nov	Dec
	£	£	£	£
Number of completed courses of dental treatment under normal procedure (other than for the provision of dentures to which the 1952 Act charges do not apply) *	363,000	388,000	414 000	333,000
Number of courses for limited treatment provided under simplified procedure †	236,000	201 000	127,000	102,000
Cost to the Exchequer	950 000	1 000 000	850 000	700 000

* Less than half the courses given were subject to charges under the 1952 Act The remaining courses were started before June 1 or were for items of treatment to which the charges do not apply or were for the exempted classes of patients

† The courses for limited treatment, which consist largely of extractions of one or two teeth, usually cost under £1 and many patients may therefore be assumed to have had the treatment privately

patients who need support can grasp the sides firmly and use the trolley as a walking-chair (fig. 2). Patients working at the sink need never lift a kettle to fill it, for the taps are fitted with a swinging delivery pipe, of the type used in operating-theatre basins, which will fill a kettle as it stands on the draining-board. Moreover, the taps turn on and off by levers.

A flap which pulls out from the front of the bench is pierced with three circular holes, one of a diameter to take a pastry bowl, one to take a pudding basin, and one fitted with a gripping lining which holds jars firmly so that their lids can be removed with one hand. A square socket fixes tins of a standard size, for the same purpose. A clamp fixed to the bench behind the pastry bowl can be used to hold a variety of tools—a potato-peeler, an egg-whisk, a mincer, a grater, and others. The hemiplegic housewife is thus able to do with one hand many jobs which normally take two. Along an overhead track, running from end to end of the bench, a sling attached to a spring can be made to travel (fig. 1). A weak arm (damaged perhaps by poliomyelitis) which cannot work against gravity will often do much more when supported in such a sling (fig. 3). A bow-fronted cupboard at one corner of the bench is fitted with circular shelves which rotate round a pivot, so that there is never any need to reach to the back of a shelf, or take out half the contents in search of one elusive tin.

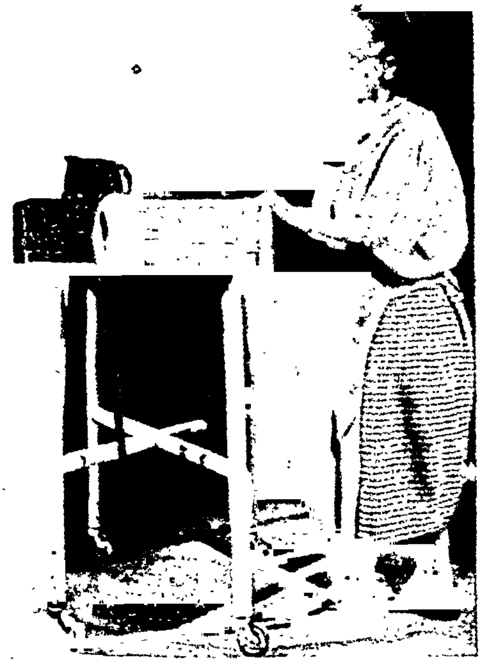
Fig. 2—The food trolley used also as a walking-chair.

The oven lights from a pilot jet when a tap is turned. Hot dishes are transferred to the trolley and wheeled to the table, where—since the table is usually the lower—a flap can be let down from the trolley to form a slope down which the hot dish is gently slid. Arthritic patients who find it difficult to sit, or to rise from ordinary chairs, are provided with stools with seats at the height to suit them, and with the seats sloping downward and forward. Such a stool, made to suit the individual in the hospital workshops, allows the patient to take the weight off her painful joints when working. Those who are not too steady on their legs find their confidence greater when using a safety-belt, clipped to the front of the bench by leash-snaps. In this very kitchen patients take it in turns to prepare the daily dinner eaten by the dozen or more patients, men and women, attending the reablement department throughout the day.

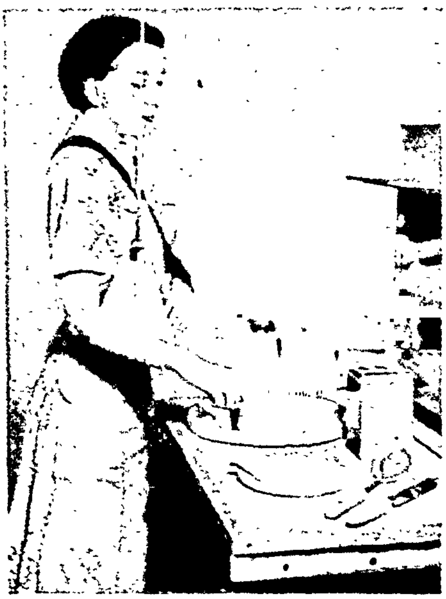
Fig. 3—Working with the sling which runs along an overhead track.

EQUIPPING THE HOME

Most of the equipment used is so simple that it can easily be copied in the patient's own home; and when the housewife leaves hospital the occupational therapist from the department goes to her home and discusses with her and her husband what she will need in her work—usually a board between cooker and sink, to save lifting, a board to steady bowls, a universal clamp for tools, and perhaps a trolley and stool. Most of these things are made by patients in the workshop and supplied at the cost of the materials used. A curtain-runner makes a good overhead track for a sling, and handrails are easily fitted in lavatories and bathrooms. If the family cannot meet the cost, the almoner helps to find ways of paying it. Recently[2] Lambeth Borough Council decided to make the necessary alterations for patients who live in their flats—a generous and sensible decision, for the time of everybody in the family is saved if the housewife is able to do her own work.

A DAILY CLUB

One need is still unfulfilled. Some men and women patients, too old or disabled to work, and often living alone, are allowed to go on attending the reablement department on two or three days a week, partly to continue with occupational therapy, and partly because they benefit from the company and activity. Dr. Cooksey would like to be able to establish a kind of club for such patients, outside the hospital though linked with it, where they could meet daily, take responsibility for the management, and cook the midday meal. Some of the disabled men, especially, would benefit by this arrangement, for it often happens that their wives, who could otherwise go out to work (and would like to do so, to relieve financial stringency), are obliged to stay at home to look after them. In such a club the disabled could look after and cheer each other. Such a reasonable project deserves success; and other hospitals would doubtless profit from the lead.

A Kitchen for Heart Cases

Hearts can be disabled as well as limbs. The American Heart Association has published a booklet[3] designed to put into the tank without loss of water or fish A satisfactory rise in temperature was recorded But darkness was falling and our patients had to go to bed The bottles needed refilling, if the fish were to survive There seemed to be no-one available to do this until our Night Sister, in common parlance, "blew in" Scorning the modified polar costume we were wearing, she retired to arrange her cap and cuffs, then, with electric torch held in her teeth, set off with the hot-water bottles, avoiding groaning and crashing trees, to the fish tank She was later reported to have been anxious lest she inadvertently crush one of the angel fish while inserting the fresh jars

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[2] *Manchester Guardian*, Nov. 22, 1952.

[3] The Heart of the Home. American Heart Association, 1775, Broadway, New York 19, New York, U.S.A. Pp. 28. 10 cents.

When our supply of electricity was renewed after two days, it was discovered that there had been one death among the fish, a neon tetra It was suggested that this might have been due to an overdose of phosphorescent material, self-administered

* * *

CRI DU CŒUR

One gropes around in darkness, kneeling on the muddy road,
To fix the jack which always slips just as it takes the load
One prises off the dust cap and by sundry feats of strength
Loosens the nuts that fix the wheel, one gets it off at length
By further skill, but mostly force, one levers out the spare,
As like as not one finds it flat so pumps it full of air
And carries it with sighs and grunts and rams it into place,
Pausing but long enough to wipe a red and sweating face
One finds the nuts and screws them on—they must be screwed on tight—
But cannot find the dust cap which has vanished in the night
Repeating strings of awful oaths which one should not repeat,
Blackened with rage and oil and grime one takes the driving seat,
Drives off at speed but two miles on is horrified to find
The wheel so painfully removed was somehow left behind
A melancholy story—which impels one to inquire
Why has nobody invented an unpuncturable tyre ?

* * *

In a country where many things are changing rapidly, the Uganda Railway is still much the same as when Treves recorded his journey on it in 1910 True it has twice changed its name, but the average speed of its trains is still less than 18 miles an hour, which allows ample time to watch the game animals and the birds which use the telegraph wires as perches

But it is the stations which provide the greatest source of interest There the features of many different tribes may be observed, while the scanty clothing permits the observation of many pathological lesions The children are most easily studied, for many of them still wear no garments Umbilical herniæ are common, and others have pot bellies on which the outlines of enlarged livers and spleens can be imagined On our journey we saw one child with the typical gait of congenital hip dislocation and another with severe flexion deformities of the knees Many natives show scars in which pigment is lacking in comparison to the remainder of their skin, while the eye conditions would provide a feast of clinical material for the ophthalmologist. The garments of the men fail to conceal the fact that hydroceles are still common, as they were in Albert Cook's early days, while there are beggars with deformities which would require further investigation

Apart from these pathological conditions, the abnormalities wrought by tribal custom are interesting—the stretched lobes of the ears, the loop of which may be turned up and suspended over the apex of the pinna, or else left hanging down perhaps as far as the shoulder, the perforated lower lip of certain northern tribes containing a metal ornament, or the ala nasæ punctured to carry a ring Finally the custom of smoking a cigarette with the lighted end inside the mouth has to be seen to be believed

Certainly a fascinating journey, and I, for one, am glad the trains go no faster

* * *

Nature Note—The first spring greens of the season evoke the same sort of response from the salivary glands that daffodils do from the spirit Ours, though looking in the dish like a wreath for Primavera, turned out to taste of nothing in particular They smelt of nothing in particular too We were puzzled until we remembered it was because of the chlorophyll

Letters to the Editor

INTUSSUSCEPTION

SIR,—We feel sure that many will share our disagreement with your leading article (Jan 31) on intussusception In the past nine years 378 children with this condition have been seen in the children's department here, and it is from this experience in which we have collaborated that our comments are made

We agree that the pessimistic statement "clinical statistics on the efficacy of any particular form of treatment are seldom very reliable" has been true for many papers on intussusception, but it need not be so if the type of case, and method of treatment, are carefully defined From this point of view the term intussusception, by itself, does not take us very far For valid comparisons we must know the exact ages of the children in the series, the proportion of small-bowel, "boundary," and large bowel invaginations, and, above all, the duration of the symptoms when treatment was applied

When these factors are comparable we find that both surgical reduction, and enema reduction combined with surgery when necessary, will be equally successful provided the operator in each case is thoroughly experienced in the technique employed This proviso of course has important professional and administrative implications which we cannot take up here

As early as 1937 Hipsley,[1] using saline enema reduction as his first approach, achieved a mortality of 4% A comparison with those series managed by surgery which were available at that time, suggested the undoubted superiority of Hipsley's method A careful scrutiny of his paper, however, supplemented by personal inquiry, showed that the majority of his children were admitted within the first twenty-four hours of the disease This early admission also applied to the careful series using barium enema reduction under direct vision described by Nyborg,[2] and by Hellmer [3] On the other hand, our own mortality with surgical reduction has always been less than 4% for cases admitted within twenty four hours, - and in 1951 and 1952, for acute cases (i e, cases admitted in under five days) the over all mortality has been just over 1% An account by one of us (J D T J) of the children treated during this two year period is at present awaiting publication The reasons why the mortality has fallen from 10% to 1% over the nine years, seem to us clear and important Firstly, in 1944 (excluding chronic intussusception) only 31% of the children reached hospital within twenty four hours and 48% in forty-eight hours whereas in 1951 and 1952 the figures were 54% and 85% Secondly, operation is always preceded by the careful correction of shock and fluid loss Lastly—and this represents a significant change from our last communication on the matter in 1950 [4]—the surgery of intussusception is now confined to a small number of surgeons who are giving much of their time and thought to the emergency surgery of childhood in this hospital

This brings us to our second major criticism You say "there seems to be no particular advantage in the Mickulicz type of two stage exteriorisation procedure", but during 1951 and 1952 bowel resection was carried out in 9 children with acute intussusception with only 1 death Although we have not used the classical Mickulicz type of operation, all these resections were carried out by a two stage procedure Our reasons for favouring this method will be given in the forthcoming article already mentioned

We must also take issue with the phrase "the inconstancy of symptoms" We find that where careful

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1 Hipsley P L *Surgery*, 1937, 1, 825
2 Nyborg S *Acta chir scand* 1943, 89 1
3 Hellmer, H *Acta radiol Stockh* 1948 suppl 65
4 Spence, J, Court, D *Brit med J* 1950, ii, 920

patients who need support can grasp the sides firmly and use the trolley as a walking-chair (fig. 2). Patients working at the sink need never lift a kettle to fill it, for the taps are fitted with a swinging delivery pipe, of the type used in operating-theatre basins, which will fill a kettle as it stands on the draining-board. Moreover, the taps turn on and off by levers.

A flap which pulls out from the front of the bench is pierced with three circular holes, one of a diameter to take a pastry bowl, one to take a pudding basin, and one fitted with a gripping lining which holds jars firmly so that their lids can be removed with one hand. A square socket fixes tins of a standard size, for the same purpose. A clamp fixed to the bench behind the pastry bowl can be used to hold a variety of tools—a potato-peeler, an egg-whisk, a mincer, a grater, and others. The hemiplegic housewife is thus able to do with one hand many jobs which normally take two. Along an overhead track, running from end to end of the bench, a sling attached to a spring can be made to travel (fig. 1). A weak arm (damaged perhaps by poliomyelitis) which cannot work against gravity will often do much more when supported in such a sling (fig. 3). A bow-fronted cupboard at one corner of the bench is fitted with circular shelves which rotate round a pivot, so that there is never any need to reach to the back of a shelf, or take out half the contents in search of one elusive tin.

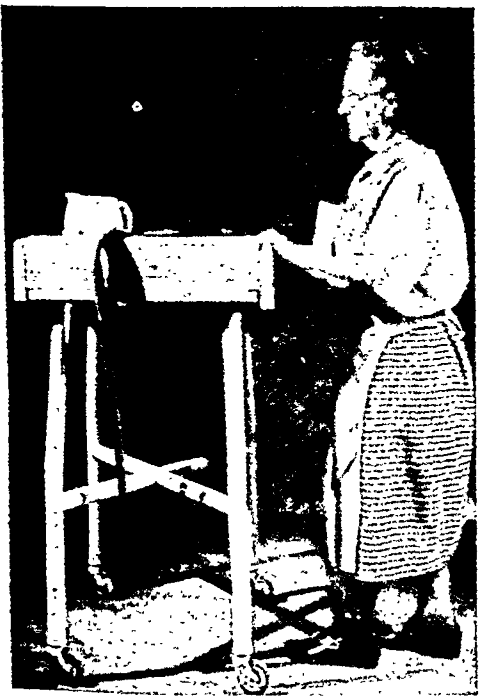

Fig. 2—The food trolley used also as a walking-chair.

The oven lights from a pilot jet when a tap is turned. Hot dishes are transferred to the trolley and wheeled to the table, where—since the table is usually the lower—a flap can be let down from the trolley to form a slope down which the hot dish is gently slid. Arthritic patients who find it difficult to sit, or to rise from ordinary chairs, are provided with stools with seats at the height to suit them, and with the seats sloping downward and forward. Such a stool, made to suit the individual in the hospital workshops, allows the patient to take the weight off her painful joints when working. Those who are not too steady on their legs find their confidence greater when using a safety-belt, clipped to the front of the bench by leash-snaps. In this very kitchen patients take it in turns to prepare the daily dinner eaten by the dozen or more patients, men and women, attending the reablement department throughout the day.

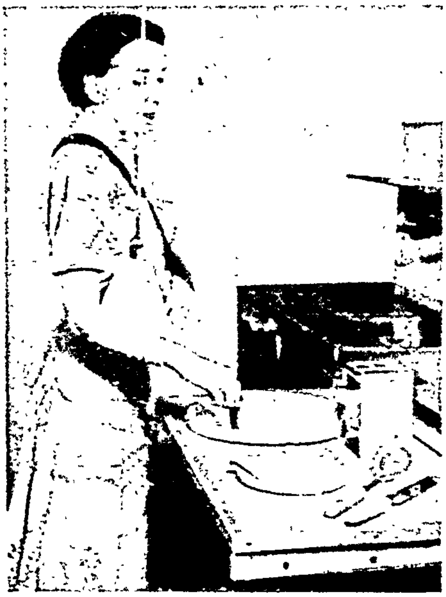

Fig. 3—Working with the sling which runs along an overhead track.

EQUIPPING THE HOME

Most of the equipment used is so simple that it can easily be copied in the patient's own home; and when the housewife leaves hospital the occupational therapist from the department goes to her home and discusses with her and her husband what she will need in her work—usually a board between cooker and sink, to save lifting, a board to steady bowls, a universal clamp for tools, and perhaps a trolley and stool. Most of these things are made by patients in the workshop and supplied at the cost of the materials used. A curtain-runner makes a good overhead track for a sling, and handrails are easily fitted in lavatories and bathrooms. If the family cannot meet the cost, the almoner helps to find ways of paying it. Recently[2] Lambeth Borough Council decided to make the necessary alterations for patients who live in their flats—a generous and sensible decision, for the time of everybody in the family is saved if the housewife is able to do her own work.

A DAILY CLUB

One need is still unfulfilled. Some men and women patients, too old or disabled to work, and often living alone, are allowed to go on attending the reablement department on two or three days a week, partly to continue with occupational therapy, and partly because they benefit from the company and activity. Dr. Cooksey would like to be able to establish a kind of club for such patients, outside the hospital though linked with it, where they could meet daily, take responsibility for the management, and cook the midday meal. Some of the disabled men, especially, would benefit by this arrangement, for it often happens that their wives, who could otherwise go out to work (and would like to do so, to relieve financial stringency), are obliged to stay at home to look after them. In such a club the disabled could look after and cheer each other. Such a reasonable project deserves success; and other hospitals would doubtless profit from the lead.

A Kitchen for Heart Cases

Hearts can be disabled as well as limbs. The American Heart Association has published a booklet[3] designed to

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[2] *Manchester Guardian*, Nov. 22, 1952.

[3] The Heart of the Home. American Heart Association, 1775, Broadway, New York 19, New York, U.S.A. Pp. 28. 10 cents.

75%—will be completely denied this type of service *Theoreticians who do not realise the practical consequences of such an action may be compared with those who have in recent years exacerbated the problem of the care of the aged by decreeing that, as every aged person can have his own doctor and hospital services are free, there is no further need for the relieving officer or compulsory financial responsibility of relatives A similar devastating error was the cause of the partial collapse of the priority dental services, when dental attention was made available to all even though the priority dental services were given special mention in the National Health Service Act itself

Finally, as some of your correspondents have pointed out, in the interests of social medicine it is surely necessary that the family doctor should, as his name implies, look after all members of the family, and to introduce a special type of pædiatrician general practitioner who would remove the child from the care of the family doctor would be a most retrograde step

I GORDON
Ilford
Medical Officer of Health

COLLEGE OF GENERAL PRACTITIONERS

SIR,—The undersigned general practitioners met informally on Jan 14 to discuss the implications for Irish doctors of the report of the General Practice Steering Committee[1] and the subsequent foundation of the College of General Practitioners in London

It was unanimously agreed that these developments were of considerable importance and that a meeting representative of all general practitioners should be called in the near future in order to have the fullest discussion on the subject and to decide upon a unified line of action Through the courtesy of the authorities of University College, Dublin this meeting will be held in the college on March 15

This promises to be the most important meeting ever held in this country in relation to general practice We hope that it will be attended no matter what the personal inconvenience not alone by all those already working in this branch of medicine whether as dispensary doctors, private practitioners, or in any other circumstances but also by the newly qualified men and women intending to make general practice their career

It may be useful for those attending if some of the points raised at the preliminary discussion are mentioned here Irish practitioners have four choices in relation to the new college

(*a*) Individuals having the necessary qualifications may join as members or associates
(*b*) An Irish faculty of the new college may be formed (the method of doing this is being investigated)
(*c*) An independent Irish college may be formed
(*d*) They may do nothing

The signatories of this letter feel that some definite step must be taken to ensure that Irish general practitioners may be enabled to secure full reciprocity with their opposite numbers in England and that nothing should be neglected which would tend to maintain the status of the general practitioner

It is scarcely necessary to point out that the field of medicine embraced by the term "general practice" has narrowed very considerably in recent years and that many G P s find themselves dealing only with the clinical trivialities while patients whom they could well treat gravitate elsewhere

In the opinion of most general practitioners there is room for great improvement in the training of medical students, for, while the great majority are destined to enter general practice, they are never taught however briefly by a general practitioner, and rarely if ever see the run of-the-mill cases which make up a G P's round and are first introduced to the G P the hard way—hard alike for the newly qualified doctor and his patients

There is no intention among the undersigned that any new group, college, or faculty formed shall be a competitor or rival of existing institutions, but rather that it shall be a co-equal partner with the object of improving the professional status of the general practitioner secondary only to the maintenance of high ethical and clinical standards in the profession as a whole.

We appeal most earnestly for a full attendance of our colleagues in University College, Dublin, on Sunday March 15, at 11 30 A M

DESMOND CARNEY
D S KEARON
NORA MCNALLY
ANDREW E H O'BYRNE
J F O'GRADY
E A O'REILLY
JOHN FLEETWOOD
JOHN J MCCANN
LAURENCE MASTERSON
J ST L O'DEA
ROBERT O'MEARA
A RYAN

DAILY PAPER PANTHEON

SIR,—I should like to congratulate you on "Daily Paper Pantheon" in your issue of Jan 31 As doctors we can count nothing human as alien and any clues to the discontents of our time must be specially welcome to us

If, as Dr McGlashan says, "the *gods*" are inevictable tenants of the human heart, how foolish have been the intelligentsia of the West in rejecting, and in persuading popular fashion to reject, that most profound and evocative version of the story of the paradoxical hero which is its religious heritage

My own conviction of the truth of Christianity does not derive from its correlation with the universal common denominator of the basic spiritual needs of mankind, but the fact is of great value for apologetics It is difficult to think too hardly of those persons who, in pursuit of a false simplicity and an allegedly higher concept, have tried to purge Christianity of its supernatural elements and have thereby done more to render it unattractive to the masses than all the atheists and unbelievers in frank opposition

JOSEPH V WALKER
Darlington

PARONYCHIA

SIR,—May I reply to some of the points raised by correspondents following the publication of my article (Jan 17)

I am sure that Dr Wheatley (Jan 24) is right when he suggests that usually paronychia can be—and is—aborted in general practice by the early exhibition of penicillin Sepsis of the hand can nearly always be aborted by the *early* exhibition of penicillin, because it is almost invariably due primarily to infection by sensitive organisms Such treatment must be very early in some cases, because in the subcuticular type of paronychia spread may be very *rapid*, and occasionally twenty four hours is long enough for a case to become out of reach of conservative measures Once pus forms the situation changes, and surgery is indicated—as it always has been Nowadays, however, operation on an abscess is incomplete if the only object is to "let pus out" Operation is also aimed at letting the antibiotic in, and this is a second principle which should activate the modern approach to minor surgery Failure to appreciate this is at the bottom of many so called "resistant" infections

The routine dosage of penicillin is that referred to by Ellis[1] We have not tested our organisms against chloramphenicol and penicillin mixed together, so I cannot comment on this, but I cannot endorse health personnel, resources and organisation, medical research, finance, special problems, and special population groups. The highlights are the recommendations for the establishment of a Department of Health and Security, and of a Federal Health Commission.

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[1] *Brit med J* 1952, ii 1321

[1] Ellis, M *Lancet*, 1951, i, 1038

DEFINITIONS

The commission defines health as optimum physical, mental, and social efficiency and well-being; and it emphasises the responsibility of society to assure its citizens access to professional services, education concerning personal health practices, and a reasonably safe environment. "Future accomplishments, however, depend to an even greater degree upon the individual's assumption of responsibility for his own health."

The doctor is defined in the introductory comments as the leader of the over-all efforts, but as one member of a well-trained team composed of dentists, nurses, technicians, and many other professional workers.

DIFFERENCES AND PARALLELS

It is difficult in Britain, still hard-pressed as a result of two world wars, and in straitened economic circumstances, to appreciate the almost adolescent vigour of the American outlook on the future; and this report must be read with two basic facts in mind. First, the population of the United States has doubled in fifty years; and secondly, Americans are still always on the move. Some 4–5 million people move from one State to another in the course of a year, and another 4 or 5 million from one county to another within a given State. Each year over 3·5 million babies are born, and the population is expected to reach 193 million by 1975.

Allowing for differences in outlook it is interesting to see how history tends to repeat itself.

> "The high number of rejectees among young men called for military service in World Wars I and II and the present Korean episode have awakened the American people to the fact that despite superior medical service and low death rates, Americans are not enjoying as good health as might be expected in this country."

The commission recommends that the Federal government develop adequate methods to measure morbidity.

HEALTH WORKERS

The report underlines the need for more health workers. The minimum estimate of the physicians needed in 1960 is 22,000 more than the predicted supply, and the commissioners are "alarmed at the progressively severe financial situation of our medical education system." Dental research is an urgent need. Dentists are too few; and the more effective utilisation of dental hygienists and of dental assistants is thought to offer the greatest hope for making dental care quickly available to more people. When the report turns to nursing it sounds a note of anxiety, amounting almost to panic, even though there are now more than 365,000 active nurses, compared with 12,000 in 1900. The shortage in 1960 may exceed 50,000. It is not always easy to understand American nursing trends; for it sometimes seems that graduate nurses are turning away from the traditional concept of nursing and becoming administrators, teachers, and clinical assistants, while bedside nursing appears to be in danger of relegation to the less highly trained. Whether that is so or not, the commissioners believe that nursing should become a part of the general educational system of the nation.

The section dealing with paramedical workers—X-ray technicians, dietitians, physical, occupational, and speech therapists, social workers, hospital administrators, and others—is of particular interest.

> "While the several groups of paramedical workers require somewhat different training, there are also basic subjects in which several groups can be trained together. Some universities are already organising schools of 'Auxiliary Medical Services' for the joint recruitment and training of several paramedical groups. This type of program points the way to better training, better use of teaching staffs, and should go a long way in developing workers for the health team."

The report calls for removal of discriminating bars against the training of Negroes in the health professions. Dr. Hinsey expresses his doubts about the advisability of Federal aid in health education, as recommended in the report, with the possible exception of that in graduate schools of public health.

HOSPITALS

The report leaves no doubt as to the place of the hospital.

> "Hospitals are at the heart of our modern medical system . . . more and more it [the modern hospital] is becoming responsible for a continuing flow of health services to the community, supplying preventive services in health centers at one end of the line and rehabilitative and home care services at the other end."

The replacement of obsolete hospitals, and especially outpatient units, is urgently needed.

> "Today a good hospital is in reality a health center which places increasing stress on preventive and restorative services which keep the patient out of a bed. Home care and rehabilitation services should be developed in association with the hospital, which should have also auditoria for medical and community health organisations, and should possess a fine medical library. Every physician in the community should have some affiliation with a hospital."

ORGANISATION

> "The genius for organisation so characteristic of American life in general, is conspicuous in the health services by its absence. . . . In reality most of the American people grope their way through a haphazard array of health services without the guidance of a personal physician."

So begins the section on organisation of health services, and similar frankness is evident in the account of unethical practices which detract from the quality of medical care. Fee-snatching and fee-splitting are touched on, and also ghost surgery—i.e., deception of the patient as to the identity of the doctor who performs an operation.

Regionalisation of health services, and in particular joint use of laboratory, X-ray, and other facilities, is suggested, and also joint purchasing of supplies by a group of hospitals; and it is recommended that Federal loans be made to local organisations wishing to institute prepayment plans associated with group practice. Organised medical bodies are recommended to review their attitude toward group practice in a spirit of tolerance.

The comments on medical research are equally outspoken. "Last year's total expenditure of 180 million dollars amounted to only three tenths of one per cent. of the Nation's defense budget. It was less than the amount spent on monuments and tombstones." The Federal government itself spends over two hundred times as much on military research as on research into heart-disease. Many medical investigators are forced to jump from project to project without any secure underpinning. Research grants should be allocated to all agencies with promise in the health field, not just to medical institutions.

On the thorny question of financing personal health services the commission favours, with proper organisation, the prepayment principle; but it is significant that Walter Reuther, Albert Hayes, and the secretary of the National Consumers' League, dissent. They feel that the objectives set forth throughout the report should be accomplished through a National Health Insurance Act supported by joint employer-employee contributions and tax revenues. Clarence Poe agrees with the

The other was in an old lady who had had a ureteric transplantation and a hysterectomy, she had only one kidney, which was subsequently found to be riddled with chronic nephritis, so the fatal hæmorrhage which ensued was not surprising This emphasises the need to include full clinical details on the request form

Dr Bjerkelund pleads for "long continued treatment of ambulant outpatients" Surely the danger of recurring thrombo-embolic incidents could be substantially reduced if the patient were maintained on ethyl biscoumacetate for longer than is now customary We cheerfully subject people to lifelong liver and insulin injections with accompanying laboratory control, and yet we are reluctant to do the same in the case of dicoumarol or its derivatives If a dosage advisory service could be arranged on the lines indicated above, most of the principal objections to the use of this drug would be overruled Is it not worth it ?

Royal Infirmary
Preston

E B LOVE

HALLUX VALGUS

SIR,—Your leader last week stimulates me to make certain observations on this important subject

Apart from terminal-phalanx hallux valgus, which is congenital, hallux valgus is, I understand, found among peoples who have always been barefoot only in adults, and the disorder appears to be due to injury of the first metatarsus or proximal phalanx Developmental hallux valgus is, I believe, virtually unknown among children who have always been barefoot

Since in this country some 50–75% of adolescents have a developmental hallux valgus (as any school medical officer will testify) only some all-embracing factor, such as tight shoes, can be involved Again, since our Ealing shoe scheme showed quite clearly among growing children that the supply of well-fitting shoes leads to the disappearance of hallux valgus, it is difficult to accept your assumption that "there is commonly no apparent cause whatever for hallux valgus"

The child with a broad foot needs no wide metatarsal angle to have difficulty in finding suitable fittings in foot wear, and children's shoes at a price within the reach of the ordinary parent are made in only one fitting At least half the children could not therefore possibly obtain satisfactory shoe fittings even if there were enough trained shoe-fitters in the shops and every parent were aware of the importance of securing correct fittings Every child needs a new fitting approximately every three months, but with shoes at their present cost it is almost impossible for parents to follow this practice

How sad it is that this preventable condition is not prevented !

Ealing

W G BOOTH
Medical Officer of Health

CONGENITAL DEFECTS FROM MATERNAL RUBELLA

SIR,—Mr Ian Robin[1] recommended that, in order to avoid danger of infection with rubella during pregnancy, every opportunity should be taken to infect girls with the disease before leaving school I am in absolute agreement, and there seems every advantage in following such a course in a school where all the girls are boarders But, as medical officer to a girls' public school in which only 153 of the 521 girls are boarders, I find the decision by no means so simple Some of the girls may be returning daily to a mother who may herself be pregnant, or they may share public transport and entertainment with pregnant women, the risk would therefore be spread over a large section of the community I should welcome the views of others who may be faced with the same problem

Northwood,
Middlesex

DUDLEY M BAKER

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[1] Robin, I G *Lancet*, 1952 ii, 1034

EXAMINATION OF RIB BONE-MARROW FOR TUBERCLE BACILLI

SIR,—The discrepancy between our findings and those of Dr Marsh and Mr Barton,[1] who found no tubercle bacilli in the rib bone-marrow of their patients, may be explained by the following facts

(1) The hæmatogenous (disseminated) form of tuberculosis is commoner in children

(2) The sternum is relatively richer in marrow than the ribs

In our work on this subject we have made comparative studies of blood, bone-marrow, and gastric-juice cultures from tuberculous children, and these have confirmed our previous results This study encouraged us to make a more detailed review of the literature, and we have found that the bone-marrow of tuberculous patients has repeatedly given positive results in the past[2–5]

University of Athens

K CHOREMIS

THE LATE Dr H W DIAMOND

Dr J B Wrathall Rowe writes "Dr Hugh Welch Diamond, who died at Twickenham in 1886, was a pioneer in the field of medical photography and photomicrography I should be grateful if any one with knowledge or early examples of Dr Diamond's work would write to me c/o the Medical Department, Kodak Ltd, Harrow, Middlesex I should also welcome information about Dr Diamond's descendants Dr Warren Hastings Diamond may have been his son, and he is thought to have had a grandson named R Hugh Clarke"

Medicine and the Law

Nationalised Hospitals and Negligence

THE degree (if any) to which the nationalised hospital and their staffs are protected from claims for negligence is still being worked out at the expense of plaintiffs and defendants In Bullard *v* Croydon Hospital Group Management Committee and Latta[6] it was alleged that a patient suffering from acute appendicitis was not operated upon till five days after admission to hospital, by that time, it was said, peritonitis had developed and death occurred on the day of the operation A claim for damages was brought against the hospital managers and the surgeon concerned The hospital managers replied that, in so far as they were responsible for the treatment of the deceased, they undertook it as their duty under the National Health Service Act, the surgeon, they contended, was acting on their behalf or as an officer under their direction in the discharge of their responsibility, and they claimed protection from liability by virtue of section 72 of the Act

Section 72 provides that section 265 of the Public Health Act, 1875, shall have effect as if the public authorities referred to therein (local authorities, joint boards, and port sanitary authorities) included a hospital management committee Section 265 provides that nothing done by such authorities or any of their officers or other persons acting under their directions, "if the thing were done bona fide for the purpose of executing" [the Act of 1875], shall "subject them personally to any action, liability, claim or demand whatsoever"

Mr Justice Parker decided in favour of the plaintiff, the administrator of the deceased patient's estate He referred to section 13 of the 1946 Act which states that hospital management committees, notwithstanding that

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[1] Marsh, K Barton G E *Lancet* 1952, ii 1059

[2] Debré R, Lamy, M, Sée G, Mallarmé J *Pr méd* 1936, 44 1853

[3] Even R Lecoeur, J, Sors, C *Bull Soc Soc méd Hôp Paris* 1947, 63, 113

[4] Bernard E Kreis, B, Lotte, A *Ibid* 1949 65, 360

[5] Katz, S, Lifschutz S *Med Clin N Amer* 1950 34, 1817

[6] *Times*, Feb 13, 1953

APPLIANCES

Surgical Appliances delivered to hospitals

—	1951				1952			
	November		December		November		December	
	No.	Estimated cost	No.	Estimated cost	No.	Estimated cost	No.	Estimated cost
		£		£		£		£
Surgical footwear (pairs) ..	3995	37,000	3996	37,000	3255	28,099	2409	20,625
Repairs to surgical footwear	6739	5000	7588	5700	2598	1763	2036	1304
Surgical abdominal supports*	8328	31,000	8430	31,500	1497	14,452	3511	11,306
Elastic hosiery (pairs or single) ..	3043	5300	3184	5600	2586	4155	2012	3105
Wigs	587	7500	581	7500	381	1830	389	4962

* Includes all types of belts, some of which are not chargeable.

Mr. BLENKINSOP asked the Minister what financial saving he estimated would result from the charges imposed under the Health Service Act, 1952; how much of this saving resulted from a fall in use of the services concerned; and how the savings compared with the estimates originally given.—Mr. MACLEOD replied: The estimated amount of the charges paid, or to be paid, in 1952–53 by patients in England and Wales under the 1952 Health Service Act is about £2 million. In addition, while figures to enable a complete estimate to be made are not available, the reduction in the demand for dental treatment and for hospital appliances for which charges are made compared with the previous year is estimated to show a saving of about £1¾ million. Comparisons cannot usefully be made with estimates framed in the expectation that the charges would operate for a full year and before modifications in the original proposals were made.

Bone-conduction Hearing-aids

In answer to a question Mr. MACLEOD said that a first consignment of bone-conduction hearing-aids had already been sent to the hospitals which distribute aids.

Flour-improvers

Mr. D. W. WADE asked the Minister of Food what progress had been made in the investigations into the existing methods of treatment of flour; and whether he would give an assurance that the process of agenisation would be abandoned.—Major GWILYM LLOYD GEORGE replied: These complex and important investigations into possible alternatives to agene as a flour-improver are requiring considerably more time than was originally thought necessary. They are being pursued with all possible speed, but it would be premature to take any action until they are completed. One or two possible alternatives have been presented, but it is obvious that very careful research must be undertaken before either can be accepted.

Health Service Resignations in Scotland

Sir THOMAS MOORE asked the Secretary of State for Scotland whether he was aware of the public concern in Ayrshire in regard to the efficiency of the National Health Service, with particular reference to the shortage of trained medical and surgical consultants.—Mr. JAMES STUART replied: If the hon. member will let me have particulars of any deficiencies brought to his notice, I shall be glad to consider them.

Sir THOMAS MOORE: While welcoming the Minister's suggestion, is he aware that there has been a disturbing number of resignations lately, especially amongst consultants; and is he satisfied that the West of Scotland Regional Board is adequately and effectively dealing with this unsatisfactory situation? Mr. STUART: I am assured that the regional board are taking proper steps to replace those who have resigned.

Mr. A. C. MANUEL: Is the Secretary of State aware that in the West of Scotland, and in Ayrshire in particular, since the inauguration of the National Health Service we have had a better full-time consultant service than ever previously existed; and that the doctors generally have expressed to me their satisfaction at the better service now available?

In England Now

A Running Commentary by Peripatetic Correspondents

LEISURE, like the conversation that goes with it, is dying; and we are hastening its end. In our fathers' day a whole section of society was dedicated to its pursuit; and none thought a whit the worse of a man for belonging to the leisured classes. But today the very word leisure bears a sting of reproach. Braving public opinion, the Chelsea Clinical Society last week met to hear from three distinguished speakers—a writer, a surgeon and a broadcaster—how we might win our way back to the Pursuit of Leisure. Mr. John Betjeman would have none of this. By speaking for only three minutes he slyly implied that he was making way for others better qualified to talk, and his brief words were largely directed to showing that no stigma of leisure could be applied to him; if, he declared, he liked what he did he wouldn't want any leisure. Leisure was an invention: and here presumably he meant that like other inventions—the safety-pin, the steam engine, and even television—it could be eradicated if only we turned our minds to the task. A similar personal disclaimer came from Mr. Gilbert Harding—the Mr. Harding who in other fields has spoken bravely. Only Sir Heneage Ogilvie stood his ground; but it was carefully chosen medical ground on which he spoke well of leisure as a counterpoise to work. The lesson seems to be that this word is now taboo except in the consulting-room: and we should thank the members of the Chelsea Clinical Society for setting aside some of their less hurried hours to establish this.

* * *

The study of man's reaction to changing environment is now a popular pastime. I have been making an unofficial pilot study of my reaction as a householder to the august body which now runs the local hospital.

The bureaucratic mills grind slowly, but with an air of majestic purpose. The first victims were some moderate-sized houses in which the ci-devant bourgeoisie once raised happy families. These were smartly converted into staff quarters and maternity units, so that our rather ordinary neighbourhood has now a busy professional air. Starched white caps and scarlet-lined cloaks charm the eye in the daytime and ambulance noises make my nights hideous. After a suitable interval a nursing-home was drawn into the net. This raised a generous amount of heat, even assuming atomic proportions, but the deed was not undone and the opposing forces have withdrawn to regroup.

But now a bureaucratic shaft has found a target right in the middle of our domestic hearth. Our invaluable daily help has decided to throw off the shackles of private enterprise and give her services exclusively to the hospital. It would take the genius of Milton to describe the despair with which we contemplate the future of our fast dwindling paradise, and my pilot study has turned a bit introspective. . . .

* * *

During the recent gales our sanatorium was soon cut off from electricity and water. On the first morning of the storm we were approached by a delegation from the patients' club, who, apparently unconcerned about their own welfare, wanted to know what was to happen to their tropical fish. We answered, civilly enough, that we were rather busy just then, and quickly retreated to our quarters to consult our small medical reference library. The fish, some three dozen of assorted species with their young, lived in a tank in a remoter part of the sanatorium property: and the fixity of their internal medium was controlled by a device of science, worked by electricity. The problem was of keeping the temperature of the tank above 75° Fahrenheit under the prevailing chilly conditions. Coal fires in the hospital numbered two, and the tank could not be moved.

On going through our literature, we found we had mislaid Dr. Bernard's paper; other oracles we had consulted in the past could give us no guidance. Our eyes fell on our stone hot-water jar which lay on the floor, where it had been blown out of the hands of a maid-servant earlier that morning. By applying the late Mr. Archimedes's principle, two hot-water jars were

Obituary

HOLBURT JACOB WARING

Bt., C B E , M S , B Sc Lond , D C L Durh , LL D Brist ,
M S Cairo, F R C S , F R A C S

Sir Holburt Waring, whose death we announced last week, made important contributions to medical education On the ward round and in the operating-theatre he was a stimulating teacher, in the hospital board room he was a generous and forceful advocate of expansion, and in the counsels of the Royal College of Surgeons, the University of London, and the General Medical Council he initiated reforms in the medical curriculum

Born in 1866, the son of Isaac Waring of Southport he was educated at Owens College, Manchester and at St Bartholomew s Hospital, from which he graduated M B with honours in 1890 In the following year he took the F R C S and in 1893 he obtained the M S and the gold medal for surgery Meanwhile in a succession of house-appointments at Barts he had quickly won recognition, and appointment to the staff and to the lectureship in operative surgery followed in due course

[Elliott & Fry

On the outbreak of war in 1914 as a Territorial he was at once called up, and with the rank of lieut-colonel he was given charge of the surgical division of the 1st London General Hospital (T F) He was mentioned in despatches, and was appointed C B E in 1919

His association with the administration of the University of London began in 1911 when he was elected to the senate, and in 1920 he became dean of the faculty of medicine, and in 1922 vice-chancellor of the university He had been appointed to the court of examiners of the Royal College of Surgeons in 1911 and to the council in 1913, and from 1932 to 1935 he was president of the college From 1917 to 1932 he represented the college on the General Medical Council, which he served as treasurer and he held the same office for the Dental Board from 1921 to 1932

Much of his work in his own specialty had dealt with the surgery of malignant disease, and the Imperial Cancer Research Fund was another academic body which appointed him its treasurer When he retired from his office last year he was elected a vice-president of the Fund

With the years accrued the honours he had earned In 1925 he was created a knight, and ten years later a baronet *The Royal College of Surgeons of Australasia* had elected him to their honorary fellowship, and he had received honorary degrees from the Universities of Durham, Bristol, and Cairo His varied work and interests had touched life at many points, and his achievements are best described in tributes from friends *of different ages and different specialties*

F R F points out that though the close connection of the London medical schools with the university is now accepted as obvious and natural, it was far from being generally accepted between the wars, and Waring worked unceasingly to bring it about

" As a first step he succeeded in obtaining a charter for St Bartholomew's Hospital Medical College, so making it administratively independent of its parent hospital, but he had to use all his influence to effect at that time what has now under the National Health Service become a required condition for all the medical schools in London It was a source of wonder to his friends and colleagues how he managed to reconcile his loyalties to the different bodies in which he held office, but he accomplished this successfully and worked continuously to promote coöperation among the many institutions concerned with medical practice and medical education in London Only those who were involved with him in obtaining the new ward block for St Bartholomew's Hospital know how hard he worked in planning it down to the smallest detail, and how carefully he studied the designs of hospitals in this country and abroad before reaching conclusion. [illegible] his colleagues, both medical and non medical, shared with him the responsibility for final decisions his was the dominant voice on all occasions Doubtless this dominance was exercised in his other activities and accounts for much of the respect, tinged with fear, that he inspired in his students and in many of his contemporaries He will not be remembered [illegible] great surgeon or a great teacher, but his methods were successful in forcing essential knowledge into the heads of many students who had difficulty in learning for themselves and many a story of his explosive language will be told for years to come His death removes a colourful personality who gave all he had to the welfare of medicine and medical education, and in so doing effected much of lasting val[illegible] He will be remembered also by those who knew him best f[illegible] his courtesy and kindnesses "

Of Sir Holburt's many excellent attributes the one that stands out most vividly in H. W 's memory, and dwarf[illegible] everything else, was his intense interest in his own hospital

" Where its welfare was concerned, it always came first and nothing else mattered Not always completely tactful in the way h[illegible] addressed his views, his persistence and thrust always sufficed to win the day and get what he wanted and thought right St Bartholomew's are very grateful for all the great improvements and advantages he secured for them Sir Holburt was a good judge of men and he possessed the valuable trait of being able to depute work successfully to others He had a beautiful pair of hands, and in his younger days he was a very neat and efficient operator When he retired, his invaluable help and the standard of service and behaviour he enforced on other people, and carried out himself in the hospital, was greatly missed, and always will be '

J E remains grateful for having had his basic surgical training from Sir Holburt

' An exact thinker himself, he insisted on his students carrying out examinations, writing notes, and expressing themselves in a similarly exact manner Brusque almost to the point of rudeness the Old Man, as he was affectionately called by all who worked with him, never forgot one of his old students, and many of them have reason to thank him for that personal letter of recommendation which can mean so much in a young man's career "

W R T admits that to all his dressers and to many of his house-surgeons Sir Holburt was an enigma, but suggests that there is no doubt that his brusque manner was something of a pose and partly accounted for by the rough handling he himself received as a young man from Harrison Cripps and others

" Sir Holburt was one of the last of the surgeons who may be said to have lived through the heyday of consulting practice the first quarter of this century , on one occasion going even as far as Nepal to operate He lived and moved in the grand manner, and to see the half hunter flicked open at just the right moment when examining a private patient was a revelation as to how this should be done As a judge of wine and cigars he had few equals, and he was most intolerant of dressers satisfied with beer from the White Hart and 'Gold flakes ' (then selling at less than a shilling for twenty) 'You young men of the present day who stand about with your hands in your pockets smoking cigarettes ' Great was the jubilation throughout the firm when someone spotted the Old Man buying a packet for himself one evening on Liverpool Street Station

' Until recent years he had substantial colliery interests and these helped to make him a shrewd man of affairs, with resulting benefits to any institution with which he was connected Although he liked to get his own way, he usually had sound reasons for wanting to do so

' His teaching was plain straightforward practical stuff and he expected his dressers under supervision, and most certainly, his residents to be able to tackle any ordinary task a attention is paid to the story and close observation made of the ways in which children react to pain, intussusception is one of the most clearly defined conditions in childhood. Certainly textbooks often give a misleading mixture of symptoms drawn from different stages of the disease; but on the first day—the period when it must be suspected for optimum results—the clinical picture is plain and the fringe of atypical cases is small. The onset is sudden; vomiting occurs in 9 out of 10 children; and blood is passed spontaneously by about half the children on that first day. Pain is always present, though we admit that sometimes it requires considerable experience to recognise it, as it will be expressed by different children in different ways. In many the traditional screaming occurs with each bout of colic: in others it is reflected in crying more often than usual: others again are exceptionally restless with whining and whimpering; while very rarely the child may simply blanch with the spasms without uttering a sound.

With proper sedation an experienced observer will feel the tumour in almost every case, except when the invagination is still confined to the small bowel; and although it is true that it is easier to feel the tumour when the bowel is in spasm, we do not agree that the tumour disappears when the bowel is relaxed. As regards surgical technique, a right paramedian incision is, in our opinion, superior to an incision in the right iliac fossa; and experience has shown that in the younger children there is no need to remove the appendix. We can certainly see no reason for the use of a combined technique of enema reduction plus laparotomy as used by Collier.

We would stress again the constancy of the clinical picture of this disease, apart from feeling the abdominal tumour, because it is upon this that we must rely if the family doctor is to suspect it with increasing frequency within the first twenty-four hours. What is more, this very constancy makes diagnostic radiography unnecessary and time-wasting except in the few subacute or chronic examples of the disease.

We hope to present our material, and with it the difficulties of this subject, more fully at a later date; but we felt that your article called for an immediate reply.

J. D. T. JONES
DENIS HINDMARSH
S. D. M. COURT
R. H. JACKSON.

Children's Department,
Royal Victoria Infirmary,
Newcastle upon Tyne.

REGISTRATION OF FEVER NURSES

SIR,—Dr. Grant's letter last week draws attention to a matter which is causing great anxiety to those concerned with the staffing of fever hospitals.

The General Nursing Council maintains that it is concerned solely with the training of nurses and not with the staffing of hospitals, but surely it can be argued that the training of nurses should be related to the nursing services required by the public.

There has been a large drop of infectious diseases over the last ten to fifteen years, but the work carried out in a modern fever hospital is still a very essential part of the health service. Much of the work consists in the treatment of acutely ill babies, and this requires possibly greater nursing skill than any other form of treatment. In a large city there is always the risk of serious epidemic disease—only a few years ago we had to treat over a hundred cases of paratyphoid fever in this hospital. The danger of poliomyelitis is an urgent one, and the recent outbreak in Copenhagen makes one view with concern any move which would lead to a precarious state of staffing in our infectious-disease hospitals. Even diphtheria is not completely absent; in the last two months we have treated ten clinical cases, including one fatal case. A too-ready belief that infectious diseases are now of little account from the nursing point of view may lead us into danger.

It must be admitted that many fever hospitals are too small to offer suitable training for nurses, but this is no reason for abolishing the two-year training course in infectious diseases in the larger hospitals where student nurses can gain a wide variety of excellent experience.

If the Fever Register is abolished the infectious-disease hospitals will face grave difficulties.

A. B. CHRISTIE
E. A. BURNS.

Fazakerley Hospital,
Liverpool.

AUGMENTED RESPIRATION

SIR,—I wish, without intending to depreciate the work of Mr. Donald and Miss Lord, to comment on a statement in their letter last week which has a wider relevance.

They claim that the negative pressures used in their respirator encourage the return of blood to the heart, and I think they mean to contrast the effect of inflating the lungs by pressure applied through the air-passages. This notion is widely held, but it is mistaken. The negative pressure exerted by a Drinker-type respirator does not enhance cardiac filling, because it is applied to the limbs and abdomen as well as to the thorax. In fact, the distribution of pressure gradients (and hence the circulatory effects) is identical with that produced by applying a similar, but positive, pressure through the air-passages. We have in this department recorded the blood-pressure during artificial respiration and have confirmed that lung inflation, whether by negative external or positive internal pressure, drops the stroke volume, whereas, of course, normal inspiration increases it.

The practical inference is that, the circulatory and other physical effects of the two modes of artificial respiration being the same, the choice between them may be made on grounds of convenience.

A. C. DORNHORST.

Department of Medicine,
St. Thomas's Hospital Medical
School, London, S.E.1.

CHILD-WELFARE CLINICS

SIR,—When considering the future of the child-welfare clinics a few facts must be borne in mind. They are:

1. The most suitable person to do this work is undoubtedly the family doctor.
2. There is no official barrier whatever to prevent him from doing this work now; for in most areas some interested doctors have their own clinics, and some of course have national reputations in this field.
3. Local authorities do this work for the undeniable reason that in the past general practitioners have neglected to do it.

It is quite impossible for the local authority to staff and equip an infant-welfare centre for every family doctor; for instance, in Ilford there are fifteen centres and about seventy general practitioners. It would be equally inappropriate to select fifteen of these seventy and ask them to look after children on the lists of other doctors.

A large number of practitioners cannot or do not wish to do this work because they are not interested or their premises are unsuitable.[1] We have all seen queues in the rain outside their surgeries in industrial towns and know how crowded the waiting-rooms must be and how they may often be filled with unsuitable fellow-patients, such as open cases of tuberculosis.

Accordingly, until such time as most family doctors are interested in health education and have suitable premises for this work (such as may be provided in health centres) the local authority must continue to provide this service. When these conditions are fulfilled, local-authority infant-welfare centres will disappear for the simple reason that they will not be wanted.

Should they be precipitately discontinued there is no doubt that the vast majority of children—say, applied his talents with great patience to each new problem, showed an impartiality which won him the regard of police and the law, and *never failed to give sound advice of a conservative kind* He appeared in many famous trials and he survived a public esteem with the same charming 'grand old man' detachment as he surveyed the Bench and Bar Many will miss this warm hearted man and will regret that he was denied the pleasures of relaxation in *retirement* He would not have lacked visitors and invitations, intellectual and more rustic diversions, conversation, and a ripe enjoyment of later years His life had been full, he had enjoyed it enormously, and it needed only a chapter of happy retirement to complete it"

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[1] See Collings, J. S. *Lancet*, 1950, i, 555.

Dr Grace is survived by his wife and two sons, one of whom took his M B at Liverpool in 1950 and is now serving in the Navy His brother, Dr A W Grace, is professor of clinical dermatology at Long Island University, New York

GORDON CAMPBELL KINLOCH REID

M B St And, L D S

Dr Reid, pathologist of the Walsall group of hospitals, died at his home in Walsall on Feb 6, at the age of 49

He was born at Elgin, but he spent his boyhood at Perth, where he attended the Perth Academy From there he proceeded to St Andrews University In 1929 he took the L D S and graduated M B He held a number of hospital posts and spent some time in general practice before he became resident surgical officer to New Cross Hospital, Wolverhampton, in 1935 Through the laboratory service of the hospital he was brought into contact with the practice of clinical pathology, which made an immediate appeal to him, and in 1938 he joined the staff of The Royal Hospital, Wolverhampton, in the joint capacity of resident medical officer and assistant pathologist

Dr Reid devoted immense energy to the development of the Wolverhampton and district blood-transfusion service, then based upon the pathological department of The Royal Hospital It was largely owing to his efforts in its early days that this service was able to bear all calls upon it at the beginning of the late war before it was merged into the Emergency Blood Transfusion Service In 1940 he joined the R A M C, and as a specialist in pathology with the rank of major served with distinction in the Eighth Army both in North Africa and on the Continent Under the pseudonym of "Pixie" he was widely known throughout the medical service of the Eighth Army After D-day he was mentioned in despatches for conspicuous gallantry and devotion to duty

After demobilisation, for a short time he again served in the pathological department of The Royal Hospital, Wolverhampton. In 1946 he became attached to the Walsall General Hospital, first as assistant and later as full pathologist, and under the National Health Service he became consultant pathologist to the Walsall hospital group In this post he unstintingly applied his immense energy, and in a short time had brought the pathological service centring upon these two hospitals to a high state of efficiency Since 1951 his work had been interrupted by his serious and disabling illness, but with great fortitude he returned to his post in the spring of 1952 and continued to fulfil its duties until December

S C D writes "Dr Reid was a great clinical pathologist, exactly of that type of which the national hospital service stands most in need He read widely and kept himself well abreast of current knowledge in all branches of his subject But the secret of his success as a clinical pathologist, and the reason for the universal regard and affection which he came to command, was that to him the welfare of the patient, whether in or out of hospital, was a major concern His years of *clinical experience*, both in general practice and in hospital posts, stood him in admirable stead in bringing the work of the laboratory and of the wards into intimate and fruitful contact His laboratory was freely open to all general practitioners of his neighbourhood, and in it both they and their patients were always sure of a ready welcome and a sympathetic and kindly hearing"

Dr Reid married Miss Dorothy Pollitt, S R N, in 1946, she survives him with two children

RANSOM PICKARD

C B, C M G, M D, M S Lond, F R C S, D P H

Colonel Ransom Pickard, who died on Feb 9, at the age of 85, was well known in the West Country as an ophthalmologist, and he was also one of Exeter's most distinguished citizens

He graduated M B with first-class honours from St Bartholomew's Hospital in 1889, and after holding house-appointments there and at Moorfields he took higher qualifications in his specialty before he settled down in Exeter in the '90s After a few years in general practice he was appointed surgeon to the West of England Eye Infirmary No man ever took his hospital duties more seriously, or took more trouble over his patients, and as a hard worker himself he expected a high standard from others It was not surprising that he soon built up a large private practice, and such was his reputation that he retained an unusually large measure of it after his retirement from his hospital post in 1932

In the 1914–18 war Pickard was mobilised as lieut colonel in command of the 1st Wessex Field Ambulance, which he had been instrumental in raising, and he saw immediate service in France He was later promoted A D M S of the 48th Division with the rank of colonel and he served in North Italy with this division until demobilisation Five times mentioned in despatches, he was awarded the Italian croce della guerra and was appointed C B and C M G

Pickard contributed fairly often to the medical journals, and he was particularly interested in glaucoma and in cases of low tension with disc cup enlargements He took immense pains over the papers which he wrote, and he would often turn up at the Eye Infirmary at 8 A M to take a tonometer reading He was also regular in his attendance at medical meetings and he seldom failed to contribute to the discussion something that was worth hearing He never talked nonsense and he never failed to command the respect of his colleague Perhaps it was for that reason that he was chosen for the unenviable position of chairman of the local committee which in the 1939–45 war had to decide which doctors should serve in the Forces and which *should* remain behind

But Pickard was a citizen as well as a doctor and for several years, until 1947, he achieved the *distinction* unique for a former member of the surgical staff, of being president of the West of England Eye Infirmary He had already served Exeter as sheriff (*1906–07*), and as mayor (1927–28), and he had a long association with the University College of the South-West, *of* which he became a vice-president He was also a vice president of the Exeter Drama League, and a past president of the Devonshire Association and of *the* Devon Archæological Exploration Society

M D B writes "One of Pickard's chief *delights* was walking Almost every Saturday of his life, dressed for the part, he went for a long walk in the country He really *loved these walks (and the planning of them)* and the Devon country they were a part of his life, and nothing—least of all bad weather—deterred him from taking them He never had a car, he always walked everywhere, and he never seemed to feel the cold I can only remember seeing him *in an* overcoat once or twice—a rather inadequate garment disliked and despised by its owner, who thought almost as poorly of a mackintosh In earlier years he was a keen mountaineer, and a member both of the Alpine Club and of the Swiss Alpine Club

"Pickard did not marry till he was 45, but he had forty years of *extremely happy married* life Mrs Pickard shared many of his interests and was *the* ideal wife for a personality which in his younger days was perhaps a little rugged and which she succeeded in mellowing into the fine old man that Exonians remember so well

"He had always been a non smoker and a teetotaller, and last but not least, *he was a life long Methodist* Every Sunday, Dr. Wheatley's suggestion that penicillin and streptomycin should be applied locally. Topical streptomycin s particularly liable to produce skin reactions, and opical penicillin is not free from the same disadvantage. I have not yet seen a skin reaction with chloramphenicol. 5% chloramphenicol in propylene glycol is not expensive; 100–150 applications cost 8s., if the solution is made up in one's own dispensary. The total cost in antibiotics of treating a case of paronychia was 3s. 7d.; it is now less.

Mr. Jones's investigation of seasonal variations (Jan. 31) interested me greatly. I agree there are so many factors that it is difficult to prove anything. I have, however, taken from last year's records on septic hands (976 cases) a few figures which may be relevant.

In the months January, February, March, October, November, and December, 58 cases of common septic hand conditions took over a fortnight to heal, 21 over three weeks, and 10 over a month. In the months April–September the corresponding figures were 26, 10, and 4. The figures for paronychia were: over a fortnight, in the winter 18 and in the summer 4; over three weeks, in the winter 4 and in the summer nil; over a month, in the winter 2 and in the summer nil.

It is the *clinically* resistant cases that we hope to abolish. Some, as I have shown, are due to bacteriological resistance, and chloramphenicol will help. Many are due to faulty surgery in the first place, and bacteriological resistance is acquired secondarily. Paronychia is the first septic condition of the hand in which penicillin-resistant organisms have been noted in significant numbers on first attendance at the clinic.

This casualty appointment, like many others, has been unfilled for some time: and in the past year no less than seventeen housemen have been detailed, at one time or another, to operate on the cases. Under such conditions it is impossible to maintain a consistently high standard. Nevertheless the 230 cases of paronychia treated since the principles I adopted have been emphasised, have had an average duration of treatment of 7·1 days. This is nearly a 40% improvement on anything we have had before, and exactly half the average disability in 1950.

Royal Infirmary,
Sunderland.

T. G. Lowden.

A SURGICAL POLICY FOR PEPTIC ULCER

Sir,—May I congratulate Mr. Orr and Mr. Daintree Johnson on their excellent article in your issue of Feb. 7? They have recognised the surgeon's dilemma: excellent as ulcer surgery is, a fairly high resection is necessary for sure relief, and the higher one goes the more likely one is to encounter untoward effects (of which we have seen examples from all over the country). The authors' plan of operation is designed to secure the benefits of gastric surgery without its disadvantages.

In my own clinic we treated a small series of patients by limited gastrectomy with vagotomy, and we were well pleased with the results, but we are waiting a little longer before going on. Meanwhile, we are giving an extended trial to another promising procedure, the results of which have not yet been assessed for publication. These latest figures from Mr. Orr and Mr. Johnson are a strong encouragement to us to begin a second series of limited gastrectomy with vagotomy in suitable cases.

It is only from the most careful personal analysis of an adequate series of cases such as this, that any important deductions can be drawn. The authors mention that they have also had access to a second series, operated upon by a colleague. I should like to emphasise the value of this method in which the same observer takes stock of both series and can therefore safely draw comparisons. We also have made a start in this direction, and we hope soon to extend similar inquiries much more widely.

Finally, may I voice one criticism? I believe they are wrong in supposing that even the most cunning questionnaire is as good as an interview: for example, the signs of riboflavine deficiency have to be looked for if they are not to be missed. Moreover, patients who have, through surgery, been relieved of their life-long ulcer pains are often reluctant, unless pressed, to admit to even so gross a feature as bilious vomiting, and, moreover, they often mistake bile for food. In this article, the incidence of bilious vomiting is about "right," but that of the vomiting of food seems to me too high.

Department of Surgery,
University of Liverpool.

Charles Wells.

METHOD OF ADMINISTERING DICOUMAROL

Sir,—The paper by Dr. Bjerkelund (Feb. 7) was very interesting to us here as, for some years, the determination of prothrombin levels and the task of working out further dosages of dicoumarol or of ethyl biscoumacetate ('Tromexan') has been entrusted to the biochemist. This arose because the requests were often inscribed "please advise dosage of anticoagulant," and also because we found commonly that inexperienced housemen either were reluctant to order enough dicoumarol or ordered excessive amounts. Furthermore, daily prothrombin estimations were becoming a burden to both staff and patients. Consequently the following scheme was devised:

The initial request form contains full clinical details, including any dosage already given. The prothrombin is determined by Quick's one-stage method using rabbit-brain thromboplastin, and the result is reported as the index and corresponding percentage normal. This is written direct on to the request form together with dosage details for the evening of the day of test, the following day or days, and the morning of the next test day. The form then goes back to the ward; or in the case of outside hospitals in the group the report is telephoned. Usually tests are done every other day—chiefly Mondays, Wednesdays, and Fridays.

The advantages are briefly:

1. The report gets to the ward quickly and treatment can be started with little delay.

2. There is no laboratory office work except to note incoming requests in the day-book; there is no typing (to save technical time, the report is written within a rubber-stamp framework), and we keep our own record of the dosages in the laboratory prothrombin-time book.

3. Tests are necessary only every other day.

4. In the case of ethyl biscoumacetate, the dosages are divided into morning and evening tablets, and usually one 300 mg. tablet is given at 6 A.M. on the day of test to maintain a satisfactory level until the result of the test is known.

5. Whilst it might be argued that it is unwise to leave the dosage to the laboratory, in practice this works very well; for the biochemist, unlike the houseman who has many such drug dosages to work out, can bring a fresh mind to the problem. Furthermore, it is obviously an asset to have someone who has been concentrating on this dosage problem for several years and who has the patient's previous figures at his finger-tips. Indeed, provided full clinical details are given, it is possible for the laboratory to point out the inadvisability of starting a course of ethyl biscoumacetate in, for example, pregnancy, if this has been overlooked by the clinicians.

6. General practitioners are more ready to treat their own patients instead of admitting them to hospital. In the case of ambulant patients the blood is taken by the laboratory, the result and dosage telephoned to the doctor, and the dosage alone telephoned to the patient. The doctor then has merely to check the clinical side every other day. He knows what dosage the patient has been instructed to take, and can alter it if he considers this necessary. This is surely a good example of a general practitioner receiving immediate and full coöperation from a hospital department and yet maintaining full control of the patient.

7. Only two cases of major hæmorrhage in the past four years can be recollected. One was in the early days, through too infrequent testing, and was controlled by transfusion.

University of Liverpool

The following have been successful in the examination for the diploma in tropical medicine and hygiene

K M Aboud A N Basu, S N Bhattacharya K R I Hariharan, *R Hecker E S Jones, G Moles, Y Na Songkhla, H C C Nwankwo, T Viriyakul

*Milne medal in tropical medicine and Warrington Yorke medal in tropical hygiene

Queen's University, Belfast

At recent examinations the following were successful

M B, B Ch B A O—D J Acheson Barbara D Allen G A Balmer, Ann T Bowden G W Donaldson, T N Elwood, Andrew Gaston Mary S Gilbody K I McD Heath, Sheila H Hoey, A K Irvine R H Johnson James Kelly, G W C McCartney, J D McDowell, A C M L Miller H R St L Ormonde, G B Purce, Ellen D Shilliday A B Siewers F A Thompson

University of Edinburgh

Dr Pierre Mallet Guy of the department of surgery, University of Lyons, will deliver a lecture on Monday, March 9, at 5 P M at the University New Building He will speak on the Manometric and Radiographic Control of Biliary Surgery

Royal College of Physicians of Ireland

On Feb 6 the following were admitted to the membership of the college

G T L Archer V T B Doyle, T M Gregg Elinor D U Powell

Betterment for Consultants

At a recent meeting of the South West Metropolitan (Western Area) Regional Consultants' and Specialists' Committee, the following resolution was passed

> "The South West Metropolitan (Western Area) Regional Consultants' and Specialists' Committee urges the Joint Committee to press for full and retrospective implementation of the Spens Report as regards salaries of Hospital Medical Staff, and only to accept a betterment factor which is comparable to that recently decided by arbitration as applicable to general practitioner remuneration"

University of Wales

Sir Cecil Wakeley, F R C S, will deliver the fourth William Sheen lecture on Wednesday, March 25, at 8 P M at the Reardon Smith lecture theatre, Park Place Cardiff He is to speak on Modern Trends in the Treatment of Cancer

Summer School in Health Education

The Central Council for Health Education is holding its summer school this year at Royal Holloway College, Englefield Green, Surrey, from Aug 10 to 20 Further particulars can be had from the medical director of the council, Tavistock House Tavistock Square, London, W C 1

Social Policy and the Social Sciences

The British Sociological Association is holding a conference on this subject during the weekend March 27–29 at Queen Elizabeth College (formerly King s College of Household and Social Science), Campden Hill Road, London, W 8 The opening address on the Relation between Social Theory and Social Policy will be given by Mr Gunnar Myrdal, executive secretary of the Economic Commission for Europe Papers will be presented for discussion on Health, Design and Planning—Buildings, Town, and Countryside, and Needs and Standards in the Social Services The contributors to the section on health will include Prof T Ferguson Rodge Dr J N Morris, Dr Milton Roemer, Mr A T Chester, Dr J H F Brotherston, and Prof R M Titmuss The conference will be open to non members, and particulars may be had from the secretary of the association, Skepper House 13 Endsleigh Street, W C 1

EMERGENCY BED SERVICE —In the week ended last Monday applications for general acute cases numbered 1730 The proportion admitted was 77 93% A yellow warning is still in force

Chesterfield Medal in Dermatology—The examination for the award will be held on March 9, 10, 18, and 19 Applications should be sent by Feb 28 to the secretary of the Institute of Dermatology St John s Hospital for Diseases of the Skin, Lisle Street, London, W C 2

Diary of the Week

FEB 22 TO 28

Monday, 23rd

UNIVERSITY COLLEGE, Gower Street, W C 1
4 45 P M Prof Jean Roche (Paris) Comparative Biochemistry of Iodoproteins

INSTITUTE OF PSYCHIATRY Maudsley Hospital, Denmark Hill, S E 5
5 30 P M Dr E Stengel Lecture demonstration.

HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4) Mr A Dickson Wright Quacks of John Hunter s Time (Hunterian oration)

MANCHESTER MEDICAL SOCIETY
5 P M (University of Manchester) *Section of Odontology* Mr R J V Battle Management of Harelip and Cleft Palate
9 P M *Section of General Practice* Dr James Kerr Legal Problems in General Practice

Tuesday, 24th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
5 P M Mr James Moroney Colonic Replacement and Restoration of Human Stomach (Hunterian lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Dr P L Mollison Life span of Red Cells

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
8 P M *Section of Medicine* Prof D M Dunlop, Dr S Leonard Simpson, Dr E N Allott Addison s Disease

INSTITUTE OF DERMATOLOGY, St John s Hospital, Lisle Street W C 2
5 30 P M Dr L Forman Skin Diseases Related to Cancer

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, W 1
5 30 P M. Dr Colin Edwards Neurological demonstration

CHADWICK LECTURE
2 30 P M (26, Portland Place W 1) Dr Georges Decharneux (Liége) Industrial Medicine and Hygiene in Belgium

Wednesday, 25th

ROYAL SOCIETY OF MEDICINE
10 A M *Section of Endocrinology* Symposium on the Thyroid Gland

ROYAL EYE HOSPITAL CLINICAL SOCIETY, St George s Circus, Southwark S E 1
6 P M Miss J M Dollar, Miss M Savory Exenteration of the Orbit (Film)

INSTITUTE OF DERMATOLOGY
5 30 P M. Dr J A Dudgeon Virus Diseases

INSTITUTE OF UROLOGY St Paul's Hospital, Endell Street, W C 2
5 P M Mr J Sandrey Vesical Neoplasms

BIRMINGHAM MEDICAL INSTITUTE, 154 Great Charles Street Birmingham 3
8 P M *Section of Psychiatry* Mr Malcolm Piercy, B A Leucotomy of Autonomic Nervous System

MANCHESTER MEDICAL SOCIETY
4 30 P M *Section of Medicine* Dr C M Fletcher Research into Occupational Dust Disease

YORKSHIRE SOCIETY OF ANÆSTHETISTS
8 P.M (Leeds General Infirmary, Leeds, 2) Dr G E Hal Enderby Reduction of Surgical Hæmorrhage by Controlled Hypotension

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW 242, St Vincent Street Glasgow, C 2
5 P M. Dr Alastair G Macgregor Thyrotoxicosis—Diagnosis and Treatment by Modern Techniques (James Watson lecture)

Thursday, 26th

ROYAL COLLEGE OF SURGEONS
5 P.M Mr L P LeQuesne Management of Water and Electrolyte Administration during Postoperative Period (Arris and Gale lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine) Dr A H T Robb Smith Functional Significance of Connective Tissue

UNIVERSITY COLLEGE
4 45 P M Prof V B Wigglesworth F R S Chemical Aspects of Insect Physiology (Second of four lectures)

ROYAL SOCIETY OF MEDICINE
8 P M *Section of Urology* Dr G I M Swyer, Mr W Selby Tulloch Male Infertility

INSTITUTE OF CHILD HEALTH The Hospital for Sick Children, Great Ormond Street W C 1
5 P M Dr G Stewart Prince Emotional Problems of Puberty

ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P M Sir Clement Price Thomas Carcinoma of the Lung

ST GEORGE S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner S W 1
5 P M Dr M A Partridge Psychiatry demonstration

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant Liverpool 3
4 30 P M Sir Russell Brain, F R C P Neurology of Cervical Spine

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small s Wynd, Dundee) Prof G A H Buttle Chloramphenicol Aureomycin and Terramycin and Resistance Developed to Them

Friday, 27th

ROYAL SOCIETY OF MEDICINE
5 P M *Section of Pædiatrics* Dr D W Winnicott Symptom Tolerance in Pædiatrics (*Presidential address*)
8 15 P M *Section of Obstetrics and Gynæcology* Dr R H J Hamlin, Mr H M Carey and Mr N F Morris Pregnancy Toxæmia

INSTITUTE OF DERMATOLOGY
5 30 P M Dr D I Williams Alopecia

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES 11, Chandos Street W 1
7 30 P M Dr Denys Ford Chronic and Recurrent Arthritis of Genital Origin

Saturday, 28th

UNIVERSITY OF CAMBRIDGE
10 30 A M (Addenbrooke's Hospital) Symposium on Dermatology (*Postgraduate course for general practitioners*)

hey may be exercising functions on behalf of the regional hospital board, "shall . . . be liable in respect of any liabilities incurred (including liabilities in tort) in the exercise of those functions." He was not to be convinced that, when section 13 plainly said that hospital managers could be liable, section 72 would prevent them from being sued. He had been pressed with a Scottish case (*Davis v. Glasgow Victoria Hospitals*) in which it was decided in 1950, on the corresponding but not identical enactments relating to Scotland, that the hospital management could not be sued. The Scottish case, he said, was not binding upon him. On the preliminary point of law, therefore, the plaintiff has succeeded; but leave to appeal has been granted. It is not a matter which should be left in doubt.

Public Health

Mortality in the North of England

THE Registrar-General's Statistical Review of the year 1950[1] drew attention to the high mortality-rate in the north of England as compared with the south. Dr. C. Metcalfe Brown, medical officer of health for Manchester, has now put before the city's health committee an analysis of the mortality figures in the Manchester area, in which he has compared them with those from other parts of the country and drawn some conclusions about the causes of the difference between north and south. He has used as illustrative figures the adjusted mortality ratio and the infant-mortality rate, which, provided areas of large enough population are considered, generally agrees with the mortality ratio when different areas are being compared.

The report sets out some examples which show that, as judged by mortality-rates, the healthier parts of the country are in the south and the least healthy in the north-east. Details are then given for those districts of Lancashire and Cheshire which adjoin Manchester, Salford, and Stockport. The parts to the south show up best—most of the county districts of Cheshire have a lower adjusted mortality-rate than that of England and Wales as a whole. But most of the county boroughs to the north have a mortality ratio close to the Manchester figure of 1·22. Along the railway line which approaches Manchester from the south-west, through Hale, Altrincham, Sale, and Stretford, the mortality ratio and the infant-mortality rate show a steady turn for the worse, the infant rate rising from 8 per 1000 live births at Hale to 37 in Manchester. Atmospheric pollution increases considerably along the same railway line, factories and workshops become more numerous, the houses crowd more closely together, and living conditions deteriorate.

Dr. Metcalfe Brown sums up the disadvantages of the north as follows:

(1) Lower temperatures.
(2) Less sunshine and daylight.
(3) Greater atmospheric pollution.
(4) Greater congestion of houses.
(5) More defective houses.
(6) More intense industrial development.
(7) Heavier industrial occupations.

He lays the chief blame for the higher mortality-rate in the north on poor housing, industrialisation, and smoke pollution; and to these he adds the high proportion of unskilled workers in the population.

"Industry needs the highly skilled craftsmen but it also needs and attracts the unskilled workers. Many of these labourers are people of high intelligence but some are not. They have not acquired the skill and greater prosperity of the craftsmen because of one or more factors such as lack of opportunity, ill-fortune, lack of ambition which is not necessarily reprehensible or physical or mental incapacity. They are not, with notable and frequent exceptions, so enlightened or educated as a skilled worker in many matters, and one of the most important of these is healthy living. They and their families tend to occupy the worst houses of the town because they are cheaper and they have learned, and in many cases have been compelled, to put up with bad conditions. Perhaps they may have never had the opportunity of knowing any other. Their wage level is the lowest in the community and that, together with the other points as well as their poor environment, has resulted in a standard of life lower than that of the rest of the community. And there they will stay unless they are helped."

There is no complete remedy within the foreseeable future, Dr. Metcalfe Brown concludes, but the greater part of the problem can be attacked by building better homes, by planning towns to avoid congestion, by improving working conditions still further, by promoting health education, and by curtailing atmospheric pollution.

Influenza

Deaths from influenza are still on the increase: in the 160 great towns of England and Wales there were 446 deaths in the week ended Feb. 7, compared with 313, 132, and 72 in the three preceding weeks. The majority of deaths were again in London and the south-eastern region, where 270 people died as against 219 in the week ended Jan. 31. There were slight increases in all the other regions with the exception of the eastern region: but there is still no evidence of any serious spread to the north, and the disease continues in its mild form. The number of first claims for sickness benefit submitted to the Ministry of National Insurance decreased in most regions, including London, in the week ended Feb. 10, though there were slight increases in some parts of the north, the midlands, Wales, and Scotland. The epidemic is discussed in an annotation on p. 383.

The epidemic has fallen heavily on a number of schools in and around London.[1] At one stage Eton had 300 of its 1160 boys ill, and at Tonbridge more than half the boys were affected, but the outbreak is now subsiding.

Appointments

CHAYTOR, R. G., M.B. Durh., D.L.O.: consultant E.N.T. surgeon, hospitals in Newcastle upon Tyne and Gateshead H.M.C. groups.

DISON, GERALD, M.C., L.R.C.P.E., D.OBST., D.P.H.: asst. administrative M.O.H., Birmingham.

KALINSKY, SIDNEY, M.B. Lpool: whole-time tuberculosis M.O., North Liverpool area.

McDOUGLE, H. A., M.B. Edin.: asst. anæsthetist (S.H.M.O.), Hull "A" and East Riding groups.

MARKS, K. L., M.B. Edin., M.CH. ORTH. Lpool, F.R.C.S.E.: whole-time asst. orthopædic surgeon, hospitals in the Chester area.

PEGUM, J. S., M.A., M.D. Camb., M.R.C.P.: physician to the skin department, London Hospital.

PERRIN, JOHN, M.B. Camb., M.R.C.P.: asst. director to clinical laboratories, London Hospital.

RICE-OXLEY, J. M., M.A., D.M. Oxfd, M.R.C.P.: consultant physician, hospitals in Chesterfield, Worksop, and Retford.

WATKINS, P. F. A., M.R.C.S.: area M.O., Swindon (British Railways, Western Region).

WELLS, C. E. C., M.B. Lond., M.R.C.P.: medical registrar, Southmead Hospital, Bristol.

WHITEHEAD, J. P. S., M.R.C.S.: asst. pathologist (S.H.M.O.), Scarborough, Bridlington, Malton, and Whitby group.

Colonial Service:

DANSEY-BROWNING, G. C., M.R.C.S., D.O.M.S.: ophthalmic specialist, Hong-Kong.

DASENT, L. E., M.B.: M.O. Grade C (late student), Trinidad.

DAS GUPTA, P. R., M.B., F.R.C.S., D.L.O.: M.O. (E.N.T.), British Guiana.

KENT, P. W., O.B.E., M.B., D.P.H., D.T.M. & H.: special grade M.O., Kenya.

McLAREN, D. W., M.B. Durh., D.T.M.: senior M.O., Nigeria.

ONWU, S. E., M.B. Edin., D.T.M. & H.: D.D.M.S., Eastern Region, Nigeria.

Dublin Corporation Tuberculosis Service:

CALLAGHAN, BRENDAN, L.R.C.P.I., D.P.H.: asst. M.O.

FLANAGAN, J. J., M.B. N.U.I.: asst. M.O.

McDONAGH, ANNA, M.B. N.U.I.: asst. M.O.

WALSH, BRIDGID, M.B. N.U.I.: asst. M.O.

Births, Marriages, and Deaths

BIRTHS

EWING.—On Feb. 11, at Hammersmith Hospital, Ducane Road, W.12, to Phyllis (née Parnall), wife of Mr. Maurice R. Ewing, F.R.C.S.—a brother for Hamish.

RIGBY.—On Feb. 5, to Joan, wife of Dr. J. P. V. Rigby, of Huntsmoor Weir, Cowley, Middl[illegible]

TURNER WARWICK.—On Jan. 2[illegible] Margaret (née Harvey Moore), [illegible] Turner Warwick, F.R.C.S.—a daughter.

WOLLNER.—On Feb. 8, at The Churchill Hospital, Oxford, to Sylvia Wollner, M.B. (née Colquhoun), wife of Leopold Wollner, M.B.—a son (Mark Edward).

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[1] See *Lancet*, 1952, ii, 1223.

[1] *Daily Telegraph*, Feb. 17, 1953.

TABLE V—OPERATIVE MORTALITY 9 (7 3%) IN 122 CASES

Year	Sex	Age (yr)	Group	Cause of death	Time of death	Operation
1944	F	32	4	Surgical shock	At operation	2nd side
1946	F	46	4	,,	1 hr postop	,,
1946	F	20	4	,,	1 ,, ,,	1st side
1947	F	48	4	,,	At operation	2nd side
1948	M	49	1	Cerebral thrombosis	2nd day	,,
1949	F	39	3	Coronary thrombosis	4th ,,	,,
1949	M	49	3	,, ,,	9th ,,	,,
1950	F	31	4	Surgical shock	4 hr postop	1st side
1951	M	52	4	,, ,,	12 ,, ,,	2nd side

Operations

Patients operated on by the Smithwick method underwent resection of the splanchnic nerves through a posterior infradiaphragmatic approach, plus removal of the sympathetic chain from the level of the 8th dorsal ganglion to the 2nd lumbar ganglion In some patients the upper limit of section varied by one or two ganglia, particularly in the earliest operations, when removal did not extend above the 10th dorsal ganglion When the more extensive procedure began to be used in 1947, the approach was by a formal thoracotomy with excision of the seventh rib The sympathetic chain was divided between dorsal ganglia 3 and 4, and through a diaphragmatic incision the dissection was carried downwards to the level of the 2nd lumbar vertebra This approach does not allow, with certainty, excision of the 2nd lumbar ganglion (Boyd and Monro 1949) Subsequently this technique was modified for reasons given below, so that through a single skin incision the posterior ends of the 5th and 9th ribs were excised, making the limits of the dissection easier, and the sympathetic chain was removed from ganglion D2 to L2 inclusive

Operative Mortality and Complications

Contrary to expectation, the more extensive operation was not associated with a higher mortality There were 9 (7 3%) operative deaths among 122 patients (table v)

Empyema developed in a patient who had the extrapleural Smithwick type of operation *Postoperative effusion* developed in all the patients who underwent the Grimson type of operation, but aspiration was necessary in less than half *Acute hypotension*, particularly during or shortly after the operation on the second side, caused much anxiety but could be controlled by blood-transfusion, with methedrine, and by elevation of the foot of the bed Though *oliguria* was often met in the early postoperative days, in no case did it occasion much worry With increasing experience of the surgical problems, and the use of noradrenaline in particular, control of the blood-pressure during and after operation has been more readily achieved

TABLE VI—EFFECT OF OPERATION ON ACTIVITY

Group	No of cases	Postoperative activity		
		Increased	Unchanged	Decreased
2	29	19	6	4
3	49	27	10	12
4	14	7	3	4
Total	92	53	19	20

Postural hypotension after operation was seen in various degrees in most patients but passed off within three to six months A supporting belt was, however, necessary in 6 patients, 5 others complained of tachycardia and breathlessness on exertion or even on standing upright In 3 patients this has persisted without alteration since operation over two years ago

Vasospasm of the hands has followed operation in 24 patients 10 have developed mild symptoms, such as increased coldness and numbness of the hands in cold weather, 11 have stated that in addition to coldness their hands go blue more often than before operation, and in 3 the changes are identical with a mild Raynaud's phenomenon All these changes took place in patients early in the series In later cases the operation was therefore extended up to and including ganglion D2, and these unpleasant sequelæ now seem to have been eliminated

2 women developed *asthmatic symptoms* after the operation In one the symptoms were mild, and in the other severe for a year, later abating In the severe case the extensive type of operation, up to and including D2, had been performed

Intercostal neuralgia has followed the operation in several patients In 2, a woman and a man, it was severe and did not appear to be relieved by injection of local anæsthetic or even division of the posterior nerve roo of the affected segment 4 other patients have complained of less severe but persistent pain in their scars It has been noticed that most of the patients who have undergone transthoracic sympathectomy for hypertension complain much more of pain in the operation site during the immediate postoperative period than do other patients on the same unit who have undergone major thoracotomy for other conditions Smithwick (1951) has noticed this increased tendency to wound pain in hypertensives, and has tried to give a physical explanation for it

TABLE VII—POSTOPERATIVE BLOOD PRESSURE

Systolic blood pressure changes	Smithwick operation	Grimson operation	Diastolic blood pressure changes	Smithwick operation	Grimson operation
Increased by more than 60 mm Hg	3		Increased by more 40 mm Hg	3	1
Increased by 30–60 mm Hg	9	3	Increased by 20–40 mm Hg	7	1
Unchanged—i e, from 30 mm Hg above to 30 mm Hg below preoperative level	11	15	Unchanged — *i e*, from 20 mm Hg *above to 20 mm* Hg below pre *operative level*	17	16
Decreased by 30–60 mm Hg	10	11	Decreased by 20–40 mm Hg	6	12
Decreased by more than 60 mm Hg	3	6	Decreased by more than 40 mm Hg	3	5

Results of Operation

Symptoms

The immediate improvement in *headaches* has been striking, and in all the patients was virtually complete immediately after the operation This relief persisted in practically all the cases irrespective of the postoperative blood pressure levels 84 patients complained of severe headaches as a presenting symptom, and 53 of these have had no further headaches after the operation The remaining 31 obtained relief from headaches for various periods, but later the headache returned to some extent In 24 it was mild and of much less intensity and frequency than previously, but in the other 7 it has again become severe Of those with serious visual impairment—i e, all grade-IV patients and some grade III (65 cases)—all but 2 showed improvement, with disappearance of papillœdema and resolution of hæmorrhages and exudates These 2 patients had already suffered permanent damage to their optic nerves one has been totally blind for seven years with optic atrophy, though otherwise fit and well, the other has lost the upper half of his visual fields and has shown no improvement over the last six years

Exercise and Work Capacity

An attempt has been made to assess results by taking as a base line the normal activity of the patient before the onset of the symptoms which ultimately led to admission to hospital "Activity increased" means that the patient had returned successfully to the employment in ctor may be called upon to do. I remember, when a dresser, at the house-surgeon suggested a dental surgeon should be sked to treat a patient then in the ward. This suggestion icited the characteristic reply 'What is the use of a house-rgeon who can't draw teeth?' Within twenty-four hours at house-surgeon and the dresser learnt quite a lot about ental surgery.

"But it was after he retired, that I really came to know ir Holburt, for he often came to stay during the time I ractised in the West Country. He was unusually well formed about the simple things that interest ordinary folk, nd on one occasion when he went to a tennis party with s he was a tremendous success. Yes, he mellowed when old."

Another former student recalls the army-like discipline hat was traditional on the Waring firm.

"Clean white jackets, well-polished shoes, sharp scissors, nd torches that worked, were expected on parade, when e waited for him near the fountain. He expected from us omplete knowledge of our cases and diagnoses as detailed nd tabulated as items listed in a Civil Service inventory. Hernia, inguinal, right,' you were supposed to say and, by ay of encouragement, he would continue in unison with you, indirect, epiploenterocele, reducible, recurrent, non-strangu-ated.' But incorrect answers would call forth his displeasure nd often his favourite epithet—'you pink flamingo!'—eaning that you were a perfectly useless creature possessing owever slight ornamental value.

"He always stood with a perfectly straight back and he xpected others to do the same: the hands were often in the ockets of the white coat. His hair was snowy white and lentiful, and his blue eyes fierce and commanding as he ooked at you in a somewhat supercilious and sometimes even defiant way. His voice, always subdued at the bedside, had nasal quality, while his address tended to be bullying in one. But his manner was assertive rather than arrogant and he inspired affection rather than fear, for conscientious work won his respect though not his praise. He never smiled, but he was not unfriendly or unapproachable.

"He was at his fieriest in the theatre, but the roar and thunder of his voice as he moved from the first table to the second disturbed no-one but the novice and the occasional visitor. His bark was always far worse than his bite, and the chief assistant and the theatre sister, for whom he had profound respect, always had the situation well in hand.

"Then there was that great formality of his famous dinner parties for his dressers. I have fleeting memories of the long mahogany table in the beautiful room, a lavish display of crystal glasses, lace and silver, the thrill of the wines, the dinner jackets of one's carefully groomed colleagues, and the affable conversation of our chief. Only then and at the firm's Christmas concert did one see the light of kindliness momentarily break through the stern blue eyes of this essentially shy man."

While Sir Holburt was treasurer, A. D. W. relates, the capital of the Imperial Cancer Research Fund was trebled and its annual expenditure quadrupled.

"The two major developments of the Fund during his time have been largely due to his instigation—the obtaining of a royal charter and the erection of the Fund's *own* premises and move from Queen Square to Mill Hill. Both were carried through under his close supervision, and the Fund will always be in his debt for the ability and devoted care which he gave not only to these major questions but to all its financial and legal affairs during his long period of office."

In 1900 Sir Holburt Waring married Annie Cassandra, daughter of Mr. C. J. Hill, who died in 1948. Their only child, Mr. A. H. Waring, who succeeds to the baronetcy, is a research engineer with Imperial Chemical Industries.

BERTRAM MITFORD HERON ROGERS

B.A., D.M. Oxfd

Dr. Bertram Rogers, who died at Oxford on Feb. 9, at the age of 92, had passed most of his professional life in Bristol. His father, J. E. Thorold Rogers, M.P., was professor of political economy at Oxford and at King's College, London. From Westminster School, Rogers entered Exeter College, Oxford, where he gained a blue for association football. He continued his medical studies at University College Hospital, London, and qualified in 1889, taking his D.M. three years later.

On first going to Bristol, he engaged in general practice, but he was soon appointed physician to the Bristol Children's Hospital, and he always took a special interest in children's diseases. He played an active part in the public and professional life of the city. For some years he was secretary of the Bristol Medico-Chirurgical Society's journal, and in 1910 he was elected president of the society. As the subject of his presidential address he chose Medical Aspects of Boswell's *Life of Johnson*. Another paper based on his wide reading was his article in the *Times* in 1937, describing his discovery of two unpublished letters of Lewis Carroll. He was chairman of the Bristol branch of the St. John Ambulance Association, and treasurer of the local Royal Empire Society branch. During the 1914–18 war he commanded a field ambulance. He was highly esteemed by his colleagues; but few if any of them are living still, to mourn his loss.

WALTER HENRY GRACE

B.Sc. Sydney, M.D. Lond., F.R.C.P.

Dr. Grace, lecturer in forensic medicine and toxicology in the University of Liverpool, and forensic pathologist for the Home Office in the north-west region, died on Feb. 10 at his home near Chester.

Born in Australia in 1892, he took his B.SC. with first-class honours in the University of Sydney. Soon afterwards he came to England, where he continued his medical education at Guy's Hospital, graduating M.B. in 1918, and proceeding to the M.D. in 1922. He held several house-appointments at Guy's before he became senior assistant bacteriologist to the hospital.

A few years later he was appointed pathologist to Chester Royal Infirmary, and he quickly won for himself an authoritative position as a medicolegal consultant in North Wales, Liverpool, and the West Midlands. He became a member of Middle Temple in 1938, and in the same year was appointed to his lectureship at Liverpool University. In 1939 he was elected F.R.C.P. For some years he was an examiner for the universities of London, Glasgow, and Leeds.

In 1947 he was appointed to his Home Office post, and he figured prominently in many murder investigations and trials in the North of England, including the "Hanging Boy" case, the Cameo, Neston, and Red Wharf Bay murders, and those associated with the names of Dr. Ruxton and Dr. Clements. About a year ago increasing physical limitations led him to retire from active medicolegal practice.

"The essence of Grace's nature," writes J. M. L., "was gentleness, kindness, charm, and an unfailing courtesy. His quiet, genial manner appealed alike to colleagues, students, and laymen. His wide sympathies, combined with a delightful sense of humour, endeared him to all with whom he came into contact. He was popular with his students, who will long remember his flashes of wit and apposite commentaries on current events and problems. He was an interested observer of the academic comedy, and he enjoyed the arguments at meetings of the faculty of medicine and found a certain relish in the business of committees."

In his picture of Dr. Grace, K. S. recalls "a leonine head of near-white hair and a slow deliberation of manner which gave him a presence which seemed far older than he was—but provided a deceptive veneer to a mind that grasped the essentials of a forensic problem, foresaw the trend of cross-examination, and could adhere with a calm unshakable determination to a view he had decided was proper. These are the fundamental assets of a good witness—for both prosecution and defence; and Grace acquired the respect of each, making many friends on the Bench and at the Bar.

"He was no iconoclast, and often sought out his colleagues to sound his opinion before committing himself in court. The Euston Hotel was his choice of milieu for such meetings—with Spilsbury, Eric Gardner, Keith Simpson, or maybe an old Guy's colleague whose special experience he wished to probe, and the hotel staff plainly allowed him much latitude in these friendly consultations, which might last far into the night. Grace presented his facts lucidly and with a nice sense of humour, showed himself a good raconteur—but never failed to listen, to test theory by his academic knowledge and experience, and to express his gratitude with a courtesy that, if it sounded a little portentous, was none the less genuine. He worked hard and relaxed little, found it impossible to detach himself sufficiently to write, and may not therefore figure greatly in the history of medical jurisprudence. He

Bechgaard (1950) for the surgical and non-surgical series are represented graphically in figs. 1, 2, and 3 with the comparable survival-time curves from our series. In group 3 separate analyses for the two sexes are made, but in group 4, because of the smallness of the numbers (20) separate analyses have not been undertaken and the composite graph is compared with the mean values for males and females from Hammarström and Bechgaard's group-4 cases. We have further corrected our results, taking into account the normal life-expectancy of patients of the same sex and age as in our series. (The results were also graphed on logarithmic paper, but the graph lines so made did not show sufficient change from those published to warrant their inclusion.)

In preparing the graphs (figs. 1, 2, and 3) of the survival-times in the various groups the number of patients surviving at the end of each yearly period has been expressed as a percentage of the number at risk. Only patients who survived the operations have been included in these graphs. Those who died as a result of the operation or in the immediate postoperative period have been detailed separately (table v). The numbers surviving from each year and the survival-times of those who have died during the following period are listed in table x.

Pregnancy

4 patients have had *pregnancies* since operation: 1 has had two children, and 2 have had one each, without any deterioration in their condition. The 4th patient had a cæsarean section at 7½ months, after developing severe toxæmia, but the subsequent course was satisfactory (Newell and Smithwick 1947).

Discussion

Ignorance of the ætiological factors as well as of the natural life-history of hypertension naturally contributes to the confusion that attends any attempt to assess the results of therapy. In recent years, however, our knowledge has been increased by Keith et al. (1939), Bechgaard (1946), Burgess (1948), Palmer et al. (1948), Frant and Groen (1950), White et al. (1950), and Hammarström and Bechgaard (1950). Bechgaard (1946), by his follow-up of 1000 cases, has provided us with a most useful base-line against which can be measured the results of any form of treatment.

TABLE X—YEARLY ANALYSIS OF SURVIVING PATIENTS AND SURVIVING TIMES OF THOSE WHO DIED IN FOLLOW-UP PERIOD

Year	Group 4		Group 3 (M)		Group 3 (F)		Group 2	
	No. operated on	No. still surviving	No. operated on	No. still surviving	No. operated on	No. still surviving	No. operated on	No. still surviving
1943	[illegible]	1	[illegible]	1	2	2	1	1
1944	[illegible]		[illegible]	1	2	2		
1945	[illegible]	[illegible]			2	[illegible]	1	1
1946	[illegible]	[illegible]			[illegible]	5	[illegible]	
1947	[illegible]	[illegible]	[illegible]	4	12	10		
1948	[illegible]	[illegible]		–	[illegible]	6		
1949	[illegible]	[illegible]	[illegible]		10	[illegible]	[illegible]	
1950	[illegible]	[illegible]	3	3	3	3	[illegible]	
1951	1	1					1	
Total	20	14	19	16	45	37	29	

Length of survival time of patients who died since op[illegible]

Group 4

Sex	aged	yr	mos
F	aged 50	6 yr	
*M	„ 29	1 „	
M	„ 58	1 „	
M	„ 39	1 „	
M	„ 49	—	4 mos
M	„ 52	3 „	3 „

* Untraced after 1 year presumed dead

Group 3

1 3 yr
1 „
2 „ 2 mo
— 6 „
1 „
„ 8 „
„
8
8 „
6 „
9 „

† D
‡ U

SURVIVAL-TIME

Palmer et al. (1948) from a follow-up of [illegible] patients for an average period of eight years, concluded that a survival-rate of [illegible]% at the end of five years in group-4 patients, or of two-thirds of the patients in group 3 for a similar period, would constitute the clearest proof of effectiveness of any form of therapy. The true effectiveness in groups 1 and 2 cannot be so easily assessed, since these groups include a great number in whom the pattern that the disease is going to follow cannot be foretold—e.g., most will be slowly progressing benign hypertensives, whose expectation of life is only little affected by the condition.

The figures available from a considerable series of cases untreated or medically treated agree, within narrow limits, on the mortality in cases of groups 3 and 4. Hammarström and Bechgaard (1950), in a series grouped similarly to ours, found that in non-surgically treated group-4 cases the mortality-rate at the end of five years was 88% (female) and 85% (male), and at the end of ten years 99%. For group-3 cases the five-year mortality-rate was 62% (male) and 30% (female), and at ten years 87% (male) and 55% (female).

We do not believe that isolated examples or small series of cases of severe hypertension as recorded by Page (1939), Flaxman (1944), Blood and Perera (1948), Burgess (1948), Perera (1948), and many other workers, which seem to have undergone subsequent remission, invalidate these figures. The mortality-rate for the present series at five years is 40%, and at seven years 43% for group-4 patients, although the series comprised many more male than female patients. In group 3 the corresponding figures were 25% (male) and 16% (female) at five years. There has been no death in group 2 (29 cases) in the follow-up period.

This significant increase of survival-time, which was one of the most striking findings of this follow-up study, accords with the experiences of Hammarström and Bechgaard (1950), Peet and Isberg (1946), Smithwick (1951), Palmer (1947), Poppen and Lemmon (1947), and Evans and Bartels (1949).

SYMPTOMS

Symptomatic improvement to a degree which can be produced by no other form of therapy has been reported by numerous workers, and objective evidence of regression, such as improvement in eye grounds, has long been noted (Wells and Welbourn 1950, Smithwick 1951, d'Abreu 1948, Hammarström 1947, Grimson 1949). Reasons for this symptomatic improvement are difficult to find in our present state of knowledge but may be contained in the two demonstrable effects of sympathec-
tomy—nam[illegible] alteration of vasomotor tone in the
non-sympat[illegible] areas, and a postural fall in
blood-pressu[illegible] may persist for years after the
operations [illegible] of headache may be due to
increased (c[illegible] vasomotor tone in the non
[illegible] thecto[illegible] which prot[illegible] the capillaries
[illegible] the [illegible]-pressure [illegible] would explain
relief fro[illegible] which oc[illegible] the subse
[illegible]t blood [illegible]ls are n[illegible] duced by
[illegible]on [illegible] shown [illegible] al. 1948
[illegible] 1948, [illegible]48, Ph[illegible] that after
[illegible] the [illegible] of [illegible] are no
reached [illegible] of [illegible] heart and
[illegible]od-ve[illegible] the stress
[illegible]ly [illegible] essential

can be
[illegible]ment

morning and evening, he attended church in Exeter, and, though he never discussed his religion there is no doubt that it meant everything to him, and guided the whole conduct of his life."

JAMES ARTHUR KERR

V.R.D., M.D., B.Sc. Glasg., D.P.H.

We have to record the death of Dr. J. A. Kerr, medical officer of health for the county borough and port of Grimsby, on Feb. 10, at the age of 51.

Born in Glasgow, he was educated at the High School and University of his native city. His undergraduate career was interrupted by service as a surgeon probationer in the Navy during the first world war, but he qualified in 1923. He took his D.P.H. two years later, and while working for this studied law and became a member of the Middle Temple. His M.D. was obtained with commendation in 1928. He held resident posts in the Western Infirmary, Glasgow, and became successively senior assistant medical officer at Manchester City Fever Hospital, deputy medical officer of health for Chester, and senior assistant medical officer of health for Birmingham.

His services to Grimsby, where he was appointed M.O.H. in 1931, were of a high order, for they were based alike on ability, energy, courage, and sympathy. Characteristically, he was fully engaged in public duties until the evening before his brief terminal illness. For twenty years he had been handicapped by severe physical disability, but he had remained an unusually dynamic figure, always a leader in planning improvements in the town's medical facilities and always ready to help his colleagues either in their day-to-day difficulties or in any cause which he felt justified his support. He was fearless in expressing his views, and he put them forward with a vigour which made him a valuable and much respected member of any committee.

In the second world war he again served in the Navy and he was awarded the King Haakon VII Liberation Medal for outstanding services in connection with the liberation of Norway. He remained a surgeon commander, R.N.V.R.

Among his local appointments, Dr. Kerr was the school medical officer and was consultant in infectious diseases at Springfield Isolation Hospital. He was a member of the Grimsby Hospitals Management Committee, the local medical and local obstetric committees, and the local executive council. His broad and accurate knowledge and his good will enabled him to maintain excellent relations between his department and his colleagues in general practice. His handling of the poliomyelitis epidemics in 1938 and 1947 and the smallpox epidemic in 1947 earned high praise from those who worked with him. Largely owing to his foresight and enthusiasm, an almoner service was established in the health department in 1949, and the mental health services were founded and steadily improved. It was with Dr. Kerr's coöperation that Dr. J. W. Brown established his well-known clinics for heart-disease and rheumatism. He was also a very active member of the Lincolnshire Joint Cancer Committee, whose pioneer scheme made specialist treatment available to many who otherwise would not have had it. His professional interests extended outside Grimsby and he was president of the East Midland branch of the Society of Medical Officers of Health for 1949–50, and an examiner to the Royal Sanitary Institute. He was also a member of the general and medical committees of the Association of Sea and Air Port Health Authorities of the British Isles. His published work includes articles on puerperal sepsis and its cardiac and pulmonary complications, on fish inspection, and on the treatment of poliomyelitis.

To the end of his life, he found time for numerous activities outside medicine. In Grimsby he was president of the Royal Naval Association, president of the Grimsby and Cleethorpes Rotary Club, and chairman of the international service committee of Rotary. He was chairman of the civilian committee of the Sea Cadet Corps, and president of the Hard of Hearing Association, which he helped to found.

In 1933, he married Doreen, daughter of the late Dr. A. M. Nevin of Birmingham, and she survives him with two sons and a daughter.

Notes and News

PRESCRIPTION COSTS

Presenting the civil appropriation accounts,[1] the Comptroller and Auditor-General remarks that in 1950 18% of all prescriptions under the National Health Service in England and Wales, and 26% of those in Scotland, were for proprietary preparations. In England and Wales the 18% accounted for 33·5% of the total cost of prescriptions. In 1951 the percentage of prescriptions for proprietary preparations increased to 23 in England and Wales and to 30 in Scotland; and in April, 1952, a sample analysis of prescriptions in England and Wales showed a further rise to 25·6%.

SCHOLARSHIPS ABROAD

The British Council has published a booklet giving details of about 100 scholarships offered by 17 foreign governments and universities to British students for study abroad during 1953–54. Further information may be had from the controller of the education division of the council, 65, Davies Street, London, W.1.

University of Cambridge

On Feb. 6 the following degrees were conferred:

M.D.—I. S. Hodgson-Jones.

M.B., B.Chir.—* I. M. Brown.

* By proxy.

Royal College of Surgeons of England

At a meeting of the council on Feb. 12, with Sir Cecil Wakeley, the president, in the chair, Mr. Geoffrey Keynes was presented with the Cecil Joll prize.

Prof. Ian Aird (Postgraduate Medical School) and Mr. F. W. Holdsworth (Sheffield) were re-elected and Mr. E. S. Lee (Westminster Hospital) was appointed to the court of examiners for the next three years. Mr. A. H. Lendon (Adelaide) and Prof. H. R. Dew (Sydney), the present Commonwealth travelling professor, were elected members for one year.

A Hunterian lectureship was awarded to Prof. Wilder Penfield, O.M. (Montreal), and a Moynihan lectureship to Dr. H. L. Jaffe (New York). The Hallett prize was awarded to A. T. Matheson (Cape Town), and the Handcock prize to A. H. Tooley (King's College Hospital).

Diplomas of membership and postgraduate diplomas were granted to those named in our report (Feb. 7, p. 303) of the comitia of the Royal College of Physicians.

Hunterian Festival Dinner.—At this dinner on Feb. 13 Sir Cecil Wakeley, the president, said that the Queen had graciously consented to lay the memorial stone of the new buildings on May 5. He was also happy to announce that the Duke of Edinburgh had promised to come to the college to receive the honorary fellowship in the autumn. Good progress was being made with the new college: the framework and floors of the Great Hall and the dining-room of the Nuffield College of Surgical Sciences were complete; and the Wellcome museums, the new council room, and the library extension were beginning to take shape. There were hopes of making a start on the main block of the Nuffield College later this year. Sir Cecil said that this was probably the last Hunterian dinner to be held in the present library, for the Great Hall should be ready in good time for the festival of February, 1955. A great deal of research work was in hand at the college, and the president referred particularly to the plans of the department of pharmacology which were being generously supported by certain pharmaceutical firms. Sir Cecil was replying to the toast of The College, proposed by the Minister of Health, Mr. Iain Macleod. Sir James Paterson Ross extended a friendly welcome to the large company of guests, for whom Sir Denys Lowson replied. Sir Reginald Watson-Jones, proposing the toast of The Hunterian Orator, said how magnificently Mr. Lionel Norbury had paid homage to the memory of John Hunter in his oration earlier in the day. Mr. Norbury, in a brief reply, spoke of the pleasure and satisfaction to be derived from a study of the history of medicine; his own researches into the Hunterian era had proved an absorbing source of interest.

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[1] Civil Appropriation Accounts (classes I–VIII), 1951–52. H.M. Stationery Office. Pp. 487. 14s.

Bechgaard (1950) for their surgical and non-surgical series are represented graphically in figs 1, 2, and 3, with the comparable survival-time curves from our series In group 3 separate analyses for the two sexes are made, but in group 4, because of the smallness of the numbers (20), separate analyses have not been undertaken, and the composite graph is compared with the mean values for males and females from Hammarstrom and Bechgaard's group-4 cases We have further corrected our results, taking into account the normal life expectancy of patients of the same sex and age as in our series (The results were also graphed on logarithm paper, but the graph lines so made did not show sufficient change from those published to warrant their inclusion)

In preparing the graphs (figs 1, 2, and 3) of the survival-times in the various groups the number of patient's surviving at the end of each yearly period has been expressed as a percentage of the number at risk Only patients who survived the operations have been included in these graphs Those who died as a result of the operation or in the immediate postoperative period have been detailed separately (table v) The numbers surviving from each year and the survival-times of those who have died during the following period are listed in table x

Pregnancy

4 patients have had *pregnancies* since operation 1 has had two children, and 2 have had one each, without any deterioration in their condition The 4th patient had a cæsarean section at $7^1/_2$ months, after developing severe toxæmia, but the subsequent course was satisfactory (Newell and Smithwick 1947)

Discussion

Ignorance of the ætiological factors as well as of the natural life-history of hypertension naturally contributes to the confusion that attends any attempt to assess the results of therapy In recent years, however, our knowledge has been increased by Keith et al (1939), Bechgaard (1946), Burgess (1948), Palmer et al (1948), Frant and Groen (1950), White et al (1950), and Hammarstrom and Bechgaard (1950) Bechgaard (1946), by his follow-up of 1000 cases, has provided us with a most useful base line against which can be measured the results of any form of treatment

TABLE X—YEARLY ANALYSIS OF SURVIVING PATIENTS AND SURVIVING TIMES OF THOSE WHO DIED IN FOLLOW-UP PERIOD

Year	Group 4		Group 3 (M)		Group 3 (F)		Group 2	
	No operated on	No still surviving	No operated on	No still surviving	No operated on	No still surviving	No operated on	No still surviving
1943	2	1	1	1	2	2	1	1
1944	2		2	1	2	2		
1945	3	2			2	2	1	1
1946	1	1			7	5	4	4
1947	2	1	5	4	12	10	10	10
1948	5	4			7	6	4	4
1949	2	2	8	7	10	7	4	4
1950	2	2	3	3	3	3	4	4
1951	1	1					1	1
Total	20	14	19	16	45	37	29	29

Length of survival time of patients who died since operation

Group 4

F	aged	50	6 yr	
*M	,,	29	1 ,,	
M	,	58	1 ,,	
M	,	39	1 ,,	
M	,	49	—	4 mos
M	,	52	3 ,,	3 ,,

* Untraced after 1 year presumed dead

Group 3

†F	aged	51	3 yr	
F	,,	40	1 ,,	
F	,	50	2 ,,	2 mos
M		52	—	6 ,,
‡M	,	39	1 ,,	
M	,,	43	2 ,,	8 ,,
F	,,	34	3 ,	
F	,	24	2 ,	8
F		36	2 ,,	8 ,
F	,,	32	1 ,,	6
F	,	43	—	9 ,,

† Died of carcinoma of pancreas
‡ Untraced after 1 year, presumed dead

SURVIVAL-TIME

Palmer et al (1948) from a follow up of 430 patient for an average period of eight years, concluded that a survival-rate of 20% at the end of five years in group-4 patients, or of two thirds of the patients in group 3 for a similar period, would constitute the clearest proof of effectiveness of any form of therapy Therapeutic effectiveness in groups 1 and 2 cannot be so easily assessed, since these groups include a great number in whom the pattern that the disease is *going to follow* cannot be foretold—e g , most will be slowly progressing benign hypertensives, whose expectation of life is but little affected by the condition

The figures available from a considerable series of cases untreated or medically treated agree, within narrow limits, on the mortality in cases of groups 3 and 4 Hammarstrom and Bechgaard (1950), in a series grouped similarly to ours, found that in non surgically treated group 4 cases the mortality-rate at the end of five years was 88% (female) and 85% (male), and at the end of ten years 99% For group 3 cases the five year mortality rate was 62% (male) and 30% (female), and at ten years 87% (male) and 55% (female)

We do not believe that isolated examples or small series of cases of severe hypertension as recorded by Page (1939), Flaxman (1944), Blood and Perera (1948), Burgess (1948), Perera (1948), and many other workers, which seem to have undergone subsequent remission, invalidate these figures The mortality-rate for the present series at five years is 40%, and at seven years 43%, for group-4 patients, although the series comprised many more male than female patients In group 3 the corresponding figures were 25% (male) and 16% (female) at five years There has been no death in group 2 (29 cases) in the follow-up period

This significant increase of survival time, which was one of the most striking findings of this follow up study, accords with the experiences of Hammarstrom and Bechgaard (1950), Peet and Isberg (1946), Smithwick (1951), Palmer (1947), Poppen and Lemmon (1947), and Evans and Bartels (1949)

SYMPTOMS

Symptomatic improvement to a degree which can be produced by no other form of therapy has been reported by numerous workers, and objective evidence of regression, such as improvement in eye grounds, has long been noted (Wells and Welbourn 1950, Smithwick 1951 d'Abreu 1948, Hammarstrom 1947, Grimson 1949) Reasons for this symptomatic improvement are difficult to find in our present state of knowledge but may be contained in the two demonstrable effects of sympathectomy—namely, an alteration of vasomotor tone in the non-sympathectomised areas, and a postural fall in blood-pressure, which may persist for years after the operations The relief of headache may be due to increased (compensatory) vasomotor tone in the non sympathectomised head, which protects the capillaries against the raised blood-pressure This would explain the relief from headaches which occurs when the subsequent blood-pressure levels are not much reduced by operation It has been shown (Wilkins et al 1948, Bourne 1948, Tuckwell 1948, Philps 1948) that after operation the higher peaks of blood pressure are no longer reached, and because of this the heart and small blood-vessels are no longer exposed to the stress of the widely fluctuating blood pressures of essential hypertension

CAPACITY FOR EXERCISE AND WORK

Increased capacity for exercise and work can be regarded as a measure of the symptomatic improvement

SYMPATHECTOMY IN THE TREATMENT OF HYPERTENSION

REVIEW OF 122 CASES

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THIS paper reviews the results of thoracolumbar sympathectomy in 122 patients with hypertension treated at the Queen Elizabeth Hospital, Birmingham, between 1943 and 1951. All except 2, who were untraced after a year, have been seen and examined regularly. Up to 1947 a limited sympathectomy was performed, using techniques similar to those described by Peet et al. (1940) and Smithwick (1940); but from then onwards the more extensive resection associated with Grimson (1941) was done. The two series are not strictly comparable; but, when some additional information is thereby gained, separate analyses have been made.

TABLE I—GROUP, SEX, AND TYPE OF OPERATION IN 113 PATIENTS SURVIVING OPERATION

Operation	Group 4		Group 3		Group 2	
	Males	Females	Males	Females	Males	Females
Smithwick ..	9	1	6	20	4	10
Grimson ..	5	5	13	25	4	11
Total ..	14	6	19	45	8	21

In classifying the patients the system described by Hammarström and Bechgaard (1950) has been adopted as being more convenient than the more complicated one of Smithwick (1951) or the method of Keith et al. (1939), which is based mainly on an accurate but personal assessment of retinal changes.

Investigation and Classification of Cases

Routine investigations included intravenous pyelography, estimation of the blood-urea, analysis and concentration tests of urine, electrocardiography, radiography of the chest, and ophthalmoscopy. In some cases early in the series inulin and diodone clearances were estimated. Much interest centred at one stage on the demonstration of the hypotensive effects of amylobarbitone, tetraethylammonium bromide, sympathetic blockade by local anæsthetics, and vasodilation by various pyrogens. These tests were gradually abandoned when it was found that they added little to the information gained by recording the blood-pressure hourly for twenty-four hours and had no prognostic value.

TABLE II—AGE-DISTRIBUTION IN 113 PATIENTS SURVIVING OPERATION

Operation	Age-group (yr.)				
	10–19	20–29	30–39	40–49	50–59
Smithwick ..	1	6	13	21	9
Grimson ..	—	3	18	21	21
Total ..	1	9	31	42	30

According to the results of these investigations the patients were divided into four groups (Hammarström and Bechgaard 1950) as follows:

Group 1.—Hypertension, with no secondary vascular complications, and either no subjective symptoms or only slight symptoms.

Group 2.—Hypertension. Marked subjective symptoms. No signs of myocardial damage or vascular change. Left axis-deviation on electrocardiography and/or a relative enlargement of the left ventricle, and heart volume radiographically within normal limits. Retinal changes grade I or II (Keith et al. 1939).

Group 3.—Hypertension, with subjective symptoms and/or signs of secondary vascular complications—i.e., retinal grade-III changes (Keith et al. 1939), including retinal hæmorrhages with or without thrombosis of the retinal vessels, or retinæ grade I or II with one or more of the following: negative T wave in the electrocardiogram; heart volume above predicted normal (transverse diameter greater than half the thoracic diameter); residual damage to central nervous system after cerebral accident; or albuminuria.

Group 4.—Hypertension, with retinal exudates and papillœdema grade IV (Keith et al. 1939).

TABLE III—DISTRIBUTION OF SECONDARY VASCULAR MANIFESTATIONS IN 64 GROUP-3 CASES

Secondary vascular complications	Grimson operation		Smithwick operation	
	Living (32)	Died since operation (6)	Living (21)	Died since operation (5)
Renal (albuminuria, &c.)	23	6	8	2
Lesions of central nervous system	23	4	16	4
Cardiac (E.C.G. changes, &c.)	19	6	6	4
Retinitis grade III ..	23	4	15	3

No. of systems affected ..	1	2	3	4
Living	23	23	6	1
Died since operation ..	4	5	1	1

The composition of each group is further analysed by sex and age in tables I and II.

Essentially, group 3 contains all the patients with evidence of secondary vascular damage of the retinal, cerebral, cardiac, or renal vessels. Many had involvement of more than one system, and it will be noted (table III) that coronary and renal damage was associated with the highest mortality since operation.

TABLE IV—PREOPERATIVE BLOOD-PRESSURES IN 113 PATIENTS SURVIVING OPERATION

Diastolic B.P. (mm. Hg)	Group 4	Group 3	Group 2	Systolic B.P. (mm. Hg)	Group 4	Group 3	Group 2
Over 180	2	4	..	Over 240	2	5	2
160–180	6	12	2	210–240	10	29	14
140–160	8	24	10	180–210	8	25	9
120–140	4	22	11	150–180	..	5	4
110–120	..	2	6				
Total	20	64	29	..	20	64	29

ESTIMATIONS OF BLOOD-PRESSURE

A very large series of preoperative blood-pressure readings was collected for each patient, and the selection of a figure which could be called "the blood-pressure" for each case was a most difficult task. We took the view that the occasional very high or very low figure in the records of most patients had little value for comparison with "casual" follow-up figures, since our patients were not readmitted for serial postoperative blood-pressure readings. We have therefore chosen as the preoperative level in each case the resting recumbent pressure taken on the second or third day in hospital. Table IV gives the preoperative diastolic and systolic levels in the 113 cases available for observation.

SELECTION OF CASES

It must be emphasised that only in a small proportion of hypertensives is sympathectomy indicated We exclude from consideration the mild symptomless hypertension which is met in group 1 of the present classification A few patients in group 2 should be considered for surgery when the symptoms have become incapacitating despite the usual remedial measures When they are first seen at this stage it is impossible to predict how the disease will progress Experience shows that many remit, some follow a slow benign course, and only a very few develop at a more rapid tempo into "severe benign" or malignant types.

The onset of secondary vascular changes characteristic of group 3 brings with it further considerations At this stage the prognosis is no longer in doubt, and the urgency of treatment is measured by the rate of deterioration, which can be assessed from the history, the age, and a short period of observation It is important that the slowly developing benign hypertensives should be recognised when met in this group They are usually aged 50–60 and are unsuitable for surgery Palmer (1947) has called attention to this type and has termed it "burnt out benign hypertension" We believe that active hypertensive disease can be arrested at this stage by sympathectomy, and that some of the apparent failures to do so are due to mistaken diagnosis and failures on technical and anatomical grounds In view of the low mortality the surgical risk is acceptable for the very considerable benefits to be gained, particularly if more conservative measures are unsuccessful Undoubtedly this group will contain some hypertensives with primary renal disease, but we have no evidence that, if the renal function is reasonably good, the operative risk is affected For group-4 patients sympathectomy is indicated if two or three months' complete rest and adequate treatment with hypotensive drugs cause no evident interruption of hypertension or its symptoms Failing improvement in these circumstances the decision should not be deferred too long, because the surgical risk is thereby increased Our best results have been obtained in malignant hypertensives under the age of 40 We regard congestive cardiac failure, poor renal function, and advanced arteriosclerosis as contra indicating surgery, and prefer our patients to be under the age of 50, although many in the present series were over that age

Summary

The classification suggested by Hammarstrom and Bechgaard (1950) has been used in reviewing the results of thoracolumbar sympathectomy in 122 patients treated in 1943–51

The results, together with those reported by other workers, support the view that operation prolongs life and produces substantial symptomatic and objective improvement irrespective of its effect on the blood-pressure

It was considered that the operation was indicated in a small proportion of group-2 cases for the relief of incapacitating headache, for most cases in group 4, and for those cases in group 3 with actively progressing hypertensive disease uncontrolled by other measures

The surgical mortality, though high in group 4, was 3% in group 3 in the series reviewed, and nil in group 2

The view is expressed that mistaken diagnoses, technical difficulties, and anatomical factors may be responsible for some of the anomalous findings

We wish to express our thanks to the physicians of the Queen Elizabeth Hospital, Birmingham, under whose care many of these patients were admitted and whose help and coöperation made the review possible The operations in addition to our own were performed by Dr William H Sweet, of the Massachusetts General Hospital, Boston, Mass (officer in charge of a neurosurgical unit "on loan" from the United States 1941–45), Prof Brodie Hughes, Prof F A R Stammers, Mr A L d'Abreu, and Mr A Gourevitch We are indebted to Dr John Waterhouse, of the department of medical statistics, University of Birmingham, for his guidance and help in the analyses

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TEMPORAL ARTERITIS AND ITS TREATMENT WITH CORTISONE AND A.C.T H.

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THE clinical picture of temporal arteritis was first described by Hutchinson more than sixty years ago (Hutchinson 1890) in the octogenarian father of a London Hospital beadle The man was quite bald and developed red painful streaks on his head which prevented him from wearing his hat The red streaks were inflamed temporal arteries the branches of which could be traced and almost met in the midline At first feeble pulsation could be detected in the arteries, but later these became pulseless, lost their redness, and were left as impervious

SYMPATHECTOMY IN THE TREATMENT OF HYPERTENSION

REVIEW OF 122 CASES

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THIS paper reviews the results of thoracolumbar ympathectomy in 122 patients with hypertension treated t the Queen Elizabeth Hospital, Birmingham, between 943 and 1951. All except 2, who were untraced after year, have been seen and examined regularly. Up to 947 a limited sympathectomy was performed, using echniques similar to those described by Peet et al. 1940) and Smithwick (1940); but from then onwards he more extensive resection associated with Grimson 1941) was done. The two series are not strictly comarable; but, when some additional information is hereby gained, separate analyses have been made.

TABLE I—GROUP, SEX, AND TYPE OF OPERATION IN 113 PATIENTS SURVIVING OPERATION

Operation	Group 4		Group 3		Group 2	
	Males	Females	Males	Females	Males	Females
Smithwick ..	9	1	6	20	4	10
Grimson ..	5	5	13	25	4	11
Total ..	14	6	19	45	8	21

In classifying the patients the system described by Hammarström and Bechgaard (1950) has been adopted as being more convenient than the more complicated one of Smithwick (1951) or the method of Keith et al. (1939), which is based mainly on an accurate but personal assessment of retinal changes.

Investigation and Classification of Cases

Routine investigations included intravenous pyelography, estimation of the blood-urea, analysis and concentration tests of urine, electrocardiography, radiography of the chest, and ophthalmoscopy. In some cases early in the series inulin and diodone clearances were estimated. Much interest centred at one stage on the demonstration of the hypotensive effects of amylobarbitone, tetraethylammonium bromide, sympathetic blockade by local anæsthetics, and vasodilation by various pyrogens. These tests were gradually abandoned when it was found that they added little to the information gained by recording the blood-pressure hourly for twenty-four hours and had no prognostic value.

TABLE II—AGE-DISTRIBUTION IN 113 PATIENTS SURVIVING OPERATION

Operation	Age-group (yr.)				
	10–19	20–29	30–39	40–49	50–59
Smithwick ..	1	6	13	21	9
Grimson ..	—	3	18	21	21
Total ..	1	9	31	42	30

According to the results of these investigations the patients were divided into four groups (Hammarström and Bechgaard 1950) as follows:

Group 1.—Hypertension, with no secondary vascular complications, and either no subjective symptoms or only slight symptoms.

Group 2.—Hypertension. Marked subjective symptoms. No signs of myocardial damage or vascular change. Left axis-deviation on electrocardiography and/or a relative enlargement of the left ventricle, and heart volume radiographically within normal limits. Retinal changes grade I or II (Keith et al. 1939).

Group 3.—Hypertension, with subjective symptoms and/or signs of secondary vascular complications—i.e., retinal grade-III changes (Keith et al. 1939), including retinal hæmorrhages with or without thrombosis of the retinal vessels, or retinæ grade I or II with one or more of the following: negative T wave in the electrocardiogram; heart volume above predicted normal (transverse diameter greater than half the thoracic diameter); residual damage to central nervous system after cerebral accident; or albuminuria.

Group 4.—Hypertension, with retinal exudates and papillœdema grade IV (Keith et al. 1939).

TABLE III—DISTRIBUTION OF SECONDARY VASCULAR MANIFESTATIONS IN 64 GROUP-3 CASES

Secondary vascular complications	Grimson operation		Smithwick operation	
	Living (32)	Died since operation (6)	Living (21)	Died since operation (5)
Renal (albuminuria, &c.)	25	6	8	2
Lesions of central nervous system	23	4	10	4
Cardiac (E.C.G. changes, &c.)	19	6	6	4
Retinitis grade III ..	23	4	15	3

No. of systems affected ..	1	2	3	4
Living	23	23	6	1
Died since operation ..	4	5	1	1

The composition of each group is further analysed by sex and age in tables I and II.

Essentially, group 3 contains all the patients with evidence of secondary vascular damage of the retinal, cerebral, cardiac, or renal vessels. Many had involvement of more than one system, and it will be noted (table III) that coronary and renal damage was associated with the highest mortality since operation.

TABLE IV—PREOPERATIVE BLOOD-PRESSURES IN 113 PATIENTS SURVIVING OPERATION

Diastolic B.P. (mm. Hg)	Group 4	Group 3	Group 2	Systolic B.P. (mm. Hg)	Group 4	Group 3	Group 2
Over 180	2	4	..	Over 240	2	5	2
160–180	6	12	2	210–240	10	29	14
140–160	8	24	10	180–210	8	25	9
120–140	4	22	11	150–180	..	5	4
110–120	..	2	6				
Total	20	64	29	..	20	64	29

ESTIMATIONS OF BLOOD-PRESSURE

A very large series of preoperative blood-pressure readings was collected for each patient, and the selection of a figure which could be called "the blood-pressure" for each case was a most difficult task. We took the view that the occasional very high or very low figure in the records of most patients had little value for comparison with "casual" follow-up figures, since our patients were not readmitted for serial postoperative blood-pressure readings. We have therefore chosen as the preoperative level in each case the resting recumbent pressure taken on the second or third day in hospital. Table IV gives the preoperative diastolic and systolic levels in the 113 cases available for observation.

and ACTH given intramuscularly or by slow intravenous drip, produced changes far beyond their usual tonic and euphoric effect Pyrexia, head pains, and arterial tenderness rapidly subsided, appetite improved, and in some cases there was a dramatic change from apathy and misery to alertness, cheerfulness, and interest One patient (case 4) had been ill for six months and, when treatment was started, had pyrexia up to 101°F, severe head pains, and grossly inflamed temporal and occipital arteries She was given eleven daily intravenous drips of ACTH , the pyrexia, headache, arterial tenderness, and inflammation rapidly subsided, and at the end of the course of treatment she felt completely well Another (case 9) had pyrexia, severe headache, tenderness of the scalp, and the grossest cranial arteritis She was so ill that a fatal issue was highly probable, but within seventy-two hours of the institution of cortisone therapy her pyrexia, head pains, and tenderness of the scalp had disappeared and she was alert and subjectively well

The answer to the second question, as to whether a brief period of treatment with cortisone is curative, seems equally definite Though symptoms and objective evidence of active disease always disappeared very rapidly, the erythrocyte-sedimentation rate remained high (cases 3, 4, 7, 9, 10, and 12) In this connection it must be pointed out that for weeks or months a raised ESR is often the only definite evidence of the disease , but, so long as it is present, vision is constantly threatened, a cerebral or coronary vascular catastrophe may occur at any time, or cranial arteritis or severe constitutional symptoms may develop One patient (case 11) died of a coronary occlusion four weeks after ACTH therapy, and follow-up of others (cases 7, 8, and 9) showed that the disease was still active months after the cessation of treatment

One patient (case 10) appeared to be cured, apart from a raised ESR , after fifteen days' intramuscular ACTH therapy, but with diminishing doses her pyrexia, head pain, and arterial tenderness returned and there was an obvious deterioration in her general condition Dosage was therefore increased, and within two or three days she was once more subjectively and objectively normal ACTH therapy was continued for a further twenty-three days, and to date (twelve months after the cessation of treatment) she has remained in normal health, apart from some residual visual loss Altogether she had ACTH for forty-two days, and for ten days before it was stopped her ESR was only just outside the normal range

Another patient (case 9) had previously had a peptic ulcer, and though cortisone therapy rapidly controlled the symptoms and signs of temporal arteritis (apart from the ESR) it had to be stopped because of a severe recrudescence of ulcer symptoms Within a few days head pains, pyrexia, and general malaise recurred and the abdominal symptoms subsided Further cortisone therapy once more produced a remission of the temporal arteritis, but ulcer dyspepsia returned For four months temporal arteritis and peptic ulceration alternately called for treatment, and three and six months after the patient's discharge from hospital the ESR was still grossly raised

It appears, therefore, that maintenance therapy is required, and in only 2 of our cases (nos 10 and 12) was it possible to continue treatment until the disease reached its natural end The cause of temporal arteritis is probably not an infection, and ACTH and cortisone presumably produce their effect by blocking some sensitisation mechanism Before they can be said to have cured the disease, their administration has to be continued until there is no longer any sensitisation to block

Visual Loss

The results obtained in the 10 of our 12 patients who had ocular involvement were as follows

(1) 4 patients (cases 3, 5, 6, and 7) had been totally blind for periods ranging from six days to four weeks when treatment was begun, and in none did any vision return

(2) 1 patient (case 1) had had partial loss of vision from five to eight months before ACTH therapy, and no improvement resulted

(3) 5 patients (cases 2, 8, 9, 10, and 11) had had partial loss of vision for periods of ten days or less All showed some improvement in their visual acuity, and visual fields after cortisone or ACTH therapy, but the degree of change was relatively small, and in none was normal sight restored

It may well be that the improvement that took place in the third group was that which so often occurs naturally after any thrombotic incident and was quite unrelated to cortisone therapy The results obtained, however, are of some value in management, both from the prognostic and therapeutic aspects, and might have been better if more prolonged therapy had been possible Total blindness and long-standing partial loss of vision are unlikely to improve, and cortisone will probably not help them When loss of vision is partial and recent, some amelioration is likely with cortisone therapy (and possibly without it), but normal sight is unlikely to return The chief value of cortisone or ACTH in such cases is without doubt to control the arteritis as long as it lasts and so to safeguard any vision that remains

CASE-RECORDS

Case 1 —A man, aged 68, was admitted in November, 1950, with asthenia, loss of weight, and pain in the right loin, where a mass was palpable The results of radiography after a barium enema and of intravenous pyelography were normal, but the urine contained pus and blood A renal neoplasm was suspected, and the right kidney was therefore explored and removed Histological examination showed chronic pyelonephritis The patient's general health did not improve, and he had severe headaches and scalp tenderness In March, 1951, the vision of his right eye suddenly deteriorated, and three months later his left eye was similarly though less severely affected He was readmitted in November, 1951, when the occipital and temporal arteries were thickened and tender but still pulsating There was no pyrexia, and the ESR was 16 mm at one hour (Wintrobe) There was no anæmia or leucocytosis The fundi were normal apart from arteriosclerotic changes, and the visual acuity was 6/6 (part) right and 6/5 (part) left The left visual field was full, but only central vision remained in the right eye The patient was given 20 mg of ACTH by slow intravenous drip each day for ten days Though his general condition improved and his head pains disappeared his visual acuity and visual fields did not alter Three months later he still had active temporal arteritis

Case 2 —A man, aged 83, was admitted to hospital with typical temporal arteritis a few days after experiencing sudden diminution in vision in both eyes On admission the visual acuity in the right eye was reduced to the appreciation of hand movements, and the visual field to a small temporal wedge The left eye had a visual acuity of 6/12 and a full visual field The patient was given a slow intravenous drip of 20 mg of ACTH daily for five days His left eye did not improve, but the whole of the right temporal field was restored, and visual acuity in this eye was 6/60 when he left hospital

Case 3 —A woman, aged 79, had six months' history of malaise, loss of weight, anorexia, and pains in the neck, arms, and legs, and five weeks' history of severe temporal and occipital pain and tenderness of the scalp Twenty two days before treatment was begun she suddenly lost all vision in the right eye, and four days later the left eye also became totally blind The discs were pale, their edges were indistinct and the retinal arteries were narrow and irregular There was a low pyrexia, the temporal arteries were tender and apulsatile, and the ESR was raised, being 29 mm at one hour (Wintrobe) She was given large doses of cortisone intramuscularly for nine days and, though there was striking subjective improvement, and the pyrexia and head pains rapidly subsided, no vision returned and the ESR remained high

Case 4 —A woman, aged 77, was admitted with six months' history of pains in the head, shoulders, neck, and ears, which

TABLE VIII—LATEST SYSTOLIC BLOOD-PRESSURES IN 35 GRIMSON-TYPE CASES FOLLOWED UP 3–5 YEARS AND IN 36 SMITHWICK TYPE CASES FOLLOWED UP 5–9 YEARS

Systolic B.P. (mm. Hg)	Group 4			Group 3			Group 2		
	Smithwick	Grimson	Total	Smithwick	Grimson	Total	Smithwick	Grimson	Total
Over 240	1	1	2	4	2	6	1	..	1
210–240	..	1	1	5	1	6	3	..	3
180–210	2	1	3	2	8	10	4	2	6
150–180	2	..	2	5	7	12	5	4	9
120–150	1	2	3	1	3	4	..	2	2
Under 120	..	..	..	..	..	..	..	1	1
Total	6	5	11	17	21	38	13	9	22

which he or she was engaged before the onset of severe symptoms. "Activity as before operation" includes many patients whose activity, though improved, has not permitted them to resume their usual work. In the lowest category are placed the patients who lead a semi-invalid existence postoperatively, and in these cases activity has been decreased since the operation. 92 cases were followed up sufficiently to allow an assessment to be made (table VI).

Blood-pressure

About a third of the patients who underwent the Smithwick type of operation, and half of those who underwent the Grimson operation, have shown an appreciable reduction of blood-pressure (table VII). Readings were taken in the recumbent position after a resting period of fifteen to twenty minutes.

The latest blood-pressure readings in the 36 Smithwick-type cases followed up for between five and nine years, and the 35 Grimson-type cases followed up for three to five years have been analysed in tables VIII and IX; those of under three years' observation are not included. 13 patients (18%) have a diastolic pressure of below 100 mm. Hg, and 40 (56%) less than 120 mm. Hg. Preoperatively no patient had a diastolic blood-pressure below 110 mm. Hg, and only 8 (11%) had one below 120 mm. Hg. 10 patients (14%) show a systolic pressure of less than 150 mm. Hg, and 32 (45%) one less than 180 mm. Hg, whereas the preoperative figures are none and 9 (13%) respectively. These figures refer to 71 patients of the 113 under observation; of the remaining 42, 21 have died since operation and 14 of the Grimson type have been followed for less than three years. The remaining 7 patients are known to be alive and well, but live away from Birmingham, and records of their blood-pressures are not available.

Electrocardiogram

Of the patients who had survived five years following operation 33 had abnormal electrocardiograms preoperatively, well-marked left axis-deviation, and, more commonly, T-wave changes of "left ventricular strain," and hypertrophy. Of these, 14 became completely normal, 6 had improved to show only left axis-deviation, and the remaining 13 showed no essential change.

Survival-time

The effect of sympathectomy on survival-time noted by various workers (Smithwick 1951, Hammarström and Bechgaard 1950)—namely, that expectancy of life in hypertensives is considerably increased by the operation—is further confirmed, and survival-time is directly related to the grouping: group 4 (those with papillœdema) has the gravest prognosis; group 3 (secondary vascular complications) has a less grave prognosis; and group 2 has the best chance of survival. Group 1 is not considered, because none in this category was operated on. The life-expectancy tables of Hammarström and

TABLE IX—LATEST DIASTOLIC BLOOD-PRESSURES IN 35 GRIMSON-TYPE CASES FOLLOWED UP 3–5 YEARS AND IN 36 SMITHWICK TYPE CASES FOLLOWED UP 5–9 YEARS

Diastolic B.P. (mm. Hg)	Group 4			Group 3			Group 2		
	Smithwick	Grimson	Total	Smithwick	Grimson	Total	Smithwick	Grimson	Total
Over 180	..	..	..	..	..	..	1	..	1
160–180	..	1	1	2	..	2	..	..	..
140–160	..	..	..	6	1	7	2	1	3
120–140	2	1	3	3	6	9	5	..	5
100–120	4	1	5	4	10	14	4	4	8
Under 100	..	2	2	2	4	6	1	4	5
Total	6	5	11	17	21	38	13	9	22

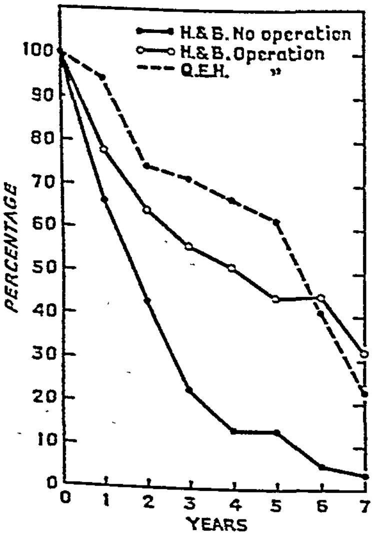

Fig. 1—Survival-times over seven years of group-4 male and female patients of Queen Elizabeth Hospital, Birmingham (Q.E.H.), compared with operated and unoperated series of Hammarström and Bechgaard (1950) (H. & B.).

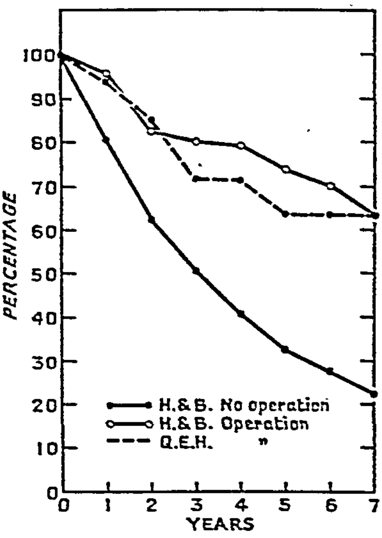

Fig. 2—Survival-times over seven years of group-3 male patients of Queen Elizabeth Hospital, Birmingham (Q.E.H.), compared with operated and unoperated series of Hammarström and Bechgaard (1950) (H. & B.).

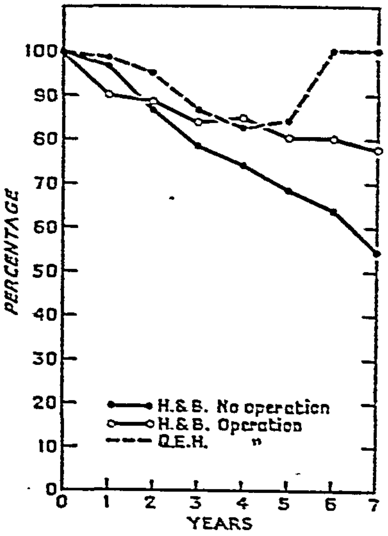

Fig. 3—Survival-times over seven years of group-3 female patients of Queen Elizabeth Hospital, Birmingham (Q.E.H.), compared with operated and unoperated series of Hammarström and Bechgaard (1950) (H. & B.).

temporal arteries were thickened, tender, and apulsatile A blood count was normal, but her E S R was 32 mm at one hour She was given intramuscular A C T H for fifty-two days Within six days of the start of therapy her headache and arterial tenderness disappeared and her general condition showed a striking improvement On discharge her E S R was 24 mm and she has since remained completely well

SUMMARY

The clinical features and pathology of temporal arteritis are briefly recounted, and the characteristics and diagnostic value of the headache and visual loss are emphasised

Twelve cases treated with cortisone or A C T H are described In ten the vision was affected.

A C T H and cortisone controlled the disease in all the cases, but relapse occurred when treatment was stopped. Maintenance therapy appears to be required until the disease reaches its natural termination

The total blindness of four patients and the long-standing partial loss of vision in one other patient were not altered by cortisone therapy, but in five patients with recent partial loss of vision there was some improvement in visual acuity and visual fields, which may have been due to cortisone therapy

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CONTROLLED HYPOTENSION IN NEUROSURGERY

WITH SPECIAL REFERENCE TO HYPOTENSION INDUCED BY PNEUMATIC SUCTION APPLIED TO THE LEGS

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A METHOD has been described (Saunders 1952) by which adequate falls of blood-pressure were produced by hexamethonium bromide (H M B) during anæsthesia with the patient maintained at or near the horizontal posture Suction was applied to the legs by encasing them in airtight metal cylinders connected to a suction pump of large capacity

We know of no report making a direct comparison between neurosurgical cases operated on with and without controlled hypotension using H M B as the hypotensive agent In the present paper we compare 150 cases in which no attempt was made to lower the pressure (normotensive group) with 150 cases in which such an attempt was made (hypotensive group)

Hypotension was produced by H M B and suction to the legs in 50 of the patients in the hypotensive group, and by H M B and posture in the remaining 100 Technical modifications have now been made to the suction apparatus (see below), though the principle remains the same

TABLE I—AGE, SEX, AND NUMBER OF PATIENTS UNDERGOING EACH TYPE OF OPERATION IN THE TWO GROUPS

—	Normotensive group	Hypotensive group
Operation		
Craniotomy	102	75
Laminectomy	10	68
Miscellaneous	38	7
Total	150	150
Sex		
Male	80	89
Female	70	61
Age (years)		
Youngest	8	8
Oldest	81	72
Mean	39	42

The 300 cases comprise all those operated on in this unit between Oct 4, 1950, and July 28, 1952, except 43 operations (leucotomy 14, abscess aspirations 2, and 27 on children under eight years of age) omitted because there were no comparable cases in the hypotensive group.

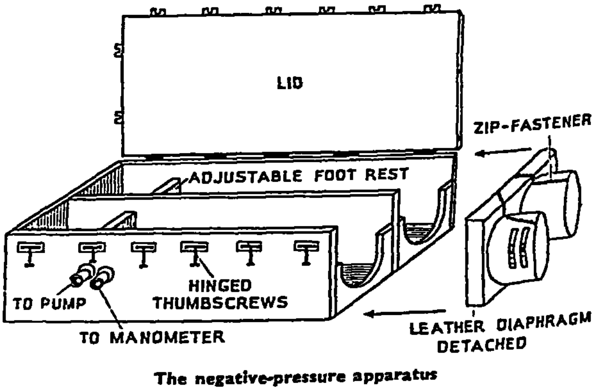
It will be noted from table I that there is a preponderance of laminectomies in the hypotensive group This is because initial experience of the technique was gained with that operation

Since it has been suggested that cerebral, cardiac, and renal ischæmia are liable to result from hypotension, electrocardiograms have been recorded and the cerebral venous oxygen content has been estimated at the low blood-pressures during operation Observations have also been made on the renal function

NEGATIVE-PRESSURE APPARATUS

By the time that H M B alone had been used in 80–90 cases its limitations, particularly in craniotomies, had become apparent In only half of them was a successful degree of hypotension and hæmostasis obtained A tilt of the operating-table of at least 30° was required, which was the maximum acceptable to the surgeon For all posterior-fossa, and for most frontal, craniotomies a much smaller tilt was essential to allow surgical access Hence H M B could not be used for these operations

For these reasons the negative-pressure device described by Saunders (1952) was devised This was similar in principle to the apparatus with which Restall and Smirk (1951, 1952) produced falls of blood-pressure in conscious persons The metal cylinders originally used (Saunders 1952) have now been replaced by a rectangular wooden box with a hinged lid (see figure) The patient's legs lie on either side of a wooden partition whose function is to prevent buckling of the lid with the negative pressure The lid is held closed by hinged



The negative-pressure apparatus

among the cases of lesser severity—i.e., group 2 and one in group 3. In more severe cases it reflects the diminution in heart size and improvement in signs of congestive failure and encephalopathy. 5 patients with congestive cardiac failure have been operated on; 2 of these have already survived three and five years and have returned to their work, an experience noted by Chavez and Mendez (1949) in 8 of 11 such patients.

ELECTROCARDIOGRAM

The finding of left ventricular strain on electrocardiography has also influenced us in undertaking operation. Canabal et al. (1945) have shown that the chances of such electrocardiographic changes reverting to normal without operation are about one in ten. After thoracolumbar sympathectomy the electrocardiogram became normal in a third, and there was some degree of improvement in a further third, of the cases. Peet and Isberg (1948) noted that 52% of their cases with abnormal electrocardiograms became normal. Similar trends were noted in our patients. Leishman (1951) suggests that this may be due to the diminution in size of the heart, and again our observations tended to confirm this suggestion. Indeed, the electrocardiographic findings are one of the truly objective measurements of benefit to be obtained by sympathectomy.

RENAL EFFECTS

Early in the series 16 renal biopsy specimens were taken. 2 patients with healed pyelonephritis and 1 with evidence of chronic glomerulonephritis underline the great difficulty that may be met in excluding patients who have a primary renal cause for their hypertension. Such patients will naturally alter the prognosis. Unless biopsies are routinely taken, even with the defects of such methods, any series would be likely to contain similar patients (Platt and Stanbury 1950), since the available clinical methods of diagnosis are insufficiently accurate. Persike et al. (1949) have operated on patients in the terminal stage of glomerulonephritis and claimed satisfactory results. Of their 10 patients 1 died as the result of the operation, 2 could not be followed, and 2 died at six and ten months, but the other 5 returned to work for periods up to forty-nine months at the time of publication. Since these patients had serum-creatinine levels varying from 2·22 to 8·75 mg. per 100 ml., blood-pressures between 184/134 and 290/185 mm. Hg, and visual disturbance, and were totally incapacitated, the reports suggest that severe kidney damage need not be an absolute bar to operation if other circumstances favour it.

BLOOD-PRESSURE

Much of the adverse criticism of the surgical treatment of hypertension is based on its failure to reduce the blood-pressure in the majority of cases (Evelyn et al. 1949, McMichael 1952, Platt and Stanbury 1950). Too much preoccupation with this single measurement of the disease tends to divert attention from other equally objective tests of improvement, such as reduction of cardiac size, and improvement shown on electrocardiography, exercise tolerance, fundi, and survival-times.

Patients were operated on because their symptoms had become incapacitating despite other forms of treatment, or because they had begun to exhibit such evidence of secondary vascular disease that steady deterioration was the only prognosis. Blood-pressure levels alone did not justify operation. Though it is true that the higher the blood-pressure the worse is the outlook (Frant and Groen 1950), it is often difficult to decide the true level of the preoperative blood-pressure. On reviewing the results it was soon evident that lability of blood-pressure was no guarantee of success in reducing it by operation, whereas a relatively fixed raised blood-pressure did not necessarily rule out a highly successful result. For example, the first patient to undergo operation, a man aged 28, had a fixed hypertension with a diastolic blood-pressure of 130–140 mm. Hg, and visual acuity limited by papillœdema to perception of light only, yet now, almost ten years later, he is working overtime as a toolsetter with only a slightly raised blood-pressure.

These observations agreed with the view, widely held, that blood-pressure readings, except in the highest levels, are of little importance in assessing the severity of essential hypertension. What are more important are (1) the rate of progress of the secondary vascular changes in the cerebral, renal, and cardiac vessels, (2) evidence of cardiac decompensation or coronary thrombosis, and (3) evidence of impending renal failure, such as constant albuminuria, hæmaturia, and inability to concentrate urine.

Comment on the effects of surgery on the blood-pressure would be incomplete without consideration of the anatomy of the sympathetic system which makes complete excision a difficult technical procedure (Mitchell 1947). This is well recognised in connection with the minimal ablations required to denervate the limbs. In the case of thoracolumbar sympathectomy not only is the resection much more extensive but also there is little opportunity of testing its completeness in the splanchnic and renal areas, and such indirect tests as may be used suggest that resection is often far from complete (Boyd and Monro 1949).

We have tried to correlate the postoperative progress of our patients with their blood-pressure levels, and have been unable to find a relationship. Some, in whom the blood-pressure has been lowered to normal and has remained so, have had their activity diminished, whereas others, whose blood-pressure was unaffected, were symptomatically and objectively improved. Several of the patients who died soon after operation showed a progressively rising blood-pressure during the period of their survival.

SURGICAL MORTALITY

Mortality from sympathectomy is related to the proportion of group-4 patients in any series. In the present review 7 of the 9 deaths within the immediate postoperative period were in group 4. 27 patients in group 4 were operated on, and the 7 deaths give an operative mortality of about 26%. We regard this high figure as a measure of our attempt to save some of the most advanced cases with cardiac and/or renal insufficiency rather than as an indication of the risk the operation entails in a fairly fit patient. In 66 cases in group 3 there were 2 deaths (about 3%), and of the 29 patients in group 2 none died. In a brief reference to his results Learmonth (1950) stated that his mortality-rate for all cases accepted for surgical treatment was "just under 3%." Recently Blainey (1952) published the results of a series of cases treated in this hospital with hexamethonium compounds. In a personal communication he has given us the mortality-rates while the patients were under medical treatment. In his series there were 7 group-4 patients, but 2 of these were aged more than 60 and are not comparable to ours. The remaining 5 patients (aged 34–36 years) all died within nine months while undergoing treatment with hexamethonium. In group 3 there were 8 patients, but 1 was over 60 years of age, the remainder being between 45 and 52. Of these 7 patients 2 died within a year of starting treatment. Blainey's figures in group 4 regarding mortality are only for a very small group of cases, but the fact that there is also a mortality from medical treatment should be borne in mind, a point sometimes omitted when the efficacy of various therapeutic substances is being assessed (*British Medical Journal* 1952).

TABLE III—COMPARISON OF RESULTS OBTAINED IN NORMOTENSIVE AND HYPOTENSIVE GROUPS

—	Normotensive group (no H.M.B.)	Hypotensive group	
		H.M.B. and posture	H.M.B. and suction
Craniotomies			
Number	102	39	36
Mean total H.M.B. (mg.)	—	104	65
Satisfactory hypotension and hæmostasis	—	54%	75%
Patients requiring transfusion	64%	69%	39%
Pints per patient of whole series	0.95	1.05	0.66
Mean duration of anæsthesia (hours)	4³/₄	4¹/₄	4¹/₄
Mortality	18.6%	15.4%	11.1%
Laminectomies			
Number	10	55	13
Mean total H.M.B. (mg.)	—	75	46
Satisfactory hypotension and hæmostasis	—	60%	92%
Patients requiring transfusion	50%	9%	8%
Pints per patient of whole series	0.5	0.15	0.15
Mean duration of anæsthesia (hours)	3¹/₄	3	3
Mortality	20%*	0	0

* The 20% mortality shown for laminectomies in the normotensive group is misleading. This represents 2 patients only, of whom one had a widespread retroperitoneal sarcoma from which she died some weeks later, and the other died from massive pulmonary embolism.

in the normotensive group. The duration of anæsthesia was again reduced, and the mortality fell to just over half the original level. With suction to the legs the number of patients in whom satisfactory hypotension and hæmostasis were obtained was increased from 54 to 75% and the requisite dose of H.M.B. decreased by a third.

With laminectomies hypotension produced an even greater fall in the number of patients requiring transfusion, and operating time was decreased as with the craniotomies. The suction technique when used for laminectomies proved especially valuable in increasing the number of satisfactorily hypotensive patients. As can be seen, an adequate fall of blood-pressure is now obtained in practically every patient.

Thus, in both craniotomies and laminectomies, the suction technique has proved more satisfactory in every way than H.M.B. combined with posture, and in addition the patient can be maintained at, or near, the horizontal posture, thus giving increased safety for the patient and increased convenience for the surgeon.

Mortality

The deaths mentioned are those which took place before the patient left hospital, all but 3 being within a month of operation. 10 patients in the hypotensive group of 150 died, compared with 24 in the normotensive group. Necropsies were made in all of these. This decrease in death-rate is attributed largely to improved surgical treatment. The 20% mortality shown in table III for the laminectomies in the normotensive group is misleading. This represents 2 cases only: one patient had an untreatable sarcoma invading the spinal canal, from which she ultimately died, and the other died from massive pulmonary embolism.

There was only one death in the hypotensive group attributable to the hypotensive technique.

This was in a hypertensive woman, aged 51, with a ruptured aneurysm on the middle cerebral artery, which was wrapped with muscle at operation. She received 25 mg. of H.M.B. in one intravenous dose and a moderate degree of suction (40 mm. Hg). This produced a satisfactory hypotensive result. Postoperatively her blood pressure rose within five hours to its preoperative level of 180/110 mm. Hg, whereupon she was given three further doses of H.M.B. at hourly intervals in an unsuccessful attempt to keep her blood pressure below 150/100. She became drowsy eight hours *after* operation, slowly lapsed into coma by next day, and died six days later. At necropsy unsuspected bilateral congenital cystic kidneys and a cystic liver were found, and the condition of the brain was satisfactory. If the condition of her liver and kidneys had been known before operation, the hypotensive technique would not have been used, and only the smallest possible amount of iodine contrast medium would have been used for arteriography.

Apart from this case, the causes of the deaths in the normotensive and the hypotensive groups were similar. The majority were due to raised intracranial pressure, in some cases associated with intracerebral hæmorrhage. In addition, 4 patients in the normotensive group died from massive pulmonary embolism. There were no such cases in the hypotensive group. Thus there seems to be nothing to suggest that the application of negative pressure involving the use of non-constricting leather cuffs round the thighs is associated with an increased tendency to thrombus formation in the legs.

Complications

Unusual complications arose in only 2 of the hypotensive group during their stay in hospital.

(1) A young man, aged 27, who had a cervical laminectomy and a partial removal of a meningeal sarcoma, became blind in one eye suddenly on the third postoperative day. This was thought to be a minor embolic phenomenon, although the ophthalmoscopic appearances were not pathognomonic of occlusion of the retinal artery. The hypotensive technique was thought not to be responsible.

(2) A man, aged 65, had a cervical laminectomy and section of the posterior roots of C8, T1, and T2 for intractable left ulnar nerve pains. On recovering consciousness he had a transient weakness of the right palate, vocal cord, and sternomastoid muscle, which was thought to be due possibly to a spasm or minor thrombosis in part of the territory of the right inferior cerebellar artery. He recovered completely. The hypotensive technique could have been responsible in this case.

No postoperative intracerebral hæmatomata have occurred in the hypotensive group. In 2 cases of pituitary tumour the conscious state deteriorated postoperatively and a re-exploration was done. No hæmatoma was found, however, in either case, and the defect of consciousness was found to be due to an endocrine imbalance and rapidly responded to substitution therapy (Caughey et al. 1952).

Follow-up

Of the 94 surviving patients who received H.M.B. alone, 74 were re-examined at intervals of one to thirteen months after discharge, with a mean follow-up period of five months. No untoward symptoms have appeared. The cases treated with H.M.B. and suction have not yet been followed for a significant period but have as yet shown no untoward effects.

Estimations of Cerebral Venous Oxygen

Samples of blood were taken under anaerobic conditions from either the cranial venous sinuses or the cerebral veins of patients undergoing craniotomies. In no case was there any undue reduction of the venous oxygen content at the hypotensive levels used.

Electrocardiography

Electrocardiograms were recorded on patients before, during, and after hypotension, and no changes were found suggesting myocardial ischæmia. Two of these patients had known coronary-artery disease.

One, a woman aged 70, tolerated a systolic blood pressure of 60 mm. Hg satisfactorily at operation. The other, a woman aged 52, who was not for operation, had hypertension (220 mm. Hg systolic) and angina of effort accompanied by pronounced electrocardiographic changes with exercise. The anginal pain and electrocardiographic changes were regularly produced by 30 paces on the flat. The systolic pressure of this patient was gradually lowered, while she was conscious, to 60 mm. Hg by H.M.B. and posture, and there was no anginal pain or electrocardiographic change suggesting myocardial anoxia at that pressure.

ends. The patient lived for several years after this lness.

Though Schmidt (1930) described a further case, it was through workers at the Mayo clinic (Horton et al. 932, 1934, Horton and Magath 1937) that the clinical nd histological features became widely known and ppreciated. It was they who suggested the name "temporal arteritis" and emphasised many of the major linical features—the mature age of the patients, the rotracted nature of the malady, the pyrexia, anæmia, nd leucocytosis, the loss of weight, and the inflammation ound the temporal arteries. Nothing has since been dded to their description of the histological changes, he features of which are round-cell infiltration round he vasa vasorum in the adventitia, the replacement f the media by granulation tissue, with the partial or omplete disappearance of the elastic laminæ, infiltration f the media with plasma cells, lymphocytes, and giant ells and sometimes areas of hæmorrhage, together with cellular thickening of the intima, often associated with thrombosis.

Horton and his colleagues held that temporal arteritis was relatively benign and its duration limited to a few months. Such prognostic optimism has, however, not been justified by the experience of subsequent workers, for Cardell and Hanley (1951) point out that in 27 of 37 published cases the patients died during the active phase of the disorder. The cause of death was in most cases coronary or cerebral thrombosis; and, though it is possible that the coincidence of such incidents was fortuitous, since temporal arteritis only occurs during the degenerative period of life, it is more probable that they were part of a generalised arteritis. Ample evidence has been provided to show that temporal arteritis is part of a generalised vascular disease, fatal cases having shown similar histological lesions in the aorta and carotid, innominate, subclavian, pulmonary, cœliac, mesenteric, renal, iliac, radial, and coronary arteries (Sproul 1942, Chasnoff and Vorzimer 1944, Cooke et al. 1946, Cardell and Hanley 1951).

Bacteriological examination of numerous biopsy specimens has not revealed a cause, and the ætiology remains unknown.

CLINICAL FEATURES

More than 150 cases have now been published and the condition has been extensively reviewed (Harrison 1948, Crosby and Wadsworth 1948, Migone and Mortara 1949, Cooke 1951, Cardell and Hanley 1951). The main features of temporal arteritis are essentially those set out by Horton and his colleagues and can be readily comprehended from the case-records given below. The condition is not uncommon, and, when once a typical patient has been seen and the modes of presentation are appreciated, most practitioners are likely to recognise examples. From our experience of more than 30 cases, two features appear to warrant further comment—namely, headache and disturbances of vision.

Headache is a constant feature of the disease. The organic causes of headache in later life are few; and, though cerebral tumour, hypertension, glaucoma, and Paget's disease have to be considered, the headache of temporal arteritis has unique features which immediately suggest the diagnosis to anyone familiar with the condition. Usually throbbing, but sometimes aching or lancinating, the headache is very severe, preventing sleep and often persisting relentlessly for weeks. It is commonly confined to the areas of the temporal and occipital arteries, and often the scalp is so tender that even mastication and laying the head on a pillow are painful. Such headaches should always lead to a careful examination of the temporal and occipital arteries and their branches.

Visual complications.—Ocular involvement has been variously estimated as 33% (Kilbourne and Wolff 1946), 40% (Anderson 1947), 33% (Harrison 1948), 35% (Migone and Mortara 1949), and 38% (Cardell and Hanley 1951). Of the 31 cases which we have observed ocular involvement occurred in 16, and 8 of the patients became totally and permanently blind. The symptoms prefacing such catastrophes have been varied. Loss of vision may be sudden "like a blind being drawn across," or it may be preceded by one or more episodes of transitory amblyopia or diplopia. Papillœdema and retinal hæmorrhages are often but not always evident, and later the features of optic atrophy develop in which the disc is slightly filled in and has a curious creamy appearance. Where total blindness does not ensue, any form of loss of the visual field may take place. Histological studies have shown that the ophthalmic and retinal arteries may be involved by the same type of arteritis as occurs in the temporal and other arteries, narrowing of the lumen or thrombosis being responsible for the visual loss. We would suggest that any elderly patient who has transitory amblyopia or sudden loss of sight should be carefully examined for tender temporal or occipital arteries, and his symptoms should be reviewed as possibly due to temporal arteritis.

TREATMENT

The treatment has until recently been limited to section of the affected artery to give relief from the severe headache. All other treatments, of which many have been tried, are relatively ineffective. The self-limiting nature of the disorder militates against accurate assessment of any form of therapy; reports, however, on the use of cortisone and adrenocorticotropic hormone (A.C.T.H.) have begun to accumulate. Shick et al. (1950) reported benefit in 2 cases. Robertson (1952) treated 6 cases with A.C.T.H. or with cortisone, and in each of them improvement was dramatic and immediate. Though, when treatment was discontinued, symptoms gradually recurred, it was thought that the course of the disease was probably alleviated and shortened. Aveling and Stevenson (1952) published details of a case in which A.C.T.H. therapy rapidly produced complete relief of symptoms. No relapse took place when, after three and a half weeks, treatment was discontinued.

PRESENT INVESTIGATION

During the past eighteen months we have had the opportunity to treat 12 unequivocal cases of temporal arteritis with A.C.T.H. or with cortisone (see below). Of the 12 patients 7 were women and 5 men, and all were aged more than 65 (mean 78, range 66–88). All except 2 had some loss of vision, amounting in 4 to complete blindness. This high incidence of ocular involvement should not be taken as an accurate reflection of the frequency of this complication, because in 8 cases consultative opinion was first sought because of visual loss. It is, however, an indication of its great clinical importance.

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Hayward (1952) suggests that, when the arterial pressure is lowered by ganglion-blocking agents, the blood-flow to the cardiac muscle may be decreased to a greater extent than the decrease in cardiac work, leading to a liability to myocardial ischæmia at the low pressures He suggests that a person with normal coronary arteries will probably come to no harm, but that in latent coronary-artery disease, symptomless under normal conditions, there would seem to be a grave risk of infarction at the low pressures The treatment of several hundred hypertensive patients in this hospital has shown that most of such patients with previous angina of effort are improved when their arterial pressure is lowered by H M B , but that some are made worse (Smirk 1952) Observations have not been made, however, on normotensive patients with angina Electrocardiograms recorded on patients in this series have shown no evidence of myocardial ischæmia at the low pressures, even in the 2 patients with known coronary artery disease It seems that, when the patient has normal coronary arteries, the degrees of hypotension used do no harm It is felt, however, that the situation is not yet sufficiently clear where there is coronary damage , so in any doubtful cases we still think it essential to record electrocardiograms during the operation, to guard against myocardial ischæmia If this is done, tragedies will be avoided and much useful information obtained

Renal damage does not appear to result from the hypotension We are in agreement with Evans and Hale Enderby (1952) that there is no significant increase in red cells or in albumin in the urine after hypotension Patients continue to excrete considerable quantities of urine at the low blood-pressures used, which would be unlikely if glomerular filtration was greatly impaired This is in agreement with the findings of Miles et al (1952) The patients in this series therefore provide no evidence that the degrees of hypotension used are damaging to the normal kidney

SUMMARY AND CONCLUSIONS

The reduction of blood-pressure has been used to reduce bleeding and intracranial tension during 150 neurosurgical operations, and the results are compared with those obtained in 150 cases in which no reduction of blood-pressure was attempted

The fall of blood-pressure was induced by hexamethonium bromide (H M B), assisted by controlled pneumatic suction applied to the legs in 50 cases, and by posture in 100

When a negative pressure is applied to the legs, the requisite dose of H M B is less and postoperative hypotension almost eliminated

The blood pressure can be varied at will over a considerable range by regulating the suction pressure

Blood-pressures of 55–65 mm Hg are used to diminish the bleeding The adequacy of the hæmostasis at any time can be examined by decreasing the suction to the legs and temporarily raising the blood-pressure

H M B when assisted by posture gave satisfactory blood-pressure falls in 54% of craniotomies and 60% of laminectomies, and when assisted by leg suction in 75% of craniotomies and 92% of laminectomies

Estimations of cerebral venous oxygen tensions, renal function tests, and electrocardiograms were made The results obtained do not suggest the likelihood of adverse effects from the hypotension, but special care is enjoined in certain cases

It is concluded that controlled hypotension, especially when brought about by H M B and variable suction applied to the legs, has led to decreased mortality, decreased transfusion, and a slightly shorter duration of anæsthesia The decrease of bleeding and of intracranial tension enable the surgeon to attain a higher standard of surgery in neurosurgical work

We should like to express our gratitude to Prof F H Smirk for suggestions and criticisms, both during the experimental work and during the preparation of this paper, to Mr R G Robinson, assistant surgeon to the unit, for permission to treat and to refer to patients under his care, and to the staff of the Neurosurgical Unit for their willing coöperation at all stages The hexamethonium bromide ('Vegolysen') was supplied by Messrs May & Baker The expenses were defrayed in part by the Medical Research Council of New Zealand

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CLINICAL TESTS RELATING TO MENTAL ACTIVITY IN INFANCY

EIRENE COLLIS
C P T , M C S P , M A O T , O N C
IN CHARGE OF CEREBRAL PALSY UNIT, QUEEN MARY'S HOSPITAL FOR CHILDREN, CARSHALTON, SURREY

THOUGHT processes are expressed in physical activity, and it is in physical activity that, in the infant, the earliest expression of developing mental processes must be sought The change from the type of activity seen *in the newborn infant to more mature activity* involving thought processes occurs gradually, and is at first intermittent Yet, normally, physical signs of advance appear which may be correlated approximately with months of age, and are useful criteria of development Failure of normal progress is not, however, necessarily significant of *mental* defect it occurs also where neural deficiency is confined to the *motor* apparatus (motor defect) The distinction between mental and motor abnormalities in the infant may be difficult, especially where these coexist, but they can, in fact, be distinguished

The observations reported here have been made over twelve years and cover more than 2000 cases of infantile cerebral deficiency and over 500 normal infants In all cases where abnormality was found to be *confined to the reflex motor apparatus* there was a history of asphyxia livida at birth

Though identical movements occur in the infant and the older child (André-Thomas and Hanon *1948), and* though the range of movement at the joints is similar, the nature of the activity into which these are integrated changes as thought processes develop Activity occurring in the presence of thought processes is described *as* "voluntary" (Hobbes 1651), though even in mature activity "a large part of voluntary movement is *both* involuntary and outside consciousness" (Kinnier Wilson 1928) When the subject's attention is focused on *the* *manner of performing* any act, a movement shows predominance of the voluntary quality (Hughlings Jackson 1893) When attention is directed towards *achievement* (e g , the preservation of an attitude against resistance, the execution of a difficult or unaccustomed task, the overcoming of embarrassment or other *emotion)* movement shows predominance of the reflex quality (Darwin 1872, Wallon 1934, André Thomas *1940)* The falling child "reflexly" throws out his arms, the athlete cords. The patient lived for several years after this illness.

Though Schmidt (1930) described a further case, it was through workers at the Mayo clinic (Horton et al. 1932, 1934, Horton and Magath 1937) that the clinical and histological features became widely known and appreciated. It was they who suggested the name "temporal arteritis" and emphasised many of the major clinical features—the mature age of the patients, the protracted nature of the malady, the pyrexia, anæmia, and leucocytosis, the loss of weight, and the inflammation round the temporal arteries. Nothing has since been added to their description of the histological changes, the features of which are round-cell infiltration round the vasa vasorum in the adventitia, the replacement of the media by granulation tissue, with the partial or complete disappearance of the elastic laminæ, infiltration of the media with plasma cells, lymphocytes, and giant cells, and sometimes areas of hæmorrhage, together with acellular thickening of the intima, often associated with thrombosis.

Horton and his colleagues held that temporal arteritis was relatively benign and its duration limited to a few months. Such prognostic optimism has, however, not been justified by the experience of subsequent workers, for Cardell and Hanley (1951) point out that in 27 of 137 published cases the patients died during the active phase of the disorder. The cause of death was in most cases coronary or cerebral thrombosis; and, though it is possible that the coincidence of such incidents was fortuitous, since temporal arteritis only occurs during the degenerative period of life, it is more probable that they were part of a generalised arteritis. Ample evidence has been provided to show that temporal arteritis is part of a generalised vascular disease, fatal cases having shown similar histological lesions in the aorta and carotid, innominate, subclavian, pulmonary, cœliac, mesenteric, renal, iliac, radial, and coronary arteries (Sproul 1942, Chasnoff and Vorzimer 1944, Cooke et al. 1946, Cardell and Hanley 1951).

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(2) If it does control the disease, is it curative, or is maintenance therapy required until the condition comes to its natural termination?

(3) Has cortisone or A.C.T.H. any power to restore sight where visual loss has occurred?

From our experience of this small series it appears possible to give a definite answer to each of these three questions, and we think our impressions may be helpful to those faced with the management of this disease, which at worst kills, often blinds, and at least produces prolonged suffering and disability.

DISCUSSION

With regard to the first question, there could be no doubt that cortisone given orally or intramuscularly, tive movements, in which Bergeron (1947) includes "bicycling" (flexions and extensions of the legs) and *battant le briquet* (crossing and uncrossing of the ankles) "Stilling" reactions (Hines 1942), trembling and shivering (Wallon 1934), "fanning" of the fingers and toes, arching of the body backward (Bergeron 1947)

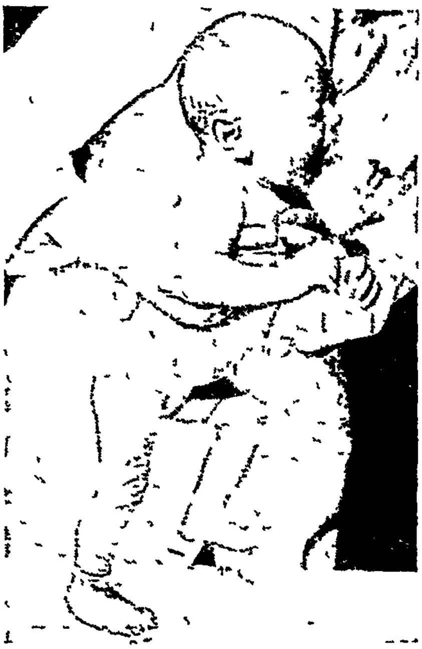

Fig 4—" Stepping reflex " of normal infant.

3 *Reactions to Handling*

(*a*) Resistance is encountered on passive displacement of the limbs, this resistance, or "rigidity," described by Minkowski (1921) and others, is decreased or absent during feeding, drowsing, and sleeping

(*b*) In the supine position, when the infant is abruptly disturbed, a diffuse "startle" reaction occurs (Moro 1918), this reaction is "pre-emotive" and cannot, therefore, be called a "fear reaction" (Wallon 1934) It involves wide displacement of the limbs from their resting attitude, and may be evoked by varied stimuli —e g, by rapidly moving the infant in space (Schaltenbrand 1925)

(*c*) Palmar and plantar grasping reactions (figs 6 and 7) (Walshe and Robertson 1933, Sturmmann 1940)

(*d*) In the supine position, the infant exhibits rolling of the trunk and flexed legs to the side to which the head is passively turned (*Halsstellreflex*—"neck-righting," Schaltenbrand 1925) On passive turning of the head with the pelvis fixed, a "tonic neck reflex" movement of the arms is seen (Minkowski 1927)

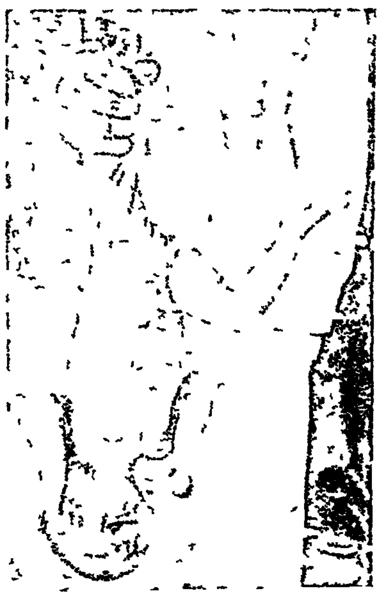

Fig 5—Reaction of bending and stretching of free leg on release of ankle in normal infant.

(*e*) "Flaccidity" (Preyer 1887) is evidenced, for example, if the infant is pulled by the arms towards a sitting position, his head does not come up with the trunk, but falls back, and when he is held upside down by the ankles his head hangs limply

(*f*) Placed on his side, the infant rolls into a supine or prone position If he is held on his side and the uppermost leg is passively abducted, extended at the hip, and then released, it falls slackly

(*g*) A "withdrawal" reaction of both legs occurs on stimulation of the sole of one foot, and if the stimulus is strong, the reaction obtained appears identical with the "startle" reflex

(*h*) There is variability of the plantar response to firm moving stimuli, occasional ankle clonus is seen, tendon jerks may be differingly described as "sluggish" or "brisk" according to the general state of drowsiness or alertness ("tonicity") of the infant at the time of examination Body curving reactions to stimulation of the skin (*Ruckgratreflex*—"back-scratch" reflex—Galant 1925) similarly vary in intensity

4 *Other Reactions*

Occasional squinting and nystagmus, "rolling" of the eyes, reflex blinking only when the eye is actually touched, crying without tears, occasional opening of one *eye at a time and only partial closure of the eyelids in sleep* (Wallon 1934) Occasional grimacing, tongue protrusion sucking and swallowing movements unassociated with feeding, as well as similar movements during feeding Nuzzling for the nipple does not occur in newborn babies, but appears during the neonatal phase Yawning and stretching, hiccuping, sneezing, and vomiting all occur There is, of course, incontinence, and speech gesture, and all other recognisable evidence of *mental activity* is absent

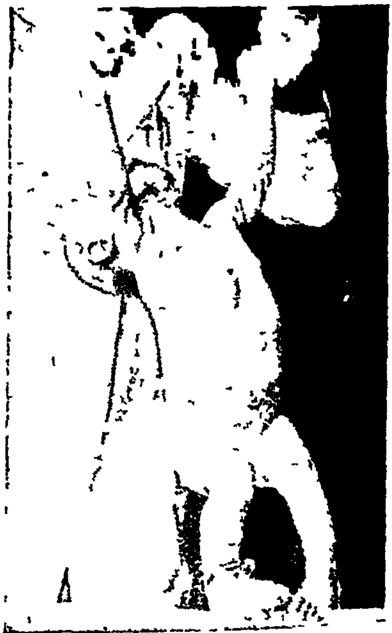

Fig 6—Palmar reflex grasping in normal infant.

NORMAL ADVANCE

When the infant is re-examined by the same method in the fourth month, the following changes may be observed

1 *Attitudes*

(*a*) In both supine and prone positions of the infant's body, the flexed attitude of the "neonatal" phase is superseded by one of relative extension (Bergeron 1947), and the "asymmetric tonic neck reflex" attitude of the *head and arms by a central position of the head* with symmetrical postures of the arms ("symmetric tonic neck reflex attitude," Gesell and Amatruda 1941) The upper limbs show variability *of* speed of movement

(*b*) As the infant is placed in the prone position, the head turns sideways or the head and shoulders may momentarily be raised

(*c*) Lifted upright, with support *under* the arms infants momentarily draw up the legs and dorsiflex the feet, the head is held steadily and the eyes look ahead The arms usually assume asymmetrical postures

(*d*) Held upside down by the ankles, the infant extends his head, the feet are fully dorsiflexed, there is some tendency to flex the hips and knees, and the arms may be *asymmetrically disposed in semiflexion* On release of one ankle, the limb falls into wide abduction with flexion at hip and knee and dorsiflexion at the ankle and *there is absence of the* bending and stretching characteristically occurring in the neonatal phase

2 *Spontaneous Movements*

(*a*) When placed in the supine position, the infant may flex the neck He smiles responsively (this reaction had been much worse for six weeks before she entered hospital. She was febrile and appeared very ill. The temporal and occipital arteries were thickened, tender, and inflamed. The E.S.R. was 46 mm. at one hour (Wintrobe). There was no anæmia, but 85% of 10,700 white cells were polymorphs. The patient was given 20 mg. of A.C.T.H. by slow intravenous drip daily for eleven days. Her pain, arterial tenderness, and inflammation rapidly disappeared, and her temperature settled down abruptly, and when she left hospital she felt entirely well, but her E.S.R. remained high (48 mm. at one hour, Wintrobe).

Case 5.—A man, aged 77, had all his life been deaf and dumb. For two weeks before admission he had had severe head pains, and nine days before he entered hospital he suddenly lost all vision in the right eye, and three days later his left eye became completely blind. There was bilateral papillœdema, and hæmorrhages were visible round the right disc. The right temporal artery was thickened, tender, and inflamed, and the E.S.R. was 52 mm. at one hour (Wintrobe). He was given large doses of A.C.T.H. intramuscularly and by slow intravenous drip for seven days, but no vision returned and he remained totally blind.

Case 6.—A man, aged 69, had had rheumatism in his shoulders and arms and had been losing weight for a year. Five weeks before he entered hospital severe bitemporal and occipital pain and tenderness of the scalp developed. After a week this diminished, but it persisted in lesser degree until the time of his admission. Four weeks before he was admitted he suddenly lost the vision of his left eye, and four days later his right eye also became rapidly blind.

He was totally blind, and both temporal arteries were apulsatile, but the fundi were normal, and no active arteritis was evident. He was afebrile, but his E.S.R. rate was 57 mm. at one hour (Wintrobe), and he had anæmia and leucocytosis (red cells 4,600,000 per c.mm., Hb 70%, white cells 14,100 per c.mm., polymorphs 77%). He was given six slow intravenous drips each of 20 mg. of A.C.T.H.; but, though all his symptoms subsided, no vision returned.

Case 7.—A woman, aged 74, had been treated by a general practitioner for hypertensive cardiac failure for some time. For a year she had been losing weight, and for four months she had had pains in her back, legs, head, and neck of sufficient severity to prevent sleep, and tender nodules had appeared on her forehead. Six days before admission she suddenly lost the sight of her right eye, and two days later her left eye also became rapidly blind. On admission she was totally blind and complained of severe head pains; her occipital and temporal arteries were tender and apulsatile. A blood-count showed anæmia and leucocytosis (red cells 4,920,000 per c.mm., Hb 76%, white cells 12,900 per c.mm., polymorphs 60%), and her E.S.R. was 56 mm. at one hour (Wintrobe). She was given a slow intravenous drip of A.C.T.H. 20 mg. daily for fourteen days; and, though she improved subjectively and her head pains and arteritis rapidly disappeared, no vision returned and her E.S.R. remained about the same. Five months later the temporal arteritis was still active.

Case 8.—A woman, aged 67, was seen as an outpatient in June, 1951, complaining of pains in the neck, shoulders, and knees. Her blood-pressure was 230/110 mm. Hg, and she had had exertional dyspnœa for two years. A month previously she had had an attack suggesting coronary occlusion, and there was electrocardiographic evidence of coronary-artery disease. She was admitted to hospital in December, 1951, having partly lost the vision of her left eye ten days previously and of her right eye three days later. She had also had severe bitemporal and occipital headache for two weeks. She was afebrile and not anæmic, but her E.S.R. was 45 mm. at one hour (Wintrobe), and 71% of 14,000 white cells were polymorphs. Her occipital and temporal arteries were thickened, inflamed, and tender. Her fundi showed arteriosclerotic changes, and there were hæmorrhages round the left disc. Visual acuity was reduced to 6/9 (part) in the left eye and perception of light in the right. Perimetry showed loss of the lower half of the left visual field, and only a small temporal segment remained on the right. She was given a slow intravenous drip of 20 mg. of A.C.T.H. every other day for three weeks. Her headaches and arterial tenderness rapidly disappeared, and her visual acuity on discharge was 6/9 left and 6/60 right. The left visual field was full, apart from a small segment in the lower nasal field, and the whole of the right temporal field was restored. Three months later there was still some tenderness of the right temporal artery, exercise tolerance was poor, and anginal pain continued.

Case 9.—A woman, aged 66, had twice been in hospital for peptic ulceration. Otherwise she had had good health until a month before her present admission, when she developed severe bitemporal headache and tenderness of the scalp, general malaise, and anorexia, and lost weight. On admission she was gravely ill, with grossly thickened, tender, and inflamed temporal and occipital arteries, and the left fundus showing papillitis and hæmorrhages. Two days after admission her vision became suddenly restricted and she could see no more than to count fingers with either eye. Systemic cortisone therapy was instituted and there was a rapid improvement in her general condition, extreme apathy almost amounting to stupor giving place to alertness and interest, and the head pains and arterial tenderness quickly disappeared. After about two weeks' treatment, however, severe symptoms of peptic ulceration developed and occult blood appeared in the stools. Cortisone was therefore discontinued and an ulcer régime instituted. Dyspepsia rapidly subsided, but pyrexia, head pains, and arterial tenderness returned, and a large area of scalp necrosis developed. Cortisone therapy was started again, and the symptoms and signs of temporal arteritis immediately came under control once again; but ulcer symptoms soon recurred. For four months temporal arteritis and peptic ulceration alternately called for cortisone and ulcer therapy, and the E.S.R. remained high; but when the patient was discharged she was symptom-free. Six months later the E.S.R. was persistently high, but the patient felt reasonably well. When last seen her visual acuity was 6/6 right and 6/18 left, but the visual fields in both eyes were considerably restricted.

Case 10.—A woman, aged 76, was first seen because of sudden deterioration of vision three or four days previously. Her fundi showed arteriosclerotic changes, hæmorrhages were present round both discs, and there was some papillœdema on the right. Vision in the left eye was reduced to counting fingers at 1 ft., and the visual fields in this eye could not be mapped. Visual acuity in the right eye was 6/24 and only the central field remained. She had not felt well for six months, her appetite had been poor, and she had lacked energy and had lost about 10 lb. in weight. For three months she had been known to have a low pyrexia and had had severe neuralgic pains in both temporal regions. At one stage both sides of her face became swollen, and mumps was suspected.

On admission she was febrile, both temporal arteries were rigid, tender, and apulsatile, her E.S.R. was 103 mm. at one hour (Westergren), and a blood-count showed 3,630,000 red cells per c.mm., Hb 70%, and 10,200 white cells per c.mm. (polymorphs 80%). She was given intramuscular A.C.T.H., and the head pains and pyrexia rapidly disappeared, and there was considerable subjective and objective improvement in her appetite and general condition, but the E.S.R. remained high (89 mm. Westergren). After two weeks the dosage of A.C.T.H. was reduced, but there was immediate evidence of relapse, head pains, pyrexia, and asthenia returning. A.C.T.H. dosage was therefore increased and continued for a further three and a half weeks. Symptoms were rapidly brought under control once again, and for two weeks before A.C.T.H. was stopped the E.S.R. was only just outside the normal range. Altogether the patient was treated for forty-two days, and twelve months after cessation of therapy there had been no relapse. Her visual acuity and visual fields showed considerable improvement, and when she left hospital she could read the newspaper with her right eye and the headlines with her left.

Case 11.—A man, aged 69, had had symptoms of coronary-artery disease for four years. Nine months before admission there was some sudden deterioration in vision of the right eye, and a week before he entered hospital he developed severe bitemporal head pains and the right eye became rapidly and almost totally blind. On admission visual acuity was reduced to perception of light in the right eye and 6/18 in the left. The left visual field was full, but vision in the right eye was so poor that perimetry proved impossible. He was given four slow intravenous drips each of 20 mg. of A.C.T.H., and most of the right temporal field returned. A month later he died of a coronary occlusion.

Case 12.—A woman, aged 72, had nine months' history of severe temporal and occipital headache and loss of weight. On admission she was apathetic and asthenic, and both in such structures, so, naturally, pathological deficiency cannot be recognised until the child reaches the age at which these structures normally show activity an extensor plantar response has no pathological significance until the child passes the age when it should have become flexor

All physical activity, both immature and mature, depends basically upon the reflex apparatus Physical activity of the newborn infant is believed to be mediated solely by reflex function, this increases in complexity with the postnatal maturation of neurones and persists throughout life, underlying all mature activity At the same time, developing mental activity increasingly modifies reflex function, the gradual change in infantile physical activity described by Schaltenbrand (1925, 1928) and others is linked with the increasing influence of thought processes There is a "transition" phase *from reflex to voluntary behaviour* (McGraw 1943), first evident clinically in the fourth month of life in full-term normal infants This change appears to consist of diminution in the reflex quality in activity, and emergence of the voluntary quality Since those responses which are most "reflex" in the adult—e g, the knee jerk—give the least information about the developing influence of thought processes in the infant, such traditional neurological signs are of little value in assessing progress

The observer can estimate the "voluntary" quality of activity only from its coherence Incoherence of movement may result from mental incapacity or from defect of the motor apparatus, in either circumstance, evidence of volition is difficult to obtain For this reason, and because the infant does not collaborate, it may be impossible to arrive by direct means at any estimate of mental growth The indirect evidence to be obtained from the study of the activity elicited by handling is therefore of special importance, though the interpretation of the activity observed may present some difficulty The history of the birth and neonatal period is of significance and should always be taken into consideration Where the birth was normal, the infant's cry was heard at once, and there was no abnormality of colour, and no difficulty (or merely transient difficulty) in establishing sucking and swallowing, then abnormality is likely to be due to *mental* defect This is the most likely diagnosis, too, when there is a history of prolonged jaundice, cranial injury, or "fits" (In both these groups signs of motor dysfunction may also be present (Craig 1950)) Babies who have no history of such abnormalities, but who had asphyxia livida at birth followed by persistent defects of breathing, sucking, swallowing, and moving, are more likely to be cases of motor defect alone

Where the four-month-old child shows little or no diminution of the reflex quality of his activity, and (apart from growth) little change in his appearance, mental deficiency can be presumed Where, on the other hand, there are signs that reflex behaviour is becoming modified, though physical activity is deficient, isolated motor defect may be inferred Mental deficiency is manifest by imperfect *employment* of the reflex apparatus, displayed not only in inefficient voluntary behaviour but also in the persistence of such infantile signs as reflex grasping Schaltenbrand (1928), Gordon (1929), and Brain and Curran (1932) observed such infantile signs up to a late age in mentally defective subjects

Motor defect, on the other hand, implies that the reflex apparatus *operates* defectively, with the result that voluntary activity—such as intended grasping—is impaired In cases of motor deficiency reflex grasping may be absent, but if it is present (provided there is no mental defect) it fades at the normal age Voluntary grasping, however, may be so incompetent that the observer does not recognise that a willed movement is being attempted Where mental and motor defect coexist, reflex grasping may be absent, and voluntary grasping may not appear throughout infancy Where mental defect exists alone, reflex grasping may persist indefinitely Moreover, as Tournay (1924) has noted, neonatal reflexes are modified on one side of the body earlier than the other thus reflex grasping has normally diminished in the right hand (in most infants) at a time when it is still definite in the left This normal asymmetry must be recognised, and differentiated from immature asymmetry (e g, the tonic-neck-reflex asymmetry) and pathological asymmetry (e g, in hemiplegia) No single sign provides convincing evidence of defect of the central nervous system, and diagnostic interpretation of signs depends upon their correlation Taken together, fragments of infantile activity provide evidence both of mental development and of the state of the reflex apparatus Where either of these is deficient the results appear in physical activity—in mental defect as the inefficient use of reflex function, and in motor defect as the use of inefficient reflex function

Summary

Physical activity of the newborn infant, it is generally believed, does not display the influence of thought processes, but is entirely reflex

As development proceeds, the reflex quality normally diminishes as competence emerges, and in the fourth month of life the change can be demonstrated

Separate criteria of assessment of mental and motor defect are discussed, and it is suggested that in full term infants at the fourth month of life deficient *mental* maturation is shown by lack of normal subordination of reflex processes, *motor* dysfunction, on the other hand, is shown, as development proceeds, by failure of the reflex processes to operate normally in voluntary activity

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thumbscrews which engage with slotted plates attached to the lid. An airtight junction between the lid and the sides of the box is obtained by a rubber gasket. Two pipes 1 in. in diameter are inset into the side of the box, one of which runs from the pump and the other to the manometer mounted on the anæsthetics trolley. Inside the box are adjustable foot-rests padded with sponge rubber. The open end of the box is partly closed by wooden diaphragms with openings about the size of a thigh. The lower part of each is fixed to the box (see figure), while the upper part is removable (not shown in the figure, for simplicity).

A suede leather diaphragm made airtight by impregnation with latex rubber is attached to the open end of the box, and is prevented by the wooden diaphragms from being sucked in. Suede leather was selected because of the ease with which it can be worked and because of its softness, thus minimising the risk of damage to the skin of the patient's legs.

The leather diaphragm is shaped like a pair of short trousers, with the legs pointing proximally and the waist around the open end of the box, attached to it permanently along the bottom and two sides in an airtight manner but detachable from the lid. Zip-fasteners which can be completely disarticulated run from the lid to the end of each leather leg. Thus when these zip-fasteners are open and the lid of the box is open, the patient's legs can be lifted in or out of the box without having to slide the legs through the holes in the end of the apparatus as in the original model. Once the patient has been lifted into the box, the upper parts of the wooden diaphragms are placed in position, the lid is closed and secured, and the zip-fasteners are closed. The leather diaphragm is next made airtight by running strips of waterproof adhesive plaster along the zip-fasteners and along the junction with the lid. Leather straps running round the leather legs can be tightened to accommodate them to thighs of different sizes.

TABLE II—MAIN ANÆSTHETIC AGENTS USED

Anæsthetic agent	Normotensive group	Hypotensive group
	No.	No.
Ether	89 (*59%*)	129 (*86%*)
Nitrous oxide	48 (*32%*)	18 (*12%*)
Cyclopropane	2 (*1%*)	3 (*2%*)
Local anæsthetic ..	11 (*8%*)	—

In the original model, when the negative pressure was applied, the patient was sucked downwards into the apparatus to the extent of 2 or 3 in., thus upsetting the position of the head on the head-rest. This is now prevented by the adjustable foot-rests.

It is essential that the box be connected to the pump by wide-bore tubing ($^3/_4$ in. internal diameter) and that the pump be of large capacity, so that the negative pressure in the box can be maintained despite the inevitable small leaks around the patient's legs.

MANAGEMENT OF ANÆSTHESIA

The management of anæsthesia in neurosurgical cases has recently been ably discussed by Hunter (1952) and Hewer (1952). Owing to shortage of nitrous oxide, ether was the main anæsthetic used in most of our cases (table II). This has the disadvantages of explosion hazard, less rapid recovery, greater incidence of nausea and vomiting, and, possibly, increased intracranial pressure. It has the advantages, however, that a high percentage of oxygen can be used, which is desirable when the blood-pressure is at hypotensive levels, and that easier and smoother maintenance of light anæsthesia is possible with less risk of straining and coughing.

The usual sequence of induction of anæsthesia was oral endotracheal intubation under thiopentone, gallamine tri-ethiodide ('Flaxedil'), and topical anæsthesia to the larynx; ether and oxygen in a closed circuit; with nitrous oxide and oxygen for the last $^1/_2$–1 hour of the operation. The amounts of ether required were surprisingly small, $1^1/_2$ oz. being the average amount used in the last 50 cases.

All the posterior-fossa craniotomies were carried out in the prone position, and the laminectomies in the prone "jack-knife" position. With increasing experience it became obvious that, with the patient prone, the chest and abdomen must be raised off the table by sandbags; otherwise the hampered respiration causes venous engorgement and increased bleeding. Initially the parietal craniotomies were performed in the lateral position, but latterly they have been done with the patient supine, one shoulder being raised, and the head half-turned to the opposite side. The sitting position was used only for exploring the gasserian ganglion.

Preliminary estimations of blood-pressure were made after the patient had been placed in position on the operating-table and while the skin preparation, injection of local anæsthetic (without adrenaline), and draping were taking place. H.M.B. was then injected intravenously. The initial dose was usually between 20 and 50 mg. We were reluctant to use the higher doses recommended by other workers, since the blood-pressure in some patients can be adequately controlled by one dose of 20–30 mg. Hypertensive patients usually require less than normotensives. Usually the blood-pressure had fallen by the time the skin was incised. It was found that in most of the patients blood began to ooze when the systolic blood-pressure reached 65 mm. Hg or more, and an attempt was therefore made to keep the blood-pressure below this level.

When the negative-pressure technique was used, the suction was not applied until the effect of the first dose of H.M.B. had been noted. The suction pressure was then adjusted to bring the systolic blood-pressure to 60 mm. Hg. If this level was not reached with a suction pressure of 40–50 mm. Hg, further doses of H.M.B. were given. The suction technique has made it possible to produce adequate hypotension with an average tilt of the table of only 5° (range 0–10°). With suction to the legs the hypotension following a single dose of H.M.B. can be maintained longer than with posture; so that once the blood-pressure has been reduced to the desired level, further doses of H.M.B. are usually unnecessary. A further advantage is that, when suction is discontinued at the end of the operation, the blood-pressure rapidly returns to normal, thus avoiding prolonged postoperative hypotension.

RESULTS

The effectiveness of the hypotensive technique was judged by the state of the surgical wound, both the intracranial tension and the amount of bleeding being recorded. Minimal or slight bleeding was considered satisfactory, whereas a normal or excessive amount was regarded as unsatisfactory. The intracranial tension practically always fell at the same time as the arterial pressure.

The hypotensive group is compared in table III with the normotensive group. The hypotensive group is subdivided into those with and those without suction applied to the legs. For simplicity the comparison has been limited to craniotomies and laminectomies. It can be seen that, with craniotomies, the hypotension produced by H.M.B. and posture resulted in *no* significant change in transfusion-rate, but that the duration of anæsthesia and the mortality were reduced. The average dose of H.M.B. required was 104 mg., and satisfactory hypotension was only obtained in 54% of patients. When, however, the hypotensive action of the H.M.B. was assisted by suction applied to the legs, the number of patients requiring transfusion was 25–30% less than

UNIVERSAL ORONASAL PRESSURE OXYGEN MASK

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The administration of oxygen to flying crews has become increasingly difficult with flight to higher altitudes since the advent of jet-propelled aircraft

Though consciousness may be maintained at rest with a lung alveolar oxygen partial pressure of 30 mm Hg, in emergencies exposure of combatant aircrew to an alveolar oxygen pressure less than 40 mm Hg is dangerous

As the combined carbon dioxide and water-vapour alveolar partial pressures remain fairly constant, with increasing altitude, at about 85 mm Hg, it is obvious that, if breathing pure oxygen, an atmospheric pressure of 125 mm Hg, corresponding to an altitude of 43,000 ft above sea level, will give the minimum required condition (85+40)

To obtain a vital extra few thousand feet of altitude it is necessary to increase the alveolar oxygen partial pressure by administering the oxygen at a pressure greater than that of the circumambient air This can be done either by pressurising the inspired gases or by increasing the expiratory resistance Both methods are used by the Royal Air Force, and both require the use of an oronasal mask sealing at positive pressure

In designing an effective mask, consideration must be given to such points as comfort, continued sealing under aerobatic conditions, and during facial contortions and speech, minimum obscuration of vision, ease of adjustment, and, equally important from the Service equipment point of view, the fitting of all shapes of faces likely to be met with from the smallest number of mask sizes

A mask mould has been developed at the R A F Institute of Aviation Medicine which appears to satisfy the above requirements in 95% of more than 100 adult males it has been demonstrated as capable of sealing an excess internal pressure of 20 mm Hg with little or no decrease in mask comfort It had been impossible to fit several of these men with any other type of pressure mask The remaining 5% of this series were able to hold 10 mm Hg pressure in the mask without discomfort

The characteristics of this universally fitting mask (from the Royal Air Force point of view) are (1) the shaping of the contour of the mask on the nasolabial folds, the nasion, and the prosthion, thus eliminating the inclusion of the lower jaw (fig 1*a*), which varies greatly in shape and size, (2) the incorporation in the mask of a malleable though firm section over the bridge of the nose, thus allowing the mask to be comfortably moulded to the shape of any nose, and (3) the reflected edge which is rounded into a soft thin flap projecting internally into the mask cavity (fig 1*b*) and abutting against the skin when the mask is applied to the face This soft rolled edge helps to seal the mask on the face, whilst the internal flap increases sealing by ballooning against the skin as internal pressure is increased

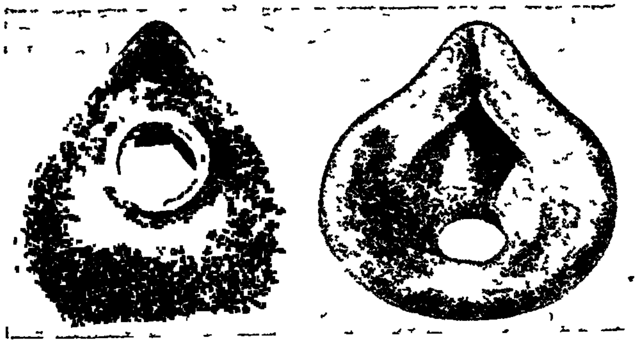

Fig 1—Anæsthesia mask *a*, external aspect *b*, internal aspect, showing reflected edge rounded into thin flap

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As the mask does not cover the chin, the dead space in the new R A F mask is reduced to an average of 60 c cm

By latex dipping cheap oronasal masks can be made from the same basic mould and used in many ways On this design of face seal several different types of mask have been evolved for use in flying, anæsthesia, mine rescue, and the Fire Service The simple shape of the mould allows a variety of accessories, valve, and harness fittings to be combined with the mask (fig 2)

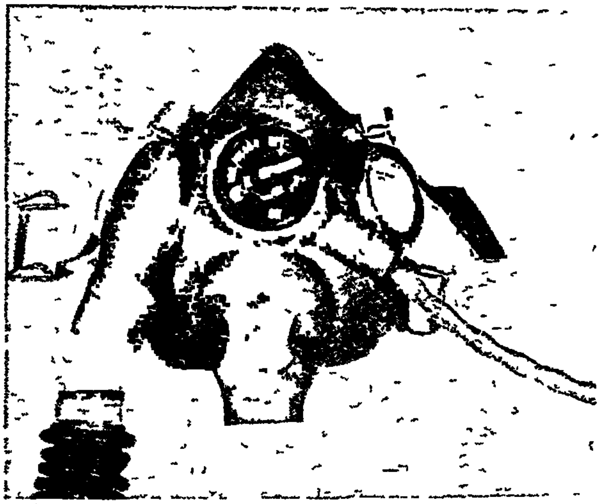

Fig 2—R A F pressure oxygen mask type M

ISOPROPYL ALCOHOL AS A SUBSTITUTE FOR ETHYL ALCOHOL IN CERTAIN BIOCHEMICAL TESTS

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Isopropyl alcohol of *B P C* quality is now available at about a third of the price of duty-free ethyl alcohol, and its purchase is free from restrictions We have therefore investigated the possibility of using it instead of ethyl alcohol in certain routine biochemical procedures So far we have confined our attention to the estimation of serum-bilirubin and of total cholesterol in whole blood, plasma, and serum, and to the qualitative tests for urobilin in urine and fæces

Serum-bilirubin

The procedure of King and Coxon (1950) was followed, a parallel test being carried out with isopropyl alcohol in place of ethyl alcohol (in the same concentration by volume) Forty-four sera from a variety of conditions, with bilirubin concentrations up to 39 mg per 100 ml, were examined, and also a few samples of icteric cerebrospinal fluid and bile diluted with serum Some of the sera were of the type which gave a "highly indirect" reaction—i e, one in which most of the colour was

Renal Function

Except for the patient with polycystic kidneys mentioned above, there has been no clinical evidence of renal damage following the hypotension. Urine taken before, during, and after hypotension in 15 patients has shown no significant quantity of red cells or albumin. It is interesting to note that all these patients produced considerable quantities of urine while the blood-pressure was low. One patient, from whom a large arteriovenous malformation was removed, produced 1000 ml. of urine during the ten hours of operation and two hours after, the blood-pressure being maintained at 60 mm. Hg, or below, throughout the whole operation.

DISCUSSION

In cranial surgery two of the major problems are to expose deep-seated structures adequately, and to obtain complete and rapid hæmostasis without unnecessary trauma to surrounding tissues. The raised intracranial tension found in such a large proportion of cases requiring surgery further aggravates the difficulties of exposure, especially when the region of the pituitary gland or the optic chiasma is being explored by the frontal approach. As soon as the dura is opened, the tense frontal lobes bulge out, and considerable difficulty is often experienced in retracting them, bruising and hæmorrhage not infrequently resulting from the retraction required. The raised intracranial pressure also aggravates the bleeding from the brain substance because of the rise in venous pressure produced. Much time and blood may therefore be lost before the pathological lesion to be treated is properly exposed, and poor surgery may result.

Ventricular tapping is one method available to lower the intracranial pressure, but it is not always convenient or completely successful. Similarly, the sitting posture will sometimes help, but there is a real danger of air-embolism in such a position. When controlled hypotension is used the intracranial tension decreases with the blood-pressure, with the result that, even in conditions where the intracranial tension is raised preoperatively, the dura is slack when the bone flap is raised and the brain does not prolapse when the dura is opened. This slackness of the brain gives increased ease of access to the pituitary and hypothalamic regions because the frontal lobes fall away from the bony floor of the anterior cranial fossa without the need of vigorous retraction.

Control of hæmorrhage is also greatly facilitated by the hypotension. Bleeding from scalp and bone is reduced; venous oozing from the brain is almost completely absent; and arterial bleeding is much reduced and more easily controlled. The complete removal of large vascular masses—e.g., vascular meningiomata and arteriovenous malformations—is much facilitated, and operations which would previously have required two stages can now be comfortably done in one.

The suction technique is also very valuable in the all too frequent emergency of a cerebral aneurysm bursting while it is being mobilised preparatory to clipping. Normally, the operating-field is at once completely obscured by a torrent of blood, and difficulty is often experienced in coping with this hæmorrhage without damage to the surrounding important structures. By increasing the suction to the legs, however, the blood-pressure can be rapidly reduced to a very low level so that the torrent becomes a trickle which can be easily and rapidly dealt with. The pressure is returned to a higher level as soon as the hæmorrhage is brought under control.

In spinal surgery, as with cranial surgery, the bleeding from subcutaneous tissue, muscle, and bone is greatly reduced. A very striking and important feature is the almost complete absence of bleeding from the epidural veins, which was formerly troublesome. Care should be taken to raise the patient's chest and abdomen off the table so that breathing is in no way hampered; otherwise these veins will be engorged. The greatly improved exposure and decreased bleeding brought about by the controlled hypotension therefore lead to a higher standard of surgery. This is borne out by the figures cited, which show that mortality and transfusion have been considerably decreased since controlled hypotension has been used. It will be seen that, although an extra 10 minutes is required to fit the suction apparatus on to the patient, the total duration of anæsthesia is reduced (table III), with the result that the increased initial expenditure of time is more than compensated for by the decreased operation time.

It is essential that the anæsthetist determine the blood-pressure frequently to avoid extremes of hypotension which would be deleterious to the patient. These can be rapidly corrected by decreasing the suction to the legs, and vasoconstrictor drugs are therefore rarely required.

To the anæsthetist the great advantage of the suction technique is that, by turning a knob, he can rapidly place the blood-pressure at any desired level over a considerable range. He can, at will and without further administration of drugs, produce extreme hypotension to cope with sudden disastrous hæmorrhage or produce an almost normal blood-pressure to ascertain if bleeding has been adequately controlled before the dura is closed. He can also more easily obtain any desired degree of hypotension and maintain it at a constant level.

Estimations of cerebral venous oxygen have shown that, when hypotension is produced with the patient very near to the horizontal posture, there is no undue decrease of the cerebral venous oxygen tension (Saunders 1953). These show that there is no cerebral anoxia, and that the cerebral blood-flow remains close to normal. Davison (1952) has pointed out that, with the patient in the head-up position, there tends to be redistribution of blood away from the head, and that this effect is far greater in the hypotensive patient. This redistribution of blood is minimised by maintaining the patient very close to the horizontal posture, and much of the danger of cerebral anoxia is removed.

It may be wondered, therefore, how the bleeding can be much reduced while the cerebral blood-flow is maintained near a normal level. Davison (1952) suggests that reduction of blood-pressure will presumably not reduce hæmorrhage from either small or large vessels unless aided by posture. This is clearly incorrect. A large proportion of the bleeding which takes place is of venous and capillary origin. The fall of venous pressure produced by H.M.B. (Restall and Smirk 1950, 1952) will considerably reduce the bleeding from these sources. This can be well illustrated by raising the cranial venous pressure of a patient undergoing a craniotomy, by squeezing the neck. The previously dry field immediately becomes covered with dark venous blood.

The arterial bleeding will also be reduced despite the arteriolar dilatation. It must be realised that the amount of blood flowing through an intact artery is vastly different from the amount which will flow from the proximal end when that artery is cut across. For the intact vessel flow = A/R, where A is the effective mean arterial pressure and R the cerebral vascular resistance. When the artery is cut across, however, the local resistance falls almost to zero; hence the blood-flow from the cut end becomes much greater than that through the intact artery. Thus, with the artery cut, the outflow depends only on the pressure in the artery proximal to the cut and is independent of the state of the general peripheral resistance. Outflow of blood from the cut end of an artery will clearly be less in a hypotensive patient than in one with a normal blood-pressure. It is therefore possible to obtain decreased bleeding during

CONCLUSIONS

Whether isoniazid will in fact prove of value in human leprosy remains to be seen An early clinical report[4] strongly suggested that it would not Moreover, the intracorneal technique with *Myco lepræ murium* is by no means established as a satisfactory screening test for drugs used in human leprosy But the results already obtained by this method, though admittedly confined to one experiment, do encourage further investigations of this kind and, indeed, further inquiries into the value of isoniazid in the treatment of human leprosy

We thank Mr D E Seymour, of Herts Pharmaceuticals Ltd, and Dr A R Martin, of Imperial Chemical Industries Ltd, for the supply of some of the drugs used in this work

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Reviews of Books

A Handbook of Radiotherapy

for Senior and Postgraduate Students WALTER M LEVITT, M D Lond, F R C P, F F R, barrister at law, associate physician, department of radiotherapy, St Bartholomew's Hospital, London London Harvey & Blythe 1952 Pp 232 30*s*

INTENDED primarily for senior and postgraduate students up to registrar standard, this book is an attempt to explain in non-technical language what are the radiations used in radiotherapy, how they are produced and applied, how they produce their effects, the diseases for which they are used, and the prospect of benefit from their use Within these self-imposed limits Dr Levitt succeeds admirably and he maintains the high standard of teaching which one expects from Barts

The opening chapters deal succinctly with the basic physics of atomic structure, isotopes, X rays, and radium, with methods of their dosage estimation and with their therapeutic application General principles, including effects on living cells, tissues, and organisms, are then discussed with useful references to radiosensitivity, tumour lethal dose, time and intensity factors, and the application of these factors in practical work The main chapters include accounts, in systematic form, of diseases treatable by radiotherapy, and there is a valuable chapter on management of the patient before, during, and after treatment The staging of breast and uterine cervical cancer and an appropriate extract from the *International Recommendations* on Radiological Protection are printed as appendices

Some minor criticisms of a first edition are inevitable For instance, the illustrations of deep and superficial X ray treatment sets and of a Geiger counter for clinical use are unconvincing for the reader to whom the book is addressed Again in a book of this kind it would seem appropriate to give a specific warning against the use of the term X ray burn to describe, in the hearing of patients and their relatives, the normal reactions of skin and mucosæ to full radiation doses Apart from the possibility of litigation which may arise, the resultant loss of confidence between the patient and the radiotherapist can make all the difference to the conduct of a case of malignant disease The reader may be confused to read (p 78) "there is at present no known certain means of sensitizing malignant cells to radiation," only to find a section (p 79) about "chemical sensitization" in which the work of Mitchell with 'Synkavit' is mentioned In discussing the gliomas, the accepted pleomorphic character of these tumours is often a deciding factor in advising radiotherapy where it might at first sight appear to be contra indicated by the histological report

The whole book is informed by good sense and practical experience, and deserves a wider public than Dr Levitt claims It will be read with advantage by anyone who habitually refers patients for radiotherapy, since it gives so much useful information in a readily assimilable form, and shows clearly how much work goes to the planning and successful execution of modern radio-therapeutic techniques

Modern Practice of Obstetrics

D M STERN, M B Camb, F R C S, F R C O G, and C W F BURNETT, M D Lond F R C S, F R C O G, obstetric and gynæcological surgeons, West Middlesex Hospital, London London Baillière, Tindall, & Cox 1952 Pp 238 35*s*

IN writing a short textbook these days an author may deal thoroughly with the more common and important conditions of his specialty or may briefly cover every aspect of the subject Mr Stern and Mr Burnett in choosing the second difficult method have achieved a concise style rather than a well-balanced account of obstetrics

For instance, more details are given of X ray pelvimetry than of the management of trial of labour, and antepartum hæmorrhage and postpartum hæmorrhage are each briefly discussed in a couple of pages or so, whereas the early development of the ovum receives the attention customary in most textbooks for no very apparent reason considering how much of this is conjectural The practice described is that of the West Middlesex Hospital, with which there will be little disagreement although the advice to leave a retained placenta in utero while awaiting spontaneous expulsion within the next few days is not likely to be generally adopted

Victor Bonney has shown what can be done with masterly line, and the clear line drawings which illustrate this book are far more serviceable than elaborate pictures, which often lose their point in a welter of irrelevant detail Though the book is neither an introduction to obstetrics nor a work of reference it should be of real help to students in need of rapid and concise revision before an examination

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Whitaker's Almanack 1953 (London Whitaker Pp 1174 15*s*)—Bigger and better than ever, this old established and incomparable referee contains as a new feature a section on broadcasting, giving the chief events of the year and a select list of Commonwealth and foreign radio stations, with their power and wave lengths To mark the Coronation Year it has as frontispiece a coloured portrait of Her Majesty

Poisons Guide (London *Chemist and Druggist* 1953 Vol II Pp 235 40*s*)—This guide has been revised by Mr W A Whatmough The first volume of the new edition, which appeared nearly two years ago, consists in poisons lists and key Volume II, now issued, describes and explains the provisions of the law on poisons and dangerous drugs The work fully earns the publishers' description of it as "a veritable encyclopædia of poisons law"

Pathology of Diabetes Mellitus (3rd ed London Henry Kimpton. 1952 Pp 336 56*s*)—In earlier editions Dr Shields Warren and Dr Philip M LeCompte, of Boston, established a secure position for their book as an oracle on all pathological aspects of diabetes This new edition, coming 13 years after its predecessor, brings the subject matter virtually up to date, especially as regards the American literature Each organ is considered in detail, and there are useful reviews of wide subjects such as experimental diabetes, the ætiology of atherosclerosis, and the ætiology of diabetes itself In the final chapter the authors attempt a synthesis of many of the heterogeneous facts that fill the earlier pages They suggest that there is a basic disturbance in the make up of the ground substance that shows itself in the arterial intima, the retinal micro aneurysms, and the lesions of the glomerular tufts It is postulated that this disturbance involves either simple polysaccharides, such as glycogen, or more complex mucopolysaccharides The volume is finely produced and illustrated with well selected photomicrographs, except for one poor one depicting hæmochromatosis An appendix gives details of necropsy and staining methods It is cheering to read that Dr Shields Warren has had occasion to revise his statement, made in previous editions, that he "had yet to see at autopsy a diabetic whose disease lasted 5 years or more, free from arteriosclerosis, regardless of age" unconsciously grimaces (fig. 1), the "nervous" subject wriggles and contorts his face and limbs. Seen in the course of activity to which they seem appropriate—taking age into consideration—such predominantly reflex reactions are recognised to have no pathological significance (Carlson 1941). When they appear to be inappropriate, however, they are often looked upon as "purposeless" and attributed to mental—though they may be due to motor—defect. The mental condition of children with abnormality of the motor apparatus should not be judged from movements seen in isolation, but from the activity in which these inhere. Unsuspected abnormalities of eye control, or defects of hearing, may alter the picture further, and so complicate assessment (Phelps 1941, Perlstein and Barnett 1952).

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[4] Lowe, J *Lancet* 1952, ii 1012

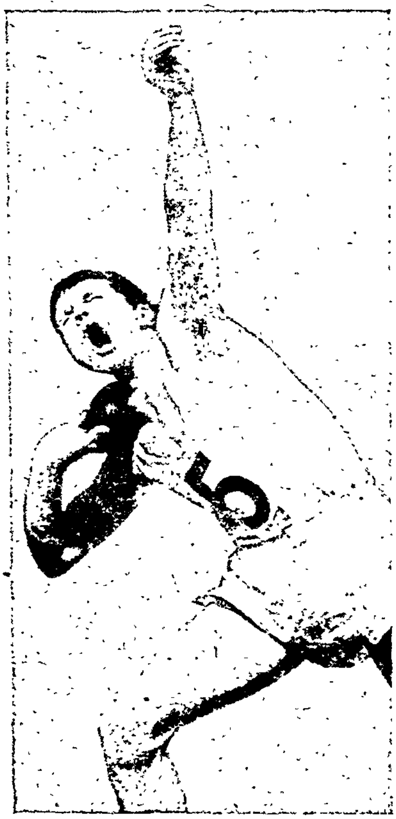
Fig. 1—Normal facial grimacing during activity.

Since motor abnormalities may be increased or decreased by the physical management of the child, early diagnosis is important. Where there is no mental defect, early treatment of motor dysfunction—that is, treatment at a time when the adaptability of the central nervous system is greatest (Gooddy and McKissock 1951)—results in the achievement of relative motor competence (fig. 2). Hence, for patients with such defects, no special educational facilities should be needed nor special provision in after life. For the mental defective, with or without defect of the motor apparatus, special provision will have to be made, probably throughout life. Mental defect (unless of a type associated with specific physical abnormality, such as mongolism or microcephaly) cannot be diagnosed in the newborn; but by the second three months lack of advancement can be detected. Signs of motor dysfunction, too, are inconspicuous at birth, but begin to be recognisable by the second three months of life. Infants with motor defects are usually brought to the doctor with a history of slowness in establishing breathing, sucking and swallowing, and other vague signs of motor dysfunction; but most of them are only later referred to a clinic for treatment when motor abnormality is obvious. This is because early evidence of motor defect is not detected by the usual methods of examination.

Fig. 2—Child with "athetosis," after treatment.

Observation of the present series of cases has shown that mentally defective children examined at the fourth month show "signs of immaturity," whether or not motor dysfunction is also present. These are signs which, though normal in early infancy, begin, in normal infants, to show modification by the fourth month. Where modification occurs—even where there is motor dysfunction—intelligence is normal. In such cases physical "retardation" is due to motor dysfunction, or motor and special sense defect. It is possible to differentiate on these signs mental from motor defect, even where these coexist. Thus, indirect evidence of mental capacity can be obtained from physical examination before direct "mental testing" is possible.

Criteria of normal physical activity at different ages have been obtained by many workers from observations on normal infants. The method of examination here suggested is based on these, and on personal observations, and consists of simple clinical tests applicable from the fourth month of life. Up to the age of six months any prematurity must be allowed for.

Method of Examination

NEONATAL MANIFESTATIONS

In the neonatal phase, infants exhibit:

1. *Attitudes*

(*a*) A general attitude of flexion in both supine and prone positions. From this attitude, movements occur at unmodified reflex speed; that is, the speed at which the reflex mechanism works in the absence (as far as we know) of cortical activity. And on cessation of activity the attitude is resumed.

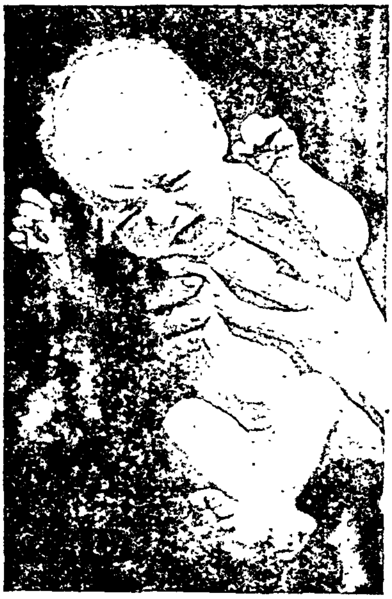
Fig. 3—Flexed attitude of normal infant held upright with support under the arms.

(*b*) A "tonic neck reflex" attitude of the head and arms is seen when the infant is at rest in the supine position (the head is turned to the right in most infants). Rotation of the head to the same side occurs when the infant is placed in the prone position (Gesell and Amatruda 1941).

(*c*) Held upright under the arms, the infant shows flexion of the limbs and dorsiflexion of the feet, with at times, crossing at the ankles and with lolling of the head (fig. 3). When the feet touch a flat surface "stepping" reactions are seen (McGraw 1943, André-Thomas and Hanon 1948) (fig. 4).

(*d*) Held upside down by the ankles, the infant shows dorsiflexion of the feet and symmetrical flexion of the arms; if one ankle is released, the leg falls into wide abduction and flexion, with dorsiflexion of the foot; spontaneous stretching and bending of the leg may follow (fig. 5).

2. *Spontaneous Movements*

Irregular respiratory movements. Arhythmic ("athetoid") movements (Minkowski 1927). Rhythmic repetiof 5% saline, and at the same time attempts to sweat out some of the excess water by a radiant-heat cradle Prophylaxis and treatment are not difficult, if the predisposing factors and the clinical picture are recognised, deaths from this cause can be prevented by tempering enthusiasm in postoperative care

Experimental Hypervitaminæmia

ALMOST all the vitamins are now obtainable in pure form, and there is nothing to prevent these being prescribed in doses greatly exceeding the amounts contained in an ordinary diet It is important, therefore, to know how the body reacts to vitamins given in excess of normal physiological requirements Early investigations told us, that surplus quantities of most vitamins may be stored for future use, and that storage is more efficient with some vitamins than with others. Experiments have also shown that very heavy doses of at least two vitamins—A and D—are toxic, and hypervitaminosis is occasionally recognised clinically More information is still required, however, about the mechanisms which distribute surpluses of *vitamins throughout* the body, and which maintain the balance between *storage and elimination by destruction or excretion*

The efficiency with which vitamin A is utilised and stored has been found to be decreased in the absence of vitamin E,[1,2] and we must obviously be alert for other such interrelationships **URBACH** et al[3] have completed a comprehensive investigation into the effect of large doses of vitamins A, C, and E and carotene on vitamin levels in the blood-plasma Twenty-five volunteer men were divided into five equal groups They continued to take their normal diet, but four groups were given one of the vitamins under investigation in daily doses at least ten times greater than the amounts normally present in the diet The fifth group acted as controls In each group all four vitamins (not only the vitamin that was administered) were estimated by chemical methods in individual specimens of blood-plasma collected once or twice weekly With each group estimations were also made for about two months before dosing was started and for two months after it had been stopped Vitamin A was given over most of the dosing period at the level of 14 mg (47,000 I U) daily, which was not toxic although greatly in excess of the minimum requirement of about 1250 I U The average level of this vitamin in the plasma was raised by only about 16%, and even this small increase disappeared soon after dosing was discontinued The levels of the other vitamins did not vary significantly from those observed in the control group Vitamin E was provided in the form of mixed natural tocopherols in daily doses of 46–125 mg The increase of vitamin E in the plasma varied at different times between 14% and 42%, and there was also an accompanying increase in carotene of about 19% When vitamin C was given as pure ascorbic acid in daily doses of 91–179 mg its level in the plasma rose by about 40% without any effect on the other vitamins The greatest change in the plasma, however, was observed in the volunteers who received carotene Daily doses of 6–62 6 mg of carotene caused increases in the plasma of 118–173%, and the level remained high during the two months after dosing was stopped

It is well known that after administration of single heavy doses of vitamins A or E their levels in the blood reach sharp maxima 5–6 hours later, and then fall rapidly as the vitamins are absorbed into the tissues **URBACH** and his colleagues give no information about the interval between dosing and the collection of blood, but the persistence of raised values for at least a week after dosing was stopped suggests that the increases observed relate to the "resting level" and not merely to the "post absorptive phase" We need not be sure on this point, however, before accepting the conclusion that, under normal conditions of nutrition, factors other than the dietary intake of vitamins are largely responsible for determining their levels in the blood Thus the differences found between individuals for vitamin A considerably exceeded the changes caused by dosing As already noticed in English work,[4] moreover, the levels found in each volunteer tended, when not affected by dietary changes, to remain at a constant level which was normal for that person Despite the known interrelationship between vitamins A and E large doses of either had no effect on the plasma level of the other

The efficiency of the mechanisms for maintaining a constant level in the plasma, however, varied somewhat for different vitamins, and with the provitamin carotene the control was much less complete Recent research has shown that although vitamin A is stored mainly in the liver it is formed from carotene in the intestinal wall, the ultimate fate of pigment which escapes conversion and passes unchanged into the blood and tissues remains uncertain The influence of vitamin E in raising the level of carotene in the blood may be related to the observation of **JOHNSON** and **BAUMANN**[5] that in rats excessive doses of tocopherol interfere with the conversion of carotene to vitamin A

Pyrexia has long been known to decrease the levels of vitamin A and C and carotene in the blood plasma The American workers found that vitamins C and E were more sensitive than vitamin A and carotene in their response to minor infections, and that their levels were also reduced by mental disturbance and physical exhaustion It even appeared that the values found for vitamin C could be related to the mental state of the volunteers at the time when their blood was collected "Whenever they were angry or truculent the vitamin C level was low If they were happy and carefree at the time of sampling the vitamin C level was high" The reductions caused by infections or stress were large, and in volunteers who did not receive supplements of ascorbic acid the vitamin sometimes completely disappeared from the plasma With the administration of ascorbic acid the frequency and severity of the variations in the plasma were much reduced The incidence of colds, however, was the same in all groups, irrespective of the supplements given

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[1] Moore T *Biochem J* 1940, 34, 1321

[2] Hickman, K C D, Harris, P L, Woodside, M R *Nature Lond* 1942 150, 91

[3] Urbach C Hickman, K. C D, Harris, P L *Exp Med Surg* 1952 10, 7

[4] Vitamin A requirement of human adults *Spec Rep Ser med Res Coun, Lond* 1949, no 264, p 14

[5] Johnson R M, Baumann C A *J biol Chem* 1948, 175, 811

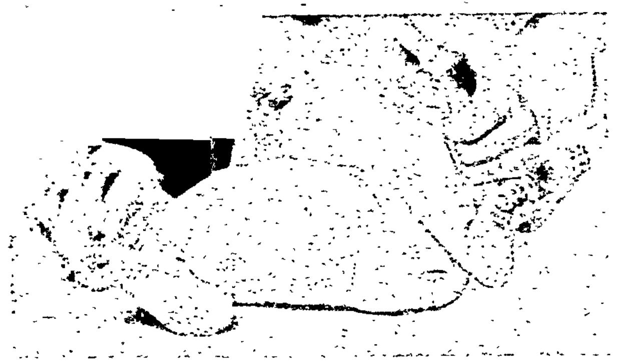

Fig. 7—Plantar reflex grasping in normal infant.

appears in the third month. fig. 8). The eyes turn in the direction of a sound and follow a moving object. Squinting is transiently seen: McGraw (1943) considers this to be part of "transitional" behaviour (see below). There is blinking on threat; the child cries with tears; the eyes watch the infant's own moving arm when it enters the field of vision. Both hands grasp for objects and both legs flex simultaneously as the grasping movements occur. Many infants suck their fingers or thumb (usually of the right hand). There is "babbling," "cooing," and other pre-speech sound.

(*b*) In the prone position, the head and shoulders may be raised. the child may support himself on his forearms and abdomen.

3. *Reactions to Handling*

(*a*) There is little or no resistance of the limbs to passive movement unless the infant is crying. when there is resistance to alteration of the flexed posture assumed during crying.

(*b*) The "startle" reaction is less than that exhibited during the neonatal period.

(*c*) The palmar reflex grasp is less easily elicited on the right side. in most infants. The plantar grasp shows little modification.

(*d*) In the supine position, rolling of the trunk and legs to the side to which the head is passively turned (neck righting reflex) is less marked than during the neonatal period.

(*e*) When the infant is pulled by the arms from a supine to a semi-sitting position the head comes up with the trunk and is momentarily held steadily; and the infant's facial expression is "responsive."

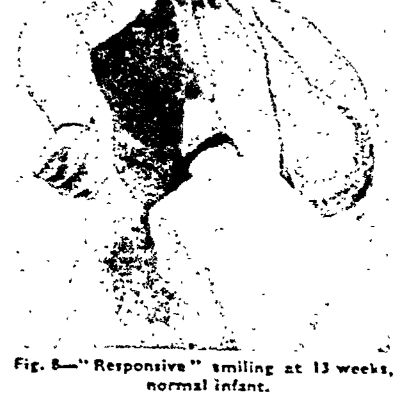

Fig. 8—"Responsive" smiling at 13 weeks, normal infant.

(*f*) In the side-lying position, the infant tends to roll on to his back or face. When held on his side, on passive extension and abduction of the uppermost hip. he shows slight but evident contraction of the hip abductors.

(*g*) "Withdrawal" and other skin reactions are less marked than at the previous examination, and tendon reactions tend to be less variable.

4. *Other Reactions*

By the fourth month there is relative absence of such neonatal characteristics as frequent crying, vomiting, clonus, trembling, nystagmus, partial or unilateral opening of the eyes during sleep, protrusion of the tongue, facial grimaces, closure of the fists with the thumb under the flexed fingers. The child gives evidence of some "awareness."

CRITERIA OF MENTAL PROGRESS

All the changes described are those normally exhibited and they illustrate the diminution of the reflex quality in physical activity which indicates *mental* advance. In cases of mental defect there is little or no evidence of such physical change. Normal motor development, on the other hand, is shown by increasing motor agility, and it is this which lags behind developing mental processes where reflex activity is abnormal. In both types of case the child fails to make normal progress; and signs of this failure, though arising from differing causes, may, in early infancy, appear in identical manifestations (e.g., unsteadiness of the head when the infant is lifted). Such signs give no evidence of value in the differential diagnosis of mental from motor defect.

Certain of the changes in reflex behaviour can. however. be used as criteria of mental progress. From the fourth month onwards, mental defect is shown by the lack of such changes in: 1*a*, 1*b*, 1*c*, 1*d*, 2*a*, and 3*a*, 3*c*, 3*d*. Mental advance is best seen in 1*a*, 1*b*, 1*c*, 1*d*, 3*a*. 3*c*. Motor dysfunction is most clearly seen in 1*b*, 1*c*, 1*d*, 2*a*, 2*b*, 3*c*. As the normal infant grows, the reflex reactions become progressively subordinated, and motor competence increases. Mental defect is consistently shown by *abnormal persistence* of reflex behaviour, and motor dysfunction by *abnormalities* of reflex behaviour. The significance of an abnormal reaction can be judged only on the presence of related abnormalities in other reactions.

Normal control of reflex function is established first in the head and upper limbs, and if, for instance, an infant fails to turn the head when placed prone (1*b*), at the age when normally this reaction is voluntary, motor defect may be suspected. Infants who are mentally defective show reflex turning of the head beyond the normal age (unless, of course, motor dysfunction is also present). From the fourth month onward abnormalities in reactions 1*c*, 1*d*, and 2*b*, taken together, attain diagnostic significance. Infants with no motor defect consistently show momentary dorsiflexion of the feet and partial flexion at hips and knees when lifted upright with support under the arms (fig. 3); while those with motor dysfunction do not show this reaction. Nor do they dorsiflex the feet when held upside down by the ankles—an important reaction seen consistently in the normal. In the differential diagnosis of different *types* of motor defect abnormalities of reactions 1*d* and 3*f*, taken together, are useful. Only when related signs show consistent defects should a diagnosis of motor or mental deficiency be accepted, and the same principle holds when differentiating types of motor abnormality.

Discussion

All physical signs are evidence of central nervous *function*, for non-functioning or absent structures produce no physical signs (Walshe 1947). Where function of the reflex apparatus is deficient from the time of birth, such deficiency may be shown by, for instance, defects of breathing, sucking, and swallowing. But these anomalies are not necessarily pathological in the newborn: it is only when they persist beyond early infancy that reflex abnormality can be diagnosed. Again, defect of neural structures which mature postnatally cannot show itself at a time when, even if normal, these structures would be immature and inactive. The central nervous system at birth is "physiologically deficient" higher proportion (75%) of malignant melanomata arise on the legs and feet, and he mentions **Baxter**'s finding[8] that among dark-skinned races as a whole 92% of these lesions are found on one of the four limbs, compared with 45% in a series of white Americans[9 10]

Two basic cell types are seen in malignant melanomata, the epithelioid and the sarcomatoid the term "*nævocarcinoma*" is sometimes applied to the first type A constant feature of the malignant melanoma is involvement of the epidermis in a bizarre kind of junctional activity The amount of pigmentation is extremely variable, and the dopa stain is invaluable for the recognition of those containing little pigment According to **Fitzpatrick**,[11] the inoculation of excised tumours with tyrosine helps to differentiate malignant melanomata from other malignant tumours and from junctional nævi The malignant melanoma, even if clinically amelanotic, forms melanin when inoculated with tyrosine because of its tyrosinase content, whereas other highly undifferentiated malignant lesions—for example, fibrosarcoma, lymphoma, squamous-cell carcinoma, and junctional nævi—do not

Discussing the treatment of malignant melanomata, **Cunningham** advises excision with a margin 6–10 cm wide and including in depth the hypodermal fat Such an excision often needs skin grafting For patients with clinically evident blood-stream metastases no surgical treatment is feasible, except perhaps the excision of the rare solitary brain metastasis, appearing after a long period of freedom following the removal of the melanoma Patients with no clinical evidence of lymphatic metastases may suitably be treated by wide excision and lymph-node dissection, and those with clinical evidence of operable regional lymph-node metastases should be dealt with by amputation—disarticulation at the hip-joint or interscapulo-thoracic amputation—with lymph-node dissection If this treatment is unacceptable because it is too mutilating, the alternative is excision and radical lymph-node dissection. Radioactive phosphorus remains of doubtful value, and hormone therapy has proved ineffective **Wright** et al,[12] however, have lately shown that the prognosis is strikingly better in premenopausal women than in other patients In a group of 132 cases of malignant cutaneous melanoma the five-year survival-rate was 74% in women under the age of 50, compared with 41% in the whole series In 744 patients with malignant melanoma treated in the period 1917–45 **Pack** et al[6] found 123 (21 4%) five-year definitive cures Analysing these results in an attempt to show how the site of the primary tumour (which was not always discovered) affected the prognosis, they found that anorectal and oronasal tumours were the ones where a five-year cure was least likely, there may be delay in the discovery of these tumours and difficulty in excising them completely **Pack** et al also showed that a delay of more than a month between local excision and definitive treatment reduced the five-year cure-rate from 39 9 to 17 0% Turning to the particulars of surgical treatment, they found that the more advanced growths (those where wide local excision was impracticable) did best with radical amputation, relatively poor results followed wide local excision combined with dissection of the regional lymph nodes, but **Pack** and his colleagues consider that their figures in this group are not yet large enough to justify any definite conclusions

Annotations

PAID SICK-LEAVE

How much personal security can we afford to offer the sick worker as we struggle for industrial survival? A somewhat daunting answer comes from recent studies of the effects of paid sick-leave on sickness absence In September, 1948, such a scheme was introduced for 330,000 industrial employees in forty-two Government departments An analysis by Buzzard and Shaw[1] of two years' experience of this scheme shows that sickness absence had doubled since its introduction, the increase being due largely to an increase in absences of four weeks or more The picture remains the same with allowances for the greater liability to absence of older workers, unskilled workers, and those with known disabilities, the proportionate increase of their absence rates was no greater than that of the other workers When the new system was put into operation workers who were on bonus schemes of payment, and who when sick reverted to a lower flat rate of pay, showed less increase in absence than workers who were on time rate only Believers in the stick-and carrot method of encouragement will not be surprised at this, for workers on time rates may be better off on sick pay than at work, since they no longer have to make insurance contributions sickness benefit is not liable to income-tax, and they are sometimes eligible for payments from a friendly society Denerley[2] also draws attention to the influence of economic incentive in reducing sickness absence He studied the effects of introducing a scheme of paid sick-leave in a company, the general results were similar to those reported by Buzzard and Shaw, but in one department where bonus earnings were extremely high the introduction of the system had no effect on sickness absence until earnings were substantially reduced

Possibly where such schemes were started immediately after the start of the National Health Service, the increase in sickness absence was accelerated by workers taking advantage of this service to have operations or long courses of treatment Moreover, the sort of advice which the general practitioner gives to such workers is bound to be influenced by his knowledge of their new economic security While there has undoubtedly been some abuse of these schemes by workers who have stayed off work unnecessarily, there is no suggestion that this is the main reason for the increase in absence Pessimists who believe that National Insurance and free medical care are creating a nation of malingerers may take heart from the opinion of management and workers in the factories where these experiments have been tried, that without pay during illness there is real danger that the sick man will come back to work when he should be at home or in hospital That increased sickness absence follows the introduction of a scheme of paid sick leave is no new discovery One of the companies studied by Denerley had had such a scheme for established workers since 1928, and had experienced this effect from the start Nevertheless the persistence of this scheme argues a belief by the management that it is good policy The benefits in

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SPONTANEOUS RUPTURE OF PROXIMAL JEJUNAL LOOP AS A LATE COMPLICATION OF GASTRECTOMY

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THOUGH many different complications have been reported after partial gastrectomy for peptic ulcer, I have not been able to find any mention of spontaneous nonulcerative rupture of the afferent jejunal loop.

CASE-RECORD

A tram-driver, aged 52, was first admitted to the Victoria Infirmary, Glasgow, on June 8, 1950, with fifteen years' history of stomach trouble, including one attack of hæmatemesis and several of melæna. Radiography revealed a prepyloric ulcer, and on June 19, 1950, he underwent a gastroduodenal resection, four-fifths of the stomach being removed, and the operation concluded as an anterior Polya isoperistaltic anastomosis of the full width of the cut edge of the stomach. Apart from a mild pulmonary complication the patient made a good recovery and returned to work on Aug. 21, 1950. He expressed himself as feeling very well, although he had some of the symptoms of the post-gastrectomy syndrome, such as fullness, weakness, and an occasional mouthful of sickness after meals. This did not incapacitate him for longer than fifteen minutes after a meal. On March 31, 1951, nine months after his operation, he was readmitted as an abdominal emergency. About noon on the previous day, while at work, he developed a dull colicky pain in the region of his umbilicus. It was of gradual onset, allowing him to finish his work at 4 P.M., but the pain became progressively worse during the night, and in the morning it was so severe as to warrant immediate admission to hospital. Though the pain had become more intense, its character had not altered, nor had there been any sudden exacerbation. There was no history of trauma. Vomiting was absent.

On admission the patient was exhausted and incapable of giving a clear history. He had upper abdominal muscle guarding and extreme tenderness indicating severe peritoneal irritation, yet with gentleness and patience relaxation took place and an ill-defined transversely lying swelling could be made out about the umbilicus. A leaking stomal ulcer was tentatively diagnosed.

Operation.—Under anæsthesia the epigastric swelling palpated by me during the clinical examination, and by two other senior members of the staff, could not now be felt. On laparotomy a large quantity of clear exudate was evacuated and the lesion was immediately revealed as a laceration of the afferent jejunal loop just distal to the duodeno-jejunal junction. It was 1 in. long, with clean-cut edges, situated in the long axis of the bowel and involving all the coats. The afferent loop, 6 in. long, showed patchy congestion and several areas of subserous hæmorrhage. The stomach in the region of the stoma was bound to the anterior abdominal wall by many broad sheets and bands of adhesions, but the stoma was patent and showed no abnormality. No ulceration was present in the adjacent stomach or jejunum. The jejunal defect was repaired.

Postoperatively the patient recovered well from the abdominal lesion, but chest complications again gave cause for concern. It soon became apparent that both lungs were affected by active tuberculosis. Radiography revealed right apical infiltration and widespread bronchopneumonic consolidation of the lower lobes. *Mycobacterium tuberculosis* was found in the sputum on direct examination and culture.

Treatment with streptomycin 1 g. daily and *p*-aminosalicylic acid 12 g. daily was started. The patient responded satisfactorily, and by the time he had received altogether 69 g. of streptomycin he was transferred, on July 10, 1951, to Ruchill Hospital, Glasgow, where treatment was completed and the tuberculosis judged to be quiescent. He was discharged on Aug. 3, 1951.

Follow-up.—Re-examined nine months later, on May 12, 1952, he looked well and had put on weight. There had been no recurrence of abdominal pain. Appetite was good, and the feeling of weakness after meals had almost disappeared. Fluoroscopy after a barium meal showed immediate filling of the distal jejunal loop. The proximal loop was not seen either before or after palpation.

DISCUSSION

Trauma, especially in conjunction with distension of the afferent loop, could have caused the present type of lesion, but there was no history of this. An acute ulcer going on to perforation could have presented a similar clinical picture. Such an ulcer described by Walton, (1934), Paterson (1909), Hurst and Stewart (1928), and others, produces an acute erosion with little or no reactionary change round it. It occurs in the first few months after gastro-enterostomy and often, apparently, in the course of an acute infection. It is situated, however, at the anastomosis or its immediate neighbourhood; and Walton has pointed out that where an ulcer is found apparently a little distance away in the jejunum, there is always a zone of reaction or fibrosis connecting it with the anastomotic ring.

The lesion found at operation in the present case had none of the characteristics of ulcer, and was situated near the duodeno-jejunal flexure at least 5 in. from the anastomosis. Everything pointed to obstruction of the afferent loop with distension having preceded rupture. Such an obstruction is a well-recognised complication of gastrectomy. It is due usually to technical errors and manifests itself in the early postoperative period. In the present case there was no suggestion of postoperative malfunction at the stoma, but the presence of extensive adhesions between the stoma and the anterior abdominal wall, together with a proximal loop longer than average, suggested that the loop might be emptying at some mechanical disadvantage sufficient to cause delay and distension, but not enough to produce clinical symptoms. With the afferent loop distended and fixed at both extremities to the flexure and to the anterior abdominal wall, ideal conditions would be present for volvulus to take place and for the mild obstruction to be transformed to a severe closed-loop type leading to rupture. Decompression would then bring about restitution of the normal lie of the loop of jejunum. We are familiar with such a mechanism in a Meckel's diverticulum which, when attached to the anterior parietes, is liable to undergo volvulus, and Russell (1950) cites Bergmann (1897) to the effect that cases of idiopathic rupture of the stomach are really cases of volvulus in which spontaneous rupture leads to reduction.

Rotation of the afferent jejunal loop is rare. Gaillard (1951) reports 1 case twelve years after the original gastrectomy, and Wells and MacPhee (1952) have seen at operation an afferent-loop volvulus associated with parietal adhesions four months after gastrectomy.

In the present instance perforation apparently took place after admission to hospital, for the swelling due to the distended loop, present on first examination, was absent after the patient had been anæsthetised. Possibly the final rupture was brought about by muscular contraction during a spasm of pain or with the upset of intubation and passage of a stomach-tube during induction of anæsthesia. The fact that the patient was tuberculous may also have been a contributory cause.

SUMMARY

A case of rupture of the proximal jejunum occurring as a late complication of anterior Polya gastrectomy is reported.

Obstruction of the proximal loop by torsion or by kinking is considered to have been the main cause.

Spontaneous rupture of the loop restored it to a normal lie.

I wish to thank Mr. Robert Mailer, in whose ward the patient was treated, for his criticism and advice in the preparation of this paper.

References overleaf

Correct handling during the early months and years of life—when the developing nervous system is at its most adaptable, and when deformities have not appeared—is essential if treatment is to be given its best chance

Not every infant with motor defect is suited to receive such intensive care those with associated mental defect cannot fully respond, and the indiscriminate acceptance of all comers for treatment along the lines used at Queen Mary's Hospital cerebral palsy unit could only lead to disappointment and disillusion The results with mentally normal children, however, can be so good that treatment should be ensured for them The difficulty, of course, is to distinguish during the early months of their lives the mentally normal motor-defective children from mentally defective children and children with combined motor and mental defect This is a hard thing to do, but Mrs Collis suggests that it becomes possible during the fourth month of the child's life, and she offers criteria based on the modifications of reflex activities normally seen at this age It may well be along such lines that a solution will be found

NEUROBLASTOMA

Though neuroblastoma is one of the commoner malignant tumours of infancy and childhood, it is still a rare condition, and Phillips[1] has usefully collected the details of some 600 published cases, including those seen at the Memorial Hospital, New York, by himself and his colleagues This tumour has a tendency to regress spontaneously or to differentiate towards the more benign ganglioneuroma, and because of this Phillips believes that all cases, however advanced, should have the benefit of treatment in order to gain time for possible spontaneous regression or differentiation The possibilities are surgery, irradiation, and chemotherapy (nitrogen mustards, Coley's toxins, folic-acid antagonists, and cortisone) and Phillips considers that any or all of them may have a place in the treatment of a particular patient

He reports the cases treated in his own hospital, accepting 58 out of a possible 61 as true cases of neuroblastoma Of these, 10 survived for three years or more, and these cases are then added to 48 treated in other centres to show the success obtained by various methods of treatment Of the 58 patients surviving, 22 were treated by a combination of surgery and radiotherapy, 19 by surgery alone, and 10 by chemotherapy Radiotherapy combined with chemotherapy was successful in 2 further cases, and chemotherapy (Coley's toxins) in another The remaining 4 patients apparently had spontaneous remissions

Wittenborg[2] has described the largest series of cases successfully treated at one centre—73 patients at the Boston Children's Centre These included 28 which received no radiotherapy, and 45 which had been treated either by surgery, by surgery followed by radiotherapy, or by radiotherapy only, and 22 patients (30%) survived for three or more years Wittenborg found that the presence of metastases and their site seemed to be the decisive factors in prognosis, distant metastases in bones ruled out successful treatment by surgery or radiotherapy Surgery followed by radiotherapy for an incompletely removed tumour offered a 60% chance of survival for three years The presence of metastases, if limited to the liver, still carried an excellent prognosis if radiotherapy was properly carried out

There can be no doubt about the value of both surgery and radiotherapy in the treatment of neuroblastoma, but this should not prevent further investigation of the possibilities of chemotherapy, particularly in patients who have distant metastases in bone when seen for the first time Nitrogen mustard, triethylene melamine, cortisone, and the folic-acid antagonists have all been shown to be capable of producing some regression and prolonging life They should not, however, be used as the first line of treatment, except where surgery and radiotherapy offer no hope at all

MITRAL INCOMPETENCE

Each generation must do the best it can with the knowledge and opinions of its time In 1849 Hope[1] recognised an apical systolic murmur as a sign of a leaking mitral valve Graham Steell,[2] Mackenzie,[3] and Lewis[4] in succession denied the importance of mitral regurgitation, but in recent years mitral incompetence has been re established as an occasional finding At operations for mitral stenosis the surgeon's finger in the left auricle may feel a regurgitant jet of blood We therefore must recognise that the diseased valve can be at the same time stenotic and incompetent, though it may be difficult to judge the volume of reflux The difficulty of diagnosing mitral regurgitation complicating mitral stenosis has been emphasised by Froment and Gravier[5] Of 26 cases of mitral stenosis which they brought to valvotomy 11 had a systolic murmur, but no recognisable regurgitant stream was felt by the surgeon's finger These systolic murmurs may be explained sometimes by dilatation of the pulmonary artery beyond the pulmonary valve ("functional pulmonary stenosis") or more rarely by slight tricuspid insufficiency The diagnosis of significant mitral incompetence is thus fraught with difficulty "Pulmonary capillary-venous pressure" tracings from a catheter wedged into branches of the pulmonary artery have been claimed to reflect left atrial pressure A rise in the pulmonary capillary venous-pressure during ventricular systole is said to show the presence of mitral incompetence,[6] but this reading is not always easy to interpret as various artefacts may obscure the results[7] Biorck and his associates[8] say that a gross (grade III-V) apical systolic murmur and left ventricular enlargement are the important manifestations of mitral incompetence Froment and Gravier think that mitral incompetence should be suspected in mitral stenosis when the systolic murmur is prominent and maximal at the mitral area and when the usual sharp first sound of mitral stenosis is absent Fluoroscopic expansion of the left auricle during ventricular systole is difficult to judge and an unreliable aid Logan and Turner[9] agree with these views, adding the absence of a mitral "opening snap" as a contribution to the diagnosis of mitral incompetence

Brigden and Leatham[10] describe a series of patients in whom mitral incompetence was the major valve disease Pathologically the cusps of the mitral valve were thickened and deformed, the left ventricle was hypertrophied, and the left auricle, though dilated, was not massively enlarged In contrast to mitral stenosis, mitral incompetence is commoner in males and seems to be the basis of bacterial endocarditis more commonly than mitral stenosis There is no clear evidence that more than a few of these cases are rheumatic in origin On auscultation at the mitral area the first sound was normal but was followed by a systolic murmur lasting until the second sound, which it obscured The second sound was better heard elsewhere over the heart In aortic stenosis, by contrast, the systolic murmur

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produced only on addition of the alcohol. Good agreement was obtained between the ethyl and isopropyl alcohol tests.

Serum, Plasma, and Whole-blood Total Cholesterol

A total of sixty-five specimens, with cholesterol concentrations up to 800 (serum), 850 (plasma), and 280 mg. per 100 ml. (whole blood), were tested by a modification of the method of Sackett (1925) using 8 ml. of ethyl alcohol and 2 ml. of ether. A parallel test was done on the extract obtained with 8 ml. of isopropyl alcohol and 2 ml. of ether. There was close agreement, the occasional slight differences being no more than might be expected between duplicates, indicating no significant difference in the efficiency of the two alcohol-ether mixtures in extracting the cholesterol.

Urinary Urobilin (including Urobilinogen)

In the Schlesinger test isopropyl alcohol may be used instead of ethyl alcohol without loss of sensitivity.

Fæcal Urobilin (including Urobilinogen)

Isopropyl alcohol, acidified with hydrochloric acid (1 ml. of concentrated hydrochloric acid to 100 ml. of isopropyl alcohol), was found to be as effective as the ethyl alcohol hydrochloric acid mixture in the preparation of an extract for spectroscopic examination.

The isopropyl alcohol used in these experiments was obtained from Laporte Chemicals Ltd. Further possible uses are being investigated.

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Preliminary Communication

INTRACORNEAL MURINE LEPROSY AND ITS RESPONSE TO ISONIAZID

THE value of any chemotherapeutic agent must be judged ultimately by the results obtained in man. As new drugs are devised, however, some idea of their potentialities may be gained, firstly, by their behaviour towards pathogenic organisms in vitro and, secondly, by their action on experimental infections in vivo. Unfortunately, so far as leprosy is concerned, such preliminary observations are out of the question; for, despite many claims to the contrary, the causal mycobacterium has never been cultured satisfactorily on artificial media, nor has the disease been transmitted to laboratory animals.

Attempts have therefore been made to use rat leprosy as a basis for experimental studies. The close similarity between this disease and that in man has been demonstrated by Carpenter,[1] while an intraperitoneal technique "for the determination of the activity of chemotherapeutic agents against *Mycobacterium lepræ murium*" has been developed by Grunberg and Schnitzer.[2]

During the past year we have developed a method for inducing rat leprosy in the cornea of mice. This communication describes the new technique and shows how such a corneal infection responds to treatment with isoniazid compared with other anti-leprous drugs used in the treatment of human leprosy—namely, a thiosemicarbazone and a sulphone.

METHOD AND RESULTS

Source of Leprous Material

The leprous material was obtained from a strain of *Myco. lepræ murium* maintained, at the National Institute for Medical Research, by successive passages through rats by subcutaneous inoculation. A large softening rat "leproma," about four months after inoculation, was excised under sterile precautions and ground down with normal saline. The suspension so obtained was only lightly centrifuged before injection into the mouse cornea. A smear of this material, stained by the Ziehl-Neelsen technique, showed myriads of acid-fast bacilli.

Inoculation

Albino mice, each weighing 25–30 g., were inoculated intracorneally with this suspension by the same procedure as that previously described for tuberculosis.[3] No attempt has been made to standardise the inoculum, but a high concentration of organisms seems to be essential for the infection to become established.

Progress in Untreated Animals

The occasional initial traumatic reactions disappeared within a few days. There then followed a "latent" period of ten to fifteen days before incipient lesions first appeared. The first signs were corneal œdema with early vascularisation. Further development was slow, in contrast to tuberculosis, but invariably progressive. The lesions spread and, more notably, they became denser. There was considerable vascularisation, but ulceration was rare. Eventually the whole cornea became involved, usually after about six months. No evidence of systemic spread has so far been detected.

Response to Treatment

40 mice subjected to intracorneal inoculation with murine leprosy were divided into four corresponding groups. Treatment was started on the same day as the inoculation and has been continued ever since. The four groups were as follows:

(1) Control (untreated): fed on M.R.C diet 41, 5 g. per mouse per day.

(2) Thiosemicarbazone (4-ethyl-sulphonyl-benzaldehyde thiosemicarbazone): same diet with 0·1% thiosemicarbazone added.

(3) Sulphone ('Sulphetrone'): same diet with 3% sulphone added.

(4) Isoniazid: same diet with 0·3 mg. isoniazid added per mouse per day.

Convincing differences between the groups have been slow to emerge, but after four months isoniazid was the only drug to show a striking suppressive effect. The eyes of the mice in the isoniazid group showed quite severe lesions at one stage, but only corneal opacities now remain. Among the other three groups, the disease seems to have been progressive. At an earlier stage the sulphone may have had a slight inhibitory effect, but there is now no significant difference between this group, the group on thiosemicarbazone, and the untreated controls.

HISTOLOGY OF CORNEAL LESIONS

The cornea of mice inoculated with *Myco. lepræ murium* four to six months previously and left untreated were uniformly thickened, threefold to fourfold. The corneal tissue was infiltrated almost throughout by large polygonal cells containing pale-staining non-vacuolated cytoplasm with a peripherally placed nucleus, but there were no signs of caseation. There were a few islands of small lymphocytes and occasional multinucleated cells. Ziehl-Neelsen preparations showed that all these polygonal cells were packed with acid-fast bacilli, and there were some extracellular organisms. The bacilli were well-defined.

In a mouse selected from the group treated with isoniazid for eighteen weeks there was a single small focal lesion with no thickening of the cornea. The cellular structure of this lesion was no different from that of an untreated lesion. By contrast, the Ziehl-Neelsen preparation showed no extracellular bacilli, and although the polygonal cells were acid-fast they seemed to consist of ill-defined acid-fast material and granules with only a few formed bacilli—an appearance consistent with dead and degenerated bacilli.

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cannot possibly have any effect. On the other hand the irradiated thyroid can no longer produce excessive quantities of hormone, so the pituitary returns to its *normal state, and once more becomes susceptible to* inhibition by exogenous thyroid extract.

Werner's argument seems unexceptionable, and his findings certainly suggest that in Graves's disease the *stimulus to the thyroid does not come from the pituitary.* But experiments of this type are difficult to carry out in a manner which defies criticism. In this instance it is regrettable that the findings were not subjected to statistical analysis. *In all groups there are wide variations* in response, and the reader is not given enough information to enable him to test the significance of the differences between groups. Another weakness lies in the use of *thyroid extract instead of a pure substance like thyroxine.* Thyroid extract contains large quantities of non-hormonal iodine, which might have been sufficient in themselves to influence radio iodine uptake. A further weakness comes from the use of large "*tracer*" *doses of radio*iodine (100 micro curies), these might themselves be sufficient (particularly when repeated at short intervals) to depress uptake in patients with Graves's disease.

An investigation along similar lines, carried out independently by Morgans et al[2] is free from some of those objections, but refers only to the effect of thyroid hormone on patients with inactive Graves's disease. They used sodium *l*-thyroxine instead of thyroid extract, and controlled the possible effect of the iodide liberated from the breakdown of thyroxine by showing that this quantity of iodide had no significant effect on radio-iodine uptake. The tracer doses used (10 micro curies) were small enough not to affect uptake. Statistical analysis showed that 0 4 mg of thyroxine daily for *two weeks caused a significant fall in radio iodine uptake* in normal subjects, and also in patients with Graves's disease in remission after thyroidectomy or a course of thiouracil. The mean fall in radio-iodine uptake was of the *same order in both groups.* Like Werner, these workers concluded that their investigations did not support the idea that the essential defect in Graves's disease is failure of the pituitary to respond to thyroxine.

Clinical experience with antithyroid drugs on the whole supports this conclusion. For if a patient with Graves's disease is overtreated with these drugs the thyroid invariably enlarges, and then subsides again when the drug is stopped or the dose decreased. This indicates a normal response on the part of the pituitary to the presence of hypothyroidism. The failure of several workers to find increased amounts of T S H in the blood of patients with Graves's disease, although not conclusive in itself, also points in the same direction. All this evidence together suggests that some agent besides T S H can stimulate the thyroid. It is clearly desirable to search for this agent, what is not at all clear is where or how the search should be conducted.

A NEW MEDIUM FOR CHOLECYSTOGRAPHY

'Telepaque,' a new radiographic contrast medium for cholecystography, has recently become available in this country after an enthusiastic reception in the United States, where it was introduced in 1951. Its chemical name is 3(3-amino-2, 4, 6 tri-iodo-phenyl) 2 ethyl propanoic acid. After the *advent* of iodophthalein ('Opacol') in 1924, little improvement in biliary contrast media took place until phenodol ('Biliselectan') was introduced just before the late war. Phenodol proved much more reliable, and gave more regular filling and better density. Hills and Trounce[3] found that a high proportion of gall-bladders in healthy young adults filled after one dose, *and that 100% filling* was achieved when the examination was repeated. Both these contrast media, however, may produce various side effects, the most serious are vomiting and diarrhœa, which may prevent *the drug being absorbed,* so that nothing is seen of the gall bladder. These drugs are unpleasant to take, they give rise to nausea and leave a hot taste in the mouth and throat.

In a recent trial Stevenson[4] repeated with telepaque 85 cholecystographies previously carried out with phenodol. He found that nausea was just as common with the new drug, but only 1 patient vomited and only 7 had diarrhœa, with phenodol 5 patients vomited and 19 had diarrhœa. The density of the gall-bladder shadow was greater with telepaque in nearly every case, and the demonstration of translucent as well as opaque calculi was simplified. These results agree with those of American workers[5] [6]

Telepaque, which is given in doses of 3 g, is eliminated *mainly through the gastro intestinal* tract and, to a lesser extent, the kidneys. Given by mouth to mice, its toxicity is about a quarter of that of phenodol. The iodine content of telepaque is 66%, whereas that of phenodol is *only* 51%, which probably accounts for the greater density of the gall bladder shadow. Concentration in the human gall-bladder is greatest after 10-12 hours, it may thus be an advantage to give the medium later in the evening than is the custom with phenodol. Traces of telepaque are often visible in the colon, but these do not seem to obscure detail in the gall-bladder. Where gall bladder function is poor, the greater *density* of the new medium may enable calculi or other abnormalities to be seen in gall-bladders at present classified as "non-functioning"

PSYCHIATRIC RESEARCH

GOOD talk is a sound corrective to cloudy thinking, for the able minded, not wishing their notions to loom vaguely out of a fog, will always get them into focus for a good listener. *Our ideas about the mind are* perhaps bound to be rather foggy at present. we are so ill informed. But some fifty research-workers, at the invitation of the Mental Health Research Fund, met last *year at* Magdalen College, to discuss what ignorances principally hamper our understanding of mental illness, and though they were well aware of the fog they were far from being lost in it. Each shone his *torch along* his own path, called out its direction to his neighbours, reviewed the distance covered, and declared that visibility was fast improving.

This *conference,* which we reported at the time,[7] brought together leading students of neuro anatomy psychiatry, biochemistry, pharmacology, sociology psycho analysis, animal behaviour, physiology, and endocrinology, and they met in a mood of mutual forbearance not perhaps strictly usual between followers of such diverse disciplines. The result was some of the best talk on the subject this century has yet heard, and the proceedings of the conference,[8] edited by Dr J M Tanner, should find many readers.

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[7]

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THE INDEX and title-page to Vol II, 1952, which was completed with THE LANCET of Dec 27, is now *in* preparation. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W C 2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

THE LANCET

LONDON: SATURDAY, FEB. 28, 1953

Water Intoxication

THE name given to a syndrome can be surprisingly influential in determining the attention subsequently paid to it. ROWNTREE[1] chose an arresting title for the ill effects of an excess of water in the body; but in retrospect we may wonder whether the element of paradox in "water intoxication" delayed clinical recognition of the syndrome as a serious cause of ill-being and even death. We are so accustomed to drinking water, or at least watery fluids, in large amount with impunity that the concept of harm from an overdose of water comes strangely to our minds; we forget that we owe our safety in this matter to the prompt diuresis which is the normal sequel to water-drinking, and also to the nausea induced by large draughts of water. When water is given to normal animals by stomach-tube, in a dose of 50 ml. per kg. body-weight, the mechanisms of water loss by vomiting, diarrhœa, and diuresis can be overcome, and a characteristic syndrome appears.[2] The animals become restless, and their muscles twitch; later, convulsions and deepening coma are followed by death. This sequence of events can be arrested by injecting hypertonic saline; but injection of hypertonic urea is ineffective.[3] Here there may be a clue to the mechanisms involved; for hypertonic saline brings about withdrawal of water from cells, whereas hypertonic urea does not do so since urea diffuses easily into the cell-fluid. The importance in water intoxication of the water being actually inside the cells is also shown by the absence of symptoms of the syndrome in patients with massive anasarca, who may have a greater excess of water in relation to body-weight than ROWNTREE's ill-fated dogs. It would seem that the essential cause of the syndrome is not an absolute excess of water in the body, but an excess of water relative to electrolyte, and particularly extracellular electrolyte, so that the water is free to pass into the cells. The emphasis placed on extracellular electrolyte is justified by the observation that sodium depletion, although usually associated with a diminished water content of the body, favours the appearance of symptoms when water is ingested in excess: this may be partly due to the increase in cerebral irritability that has been shown to accompany lowering of the plasma-sodium.[4] We could wish to know more of the intimate mechanisms of experimental water intoxication; but it is at least possible to derive from the experimental work some notion of the clinical situations in which the syndrome might arise.

Voluntary intake of fluid is not likely ever to cause water intoxication, for water is an exception to the general rule that appetite grows by what it feeds on; whatever else sufferers from water may feel, they do not feel thirst. If we remember that water cannot harm thirsty patients, no fears of water intoxication will condemn them to semi-dehydration. Danger both of dehydration and of water intoxication arises when the patient cannot control his own water intake; and our responsibility is still greater when circumstances force us to give fluid by some route, such as the rectum or a vein, where the patient's own inclination can scarcely find expression. A patient's daily maintenance requirements for water can be covered by two litres of 5% glucose[5]; and it is unwise to give fluid in excess of this amount, except with its quota of dissolved electrolyte. In this way we would avoid experiences such as that of HELWIG et al.,[6] who reported convulsions and death in a patient given 9 litres of tap water by rectum; they found that similar effects could be regularly induced in rabbits by proctoclysis.

How can we reconcile our wonted immunity to the water we drink with the susceptibility of some patients to what may seem almost moderate amounts? Without doubt such susceptibility is due to failure of a prompt diuretic response. This failure is, of course, greatest in patients with anuria; and LATTIMER[7] was perhaps the first to point out how greatly the recovery of patients with anuria depended on restraint in giving them fluid. In the same way the fluid intake should be restricted in patients with oliguria in acute nephritis. It is important to remember that the normal kidney conserves water in response to the posterior pituitary antidiuretic hormone (A.D.H.); and also that water diuresis is inadequate in adrenocortical insufficiency.[8] The pitressin test[9] for unmasking latent epilepsy is based on water intoxication secondary to a contrived antidiuresis; and adrenalectomised animals are specially susceptible to water intoxication.[10] After a surgical operation patients retain a higher proportion of an administered water load[11]; more work will be needed to assess the relative importance here of diminished renal blood-flow and of hormonal influences on the renal tubule. The early retention of water after operation has the character of an A.D.H. antidiuresis,[12] but this would not explain the later changes in electrolyte excretion. Meanwhile we cannot escape the important practical conclusion that for some days after operation patients are in no condition to withstand excessive dosing with fluid; and the amounts we give should be limited by their needs, not inflated by our enthusiasm. Symptoms of water intoxication call for the injection of 50–100 ml.

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[1] Rowntree, L. G. *Physiol. Rev.* 1922, 2, 116.

[2] Weir, J. F., Larson, E. E., Rowntree, L. G. *Arch. intern. Med.* 1922, 29, 306.

[3] Harding, V. J., Harris, L. J. *Trans. roy. Soc. Canad.* 1930, sect. v, 24, 101.

[4] Woodbury, D. M., Davenport, V. D. *Amer. J. Physiol.* 1949, 157, 234.

[5] Gamble, J. L. Companionship of Water and Electrolytes in the Organisation of Body Fluid. Stanford, 1951.

[6] Helwig, F. C., Schutz, C. B., Curry, D. E. *J. Amer. med. Ass.* 1935, 104, 1569.

[7] Lattimer, J. K. *J. Urol.* 1945, 54, 312.

[8] Slessor, A. *J. clin. Endocrin.* 1951, 11, 700. Oleesky, S., Stanbury, S. W. *Lancet*, 1951, ii, 664.

[9] McQuarrie, I., Peeler, D. B. *J. clin. Invest.* 1931, 10, 915.

[10] Gaunt, R. *Endocrinology*, 1944, 34, 400.

[11] Cooper, D. R., Iob, V., Coller, F. A. *Ann. Surg.* 1949, 129, 1.

[12] Le Quesne, L. P., Lewis, A. A. G. *Lancet* Jan. 24 1953, p. 153.

of the South-West representing the medical activities of the whole of the South-West Region. It remains under the control of the Bristol Medico-Chirurgical Society, but its editorial board has been enlarged to include representatives of other regional activities. It is an impressive production.

The *Newcastle-upon-Tyne and Northern Counties Medical Journal* is another medical society publication. It began life in 1848 as the *Transactions of the Newcastle and Gateshead Pathological Society* and has run an uninterrupted course under various titles apart from the years 1914–20. It is well illustrated and of a high standard, many of its papers being worthy of wider circulation. Normally a quarterly publication, it has only been possible since the war to publish two numbers a year. The annual subscription of the medical society is £1, each member receiving the journal free of charge.

The *Birmingham Medical Review* first appeared in 1872 and with the exception of the seven years between 1919 and 1926 has been regularly published by the Birmingham Medical Institute. It is a comparatively inexpensive publication distributed free of charge to members of the institute. To others the subscription is 10*s* for four issues. It is essentially a regional journal with many pages devoted to the times of outpatient clinics and other health services. It circulates widely to general practitioners.

The *University of Leeds Medical Journal* began life in 1931 as the *University of Leeds Medical Society Magazine*. Its editorial committee is elected partly by the board of the Faculty of Medicine and partly by the Medical Students' Representative Council with one member of the Leeds Medico-Chirurgical Society. It caters both for graduates and undergraduates, but has a graduate editor. In the recent post-war years it lost a lot of its distinguished appearance though it remained an impressive and serious publication. Last year it appeared in new guise with the avowed intention of obtaining recognition in the *World List of Scientific Periodicals* and the *Index Medicus*. It now clearly places the interests of graduates over the requirements of undergraduates and well deserves a wide circulation. Three numbers are published annually for a subscription of 1 guinea (for students 4*s* 6*d*). One number each year is a symposium. The other two contain mixed articles. It is wholly medical and wholly serious.

SECRETS OF LONGEVITY

It is tempting to ask why some journals have kept going while others have fallen by the wayside. The clues lie in two opposing groups of forces which work for or against the continued publication of a journal. The former are the keenness, drive, prestige, and skill of the editor and his board, and the demand for the particular publication. The latter include financial solvency at a time when costs are rising steeply and there is increasing difficulty in obtaining suitable material, because of the modern tendency to transfer support from the parochial to the wider national field of medical publications.

Charles Hastings and his heirs exemplify the influence of the individual. On the other hand the demand for local journals is losing ground to the greater force of the national ones. If a regional publication is to survive it must meet a demand not covered by these giants. One reason for the wide general-practitioner circulation of the *Birmingham Review* is that it provides much useful local information. A wide circulation maintains financial solvency, a state which many provincial journals are finding difficult to achieve. Rising costs require either a wider circulation or a higher subscription, and often neither is forthcoming. Liverpool found it impossible to support on one subscription an institution, a society, a library, and a journal—the journal had to go. Libraries are costly to maintain adequately, and it is noteworthy that Newcastle, Leeds, and Bristol, free from that expense, keep up their publications, but not without financial troubles. The Newcastle journal now appears only twice a year, and Bristol, in attempting to increase the circulation, has been forced to widen its scope to cover the whole region, though this is a good move apart from the expected financial gain. Leeds must be congratulated and surely has our good wishes in its attempt to gain international status as a medical publication. Its fortunes will be watched closely.

UNDERGRADUATE JOURNALS

There remain the journals published by undergraduate organisations. Of these the three that seem best are the *Oxford Medical School Gazette*, which publishes three numbers annually for a subscription of 5*s*, the *University of Durham Medical Gazette*, which costs half a crown more, and the *Manchester University Medical School Gazette*, a larger publication, and in my view the best of the three. It appears quarterly for a subscription of 8*s* 6*d*, and can afford a considerable number of well reproduced illustrations. A close liaison with the Royal Infirmary's department of medical illustration is a great help. These journals mix serious medical articles, written mainly by graduates, with articles on a variety of theme written by students. The Oxford and Manchester journals include excellent caricatures, and the latter a regular flow of light and often witty verse. Each is a credit to its university and, though read mainly by students, has a distinct appeal to graduates as well. The other medical school journals are not so successful. Some are too frivolous and immature, tending too much to the rag-mag type of publication. They seem to lack some fatherly influence from a mature member of the medical staff who is prepared to discuss with and advise the student editor while remaining in the background.

What I like about the best provincial undergraduate journals—and it applies equally to their London counterparts—is the type of medical article they often provide. For example, an undergraduate guineapig after a scientific evening wrote a most interesting and amusing essay entitled An Evening in the Iron Lung. I like reading the medical articles written mainly for the benefit of the undergraduates. They are often surprisingly instructive to a clinical teacher. And I like reading many of the non-medical articles.

WHAT THE PROVINCIAL JOURNALS SHOULD OFFER

Is it a pity that the provincial journals have almost died out? From the point of view of major scientific papers they are not required, for such papers, if printed in them, are lost. There are plenty of journals with national and international circulations in which work worthy of wide publication will find a place, and to which the staff of provincial hospitals must make their contributions. A case can be made out against the provincial journals. There is no need for them, as there are already national journals in sufficient numbers—too many for the reading capacity of some. They won't be read anyway. There is not even enough time for practice, let alone reading a journal, and the occasional moments of leisure will be filled with golf, bridge, wireless, and television. There is a limit to the number of journals a doctor will buy—and look at the price!

But they can put up a good defence too. Provincial (or should they be regional?) journals do not compete with the national journals but supplement them. If they have well-edited sections of local information they should become essential for successful practice in the area. A provincial journal often gives an encouraging start to a keen young graduate. Sir Harry Platt said proudly the other day "I published my first paper in the *Medical Chronicle*." A provincial journal has a great exchange value, bringing free copies of many contemporary journals into the local medical library. If the journal is part of a society's subscription there will be a relief of income tax under schedule D. Unfortunately this does not apply to those working on a full time basis. In

Moles and Melanomata

THE origin of pigmented nævi is still in question: those who support the epidermal theory say that the nævus cells originate from epidermal cells by gradual differentiation and a process of dropping off into the dermis; on the other hand, the supporters of the more widely accepted neurogenic theory maintain that nævi are derived neoplastically or disontogenetically from two sources—the intradermal dendritic melanoblast formed in the neural crest and the Schwannian syncytium around the dermal nerves. The syncytium proliferates and the Schwann cells fuse to form a complicated nævic plexus. Discussing the whole subject of nævi and melanomata in a recent review of medical progress,[1] J. A. CUNNINGHAM uses "melanoma" and "nævus" as synonymous with "malignant melanoma" and "mole" respectively. Pigmented skin tumours that may be confused with melanomata and nævi include senile warts, pigmented basal-cell carcinomata, sclerosing hæmangiomata, and dermatofibrosarcoma protuberans. Histological examination usually makes it easy to recognise the true nature of these lesions.

A melanoma is more often than not preceded by a pigmented nævus. CUNNINGHAM recommends the classification of nævi into four groups:

(1) Junctional (dermo-epidermal) nævus.
(2) Intradermal nævus (mole).
(3) Compound nævus (a combination of 1 and 2).
(4) Blue nævus (persistent Mongolian spots).

The cells forming these nævi vary; the deeper lesions have a complicated neurofibromatoid appearance, while those beneath the epidermis are cellular and alveolar.

The *junctional nævus* is clinically a smooth, hairless, brown to black macule, flat or slightly elevated. It may be present at birth or it may develop later, sometimes in a sudden outcrop of several nævi. Pigmented nævi of the palms, soles, or scrotum are always of this type, for intradermal nævi are never found at these sites. The junctional nævus, however, may appear on practically any part of the body. Histologically, the nævus-cell proliferation is seen to start at the junction of the dermis and epidermis. Clusters of nuclei in what seems to be an empty space adjoin typical epithelial elements. Junctional nævi have a tendency to show "skip areas" which may lead to recurrences around the operation scar unless excision is sufficiently wide. But what is more important, a frank melanoma may develop later in one of these areas. It is widely believed that junctional nævi are the true precursors of the malignant melanoma.[2]

The *intradermal nævus* is the common mole, a pink to brown, papillary or flat, and often hairy growth. Infection of the hair follicles may lead to suspicions of melanomatous change; but in fact it is believed that this type of nævus rarely, if ever, becomes malignant. Histologically there are combinations of hyperkeratosis, parakeratosis, acanthosis, and atrophy in the epidermis, with irregular epithelioid or alveolar clusters of nævus cells in the upper dermis. The middle and lower dermis show the complicated nævic plexus. The nævus cells are more fusiform and grow around the sweat-glands, and leaf-like laminæ are seen caricaturing Wagner-Meissner corpuscles.

The *compound nævus* is a combination of the junctional and intradermal forms, and its junctional component makes it a possible precursor of the melanoma. Most nævi in children are reported to be of this type.

The *blue nævus* is fundamentally different because the melanoblasts in it are thought to come from the mesoderm. It is smooth and hairless, flat or slightly raised, round or oval, sharply circumscribed, and blue-grey or blue-black in colour. It usually occurs on the face, buttocks, or backs of the hands and feet. Histologically there are heavily pigmented and greatly elongated fusiform cells arranged in bundles. The cells have bipolar, often branching, processes, with each cell having its long axis parallel to the surface of the skin. The cells are mostly situated in the lower and mid dermis. This type of nævus is essentially benign.

A knowledge of the natural history of nævi is very important in deciding how to deal with them. Nævi in children rarely behave like malignant tumours in spite of the fact that 98% of those that are excised show junctional activity; but the profound hormonal stimulus of puberty may be followed by rapid malignant proliferation and metastases. In the adult, pregnancy may have a similar powerful effect. CUNNINGHAM recommends surgical removal of all pigmented lesions on the palms, soles, or scrotum; all ulcerated pigmented lesions; pigmented lesions at sites subject to repeated pressure or friction; pigmented lesions with irregular borders, finger-like projections, or accompanying satellites; suspected nævi in children; and any pigmented nævus on the genitalia, feet, or sites subject to repeated trauma in women in the early stage of pregnancy, or even as a prophylactic measure before pregnancy. In 1944 TOD[3] opposed the removal of any pigmented lesion for cosmetic reasons, quoting 34 instances in which a patient died of malignant melanoma after treatment of an apparently simple mole by local excision, ligature, or cautery. But WIGLEY and BRAIN[4] criticised her implication that the malignancy of these tumours was in any way the result of injury or injudicious treatment; and McEVEDY[5] also thought that removal for the sake of appearance alone was justified. If the term "simple mole" is confined to the light brown, fleshy, slightly elevated, and often hairy lesion, then the surgeon can be confident that the nævus is both intradermal and benign, and excision for cosmetic reasons is justified. But if the lesion is dark brown and flat, or only slightly elevated, it should be regarded as a junctional nævus and treated accordingly, even though it is not enlarging. If it is decided to excise it, the incision should be wide, and on no account should the nævus itself be held or squeezed by the forceps in the process of removal. The use of the cautery or any other traumatic manipulation of doubtful nævi is indefensible, not only because of the risk of disseminating malignant cells but because the destruction involved means that valuable information about the precise histological nature of the lesion is lost.

From the distribution of 960 tumours, CUNNINGHAM concludes that malignant melanomata are found most often on the lower limb (27%), followed by the head and neck (23·5%), the trunk (19%), and the upper limb (13·5%), the remainder being in the eye and elsewhere. PACK et al.[6] found rather less on the arm and more on the trunk in their series of 1190 melanomata; but their figures for the lower limb (27·3%) and the head and neck (22·1%) are very nearly the same. SIRSAT[7] suggests that in Indians a much

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1. Progress in Fundamental Medicine. Edited by J. F. A. McManus, M.D. University of Virginia. London: Henry Kimpton. 1952. Pp. 316. 67*s*. 6*d*.
2. Sachs, W., Macke, G. M., Schwatz, O. D., Pierson, H. S. *J. Amer. med. Ass.* 1947, 135, 216.
3. Tod, M. C. *Lancet*, 1944, ii, 532.
4. Wigley, J. E. M., Brain, R. T. *Ibid*, p. 707
5. McEvedy, P. *Ibid*, p. 806
6. Pack, G. T., Gerber, D. M., Scharnagel, I. M. *Ann. Surg.* 1952, 136, 905.
7. Sirsat, M. V. *Ind. J. med. Sci.* 1952, 6, 806.

The 2 cases in December, 1950, were sisters There was delay in diagnosing the first case, and before she was isolated she had infected her sister In the conglomeration of urban areas of which Birmingham is a part, the local-authority boundaries are of very little significance in the life of the community It was therefore not surprising to find that, at the same time as the Birmingham cases, there were 3 in Smethwick, and 1 each in Oldbury, West Bromwich, and Aldridge, which are urban areas to the north-west of Birmingham

The geographical distribution of the cases suggested that the focus of infection would be found in Smethwick, but, through the cooperation of the five public-health departments concerned, it became clear that at least 6 of the 7 primary cases had eaten cream cakes made by a Birmingham firm whose area of distribution coincided with the distribution of the cases The evidence was strong enough to warrant investigation of the fæces, urine, and blood of the employees of this firm All the tests were negative except the Widal reaction in 1 woman, where *Salmonella paratyphi B* O agglutinated to a titre of 1 in 125 Two specimens of fæces and one of urine were negative, but, having given up work, she refused further investigation However, the Widal reaction was regarded as evidence of recent infection, for O agglutination disappears relatively quickly after infection or inoculation, although H agglutination may persist for years

FURTHER OUTBREAKS

May and June

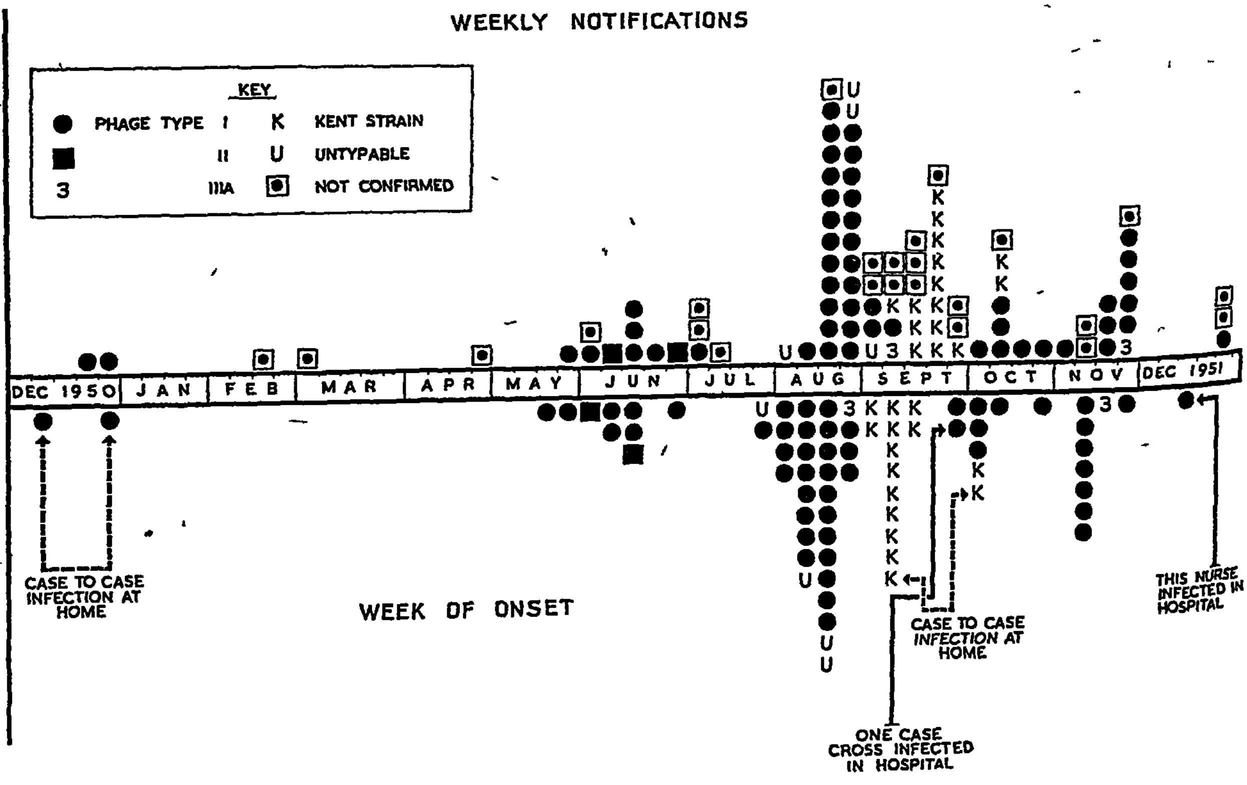
At the same time as the 9 Birmingham cases in May and June, there were 2 cases in adjoining areas It was reasonable to assume that, coming after a period of freedom, a sudden outbreak indicated infection from a single source At the time of the investigation, however, it was not possible to link all cases with food from a single source 2 of the 11 patients had definitely eaten cream cakes from a large Smethwick bakery, and Dr Hugh Paul, medical officer of health for Smethwick, quickly discovered a carrier in this bakery Almost immediately afterwards this man joined the Army Later, when reports upon the phage-typing of the organisms became available, this carrier and 9 of those infected were found to be of phage type I Still later in the year, while investigating further cases, it was discovered that the Smethwick bakery sells some of its cakes under a trade name, and this might well have accounted for the failure to associate 7 of the 9 type-I cases with this source It was also surprising to learn that there were 2 cases of phage type II Evidently there had been two simultaneous outbreaks, but the lapse of time between onset of illness and diagnosis, and the further interval between diagnosis and the phage type becoming known, was a great handicap to the investigation From the stools of one patient, a baby aged 2½, both *Shigella sonnei* and *S paratyphi B* were recovered

August

The August outbreak was at first very hard to explain, for many cases had no apparent connection with a small suburban Birmingham bakery where a carrier was discovered But it turned out that casual meals had been taken at a canteen and an eating-house supplied by the bakery Cases in Droitwich and Ilfracombe were a help in identifying the source of infection The bakery employee had no symptoms and had had T A B during the war His Widal reaction was

S typhi	*S paratyphi A*	*S paratyphi B*
H 1/25	H 1/250	H 1/250
O 1/25	O 1/25	O 1/250

It was the O agglutination to 1 in 250 with *S paratyphi B* which pointed to his being a carrier, a suspicion confirmed by isolating the organisms from his stools He had been employed at the bakery for seventeen months, and he alleged that employees had to make special application to the management to use soap and a towel, so that effective washing of the hands was a rarity As judged by this and the dates of onset of the cases, he seemed to have been a carrier for a month After seven days'



Weekly notifications, week of onset of individual cases, and phage type in confirmed cases terms of improved relations between labour and management and of sounder recovery from illness are difficult to estimate, but may be great. Denerley points out that in the factory with twenty years' experience of such a scheme the older established workers who benefited from the scheme showed a relatively smaller excess of sickness absence compared with their unestablished contemporaries than the younger established workers; and he suggests as one reason that when younger they had benefited from being enabled to recuperate soundly from illness. Buzzard and Shaw, on the other hand, indicate the danger that such schemes may encourage absence that is not to the real advantage of the worker, when his health and morale might be improved by return to work, especially if arrangements could be made for his reablement on the job.

Schemes of sick pay underline the general need for closer liaison between industry and general practitioners, to achieve a smoother and more constructive restoration of the convalescent worker to his job. About the enthusiasm of employees for schemes of payment during sickness there is no doubt. A typical comment was: "It gives a sense of security during illness and removes the nagging fear about your family." As Davis[3] has lately remarked in discussing psychological conflicts caused by group bonus payments, the effects of different systems of payment are an unexplored field for students of social psychology and of social medicine.

SEARCH FOR TUMOUR INHIBITORS

THE search for substances which have the power to inhibit the growth of tumours is one of the rational ways of tackling the cancer problem. Many attempts have been made to find such substances, often by the patient trial of the most unlikely compounds. Inhibitors should preferably come into contact with the tumour cells via the blood-stream rather than by local application, partly because of the mechanical difficulties of reaching deep-seated tumours, and partly because, even when the tumour is accessible, local applications may fail to reach all parts of it. A hopeful approach to this kind of work is to examine substances related to known inhibitors, however weak and ineffective. For example, a good deal of attention is being paid to the inhibitory effects of hormones and other closely related chemical compounds. This is a method comparable to those by which the effective sulphonamide derivatives and the synthetic antimalarial drugs were discovered. Another approach is to test compounds which might be expected to interfere with known cell mechanisms, such as mitosis. Quastel and Cantero,[4] working in Montreal, have now examined the properties of a new tumour inhibitor, D-glucosamine. Previous work had shown[5] that the addition of D-glucosamine to a tissue diverted adenosine triphosphate (A.T.P.) from its normal metabolic paths. As the energy required by rapidly proliferating tumour cells seems to come largely from the breakdown of glucose—a process in which A.T.P. takes part—it seemed possible that parenteral administration of D-glucosamine might divert A.T.P. activity sufficiently to affect the rate of mitosis in the tumour cells. Even if the diversion was only slight, it was hoped that it might be enough to impede the rate of proliferation of rapidly growing tumour cells.

Daily intraperitoneal injections of 2·5 mg. or 5 mg. of D-glucosamine hydrochloride in aqueous neutral solution were given to mice on which small tumours (sarcoma 37) had been grafted. The rate of growth of the tumours became considerably slower, and cytotoxic effects were observed in the tumour itself. Instead of dying before the 50th day, as was usual, nearly all the treated animals survived longer. The level of liver catalase, which is known to fall in tumour-bearing mice, did not fall in sarcoma-bearing mice treated with D-glucosamine. No immediate toxic effects or signs of shock were noted as a result of the injections.

No claim is made that this treatment causes complete regression of the tumours: the effect lies in the retardation of the growth-rate. Indeed, on the theoretical basis suggested, no more than a 50% retardation could be expected. As the mechanism of carbohydrate utilisation is common to tumour and host cells it seems possible that D-glucosamine has some specific toxic action on this particular tumour—a view supported by the fact that no similar action could be demonstrated on the Ehrlich carcinoma in mice.[6] It is thus clear that before this substance could justifiably be used for human tumours, a wider variety of animal tumours must be tested and the long-term effects of D-glucosamine on normal tissues must be studied. None the less, this type of experiment, based on reasonable theoretical grounds, should be encouraged and extended.

THE INFANTILE CEREBRAL PALSIES

SINCE the classic studies of Little, the medical profession has paid only sporadic attention to the infantile cerebral palsies. In recent months, however, a variety of papers have appeared on this subject, and interest has spread to the lay press, in which have appeared reports, articles, appeals, and even a strip cartoon. Present enthusiasm carries with it some risk of rash action because of the emotional appeal of any project which aims at helping cripples, and especially crippled children. The value of any proposed action should therefore be carefully weighed. Already, in the words of Nissen,[7] "the actual surgery of spastic paralysis suffers a great deal from unwarranted enthusiasm for techniques used with success in lower motor neurone paralysis." His remarks apply especially to operation before the age of 6 years: "operation," he says, "is too often advised in desperation when a child cannot walk, even round a table; the results can be deplorable." It will be of no service to the palsied child if our efforts lead only to the widespread use of methods which fall so far short of Little's ideal of "treatment based on physiology and rational therapeutics."

A child with a purely motor handicap is in quite a different category from a child with mental defect. As Eirene Collis points out on p. 416, mentally deficient children, whether palsied or motor normal, need provision primarily as mental defectives. In contrast, mentally normal children with motor defects have the possibility, she holds, of living full, useful, and normal lives. Thus those planning new provision for cerebral palsy cases must make mental assessment their first concern. But it is notoriously difficult to distinguish the motor defective from the mental defective during the first year of life, and sometimes later. Moreover defects of hearing, sight, or neuromotor speech mechanisms may complicate the picture. In such cases the physical handicap must be allowed for, and not every psychologist has the necessary knowledge and experience to make such allowances. Certainly the accuracy with which it can be done, even by the most experienced, is not such as to justify the estimation of the intelligence in terms of a numerical intelligence quotient. Even if intelligence tests could be relied on in these cases, they cannot be applied until the child is old enough to coöperate to some extent; and *that* means a waste of time just when, from the point of view of treatment of motor defect, it is most precious.

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[3] Davis, N. M. *Ibid*, 1953, 10, 18.
[4] Quastel, J. H., Cantero, A. *Nature, Lond.* 1953, 171, 252.
[5] Harpur, R. P., Quastel, J. H. *Ibid*, 1949, 164, 779.
[6] Lustig, B., Wachtel, H. *Z. Krebsforsch.* 1935, 41, 465; *Ibid.* 42, 397.
[7] Nissen, K. I. *Proc. R. Soc. Med.* 1951, 44, 87.

In England Now

A Running Commentary by Peripatetic Correspondents

ALTHOUGH in our more cynical moments we may think, or even speak, disrespectfully of experts, it is only the more self-confident among us who imagine that we could get along without them Indeed, in the complexities and perplexities of modern life we are continually and gratefully turning to them for help Most of us, though not ourselves expert in anything, are quick to spot mistakes, or what appear to us to be mistakes, made by experts in divers spheres of human activity of which we have little or no knowledge or experience Thus, many of us who never aspired to anything higher than to be twelfth man (in braces) on the village green will freely criticise the performances of Mr Hutton or Mr Compton Others who could not say boo to another goose at the local debating society will denounce with vigour and pot-valiance in the local pub the policies and speeches of Mr Churchill or Mr Attlee, and, on a humbler plane, which of us in matters affecting our health does not know better than that fool of a doctor?

It might be all too readily assumed that this alacrity displayed by the inexpert to turn and rend the expert is what the psychologist might describe as a sour-grapes reaction, but this may not necessarily be true The zoologists tell us that many of what we loftily call the lower animals have reached the end of their evolutionary tether and cannot hope for further improvement The lobster, for instance, by specialising in the matter of claws and so forth, has achieved the acme of lobsterdom, but in doing so has come to a dead end He is, in fact, an expert in lobsterism whom we may admire without wishing to emulate, of whom we may expect so much, but no more Never, try as he may, will he become, say, a sound golfer or capable of making up a four at bridge

Mutatis mutandis, may not the same argument apply to your human expert? Must he not, in acquiring that enviable degree of expertness in one direction, have shut himself off inevitably from the possibility of development in a thousand others? If there is a moral to be drawn here it is that we should employ experts whenever we must and can, but should resolutely, refrain from becoming experts ourselves

* * *

The other day, browsing respectfully among the writings of some of my colleagues, I came across the sentence "The patient's blood groups were O, NsNs, P +, Lu(a −), kk, Le(a − b +), Fy (a +), Jk(a −), Tj(a +), Mi(a −)" The authors added nonchalantly: "Only the Rh grouping presented *any difficulty*" The whole affair reminds me of the story of the laboratory technician who used to play postal chess with a friend One day he left a postcard by mistake on the Professor's bench, "*QKtP × KBCh*" read the Great Man "Impossible" he muttered, and spent the rest of the day in the library and most of that night writing an abusive letter to a medical journal about the Wiener versus the A-Z notation

* * *

The commode was discussed so fully in your columns some years ago that I hesitate to revert to it But I do so because I have just realised that it is not a sub-umbilical problem alone By that I am not wanting to start the problem of mind over matter, or spirit over stool, fancy over fæces Recent experience has necessitated a stately throne being trundled beside my bed each morning—in other words, as my nurses chastely say, the chair on wheels I have been surprised how regularly, despite my decubitus, the daily function has been performed without the aid of roots, recipes, or paraffin I was dimly aware how pleasant it was to lean back, almost as comfortably as in an easy chair, and particularly conscious of how the arms of the newfangled contraption gave a sense of ease But I related none of this to my regularity of function

Then came the blessed moment when I was bed-ridden no more, and recuperation entailed visits down the passage But alas my diurnal duty ceased to be done with any ease Now the "cottage" in the hospital where they cared for me so well is an admirable chamber, almost worthy of an auctioneer's advertisement, "pleasant outlook, luxuriously appointed, well warmed" But the throne, like my own here at home, had a very hard back, and it was without arms Now I am prepared to admit that in my convalescent state I may be more dependent on such aids than when I am out and about But I find it hard to believe that the gentle pressure on the arms and the back of the chair on wheels doesn't enhance and smooth the contractions of the abdominal and femoral muscles upon which the ordinary architecture of Messrs Doulton and Goslett so largely depend

I can hear the storm of protest that a proposal for back-rests or simple arms on the ordinary water closet will create I wonder how far all of it will really stem from a calvinistic conception that unless everything to do with the genito-urinary and rectal processes is less than comfortable, some shocking moral turpitude will overwhelm mankind

* * *

The renewal of the import prohibition for parrots has far-flung consequences In Aden troopships returning from the Far East disgorged numerous enterprising members of Her Majesty's Forces who had to sell their cockatoos in a hurry before they reached the shores of a psittacosis-conscious Britain There can now be few places with a better buyers' market for these splendid creatures than this volcanic peninsula on the coast of southern Arabia A sale calls for great ingenuity on the part of the local salesmen—known already to be most capable An Arab youngster pressed an unwilling victim to buy a couple of magnificent birds, asked whether they could talk, the answer was "No, master, but they understand"

* * *

The hula-hula girl was gliding gracefully towards me when I was rudely roused from my postprandial nap "The gas man wants to blow your fire" "Blow the man down," I muttered as I retreated to another room "And now, where had we got to?" I asked myself drowsily I had hardly composed myself when the unmistakable sound of the window-cleaner roused me again "A Happy New Year to you, Sir," he bellowed genially, framed like a tattered saint in a stained-glass window "Thanks, and the same to you," said I, speeding his departure with half a crown Back in my own room, I found that the gas man had brightened things up a bit Now let me recapture that first fine careless rapture That swishing sound must surely be the gentle caress of waves on a coral strand No, it is my clean collars slithering on to the floor "It's only your laundry," the bearer explained All quiet now, apart from the blended murmur of distant aeroplanes, buses, and radios A loud rattle—parakeets in the tropical jungle, of course No, that's my nephew's tommy-gun It's time that imp went home, it's dark so soon at this time of year Tea-time and peace at last But that's the front-door bell, with four visitors behind it "It's a long time since we saw you, doctor, and we heard you were having a day off" All the best, I mused, to each and all, and the best of all to the hula-hula girl I left behind me

* * *

A clinical education undoubtedly predisposes to a narrow preoccupation with purely human problems, but glimpses of the larger life keep breaking through Only the other day our attention was diverted to a letter in *Nature* advocating A Simple Method for Sexing the Confused Flour Beetle Speaking personally, we had always thought of flour beetles as brisk purposeful creatures, and it is vaguely comforting to learn that they are subject to doubts and hesitancies much as we are, and about much the same subject too

Now we come to think of it, perhaps this is what is wrong with all insects, this is the tragedy that explains the aimless buzzing on the window pane, the dispirited cockroaches in the scullery This is what underlies the dry flutterings in the wardrobe, the forlorn cobwebs on the ceiling They are all confused, poor things, and a good sexing would soon set them right All except the ants and bees, that is, they have sublimated their difficulties in a thoroughly nasty inhuman ant-like way, and we cannot help feeling that they stand in no need of help, or even of sympathy ends before the second sound. In some cases of mitral incompetence there may be a short diastolic murmur, but the so-called mitral opening snap is not heard. Radiologically Brigden and Leatham found enlargement of the left auricle with gross systolic expansion in all views. None of the patients showed electrocardiographic signs of right ventricular hypertrophy; instead there was a tendency to left ventricular preponderance.

This subject is important; and Brigden and Leatham's paper leaves an impression of highly developed diagnostic finesse, especially by radiological and phonocardiographic methods. Amid all these difficulties the diagnosis of mitral incompetence has returned to stay. Operations are being devised for its relief,[9] and on physicians falls a new diagnostic responsibility which they cannot shirk. Biörck and his colleagues have achieved reasonable accuracy in diagnosis by using nearly all the modern instrumental techniques as well as the older clinical methods. Careful auscultation, however, proved the best technique of all.

VIRUSES AND HERESY

SCIENTISTS have deservedly earned a reputation for worshipping truth; but now that their tools are turning out observations so much faster than the facts can be explained, some of their devotion is being given to hypotheses. Two examples of this heresy can be detected in some recent work on viruses. Gaylord and Melnick[1] have described developmental forms of vaccinia virus which they have seen in thin sections of infected tissue under the electron microscope. Within the cytoplasm of infected cells round or oval-shaped bodies were seen which were of the same size as, or slightly larger than, mature virus. The bodies were less dense than mature virus and presented a variety of internal structures. For example, some bodies were seen which seemed to be empty shells, giving the appearance of concentric circles. These and other odd appearances are described by Gaylord and Melnick as developmental forms of virus, although it is not clear what form the development takes. Moreover, since no single body can be identified as a virus by its appearance alone, this interpretation is particularly hard to accept. Similar developmental forms were described for the virus of molluscum contagiosum[2]; but, if the term "developmental form" is to mean anything, it must be defined in much greater detail than this.

Something similar seems to be happening with the influenza viruses. Hoyle[3] has found that the influenza soluble antigen appears in infected cells before the virus, and, on this basis, he suggests that the soluble antigen is the form in which the virus multiplies inside the cells. Other observations[4] have suggested to him that the virus consists of aggregates of soluble antigen surrounded by a lipoprotein envelope and Hoyle et al. have now published some electron micrographs which, they claim, give support to these hypotheses. But the experimental fact on which this theory is based—the prior appearance of soluble antigen in the cell—is disputed by other workers in this field.[6,7] Moreover, even if it were true that soluble antigen preceded the appearance of virus in the cell, the crowing of the cock before sunrise should be enough to remind us that what is first to appear is not necessarily the precursor. As for the electron micrographs, they may indeed contain virus particles or soluble antigen: but, if so, these are so heavily camouflaged that adequate controls and further experiments would be required to identify them. Fascinating though the suggestions may be, they strengthen the plea of astronomers for a new unit of speculation, the hoyle, with the micro-hoyle and the mega-hoyle expressing lesser or greater quantities of imagination.

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[1] Gaylord, W. H., Melnick, J. L. *Science*, 1953, 117, 10.

[2] Banfield, W. G., Bunting, H., Strauss, M. J., Melnick, J. L. *Proc. Soc. exp. Biol., N.Y.* 1952, 77, 843.

[3] Hoyle, L. *Brit. J. exp. Path.* 1948, 29, 390.

[4] Hoyle, L. *J. Hyg., Camb.* 1952, 50, 229.

[5] Hoyle, L., Reed, R., Astbury, W. T. *Nature, Lond.* 1953, 171, 256.

[6] Henle, W., Henle, G. *J. exp. Med.* 1949, 90, 23.

[7] Fulton, F. *Nature, Lond.* 1949, 164, 189.

PITUITARY-THYROID RELATIONS IN GRAVES'S DISEASE

IN normal people reciprocal arrangements between the pituitary and the thyroid ensure that the level of circulating thyroid hormone remains more or less constant. If that level falls the pituitary secretes more of its thyroid-stimulating hormone (T.S.H.); if the level rises the pituitary ceases to secrete T.S.H., and the thyroid becomes less active. These reciprocal arrangements, constituting what engineers call a "servo mechanism," would be expected to maintain a constant mean level of circulating thyroid hormone, with more or less rhythmic oscillations round the mean value. Since the thyroid hormone is slow in producing its effects on the tissues these oscillations (which the engineers would call "hunting") would be without physiological significance.

Such a mechanism should prevent people from getting Graves's disease. Since it does not, we may infer that in this condition either the mechanism is faulty or else some other factor is powerful enough to overcome the normal control arrangements. We know that in Graves's disease the level of circulating thyroid hormone is abnormally high. Does this high level fail to inhibit the pituitary (as it would in a normal subject); or is the pituitary effectively inhibited, the thyroid stimulation being due to some quite other cause? S. C. Werner and his colleagues[1] in New York have been trying to answer these questions. They tested the response of the thyroid to T.S.H. and to thyroid extract, assessing it both by the radio-iodine uptake and by the level of protein-bound iodine in the serum. In normal subjects T.S.H. could be shown to increase both of these functions. In patients with active Graves's disease there was no effect on radio-iodine uptake, but the serum protein-bound iodine rose. This seems to indicate that T.S.H. can cause a further release of preformed thyroid hormone, even if it cannot increase the gland's synthesising powers. In other words, in Graves's disease the thyroid does not behave as if it were being subjected to maximal stimulation by T.S.H. Similar results were obtained in patients whose hyperthyroidism had been controlled by past treatment with radio-iodine.

Observations on the effect of giving thyroid extract gave more interesting results. It could readily be shown that, in normal subjects, this procedure depressed radio-iodine uptake, usually without any appreciable rise in serum protein-bound iodine. This is the response to be expected from an efficient servo mechanism. In patients with active Graves's disease there was no such depression although the serum protein-bound iodine rose. When, however, the same procedure was repeated in treated patients, without active hyperthyroidism, it was found that radio-iodine uptake fell, as in normal subjects. Werner argues that an intrinsic pituitary defect (such as insensitivity to thyroid hormone) would have persisted after treatment aimed at the thyroid; and that in this case thyroid extract should have no effect on radio-iodine uptake in treated patients. The results are, he claims, much more in accord with the hypothesis that the thyroid in patients with Graves's disease is being stimulated by a non-pituitary agent. He supposes that in active Graves's disease the pituitary is completely inhibited; hence giving exogenous thyroid extract from a lack of knowledge of the acute and skilled nature of the work which goes on in a modern hospital specialising in infectious diseases

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[1] Werner, S. C., Hamilton, H., Nemeth, M. *J. clin. Endocrin.* 1952, 12, 1561.

We agree that this work should be available to enrich the training of general nurses, but we do not agree that any such scheme can replace the two years of training for the fever certificate

It is hoped that Dr Grant's letter will draw attention to the disquiet that exists among those responsible for the staffing of infectious-disease hospitals If nothing is done and the Fever Register closes, we fear that very soon these highly specialised hospitals will be unable to provide the services required by the public

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D Blanchard
Matron, Leicester Isolation Hospital and Chest Unit
G D Bradford
Matron, Plymouth Isolation Hospital
R Devonshire
Matron, Grove Hospital, London
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Matron, Western Hospital, London
M. R Hills
Deputy Matron, Park Hospital, London
A Holder
Matron, Lodge Moor Hospital Sheffield
L Holland
Matron, Fazakerley Hospital, Liverpool
S Hunter
Matron, West Lane Hospital, Middlesbrough
M Moffat
Acting Matron, City Isolation Hospital, Cardiff
M M O'Kane
Matron, Hospital for Infectious Diseases, Havelock Hospital, Grindon Hall Sanatorium, Sunderland
M Philips
Matron, Monsall Hospital, Manchester
E Spencer
Matron, Little Bromwich Hospital, Birmingham
E L S Strachan
Matron, Walker Gate Hospital, Newcastle upon Tyne
L White
Matron, Sheriff Hill Infectious Diseases Hospital, Gateshead
M T Wilson
Matron, Isolation Hospital, Chester-le-Street co Durham

Sir,—Dr Grant's letter gives a factual and moderately worded description of the impossible situation which has arisen in all large isolation hospitals during the past five years Dr Grant does not, however, fully depict the despair felt by clinicians endeavouring to run these hospitals at the high standard of efficiency to which they had attained

Since 1949 the General Nursing Council has maintained a completely autocratic and unbending attitude towards fever nurses' training It is an attitude which appears to be compounded of ignorance of the value of such training and of a determination to accept no advice which will prevent the complete destruction of the isolation hospitals as they exist in this country today

Since 1949 we have been expected to recruit nurses for the Fever Register while at the same time the General Nursing Council has held over our heads the threat of closure of the Register It is not surprising that very few intelligent girls feel it worth while to embark on such training At the same time fever-hospital nurse recruitment has lost the advantages of pay and earlier age of entry which were enjoyed before the war

It has been suggested that the difficulty of staffing large fever hospitals can be overcome by secondment of nurses from general hospitals, and, indeed, the General Nursing Council grants no other option In this hospital we have for the past two years attempted to maintain our staff by secondment from local general hospitals We have found that such secondment depends entirely on the good will of the matrons in charge of these general hospitals, but even with the best cooperation there is no guarantee that seconded staff can be regularly transferred to us In fact, the numbers have been altered considerably from time to time, and there have even been suggestions that the general hospitals can no longer afford to allot such staff

When this scheme of secondment was suggested it was understood that comprehensive training would take the place of the Fever Register and that infectious diseases would be properly incorporated in the general syllabus Now the new syllabus has been issued by the General Nursing Council and there is no mention of such secondment, and the minimum amount of time given to communicable diseases is four hours There is no other requirement which might take the place of the Fever Register now threatened with closure

Thus a scheme of secondment can easily break down since it has not been made a requirement of the new comprehensive training Secondment has many difficulties, particularly associated with rapid turnover of staff, and the attempt to teach isolation nursing technique in no more than three months has, for practical purposes, not proved a success

The fever hospitals are losing all opportunity to recruit fever-trained senior staff and are now operating successfully by means of senior staff who are overworked and irreplaceable This present success cannot last long

I do not think that the value of fever training to a nurse is fully realised, and it would be a pity if its value is demonstrated only when such training is no longer available Assistant nurses, nursing orderlies, and indeed ordinary general-trained nurses do not compensate for the loss of the fever nurse, and in many cases are more of a menace to the workings of a fever hospital than any real value

It is suggested, from many quarters, that common infectious diseases have declined in prevalence, and if one regards the work of a fever hospital as the care of scarlet fever, diphtheria, and typhoid fever, this is certainly so In actual fact the large fever hospital anticipated this trend some twenty years ago and now treats efficiently all sorts of infections In the hospital from which I write, numbers of cases increase from year to year, and the work is limited only by the available nursing staff It would be unwise to assume that infectious diseases hold no terrors for the future, and when they develop, as they may at any time, it would be a national disaster if the trained fever nurse and the fever hospital had already disappeared The community cannot afford to lose the insurance that these hospitals offer

To meet the situation there seem to be but three possible lines of action

1 To allow the policy of the General Nursing Council to take effect towards the disintegration of the fever hospital service, with the certainty of being able to say "I told you so" when infection demonstrates its strength and when cross infection in general hospitals reaches a new zenith This would be costly and cynical

2 To re establish the well proved methods of fever nurse training with the inducements of a register, higher pay, and an age advantage on entry

3 To establish a fever nurse's certificate of training dissociated from the General Nursing Council, but possibly approved by the Minister of Health, and with inducements of age and pay

Ham Green Hospital
Pill near Bristol

James Macrae

Sir,—We are in entire agreement with Dr Grant At this hospital also, there has been a steady increase in the admission and bed-occupation rates since the war, while the scope of the work has enormously widened

If the Fever Register is discontinued, the effect will be disastrous, for we depend almost entirely on our

Special Articles

THE HISTORY AND PRESENT STATE OF PROVINCIAL MEDICAL JOURNALISM *

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THE earliest journal that could be classed as a provincial medical publication is the *Memoirs of the Literary and Philosophical Society of Manchester*, first published in 1785 and rapidly nearing its 200th year of publication. This society was founded in 1781, with Thomas Percival one of its two presidents, and Charles White, one of its vice-presidents. It had wide interests and was by no means confined to medical men or medical subjects. Nevertheless, one-third of its members were doctors and the *Memoirs* contained many important medical papers. Charles Hastings in 1832 regarded it as the only provincial medical publication before 1828 and described it as a "brilliant success." Appropriately enough, the first paper presented to the society was read by a doctor—George Bell, M.D.—his subject being "Some remarks on the opinion that the animal body possesses the power of generating cold." The opinion had been expressed at a meeting of the Royal Society and was based on the fact that when a man went into a room heated to a degree far above body-heat, and remained there for half an hour, the heat of his body did not increase by more than three or four degrees. Therefore, the body must possess the peculiar property of generating cold in some occult way. Dr. Bell argued that this was nonsense, explaining the phenomenon along reasonable physiological lines.

Another early publication was the *Transactions of the Society for promoting general inoculation at stated periods and for preventing the natural small-pox in Chester*. This was a mixed lay and medical body with which James Haygarth was associated. The society met regularly for six years from 1778. By 1784 smallpox had been eradicated from the district and the society ceased to function. The *Transactions* were finally published in 1785 by Haygarth.

EARLY MEDICAL JOURNALS

The first wholly medical journal published in the provinces was the *Midland Medical and Surgical Reporter and Topographical and Statistical Journal* published at Worcester in August, 1828, and thereafter quarterly. It was founded by Charles Hastings with the assistance of a number of his friends who formed the editorial board. The journal continued until July 18, 1832, when the Provincial Medical and Surgical Association was born in the board-room of the Worcester Infirmary, largely as the result of the efforts of Hastings, who delivered the opening address. Among other things it was decided to publish the *Transactions* of the association in place of the *Reporter*. The first volume appeared in 1833.

It was a thorough-going provincial organisation. There were at first 150 members but these rapidly increased to 300. One member only was not strictly provincial: T. S. Traill, M.D., late of Liverpool, was professor of medical jurisprudence in the University of Edinburgh. Sir Charles Hastings was the father of provincial medical journalism; but so successful was his association that it absorbed the Metropolis and became a national body. His journal ceased to be purely provincial nearly a century ago, for the *Transactions* became the *British Medical Journal* in 1857.

Hastings's example was quickly copied in other provincial centres. The *North of England Medical and Surgical Journal*, based on Manchester, appeared in 1830 but only lasted a year. So did the *Liverpool Medical Gazette* in 1833. The *Transactions of the Cornwall Medical Society* appeared in 1842 and had a similar fate. The *British Record of Obstetrics, Medicine, and Surgery* (another Manchester journal) was born and died in 1848–49, and the *Manchester Homœopathic Lancet* appeared in 1852 lasting for six months only.

Rival medical journals were published in Liverpool in 1834. Dr. Hunter Lane edited the *Monthly Archives of the Medical Sciences*. This began publication early in the year. In May there appeared in hot competition the *Liverpool Medical Journal published monthly under the supervision of an association of physicians and surgeons* (and then in block letters) *chiefly attached to the Medical Charities of Liverpool*. The anonymous editors were clearly unfriendly to Dr. Hunter Lane. Neither journal lasted more than twelve months. But with the passage of time some of the local journals took root and become firmly established, and, although they are no longer with us, they did excellent work for many decades, both from provincial and national standpoints. There was for example:

The *Medical Chronicle* published in Manchester. A monthly record of progress of medical science, it consisted of original articles and a particularly well-written series of abstracts. This was its most notable feature—and what a team of abstracters the editor could command in the early 1900s: Gordon Holmes; A. E. Johnson (the Webb was missing in those days); A. J. Jex-Blake; Percy Stocks; John Hay; G. E. Gask; I. Walker Hall; in addition to the staff of the Manchester Royal Infirmary. The *Medical Chronicle* ran from 1884 for thirty-two years and was a casualty of the first world war.

The *Liverpool Medico-Chirurgical Journal* was another good example. This contained original articles, reviews, and the transactions of the Liverpool Medical Institution. It began life in 1857 in order to stimulate the writing of scientific papers, but it lasted only two years. It was revived in 1881 and ran without a break until 1916. It was again revived in 1929 as the journal of the institution, but ceased publication in 1948 "because of the increasing costs of production and the limited circulation." This is hardly surprising when it is realised that the society had to finance a building and a library in addition to the journal. When it was revived in 1929 the editorial said:

> "A Scientific Society without Transactions is as imperfect as a man without a shadow. It is generally admitted that the papers read before the Medical Institution are for the great part papers of high merit. Some of them naturally find their way into one or other of the larger medical journals. Others are allowed to drop into unmerited oblivion. A local journal saves some of these for posterity and of others a readable synopsis."

This surely means that it was expected that the journal would not attempt to compete with the national journals but could well supply a local need.

PROVINCIAL MEDICAL JOURNALS TODAY

Which are the best provincial journals now? Let us start with those published by graduate bodies. There are only four.

The *Bristol Medico-Chirurgical Journal* holds pride of place. It began life in 1883 and has continued without a break. No other present-day provincial medical journal has survived intact for so long, and its sponsors the local medical society are justly proud of this. A quarterly publication for a subscription of 16s., it embarks this January on a new lease of life as the *Medical Journal*

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* A paper read to the Osler Club on Jan. 16, 1953. For the purpose of this essay "provincial medical journals" were defined as those published by local English organisations operating outside the London area.

CALCIUM CHLORIDE AEROSOL IN BRONCHITIS

SIR,—In an earlier letter[1] an account was given of the use of calcium inhalations to relieve wheezing The fogs of December, 1952, and the respiratory manifestations of the current epidemic of influenza have allowed a further trial of the technique in acute bronchitis

During the past two months, inhalations of 3 ml of a 10% solution of calcium chloride have been administered thrice daily to 35 patients who had wheezing and respiratory distress Of these 35, 24 were completely relieved of their symptoms, of the remainder, 4 were partly relieved, while 7 were not relieved or else refused treatment Some of the patients used the solution in hand nebulisers These did not yield such effective results, on the whole, as an aerosol with oxygen None of the patients were given other drugs to relieve their wheezing

These results suggest that inhalations of calcium chloride solution are of considerable value in the treatment of the common respiratory diseases

Queen's Hospital
Croydon

T H. HOWELL

INTRACRANIAL HYPOTENSION

SIR,—In your issue of Jan 3 Dr Page discusses the *significance of intracranial hypotension* He also describes a series of cases in which he regards the clinical manifestations as the result of intracranial hypotension In considering the possible ætiology of the condition, Dr Page makes a number of assertions which call for correction or modification

He tells us that "hypotonic solutions increase the production of cerebrospinal fluid," and gives Weed and Hughson[2] as his authority Although Weed and Hughson did not deny the possibility that hypotonic solutions may increase the production of cerebrospinal fluid, they never claimed to have demonstrated the phenomenon in the course of their experiments Indeed, in a paper submitted for publication in the same year as that to which Dr Page refers, they state

> "Thus far it has not been possible to demonstrate with certainty whether, following the intravenous injection of the *hypotonic solutions, there is an increase in the quantity of* the cerebrospinal fluid, nor has it been possible to determine an additional absorption of the fluid due to injection of a hypertonic solution"

Thirteen years later, Flexner[3] states clearly when discussing the results of Weed and Hughson's experiments that "the effect of solutions of high or low toxicity on the rate of formation of cerebrospinal fluid remains undetermined" Even today our knowledge of this problem has not advanced beyond the stage of speculation

When considering the mode of formation of the cerebrospinal fluid, Dr Page tells us "Its formation within the choroid plexus depends on active secretion by these cells and not a simple filtration," and cites Flexner[3] as his authority This statement does not represent fairly the guarded conclusion reached by Flexner in summing up the results of his experiments Flexner never claimed to have produced unequivocal evidence that cerebrospinal fluid is formed by a process of secretion It is true he says "The fluid, on the basis of present evidence, is to be considered a secretion with the understanding that the term secretion means that cells must do the work in the formation of the fluid", but in the very next sentence he adds that "these conclusions, however, are based on evidence which is far from ideal"

Finally Dr Page describes some of his own experiments in which, he suggests, an increased formation of cerebrospinal fluid had been induced

> "We have," he says, "been able largely to abolish lumbar puncture reactions after removal of 30 ml of cerebrospinal fluid in a few cases of disseminated sclerosis in which reactions are common, by the immediate introduction of physiological saline solution Only 20–25 ml of physiological saline solution is needed to restore the original pressure, which fact suggests that a reactive increase in the production of cerebrospinal fluid has taken place"

It is difficult to understand on what grounds Dr Page arrives at this conclusion If he had repeated the process of withdrawal and "immediate" introduction of saline, he would have found that the volume of saline required to restore the original pressure continued to decrease *and that the total volume of fluid that could be withdrawn* likewise diminished If Dr Page's conclusion is correct, it should be possible to drain an equal or increasing volume of fluid In my series of experiments in dogs in which this procedure was prolonged, the brains were found after death to be swollen and frequently presented punctate hæmorrhages, especially in the basal region It is evident, therefore, that Dr Page could only restore the pressure of the cerebrospinal fluid to its original level by introducing a reduced volume of fluid because of reduction in the capacity of the subarachnoid space This reduction must be caused by swelling of the central nervous system which itself was brought about by the sudden lowering of subarachnoid pressure by the withdrawal of cerebrospinal fluid

It would, of course, be unreasonable to deny that changes in pressure may induce variations in the rate of formation of cerebrospinal fluid Unfortunately no conclusive observations are yet available However, whatever these changes may be, I submit that they are entirely overshadowed in the experiments I have mentioned by changes in the volume of the central nervous system

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T H B BEDFORD

PRACTICAL PENICILLIN

SIR,—In reply to Dr Ryle (Jan 31) may I ask him to give me credit for having treated many more cases than 135 with 1 5 mega units of 'Distaquaine' This was a continuous series in general practice, not selected by me but merely supervised by me I am sure Dr Ryle will agree that those 35 patients who failed to return did so because they were earning a living Had their sepsis not become quite better the patients would have had to return to one of the general practitioners of the group for his "first certificate and one for work"

With regard to Dr Ryle's second point, a "higher daily level" is not the aim The aim is a high initial level with a daily fall so that the patient has time to *make a personal resistance* to the infecting organism A secondary aim is to substitute a single massive injection for daily injections, however easy these may be Organisms become penicillin-resistant by being subjected to daily low increases in penicillin blood level When I arrived in Fiji I was told that more than half the infections were *penicillin resistant*, administration of 1 5 mega units of distaquaine has proved otherwise

In my article no mention was made of bacteriology *because general practitioners* in Liverpool have neither time nor facilities to subject pus to examination, culture, and penicillin sensitivity tests Clinically I have not seen, *in many thousands of injections*, a case where the result did not support one's clinical judgment It is much nicer to have a single injection of fixed dosage than 500,000–600,000 units daily as suggested by Dr Ryle

The article was written to reduce the work of general practitioners and to suggest how the patient may be restored to work *or school in the shortest* time and with the minimum of suffering The cases at hospital were in groups of 200 and 100 chosen for penicillin treatment by

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1 Howell T H *Lancet* 1952 ii 1230
2 Weed L H Hughson, W *Amer J Physiol* 1921, 58, 101
3 Flexner L B *Physiol Rev* 1934, 14 161

any case, the cost is small. If the journal is doing its job it should dispense valuable local information, but how many of them do this? The Birmingham journal certainly gets near the mark.

It seems to me that an efficient provincial journal should include at least one article for the benefit of the local general practitioner, and a section of local information applying to all hospitals in the area. The sort of cases required by a particular hospital for a particular form of research. The length and reason for the various outpatient or inpatient waiting-lists. There could well be frank discussion of the regional geriatric problem and the steps being taken to overcome it. Special advice could be given on local medical problems, such as catarrh or byssinosis in Lancashire, silicosis in mining areas—matters of local interest that would find no place in a national journal. The journal must be allied to the local medical society or university and should report at length important discussions. It should act as the channel for exchange of opinion in its correspondence columns. Why does it take so long to get a report from a hospital? How do I deal with a particular patient complaining of this and that, who has been the round of the consultants without benefit? Could we have a symposium on the treatment of peptic ulcer? Opinions on the activities of the local medical society, refresher courses, the use and abuse of new drugs and methods—and for that matter of some of the old ones as well—and so on.

A regional journal could help to foster coöperation and camaraderie between the general practitioners themselves; between the general practitioners and the hospitals and consultants; and between the hospitals.

But the journal should not be wholly serious. It should include items of local medical history. It should include as a regular feature some light-hearted verse and, if possible, a clever but kindly caricature.

I wish to acknowledge my indebtedness to Mr. George Wilson, librarian at the Manchester University medical library and to my senior registrar, Dr. R. S. Savidge. Their opinions and advice materially assisted in the writing of this paper.

BIBLIOGRAPHY

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SCOTTISH HEALTH SERVICES COUNCIL AND STANDING ADVISORY COMMITTEES

The Secretary of State for Scotland has appointed new members to the council and standing advisory committees in place of those who retired on Dec. 31, 1952, and has reappointed other members whose term of office had expired on that date. Medical members have been appointed or reappointed as follows:

Health Services Council.—Dr. W. Mackie (Perth) appointed until Dec. 31, 1953; Dr. W. Boyd (Stratheden Mental Hospital), Dr. C. W. Clayson (Lochmaben), Dr. J. G. M. Hamilton (Edinburgh), Prof. J. L. Henderson, F.R.C.P.E. (St. Andrews), until Dec. 31, 1955: Dr. I. D. Grant (Glasgow). Mr. W. W. Galbraith, F.R.C.S.E. (Glasgow), reappointed.

Medical Advisory Committee.—Dr. D. P. Cuthbertson (Aberdeen) reappointed.

Nursing and Midwifery Advisory Committee.—Prof. W. L. Burgess, M.D. (St. Andrews) reappointed.

Pharmaceutical Advisory Committee.—Dr. I. M. Macleod (Inverness) reappointed.

Advisory Committee on Hospital and Specialist Services.—Dr. J. T. Curran (Lennox Castle Mental Deficiency Institution) appointed.

Advisory Committee on Local Authority Services.—Dr. I. B. K. MacGregor (Kilmarnock) appointed.

Advisory Committee on Health Services in the Highlands and Islands.—Dr. C. S. Sandeman (Durness) appointed.

Public Health

PARATYPHOID IN BIRMINGHAM IN 1951

E. L. M. Millar
M.Sc., M.D. Sheff., D.P.H.
DEPUTY MEDICAL OFFICER OF HEALTH FOR BIRMINGHAM

Although typhoid fever is now quite a rarity, paratyphoid is not at all uncommon. In fact there has recently been a considerable increase in the notifications of this disease. In the absence of epidemics or even of individual known cases, the organisms can often be found in sewage. Diarrhœa and pyrexia persisting for some days should automatically lead to an examination of the blood and stools.

Starting with 2 cases at the end of December, 1950, 75 people in Birmingham had been found to be infected by the end of 1951; and these infections were traced to at least eight apparently quite separate sources, as shown by phage-typing of the organisms and by the discovery of the foci from which the disease had spread.

While one or two typhoid bacilli will set up disease, a much greater dose of paratyphoid organisms is needed to cause clinical infection. Such a dose is often provided by a nutritious food at first contaminated with only a few organisms, which then multiply to produce a dose sufficient to cause paratyphoid fever. Experience in Birmingham reflected that in many parts of the country, several of the outbreaks being caused by confectionery containing synthetic cream.

SYNTHETIC CREAM

The manufacture of synthetic cream is a relatively new industry, and in its early days samples from unopened containers often gave alarming bacteriological results; but such samples are normally free from serious contamination. However, between the moment that the bulk container of synthetic cream is opened by the confectioner and the time that the cream cakes are consumed, a series of hazards arise. Contamination may occur during the mixing of the cream with sugar, the filling of the cakes, and the transfer of cakes to trays, shelves, paper bags, or boxes. Moreover a further train of dangers lies between the shop and the tea-table. Any one of the people handling the cakes, and any one of the flies settling upon them may be a carrier of paratyphoid. Transient carriers are probably commoner than is realised; for positive Widal reactions are found in 2% of blood samples from the uninoculated population, and paratyphoid organisms may be unexpectedly isolated from the stools of people not affected clinically.

SEVERITY AND AGE-DISTRIBUTION

There were no deaths, but illness of all grades of severity occurred: some patients had an almost symptomless pyrexia and nothing else, and in 2 people, one of whom was a baby, the organisms were recovered from the stools, but there were no symptoms and the Widal reaction remained negative.

A striking feature was the high proportion of young children infected, the incidence being greatest at about 9 years of age, when it was six times that among adults. The cause may be the children's liking for cream cakes, or it may be due to children developing symptoms of the disease more often than adults when the organisms are ingested.

THE FIRST CASES

The accompanying figure shows the notifications received week by week, and the phage types in confirmed cases. The date of onset of each infection is important in investigating an outbreak, and the lower half of the figure therefore shows the individual outbreaks more clearly.

addition, direct sensitivity tests have been performed by culturing from sputum on to sets of Lowenstein-Jensen slopes containing isoniazid with and without the addition of fraction-V albumin It is hoped soon to publish an account comparing these results with those obtained by indirect methods This work has been done in collaboration with my colleagues in this department, Dr K Anderson, Dr D G Chalmers, Dr P Collard, and Dr M B King

Our remarks *on* the effect of temperature on isoniazid sensitivity seem to have been misinterpreted The effect of temperature is complicated, but our general conclusion was that the bactericidal efficiency *of* isoniazid appeared to be *increased* at temperatures above 37°C The conclusions of Dr Mitchison and his colleagues, however, do agree broadly with our own and with the experimental results of Goulding and Robson [1]

Department of Bacteriology,
Guy s Hospital Medical School
London S E 1

ROBERT KNOX

PNEUMOTHORAX THERAPY

SIR,—Your leading article on this subject (Feb 14) draws attention to the need for a rational policy with regard to the duration of pneumothorax therapy and the benefits that would ensue from such a policy There is undoubtedly a good deal of evidence that an artificial pneumothorax which has not substantially achieved its object within three years should be abandoned in favour of some other method of achieving control of the disease in the affected lung Even this period may possibly prove to be rather long, as sufficient time has not yet elapsed to assess the effects of combined chemotherapy and pneumothorax treatment

The use of the artificial pneumothorax may be becoming less popular, but that is surely right if the reason is a more critical selection of cases If the patient is to finish with a good functioning lung the same critical standards should be applied to the management of the pneumothorax, and the period for which it is maintained, from the time it becomes effective Much will depend on the size and extent of the initial lesion and its response to rest and chemotherapy, but perhaps we should not necessarily wait the three years suggested by Harris et al [2] before reviewing our pneumothorax cases with a view to termination, but should start a year or even eighteen months earlier

London W 13

HUGH CLIMIE

FATALISM ABOUT CANCER OF LUNG

SIR,—The great majority of smoking doctors seem to have adopted a fatalistic attitude towards their developing cancer of lung They usually argue that if they *are* going to develop cancer of lung, carcinogenesis has doubtless been going on in their bronchial stems for years, so why should they bother to stop smoking now, when it would almost certainly be too late ?

The carcinogen has not so far been found, but it is probable that carcinogenesis resulting from chronic irritation by tobacco smoke goes on all the time in the bronchial stems of all smokers, to an extent which corresponds mainly with the heaviness of their smoking Only occasionally does carcinogenesis go on to carcinoma, and so long as no symptoms of cancer of lung have developed, there is a good chance that stopping smoking —cutting off fresh supplies of carcinogen—will prevent this happening Doll and Hill [3] found that out of 1350 male smokers who developed cancer of lung, 70 (5 1%) had given up smoking for a year or more, whereas in the case of 1296 matched control smokers, the corresponding figure was 124 (9 6%)

Wallasey

LENNOX JOHNSTON

REMUNERATION OF SENIOR PRACTITIONERS

SIR,—I am a senior member of our profession (being now aged 68) and have only a small list of National Health Service patients which it is virtually impossible for me to increase Those who found themselves in the same position as myself were, prior to the Danckwerts award, allowed certain extra sums out of the general sums available for the payment of doctors Following this award these sums are all to be reduced, and in my own case this will mean that I am likely to lose not less than £100 per annum The loss may be greater, for the precise figures are not yet worked out The sums which we lose are to find their way into the pockets of younger men with larger lists, most of whom have never been called upon to do the vast amount of unpaid work which was our lot when we entered the profession

It will be probably agreed by everyone that this state of affairs involves a flagrant injustice which should, since our own committees seem unable to cope with it, be corrected by Parliament itself I recommend all those in the same position as myself to write forthwith to their Member of Parliament, and to their local representatives on any Professional Committees, asking that this matter may be given urgent attention

Sevenoaks

GORDON WARD

TUBERCULIN SENSITIVITY

SIR,—In his letter of Feb 14 about our paper on tuberculin sensitivity (Jan 10), Dr Daniels says "there is no doubt they mean ['*low grade*' *sensitivity*] is *always* non-specific" Even in our most expansive moods we should hesitate (I hope) to suggest such an absolute and uncompromising concept, particularly in medical-biological sciences

I believe our results show that *groups* of persons may be characterised as having high-grade, low grade, or relatively no sensitivity, and this is quite different from implying that every single person can be precisely allocated to one group or another With the tuberculins in use today the different kinds of sensitivity overlap to some extent on the quantitative scale, *a perfect separation of one group from another cannot be made* If for *no other reason than errors of observation*, some persons will be incorrectly classified One of the points we tried to make, and this was based on the results in that paper (and in some half-dozen other papers in the last ten years), was simply that a special kind of low grade sensitivity exists it is characterised *in groups of persons* by small reactions to a weak dose of tuberculin (5–10 T U) and larger reactions to a strong dose (100 T U or more), this low grade kind of sensitivity has not been shown to be related *to other evidences of tuberculous infection*, but is clearly related to still unidentified geographic factors

I *do* not think this is a "surprising" postulate in view of the findings reported during recent years, and especially as I know of no strong evidence which contradicts it in the literature on tuberculin sensitivity of human beings

Evidence that high-grade (specific) tuberculin sensitivity wanes in the absence of repeated infection is, I believe, very difficult to assess One must be confident of the uniformity of the tuberculin and of the methods of testing (especially the reading of reactions) and, above all, of the absence of bias I would not disagree that tuberculin sensitivity has been observed to fluctuate, but I am not at all convinced that it generally or even frequently wanes in persons below 50 or 60 years of age Other attempts have been made to explain troublesome questions in the epidemiology and pathology of tuberculosis in terms of waning tuberculin sensitivity It was used a number of years ago to discourage the search for a cause other than tuberculosis of pulmonary calcification in "negative" tuberculin *reactors*, and it was advocated as a reason for disbelieving that histoplasmosis causes pulmonary calcification treatment with chloramphenicol, his carrier state ceased and did not recur.

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[1] Goulding R, Robson, J M *Lancet*, 1952, ii, 849
[2] Harris, W C Poles F C Anderson, A W *Quart J Med* 1952, 21, 447
[3] *Brit med J* 1952 ii 1275

In spite of eliminating the carrier and cleaning up the bakery, new cases continued to arise even after the incubation period had expired. As further cases were investigated, it became clear that a new source of infection was in operation. The factor common to all these cases was again cream cakes from the Smethwick factory which had been partly responsible for the May–June outbreak. Organisms from the new cases were reported as of phage type K. It was, therefore, clear that a new source of infection had arisen in the factory, and a cleaner who occasionally handled cream cakes was identified as a carrier.

Though this new danger was eliminated, further cases arose, all characterised by severe headache at the onset. All these patients had eaten a popular make of ice-cream. The cases were of phage type I, and the evidence to incriminate the ice-cream was slender.

November.

A further group of phage type-I cases arose in the northern two-thirds of Birmingham between Nov. 4 and 10. All the patients had eaten synthetic-cream confectionery from a firm supplying this area, and suspicion fell upon 2 of the 130 employees. They had been immunised with T.A.B. during the war, and still gave *S. paratyphi* B O agglutination to 1 in 50. Repeated examinations of fæces and urine were negative.

On Nov. 16, 3 more cases of paratyphoid B appeared; 2 of them lived just beyond the city boundary. They were all of phage type IIIA and almost certainly from the same source, but this could not be found. There had also been a patient with the same phage type at the end of August.

CONCLUSIONS

Our experience focused attention upon (1) the importance of synthetic cream as a vehicle of infection; (2) the great value of rapid identification of the phage type; (3) the fact that the carriers responsible gave no history of illness; and, above all (4) the need for scrupulous cleanliness of persons and premises, and for the proper training of workers in the preparation and handling of food. It is easy enough to assess premises, but very difficult to assess the people who work there.

Health Visitors

"The front-line troops in the campaign of health education are the health visitors, those devoted workers the nature of whose services, perhaps because they are so little spectacular, are so little understood." This is the judgment of Dr. A. C. T. Perkins, medical officer of health for Middlesex, in his report for 1951.

". . . the health upbringing of young children," says Dr. Perkins, "is not revealed to their parents by instinct and it is the health visitor who teaches the inexperienced—and the not so inexperienced—mother how to avoid the many simple and common mistakes in the care of her children's and her own health which can have all too disastrous consequences. Evidence of their value and success is abundantly furnished by the constantly falling figures of infantile mortality . . . the maternal mortality rate . . . was by far the lowest ever recorded in the County."

There is no doubt, Dr. Perkins adds, that much of the credit for these achievements is due to the county council's health visitors. "Were their services equally readily available in other fields of human health, particularly in connection with the care of the aged, there is every reason to expect that their influence would prove no less beneficial." Unfortunately, however, the number of trained nurses adopting health visiting as a career is far too few to meet the needs: in Middlesex during 1951 the average number of health visitors was some 14% below the target establishment. The training school for health visitors that has been set up in conjunction with the education committee has thoroughly proved its worth.

Influenza

The number of deaths from influenza again increased in the week ended Feb. 14, but the rise was not so steep as in earlier weeks. In the 160 great towns of England and Wales there were 530 deaths from influenza, compared with 446, 313, and 132 in the three preceding weeks. The increase was largely due to more deaths in the northern half of the country. In the London and south-eastern region there were 274 deaths, compared with 270 in the week ended Feb. 7. Of the 530 people who died, 409 were aged 65 or over. First claims for sickness benefit received by the Ministry of National Insurance continued to decline in London and the south, but there was a moderate increase in the north. The subsidence of the epidemic in the London area was reflected in the admission-rate of 84·3% reported by the Emergency Bed Service for the week ended Feb. 23; in the preceding week the rate was 77·9%. The service's yellow warning changed to white on Feb. 19.

Births in 1951

The Registrar-General[1] reports that in 1951 the birth-rate in England and Wales was 15·4 per 1000 population: this was a decrease of 0·4 per 1000 from the rate for 1950. The stillbirth-rate was 23 per 1000 total live and still births. Of the legitimate maternities 39·7% were to mothers with no surviving previous children, 31·9% to mothers with one surviving child, and 15·3% to mothers with two surviving children.

Rural Sanitation in the Tropics

The greatest defect in the development of hygienic living conditions in tropical and subtropical countries is the failure to produce systems of sanitation and water purification applicable to village and rural conditions. The alimentary infections remain today a prolific cause of death and invalidism, whether they are viral, bacterial, or helminthic in origin. But, whereas the use of insecticides for the control of insect-borne disease brings results which are obvious to all, even to those of low intelligence, a simple system of sanitation has no immediate demonstrable advantage and involves accumulation of the unclean waste products of the body. Indeed misused or badly constructed systems produce a filthy locale, and a greater incidence of illness, than the natural use of the "clean" jungle or bush.

Most textbooks on public health describe in detail the large sewage purification plants of the modern city but pay little attention to the problem of the individual house in the rural areas. Hence there will be a wide welcome for Dr. Macdonald's practical account of the different kinds of small sewage-disposal systems.[2] He demonstrates in particular the usefulness of the household aqua-privy, a domestic system which, besides being relatively cheap, is eagerly accepted by the user and is effective, safe, and inoffensive.

Though his book will be useful to doctors working in underdeveloped regions, Dr. Macdonald has written it mainly for public-health workers and for those whose actual task it is to supervise the construction of sewage-disposal systems at bungalows or at the quarters of labourers. Clear and unelaborate drawings indicate measurements in plan and section, and his chapter on maintenance will please everyone with experience of sanitation among tropical populations: too often a sewage-disposal system, once correctly installed, is left to take care of itself—a practice which brings these methods into disrepute. Sewage digestion, and the various designs of septic tanks and aqua-privies, are also well illustrated. Though some of the drawings are on a very small scale, the sanitary engineer should nevertheless be able to prepare his own plans quite readily from them.

Bulletin no. 8 of the Ross Institute Industrial Advisory Committee, dated December, 1952, deals with Sanitation for Estate and Mine Labour Forces and reproduces some of Dr. Macdonald's illustrations. It may be had from the secretary of the institute, London School of Hygiene and Tropical Medicine, Gower Street, W.C.1.

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1. Registrar-General's Statistical Review, 1951. Tables. Part II. Civil. H.M. Stationery Office. Pp. 151. 5s.
2. Small Sewage Disposal Systems: with special reference to the tropics. By O. J. S. MACDONALD, M.D., assistant director, Ross Institute of Tropical Hygiene. London: H. K. Lewis. 1952. Pp. 309. 20s.

indefinite periods—e g , paratroopers But I am certain that the policy in Korea is the correct one I am also fairly certain that the American equivalent of R M O s and field ambulances did not carry blood as a routine, though they could have it flown in by helicopter if necessary

I am quite sure that if we had a C C S in Korea to which casualties were evacuated for primary surgery it would be adequately supplied with blood, as was the base hospital at Kure

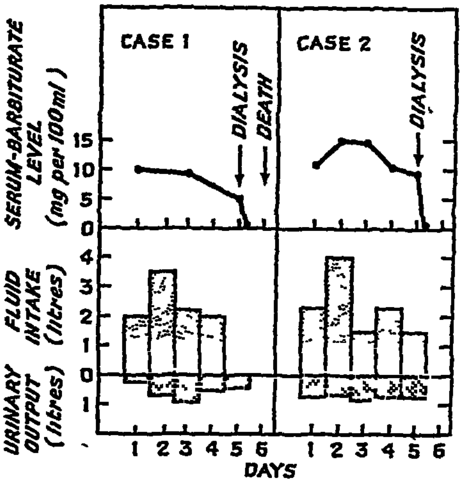
Children's Hospital, Birmingham P D HOOPER

TREATMENT OF BARBITURATE POISONING

SIR,—Your annotation of Jan 10 mentions the 2 patients with barbiturate poisoning whom we treated by the method of dialysis described in 1948[1] Your readers may be interested in some of the details

Two patients were treated with dialysis after the customary forms of treatment had been ineffective for five and four days respectively The accompanying figure shows the changes in the serum-barbiturate level, the fluid intake, and the urinary output

CASE 1 —A woman, aged 29, was admitted to this clinic in a poor condition the respiratory tract contained much secretion, and there developed *purulent bronchitis*, bronchopneumonia, and pulmonary œdema The urinary output was low in spite of an abundant fluid intake and the use of mercurial diuretics, suggesting that renal function was impaired Blood and dextran were given to combat shock, and because on the second day the hæmoglobin level fell from 81 to 51% There was no sign of hæmorrhage at the time, so the decrease was presumed to be due to dilution



By the fifth day the serum barbiturate level had fallen to 5 mg per 100 ml Nevertheless, the patient became worse and more comatose The pneumonia and pulmonary œdema produced persistent anoxia despite the use of oxygen

Treatment by dialysis began on the fifth day, when she was almost moribund We undertook this particular treatment with great hesitation, for we feared the possibility of pulmonary hæmorrhage complicating the pneumonia and œdema After seven hours' dialysis the serum barbiturate level had fallen from 5 to 2 mg per 100 ml —in other words, by 60% The patient recovered consciousness and was able to speak to her relatives

However, severe intestinal hæmorrhage occurred during the dialysis, and this later proved to be due to gastric erosions of the type sometimes met with at childbirth

The improvement was only temporary and she died of pneumonia and pulmonary œdema the following day

CASE 2 —A woman, aged 59, was admitted twelve hours after taking an overdose of a barbiturate It proved impossible to induce polyuria by raising the fluid intake Her condition deteriorated, and purulent bronchitis developed

Dialysis was started on the fourth day, the narcosis was still so deep that the cannulæ could be inserted without local anæsthesia The serum barbiturate level fell rapidly from 8 2 mg to about 1 mg per 100 ml , or by about 85% At the end of the treatment, the patient had recovered consciousness completely, and she eventually went home, physically and mentally restored

Our experiments[2] with rabbits show that the effect of dialysis is much superior to that of forced polyuria, even when the output is as great as half the body weight over a period of six hours

So far, we have treated only these 2 patients with severe barbiturate poisoning During the dialysis the serum-barbiturate level was reduced by 60% and 85%, and both *patients were conscious and lucid immediately after treatment We suggest that dialysis should be used* as early as possible in cases of severe poisoning with *barbiturates, for these drugs are otherwise slowly eliminated*

Medical Clinic
University of Lund, Sweden.

NILS ALWALL
ANDERS LUNDERQUIST.

CHILD-WELFARE CLINICS

SIR,—Dr Gordon's clear and reasoned letter last week contains, I think, some misunderstandings of the past and at least one very doubtful prophecy He writes "Local authorities do this work for the undeniable reason that in the past general practitioners have neglected to do it" It is undeniable that they did not do it, but the reason was not neglect on the doctor's part but the poverty of the patient This was also the reason for the inadequate accommodation and queues in the rain Doctors working in slum areas before the health service saw a very meagre return for their labours, and suitably sized houses did not exist in those areas

As to Dr Gordon's prophecy that welfare clinics will disappear, I fear that he is himself something of a "theoretician" They represent a vested interest of the *local authorities, and cannot simply disappear* Occasionally, of course, they can be converted to occupational centres or mother and-baby homes

May I also comment on the remark *of Dr Owen (Jan 31) that proprietary foods account for half* the attendance at the clinics ? I have proved that a general practitioner and a health visitor can achieve the maximum possible attendance from a practice without resorting to this rather paltry " draw "

York F. CHARLOTTE NAISH

Parliament

Scottish Hospital Endowments

IN the House of Lords on Feb 18, the EARL OF SELKIRK moved the second reading of the Hospital Endowments (Scotland) Bill[3] He explained that under the *health service legislation the procedure* followed in Scotland in transferring hospital endowments was different from that in England In Scotland all endowments were *transferred to the hospital* boards of management and at the same time the Hospital Endowments Commission was set up to prepare schemes for the *manage*ment of these endowments In England, on the other hand, endowments were transferred to the Endowments Fund and then distributed by the Minister of Health

The Endowments Commission, under the chairmanship *of Sir Sydney Smith,* M D , *had recommended* that part of these funds should be devoted to research Though individual hospital boards could use their funds for research, Sir Sydney had felt that this could be more usefully done by an independent body of trustees acting for the whole country He estimated the funds available at £120,000 a year There was a wide measure of support for the scheme both from the hospitals and from the universities In proposing this arrangement Sir Sydney had, of course, borne in mind that adequate funds must *be available to provide reasonable amenities* at individual hospitals and that the spirit of the intention of the original founders of an endowment must be respected

The chairman and members of the new trust would be appointed by the Secretary of State, and it was considered that a small body would be adequate—probably about seven people The trust could also receive legacies

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[1] Alwall N Norvit L , Steins A M *Lancet,* 1948, i 60

[2] Alwall N , Lindgren, P , Lunderquist, A. *Acta med scand* 1952, 143 299

[3] See *Lancet,* 1952, ii 251

Letters to the Editor

POLIOMYELITIS IN DENMARK

SIR,—A striking feature of the recent epidemic of poliomyelitis in Denmark [1] has been the great number of cases of respiratory insufficiency resulting from bulbar and bulbospinal paralysis. We have lately visited the Blegdam Hospital in Copenhagen and we are most grateful to Professor Lassen, Dr. Neukirch, Dr. Ibsen, and their colleagues for their hospitality and for giving us every facility to study and discuss their cases with them.

The magnitude of the task the Danish doctors have had to face can be gauged from Professor Lassen's preliminary communication in your columns.[2] At the time of our visit over 3000 cases of the disease—a third of them paralytic—had been admitted under their care since the epidemic started in midsummer. 310 of these had respiratory complications of a degree requiring special treatment. This treatment consisted in most cases of a high tracheotomy performed under general anæsthæsia, the insertion of a cuffed endotracheal tube, and, through this tube, intermittent positive-pressure ventilation by means of manual compression of a rubber bag.

In the earlier stages of the epidemic the mortality was considerable, but Professor Lassen has shown that the introduction of the new treatment significantly improved the survival-rate. As many as 70 cases had been ventilated at one time by relays of medical students, and at the time of our visit 43 such cases were still receiving artificial ventilation. Several of them had been on bag ventilation for as long as four and a half months and it was surprising to see so little evidence of tracheal damage from prolonged intubation.

It is a triumph for the anæsthetist that so many students were trained to maintain adequate ventilation for such long periods by a method in which over-ventilation, under-ventilation, or circulatory disturbances from excessive pressure can so easily occur. It is also of interest that none of the great number of persons employed in these procedures contracted the disease.

The techniques used in dealing with complicated bulbar or bulbospinal cases have been widely discussed in recent years, particularly in the U.S.A., and there is no general agreement on the most satisfactory method. The tank and cuirass types of respirator are of proven value in pure spinal paralysis, but in bulbar cases with pharyngeal paralysis these machines may be disastrous because they may cause aspiration of pharyngeal secretion. The accumulation of secretions and consequent pulmonary complications are a constant source of anxiety in the treatment of respiratory paralysis. The full postural drainage régime, as carried out in most thoracic units in this country, should be an essential part of any method of treatment and could be employed much more widely. Too often the supine or lateral position with a few degrees of head-down tilt is wrongly regarded as adequate. The prone (or "face-down") position, even with little or no head-down inclination, is normally effective in draining the main bronchi and is no more uncomfortable for the patient.

The tracheotomy and bag ventilation technique provides a practical way of treating bulbospinal paralysis, especially in the early stages. It has the advantage that the patient can readily be nursed in any posture and there is easy access for the physiotherapist. A small mobile team consisting of an anæsthetist, a surgeon, and a nurse has been able to initiate this treatment in the patient's home in the outlying districts of Copenhagen, and the adequately ventilated patient has then been transported to the hospital.

It is our opinion that the method pioneered by the doctors at the Blegdam Hospital has a definite place in the treatment of those cases of bulbospinal respiratory paralysis where postural drainage alone is insufficient and the tank respirator is contra-indicated or difficult for technical reasons.

The experiences of Copenhagen could well be reproduced here. Most of the deaths that occur in the acute stage are in the complicated bulbospinal types and the obstructed airway provides the problem. The mortality in such cases is extremely high. Although the Copenhagen technique has not been claimed as perfect, it does at least appear to provide a means of saving many lives. We feel that those who may ever have the responsibility to treat such cases should consider now whether the technique offers advantages, and, if so, how best to organise the necessary team-work and equipment. We are now in the process of organising such a team or teams which could provide cover for the emergency should it arrive. It should not be overlooked that the emergency is one calling for twenty-four-hour cover.

We are grateful to our respective boards for providing us with the opportunity to see this unique experiment being conducted.

Western Hospital, London, S.W.6. W. HOWLETT KELLEHER.
The Middlesex Hospital, London, W.1. BRIAN A. SELLICK.

REGISTRATION OF FEVER NURSES

SIR,—As matrons of infectious-disease hospitals we have read with great interest and considerable relief the letter from Dr. Grant in your issue of Feb. 14. The difficulties described by Dr. Grant have been felt by all of us since the closure of the Fever Register was first mentioned by the General Nursing Council several years ago. We have found it increasingly difficult to recruit student nurses, and the supply of post-registration nurses taking the fever certificate has almost ceased. Quite naturally nurses do not wish to spend time qualifying for admission to a register which they believe will soon be closed, and there is no doubt that student nurses in general hospitals are being advised, quite understandably, not to spend time taking the fever certificate. Meanwhile we have had to carry on under increasing staffing difficulties which will certainly be much worse if and when the register is finally closed.

In hospitals of every type, the student nurse plays an indispensable part in the ward team; and no matter what may be said regarding her student status, it is impossible to run a modern hospital without her services. Under the most favourable scheme of combined training likely to be approved by the General Nursing Council, matrons of infectious-disease hospitals will lose the services of their student nurses to general hospitals after a period of training for the preliminary State examination. In certain cases she will be able to keep her students for a few months only. This means that no second-year students at all will be available to fever hospitals. There will be no source from which to recruit staff nurses and no provision for the future supply of sisters specially trained in the nursing of infectious diseases. The difficulties of staffing under such conditions can well be imagined.

The nursing work done in these special hospitals compares very favourably with that done in children's and general hospitals. A high proportion of the patients are young babies who require highly skilled nursing. We find that nurses who come to us from general hospitals have commonly had no experience at all of such nursing. The management of infection in open wards and cubicles also requires a rigid technique which can only be acquired by careful training. We feel that much of the misunderstanding which has arisen over the question of the closure of the Fever Register derives

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1. See *Lancet*, Jan. 3, 1953, p. 33.
2. Lassen, H. C. A. *Ibid*, p. 37.

Obituary

HAROLD BALME

O B E, M.D Durh, F R C S, D P H.

As we announced last week, Dr Harold Balme died on Feb 13 at the age of 74 His eventful life had ranged from China to Whitehall, and he had done fine work as a teacher, an administrator, and a clinician

Balme entered King's College Hospital in 1898 with a Worsley Scholarship, and from then onwards obtained his fair share of prizes, including one in divinity He broke off his training at King's to serve in the Imperial Yeomanry Hospital in the South African War After qualifying in 1903, he became house-surgeon to the late Albert Carless and a clinical assistant at Moorfields Hospital, taking the F R C S in 1905 and later the D.P H.

Lafayette

He then felt himself adequately qualified to begin the work he had chosen as a medical missionary He learned his job in an up-country hospital in Tai Yuan Fu, the capital of Shansi, and he became a good general surgeon and an adequate ophthalmologist His clinical success came from method rather than from instinct, but he was a remarkably able speaker and teacher in both English and Chinese While in the interior of China he convinced himself that higher education there must conform to Western standards and should not be directed to training half-baked assistants At that stage of evolution he thought that, in one centre at least, teaching should be in Chinese He then went to Tsi-nan-fu, the capital of Shantung, and with the active coöperation of the Rockefeller Foundation and the mission boards he played a large part in building Cheeloo University, with faculties of art, history, science, and medicine In 1913 he was appointed professor of surgery there, and later he became dean of the medical school and president of the university. He described this part of his work in his book *China and Modern Medicine* (1921)

About 1927 he returned to England; and the following year he took the M D Durh before settling in Surrey into what became a model general practice In 1936 his monograph on *The Relief of Pain* appeared But ill health forced him to give up his practice, and his work was for some time relatively limited When war came in 1939 he was appointed medical superintendent of Haymeads Hospital, Bishop's Stortford, and later of Pinderfields E M S Hospital, Wakefield For his work at Haymeads he was appointed O B E

After the war he became immersed in reablement, which he regarded as an attitude of mind rather than as an affair of apparatus He became successively medical officer in charge of rehabilitation and consultant adviser to the Ministry of Health Later he was director of welfare services to the British Red Cross At this time his interests became international and he served successively as a consultant in rehabilitation to the United Nations, UNICEF, and the World Health Organisation He travelled widely in Europe advising on the rehabilitation of refugees and of physically handicapped children and on the aftercare of the disabled All these activities drew heavily on his reserves of strength, and the last months of his life were a struggle with physical disabilities

H W S W writes "Harold Balme had solved the problem of how to be intensely stimulating and effective and yet remain simple and selflessly unambitious He found his greatest self-realisation in educational administration, for which he had a rare and happy gift He had the capacity of seeing the basic needs of any situation and could create machinery by which they could be realised in terms of harmonious action This for him was a sort of religious activity, for he believed that creative ideas for the betterment of humanity were a part of divine activity He believed this in a much more vivid and personal way than most of us do, and he held that these ideas have a dynamic of their own, he therefore held it his duty to crystallise them all as functioning institutions His life was the embodiment of the Confucian ideal of the Superior Man The Superior Man strives after what is fundamental, and from fundamental principles everything else follows"

Dr Balme married in 1910 Hilda Elizabeth Carr She survives him with two sons and two daughters

The late Sir HOLBURT WARING

Mr Charles Noon writes

Sir Holburt Waring belonged to the distinguished group of surgeons described by Sir Norman Moore in his *History of St Bartholomew's Hospital* as the "successors of Abernethy" During the first half of the 19th century, after Abernethy's retirement, "Sir William Lawrence became the dominating influence in the School of St Bartholomew's He was regarded by the students as the Lord paramount of surgery there" During the greater part of the second half of the century, Sir James Paget stood apart from the rest "After Abernethy he was the greatest benefactor of St Bartholomew's" The career of Lawrence in the 19th century, and that of Waring in the 20th, bear to one another a marked similarity Each man had been a demonstrator of anatomy, a Jacksonian Essay prizeman, surgeon and senior surgeon at St Bartholomew's, Hunterian orator, and finally president of the College of Surgeons

I first met Waring in 1906 He was a slim, well built, upright man, proud of his grey hair and striking appearance his facial expression revealed a dominating personality He was an outstanding clinical bedside teacher The lessons he impressed upon his house surgeons and dressers, both in the wards and operating-theatre, were unforgettable He was not given to praise work which it was a duty to perform, but by his example he gave guidance, inspiration, and encouragement "He made one feel anxious to do better work and to be capable of greater effort" He was stern and exacting, and at times seemed almost unapproachable Many of his house surgeons, however "held him in affection" Before I finished my term of office I felt I was beginning to know something of the man He would indicate, in his own particular way, that your interests were his He was a surgical autocrat, but he could be a real friend and adviser

I saw him for the the last time about two years ago in his Gloucestershire home He talked of the work he had done at St Bartholomew's and the College of Surgeons He had done the things he had wanted to do, he had done what he thought was right, and the memory of his life and work will be treasured by his friends

Appointments

AIRD, P J, M B N U I, D P H D P M resident medical superintendent, District Mental Hospital, Ennis, co Clare

BARCLAY, RENÉ, M B Lond, D P H M O H, borough of Newbury, and rural districts of Bradfield, Hungerford and Newbury, and asst county M O Berks

DEARNALEY J N M B Lpool, D C P asst pathologist, Leicester Royal Infirmary

GRIFFIN, S G, M B Lpool, F R C S consultant thoracic surgeon regional thoracic service, Newcastle upon Tyne

HALL, T S, M B E M D, B SC Belf, D OBST, D P H M O H and school M O Salop

HILL, J P, L R C P I, D P M resident medical superintendent District Mental Hospital Portlaoise

MCROBERT, CATHERINE, M B Madras resident M O, Tadworth Court, Surrey

MANNING, F R C, M R C S appointed factory doctor, Epsom Surrey

MILLIGAN, A B, M B Edin, D C H appointed factory doctor, Worcester

MILLIKEN, T G M D Belf M R C P I second consultant South Tyrone Hospital Dungannon and Mid Ulster Hospital, Magherafelt

TRILLING RUTH, B M Oxfd, D C H asst resident M O, Tadworth Court Surrey

VINE, R G M D Belf, M R C P second consultant to north west area hospitals in Londonderry and Limavady

South Western Regional Hospital Board

HOFFMAN, J N, M B Lond registrar in diseases of the chest, Bristol clinical area

PATON, S I opædic and traumatic tal, and the traumatic surgery centre

TROTTER, J strar Frenchay Hospital Bristol

WALKER, W LUMSDEN, M B Aberd, D P H, D P M senior registrar, in psychiatry, Moorhaven Hospital Ivybridge

YORSTON R A., M B St And registrar in ear, nose and throat surgery, Bath group of hospitals own student nurses in training for the Fever Register. Most of our senior staff, including six ward-sisters, have done their fever training here. It is true that for four years we have participated in a comprehensive scheme, general students spending three months here, but from our point of view this has not been as successful as was originally hoped. The time is far too short for them to be of use, while the numbers in each batch are tending to decline; in one group recently there were only three. (Those that return for the postgraduate course are surprised by the amount that they still have to learn.) In fact, this scheme is to be replaced experimentally by another. Otherwise, our recruitment is satisfactory now that we have recovered from the setback which lasted for two years after the premature announcement of the General Nursing Council in 1949 that they proposed to close the Fever Register.

The council apparently realises that the staffing of fever hospitals will be seriously upset if they persist with their plan, but consider that they are only responsible for education. Clearly, the two cannot be separated. All professions exist primarily to serve the public, and professional education has been designed for the adequate fulfilment of this basic principle. Properly trained staff must be provided to meet *all* requirements; and any experimental changes in "education" which conflict with this principle are retrograde and contrary to the interest of the patients and, in this instance, of the public health of the nation as well.

It is agreed that trained staff would still be available for teaching purposes, ignoring the probability that many might leave institutions which ceased to be recognised as training-schools. Much more important, can anyone say whence the necessary future replacements of this senior staff will be forthcoming? There will be none, and the whole infectious-disease service in England and Wales with its fine traditions will be lost. This is quite indisputable.

If the responsible authorities sanction such a retrograde step, they will be taking a serious risk with the nation's health. Should an epidemic of poliomyelitis of the magnitude of the recent catastrophe in Copenhagen strike this country—and it is very possible—with its fever hospitals inadequately staffed, they could be open to the most serious criticism. Seconding comparatively inexperienced staff from other hospitals would be no solution to the problem.

The whole history of infectious diseases is a warning against facile optimism that they are no longer of any account. It is our excellent public-health service that keeps them in check, and in this the modern adequately staffed isolation hospital still has an important part to play.

The General Nursing Council should think again before allowing their experiments in education to tamper with the safeguards that protect the nation's health.

Isolation Hospital,
Plymouth.

D. F. JOHNSTONE
J. L. FLUKER.

SIR,—For over twenty-five years now the General Nursing Council for England and Wales has maintained a State Register for fever-trained nurses. Prior to the 1920s, the Fever Nurses' Association and the Metropolitan Asylums Board held examinations and kept registers of successful nurses. In order to qualify for recognition from any of these bodies, nurses had to undergo two years' arduous training in the nursing of infectious diseases; so for almost fifty years "fever" nursing has been appreciated at its full worth.

Two years is none too long a period in which to teach student nurses the special techniques that are necessary to prevent the spread of infection and to guard their own health. It can be said with truth that there is more cross-infection in the wards of general or children's hospitals than in an infectious-diseases hospital, where it is practically unknown.

The General Nursing Council suggests that the nursing experience available in isolation hospitals should be used to "enrich" the training of the general nurse. In fact it will burden the already overcrowded syllabus which is about to be imposed upon young student nurses entering for three years' general training. On Jan. 1, 1954, the revised syllabus comes into force, and we shall require superhuman beings with first-class brains to master completely all the subjects required of them and at the same time to undertake bedside nursing duties. Sister-tutors also will have so many class administrative duties that it will be a miracle if they find time to do any teaching. In order to grasp all the information indicated by the new syllabus, six years' general training would not be too long. One wonders whether the council is seriously attempting to train first-class bedside nurses, or whether it is endeavouring to give to nursing students a kaleidoscopic view of as many subjects allied to nursing as can be named.

By this new syllabus the nursing of infectious diseases is to be mastered in four teaching hours. It will take much longer than that merely to teach the basic facts about immunity and susceptibility and protective measures against infections.

Fever training is essential for sisters in charge of infectious-disease wards, and indeed for sisters of any children's wards, for school nurses and health visitors, and for nurses in the missions and in hot climates. This specialised training should be available for those who want it.

Many matrons of isolation hospitals will despair of ever obtaining sufficient nurses to care for their patients adequately. The General Nursing Council may argue that they are interested not in staffing hospitals but only in training nurses. But surely the training of nurses must be related to the nursing needs of the population? So long as patients with infectious diseases are segregated in isolation hospitals then nurses should be trained in their care and management.

It would seem to be more sensible if the General Nursing Council were to extract some of the material from the general syllabus and allot this time to fever training. At the same time young women of 17 to 18 years should be permitted to enter for this training in infectious diseases before starting their general training. Thereby their health would be safeguarded and their early studies would gradually lead them to the fuller syllabus.

The country is not yet in a position to give student nurses a purely theoretical training, however desirable this may be. Student nurses are important members of the working staff of a hospital; and, as their physical work is quite arduous, their academic studies should not overtax their mental powers. Unfortunately we do not attract educated students with superior intelligence in sufficient numbers: we do not seem to produce the quality of nurse we trained twenty years ago. How then will it be possible to train a less well equipped nurse in a lesser number of years and less hours per week from a more comprehensive and academic syllabus—especially when the sister-tutors will obviously have less time for teaching and coaching than formerly?

Let us be reasonable and keep open the Fever Register, first of all to ensure that our infectious patients can be adequately nursed, and secondly to secure good medical training for our young student nurses and to instil into them the principles of prevention of spread of infection.

Western Hospital,
Seagrave Road,
London, S.W.6.

GLADYS M. HARDY
Matron.

Society of Apothecaries of London

At recent examinations the following were successful

L M S S A—G Hamlet J V Parson, A McL Keil, J S Bennett P M Teng, N Kaan, W I G Hughes, F L D Steel, C E Lay

D I H—M S Bopari P K Bose, I Fairlee, A Munn P N B Peacock, S Mukherjee, W E Scott, D K Ramadwar

Mr E J Dearman, bedel to the society, has retired after 52 years' service

Gilbert Blane Medal

On Feb 17 at the Royal College of Physicians of London, with Sir Russell Brain, the president, in the chair, and in the presence of the president and vice presidents of the Royal College of Surgeons of England, Surgeon Vice Admiral Sir Alexander Ingleby Mackenzie, medical director general of the Navy, presented the Gilbert Blane medal to Surgeon Commander H L Belcher, R N

Research Board for the Correlation of Medical Science and Physical Education

This board has given the William Hyde award for 1951 (£300) to Dr Richard Scott, of Edinburgh, in recognition of his work with students—both in the student health service and in the general practice of medical work in the home

Anglo-French Exchange Bursaries

Short term grants for work in France are offered again this year to British doctors and medical research workers by the Institut National d'Hygiène, Paris Details and application forms can be obtained from Dr G W Wolstenholme, director of the Ciba Foundation, 41, Portland Place, London, W 1 The closing date for applications is March 31

College of General Practitioners

The membership of the college now stands at 1600 Eleven additional general practitioners from different parts of th British Isles have been elected to the foundation counci Until the first annual general meeting is held in the autum the council will consist of

G F Abercrombie (London), chairman, G O Barber (Esse I Cottrell (Lincolnshire), D G F[illegible] Gillie [illegible] s [illegible] J M [illegible] Hughe[illegible] [illegible]unt (London), hon secretar[illegible] R M [illegible] J G [illegible] R J [illegible] F M [illegible] chairman, Richard Scott (Edinburgh), J G Swift (Hampshire), A Talbot Roge (Surrey), J C Young (Belfast)

The college is collecting plans and photographs of up to dat surgeries, consulting rooms, dispensaries, and waiting room It is hoped to provide a centre where plans of these projec can be studied General practitioners who have recentl adapted old houses, or who have built new premises, a asked to send plans and photographs to the secretary of th college, 14, Black Friars Lane, London, E C 4

EMERGENCY BED SERVICE—In the week ended last Monda applications for general acute cases numbered 1472 The proportio admitted was 84 3% The yellow warning was withdrawn an a white warning imposed on Feb 19

The Ministry of Education has prepared a new edition of the Li of Special Scho[illegible] or Handicapped Pupils an Institutions for [illegible] Training of Disabled Perso in England and [illegible] ublished by H M Statione Office, price 2s

Diary of the Week

MARCH 1 TO 7

Monday, 2nd

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W C 1
5 P M Prof R W Russell, PH D Comparative Study of Effect of Electric Shock Convulsions on Behaviour
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W 1
8 30 P M Dr E R Cullinan Disorders of the Liver and Bile Passages (First of three Lettsomian lectures)

Tuesday, 3rd

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street, W C 1) Prof E P Sharpey Schafer Causes of Hypotension in Man
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
8 30 P M *Section of Orthopædics* Mr H Jackson Burrows An Even Keel in Orthopædics (Presidential address)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W C 2
5 30 P M Dr S Thomson Animal Diseases
WEST END HOSPITAL FOR NERVOUS DISEASES, 10, Marylebone Lane, W 1
5 30 P M Dr G Parsons Smith Neurological demonstration

Wednesday, 4th

ROYAL SOCIETY OF MEDICINE
5 30 P M *Section of History of Medicine* Sir Gerald Kelly P R A Value and Significance of Representational Painting, Especially in Regard to History
8 P M *Section of Surgery* Sir Stanford Cade, Mr Ronald Raven Mr J P Reidy Surgical Treatment of Carcinoma of the Pharynx
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Animal Parasites in Dermatology
INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray s Inn Road, W C 1
5 30 P M Dr B Larsen (Denmark) [illegible]
INSTITUTE OF UROLOGY, St Paul s Hospi[illegible] C 2
5 P M Dr Cuthbert Dukes Patholog[illegible]
UNIVERSITY OF OXFORD
5 P M (Radcliffe Infirmary) Sir James Learmonth Portal Hypertension (Litchfield lecture)
MIDLAND MEDICAL SOCIETY
8 15 P M (Birmingham Medical Institute 154 Great Charles Street) Discussion on Deficiency Diseases in Animals and Man
MANCHESTER MEDICAL SOCIETY
4 30 P M (University of [illegible] Howell Hughes Gastroscopy Dr [illegible] Rheumatic Carditis (Joint [illegible]ool Medical Institution)
MEDICO CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (Royal College of Surgeons 18 Nicolson Street) Mr Colin S Penn F F A R C S Life Assurance and the Medical Profession

Thursday, 5th

ROYAL COLLEGE OF SURGEONS Lincoln s Inn Fields, W C 2
5 30 P M Prof E C Dodds, F R S Biochemistry of Endo lymph Perilymph and Cerebrospinal Fluid
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicin Prof G W Pickering Natural History of Essenti Hypertension
UNIVERSITY OF LONDON
5 P M (St Mary's Hospital Medical School, Paddington, W Prof P Mallet Guy (Lyons) Les opérations sympath ques dans le traitement des pancréatites chroniqu récidivantes
UNIVERSITY COLLEGE, Gower Street, W C 1
1 45 P M Prof V B Wigglesworth, F R S Chemical Aspec of Insect Physiology (Third of four lectures)
ROYAL SOCIETY OF MEDICINE
5 P M *Section of United Services* Wing Commander A J [illegible] D G V Whittinghan [illegible] Brennan Survival an Rescue
8 P M *Section of Neurology* Sir Geoffrey Jefferson F R [illegible] Dr G C Evanson Smyth Dr J W D Bull Differentia Diagnosis of Lesions of the Posterior Fossa
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Childre Great Ormond Street, W C 1
5 P M Dr J A Fraser Roberts Genetic Background of th Dull Child
ST GEORGE S HOSPITAL MEDICAL SCHOOL Hyde Park Corne S W 1
5 P M Dr Denis Williams Neurological demonstration
[illegible] Small s Wynd, Dundee) Dr [illegible] Embryology of Twins, Triplet [illegible]uintuplets

Friday, 6th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS, 58, Quee Anne Street, W 1
5 P M Mrs Ruth Graham (Boston) Value of Vaginal Smea to the Gynæcologist (John Shields Fairbairn lecture)
UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medicine) Prof G F Marrian, F R S Metabolism of the Steroid Hormones
ROYAL SOCIETY OF MEDICINE
10 30 A M *Section of Otology* Mr R S Venters Prof Alexander Kennedy Tinnitus
2 30 P M *Section of Laryngology* Dr W Goodd[illegible] Mr T E Cawthorne, Prof Robert McWhirter Early Diagnosis of Nasopharyngeal Carcinoma
5 30 P M *Section of Anæsthetics* Dr Robert Forbes Dr Alistair French Medicolegal Aspects of Anæsthetic Accidents
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H J Wallace Clinical demonstration

Saturday, 7th

NUTRITION SOCIETY
10 15 A M (King's College of Household and Social Science, Campden Hill Road W 8) Symposium on Education in Nutrition in the United Kingdom
MIDLAND TUBERCULOSIS SOCIETY
3 P M (Chest Clinic 151 Great Charles Street, Birmingham 3) Prof Thomas McKeown Inheritance and Environment in Tuberculosis

the casualty officer and followed up by me. The graphs were put in to show that in general practice an injection of 1·5 mega-units procaine early in sepsis enabled the patient quickly to return to work and at the same time relieved the casualty department and the busy practitioner of unnecessary work. I would go one better than Dr. Ryle and say that an early return to work is for the good not only of the patient, hospital, and general practitioner but of the country as a whole.

Colonial War Memorial Hospital,
Suva, Fiji.
ROBERT I. COHEN.

FOG AND FALLACY

SIR,—May I throw into the arena my figures for the effects of the fog on a suburban general practice of approximately 3250 on the outer edge of East London:

Date		*Influenza*	*Other respiratory complaints*	*Other complaints*
Nov. 24–30	..	3	24	54
Dec. 1– 7	..	4	39	66
„ 8–14	..	6	69	66
„ 15–21	..	5	32	56
„ 22–28	..	5	34	64

The weekly figures represent only first attendances, the increase reflecting the effect of the fog on Dec. 5–9. The severity of the effect would only have been shown by the total number of attendances on both fresh and old cases together.

It will be seen that the increase in respiratory affections of just over 1% agrees with that found by Dr. Fry (Jan. 31).

Ilford, Essex.
R. M. C. SMITH.

SIR,—I was surprised to see the figures given by Dr. Cort (Feb. 14) of the attendances in his practice in Durham. The accompanying table shows figures for my practice, which is of similar size to Dr. Cort's, for the past twenty-three years.

Taking the average since July 5, 1948, my figures are as follows: number on list 2466; visits 836, attendances at surgery 5633, total items of service 6469, per annum; average number of items of service per person 2·62 per annum; percentage of items of service as visits 12·9.

Dr. Cort's figures are: number on list 2600; visits 11,900, attendances at surgery 18,700, total items of service 30,600; average number of items of service per person 11·8; percentage of items of service as visits 38·9.

Thus in Dr. Cort's practice, compared with mine, visits are 14 times as many, attendances at surgery 3 times as many, total items of service about 4 times as many, and percentage of items of service as visits 3 times as great.

ATTENDANCES ON N.H.I. AND N.H.S. PATIENTS

Year	No. on list	Visits	Attendances in surgery	Total items of service	Av. no. of items of service‡	Distribution of items of service (%)	
						Visits	Surgery
1930	2051	788	7527	8315	4·05	9·5	90·5
1931	1950	979	6939	7918	4·06	12·4	87·6
1932	1971	775	6449	7224	3·67	10·7	89·3
1933	1929	810	5987	6797	3·52	11·9	88·1
1934	1838	657	5906	6563	3·57	10·3	89·7
1935	1703	662	5518	6180	3·63	10·7	89·3
1936	1667	647	5768	6415	3·85	10·1	89·9
1937	1649	673	5456	6129	3·72	10·9	89·1
1938	1637	546	5310	5856	3·58	9·3	90·7
1939	1592	667	4741	5408	3·39	12·3	87·7
1940	1561	605	4765	5370	3·44	11·3	88·7
1941	1422	396	4117	4513	3·17	8·8	91·2
1942	1368	374	4639	5013	3·67	7·5	92·5
1943	1396	392	4766	5158	3·69	7·6	92·4
1944	1403	341	3995	4336	3·09	7·9	92·1
1945	1346	490	3912	4402	3·27	11·1	88·9
1946	1634	382	3914	4296	2·63	8·9	91·1
1947	1682	467	3920	4387	2·61	11·3	88·7
1948*	1639	146	2015	2161	2·64	6·9	93·1
1948†	2505	380	3129	3509	2·80	10·8	89·2
1949	2596	1050	6549	7599	2·93	13·8	86·2
1950	2557	846	5746	6592	2·58	12·8	87·2
1951	2466	766	5123	5889	2·39	13·0	87·0
1952	2245	683	5115	5798	2·58	11·8	88·2

* Up to July 4.
† After July 4.
‡ Average for all patients registered.

One explanation might be that in Dr. Cort's district morbidity is much more prevalent; but this could hardly account for such a large difference. It would be interesting to know the number of prescriptions issued by Dr. Cort, and their cost, during his 30,600 attendances in one year.

London, S.E.25.
A. FRY.

SIR,—I was delighted to read Dr. Fry's reply to Dr. Cort's letter, and also your editorial comment. The number of visits made and the number of bottles dispensed are often cited as evidence of the excellence of a practice.

A bottle of medicine can be dispensed in a matter of minutes, whereas probing into and straightening out a problem often takes half an hour. Such a half-hour is well spent and probably the patient will not have to return; whereas the patient who has received the bottle of medicine without thought comes time and again for a repeat until he tires or the problem resolves itself.

I am of the opinion that the value of a practitioner is in inverse proportion to the number of bottles of medicine he prescribes.

Newent,
Gloucestershire.
K. M. TOMLINSON.

RESISTANCE TO ISONIAZID

SIR,—We have previously discussed some of the puzzling problems met with in studying the resistance of tubercle bacilli to isoniazid.[1] In their article of Feb. 14, Dr. Mitchison and his colleagues touch on certain aspects of this subject which we have for some time been actively investigating, and ask certain questions which we can, partly at least, answer now.

We have found that the in-vitro resistance to isoniazid, which developed in tubercle bacilli isolated from the sputum of patients during a course of treatment with the drugs[2] did in fact almost or completely disappear after treatment was stopped. To test the clinical significance of this finding, our colleagues, Dr. K. S. MacLean and Dr. C. L. Joiner, in the department of medicine, started some six weeks ago to give a second course of isoniazid to 7 of these patients. These patients as a group at first showed an improvement in clinical condition, in weight, and in sputum-count which was of the same order as the improvement they showed at the beginning of the first course of isoniazid. But it is already clear that they are again showing signs of relapse just as they did in their first course of treatment. We hope shortly to publish a full account of these investigations.

Dr. Mitchison and his colleagues criticise the use of methods of testing isoniazid sensitivity which involve subculture in isoniazid-free Dubos medium before the final test in the same medium. But they themselves have made primary cultures from sputum on to isoniazid-free Löwenstein-Jensen medium. Now Fisher's work[3] suggests that the fraction-V bovine albumin in Dubos medium contains a substance essential for the growth of isoniazid-resistant strains of tubercle bacilli. Results obtained in this laboratory agree, partially at least, with Fisher's, and suggest that Löwenstein-Jensen medium itself may be somewhat deficient in a factor required by isoniazid-resistant strains. For these and other reasons, it is unwise to be dogmatic about the best medium or method for performing tests of isoniazid sensitivity until more facts are available. In the meantime it might be wise to add albumin or serum to Löwenstein-Jensen medium, and we have in fact been doing this as a routine in all our cultures for some weeks. In

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1. Knox, R., King, M. B., Woodroffe, R. C. *Lancet*, 1952, ii, 854.
2. Joiner, C. L., MacLean, K. S., Pritchard, E. K., Anderson, K., Collard, P., King, M. B., Knox, R. *Ibid*, p. 843.
3. Fisher, M. W. *Amer. Rev. Tuberc.* 1952, 66, 626.

Case 2.—A man, aged 52, a physical training instructor, headed a football backwards with neck hyperextended. He immediately experienced the feeling of an electric shock throughout his whole body, with cramp in his hands and feet and a burning sensation round the trunk. The radiograph taken after the injury was said to have shown cervical spondylosis with narrowing of the disc spaces, especially between the fifth and sixth cervical vertebræ, and a decompressive laminectomy did not improve his signs, which, when I examined him three years after the accident, were as follows: Weakness of extension of right wrist and fingers, and slight spastic weakness of the legs, the right being the weaker. The reflexes were as follows: biceps feebly present; supinators absent with finger flexion; triceps, right absent, left feebly present; abdominals present and equal; knee and ankle jerks present and equal; plantars, right strongly and left weakly extensor. There was no sensory loss.

This was a hyperextension injury, again with evidence of pre-existing cervical spondylosis.

It is highly probable that in the past, before the importance of cervical spondylosis as a cause of compression of the spinal cord was recognised, the accidental injury in these cases would have been regarded as the sole cause of the spinal cord lesion.

SUDDEN PARALYSIS IN CERVICAL SPONDYLOSIS WITHOUT INJURY

It is clear that sudden severe flexion or hyperextension of the cervical spine can cause immediate spinal cord compression from protrusion or tearing of a disc without pre-existing disc disease, that disc disease in itself can cause gradual spinal cord compression without injury, and that disc disease and injury of the types described may operate together in determining the sudden onset of a spinal-cord lesion. The next question is whether sudden compression of the cord can result from disc disease without injury. The evidence to be presented on this subject lacks the support of post-mortem examination, but is suggestive.

Case 3.—A man, aged 66, took his wife out for a drive and stopped by the roadside to empty his bladder. As he had been gone some time, his wife got out to look for him and found him collapsed *on the ground and unconscious*. He was eventually taken to hospital and in the course of the journey recovered his senses, about twenty minutes after his wife had found him. He was then mentally clear but was paralysed in all four limbs and had retention of urine. There was no evidence of any external injury. A lumbar puncture was done that day and the fluid reported clear with normal constituents. Manometry was not done. Next day there was considerable return of power in the lower limbs, and thereafter improvement in the upper limbs with recovery of bladder control.

When examined on the fifth day after the onset he showed the following abnormalities: The upper limbs were slightly, and the lower limbs moderately, spastic, and all movements of the limbs were weak. The weakness was symmetrical. In the upper limbs abduction at the shoulders was fair, adduction very weak. There was gross weakness of flexion and even more of extension at the elbows. There was hardly any power of extension of wrists or fingers, but flexion was a little better; the intrinsic muscles of the hands were powerless. The lower limbs showed a moderate degree of weakness of upper neurone type. The reflexes were as follows: biceps, supinator, and triceps brisk and equal; abdominals absent; knee and ankle jerks brisk and equal; both plantars extensor. Sensory examination showed hypalgesia below the fourth cervical level, extending downwards to the fourth thoracic. Postural sense was impaired in the left fingers. Vibration sense was nowhere lost but relatively impaired over the left tibia and foot. All neck movements were free, but not without pain, and he complained of spontaneous pain across the shoulders. The radiograph showed cervical spondylosis, with osteophytes protruding into the vertebral canal, especially from the adjacent margins of the third and fourth cervical vertebræ.

There was no history in the past of any relevant injury, but three years previously he had had what was called neuritis in his right shoulder and arm. The pain at that time was severe and radiated from the shoulder down the arm, but not below the elbow.

The onset of the paralysis in this case was in June, 1949. The patient was treated with strict rest in bed and gradually made a very fair recovery, being able to return to his business. When I last examined him in January, 1950, he complained of a good deal of pain in his shoulders as well as of weakness of the limbs, and then showed a spastic quadriparesis, with slight wasting in the intrinsic muscles of both hands. All deep reflexes were exaggerated, including the finger jerks, and both plantar reflexes were extensor. There was no sensory impairment.

This case is representative of a small group of which I have seen several examples having the following features in common. The patient is in the 60s or 70s. The onset of quadriplegia is quite sudden and often attended by loss of consciousness, the physical signs being those of a partial transverse lesion involving the anterior part of the cord, and there is a satisfactory degree of recovery. In the past I have thought thrombosis of the anterior spinal artery the explanation, but this was before attention was directed to cervical spondylosis as a cause of lesions of the spinal cord. Whether this patient fell and sustained an injury we do not know, but if so it cannot have been a severe one. In the next case there was no question of injury at all.

Case 4.—A woman, aged 76, was standing in her room pouring out a glass of water, when her legs suddenly gave way and she collapsed. She was taken to a nursing home and there found to have severe weakness of the lower limbs, the left more than the right, with retention of urine, which had persisted despite some return of power in the lower limbs, until I saw her a week later.

At that time there was no wasting, weakness, or dystonia of the upper limbs, but moderate weakness of upper neurone type, with spasticity, of the lower limbs, the left more than the right. She was just able to lift the left lower limb off the bed. The tendon jerks in the upper limbs were brisk, but without finger jerks; knee and ankle jerks were present and equal; both plantar responses were extensor. She was a poor sensory witness, but there appeared to be hypalgesia up to about the fourth thoracic segment without impairment of tactile sensation. Postural sense was normal in hands and feet, and vibration sense relatively diminished over the left lower limb. The radiographs showed severe cervical spondylosis with disc narrowing most evident between the fifth and sixth, and sixth and seventh, cervical vertebræ, and osteophytes protruding into the vertebral canal, especially between the fifth and sixth.

The patient was said to have had a bad fall eighteen months previously, after which she complained a great deal of pain across the shoulders. The onset of paralysis was in January, 1952. She was treated by rest in bed for a further three weeks, with gradual convalescence, and was reported eleven months later to have made a satisfactory recovery, being left only with a little weakness of the legs.

The clinical picture observed in this case a week after the onset was such as is often found in a case of gradual compression of the spinal cord by cervical spondylosis at the level of the fifth and sixth or sixth and seventh cervical vertebræ. When the disability is mild, the signs are not infrequently confined to the lower limbs, with hypalgesia extending no higher than an upper thoracic level. The radiological evidence was in keeping with this diagnosis, as also the improvement with rest. The only argument against it is the sudden spontaneous onset. We know, however, that protrusion of a lumbar disc may cause the sudden appearance of root symptoms without any injury deserving the name. The patient may experience sudden sciatic pain, with numbness and loss of ankle jerk, after tying a shoelace, or he may wake with these symptoms in the morning, presumably as the result of an unguarded movement during sleep, and the same is true of root symptoms resulting from protrusion of a cervical disc. Compression of the cauda equina from protrusion of a lumbar disc may also be of sudden onset with no more precipitating cause than may occur in the daily round. I have observed two cases of sudden paralysis from compression of the cauda equina—one in

As to the stability of low-grade, non-specific tuberculin sensitivity, *that* is quite another matter.

Dr. James (Feb. 7) mentions the work on Africans as evidence against the non-specific nature of low-grade sensitivity. I see little reason to doubt that some races, in some circumstances, may have the capacity to develop very high sensitivity to tuberculin, but the point we were making was that within a single population there may be groups showing distinctly different kinds of sensitivity. Dr. James's comments serve to emphasise how little we understand tuberculin allergy in human beings, especially on an international scale, and the obvious need for careful, quantitative studies.

W.H.O. Tuberculosis Research Office,
Copenhagen.
CARROLL E. PALMER.

MEDICINE BOTTLES

SIR,—If everyone taking a prescription to the chemist's would bring along a clean medicine bottle Britain would save £1,000,000 a year. At present National Health Service patients lose roughly half of the 100,000,000 handed to them each twelve months.

Nottingham.
MARY A. BURR.

THE BRITISH X-RAY AND RADIUM PROTECTION COMMITTEE

SIR,—A disturbing series of deaths amongst early workers with X rays led a small group of their surviving colleagues in 1921 to formulate some rules which would prevent a continuance of such casualties. Thus was born the British X-Ray and Radium Protection Committee. The late Sir Humphry Rolleston consented to become its first chairman. Under him, and largely financed by him, the first memorandum was issued in July of that year, and the first detailed report followed in 1923. The code was welcomed by all classes of radiological workers and formed the basis for similar recommendations in most countries of the world and for subsequent international recommendations.

Towards the end of the war the Medical Research Council set up a Committee on the Medical and Biological Applications of Nuclear Physics. Its subcommittees, and particularly the Tolerance Doses Panel, under the chairmanship of Prof. W. V. Mayneord, produced a large series of papers dealing with the fundamental data upon which protection measures for all those dealing with sources of ionising radiations could be formulated.

With the passing of the Radioactive Substances Act, a statutory committee came into existence. Whilst the Medical Research Council groups are concerned with the research aspects, the statutory committee has a duty in respect of regulations and licences, and is concerned with codes of practice over the whole extensive field now to be covered.

In these circumstances the British X-Ray and Radium Protection Committee, which despite its lack of any statutory authority had attained international status, had lost its raison d'être. A final meeting was held in September, 1952.

The passing of a committee through which Great Britain set a pattern for the world would seem to be a landmark that deserves record. At the suggestion of its last chairman, this letter is signed by the two surviving members of the 1921 meeting.

CUTHBERT ANDREWS
SIDNEY RUSS.

TABLET-INDENTIFICATION BOX

SIR,—Mr. Smith's remarks (Feb. 7) on tablet-identification boxes show the perils but do not overcome them.

It is common practice with N.H.S. prescriptions in retail pharmacy to keep records only of D.D.A. preparations that have been supplied; the tracing, therefore, of a script, especially if issued in the previous calendar month, may be difficult.

I would suggest that the easiest solution is to write the contents on dispensed medicines, as is already done on the Continent. It has been suggested that this would be a breach of professional secrecy; but the objection could be easily overcome by agreeing on a suitable sign or abbreviation which the doctor would put on the prescription when the chemist was not to mark the container.

Such a system would have the merit of simplicity.

Newcastle upon Tyne.
A. FORSTER.

THE MEDICAL SERVICES IN THE KOREAN WAR

SIR,—Dr. Binning (Feb. 14) can rest assured that we have not forgotten the lessons of the last war and we still regard blood as the fluid of choice in the resuscitation of battle casualties. I think it is clear from your correspondent's article (Jan. 17) that the medical arrangements in Korea are in many respects different from those existing in the Western Desert and Tunisia. I am sorry that, as Dr. Binning cannot be in full possession of all the facts about medical planning in Korea, he should have been forced to arrive at the conclusion " that blood is not as readily available to the Commonwealth medical units in Korea as it should be." Supplies of blood for the Commonwealth forward medical units have always been, and are, readily available from American blood-banks as and when required. Blood has never been in short supply in Korea.

The Commonwealth forward field medical units are only a small part in the over-all framework of the United Nations medical organisation in Korea. As mentioned in your article, these forward Commonwealth medical units serve one of the U.S.A. or Norwegian mobile army surgical hospitals (M.A.S.H.) and nearly all major emergency definitive surgery is carried out in a M.A.S.H. Considerable numbers of casualties are also evacuated direct from the regimental aid posts to the M.A.S.H. or other definitive-care hospitals by helicopter without passing through a field ambulance.

Dr. Binning may be interested to know that the Americans were perturbed in the early days of the campaign by the high incidence of infective hepatitis which followed the use of their plasma, even when irradiated beforehand, and this is one of the reasons why they prefer fresh blood to plasma.

F. HARRIS
Director-General,
Army Medical Services.

The War Office,
London, S.W.1.

SIR,—As a R.M.O. fairly recently returned from Korea I would like to comment on the letters by Dr. Binning.

One has to be quite clear what is meant by the term " forward areas." To me it means forward of Corps H.Q. Up to the time that I left the theatre (August, 1952) we had no medical organisation dealing with battle casualties greater than a field ambulance in the forward areas, and at none of these were major or even moderate surgical procedures carried out. At the American mobile army surgical hospital (M.A.S.H.), to which all our casualties were evacuated from the divisional field ambulances for primary surgery, blood was, of course, used.

I consider that to provide a R.M.O. or field ambulance with blood, where there is little or no chance of cold storage and relatively little call for its use (in nine months I used no more than 15 pints of plasma), would be a gross wastage of blood. The task of these units is to evacuate the casualty in reasonable condition so that when he arrives at the M.A.S.H. surgery can be undertaken with the minimum of delay. For this plasma is adequate; and it is devoid of storage problems and is cheaper. A casualty who is so ill that he must have blood is better evacuated from the R.M.O. or his company area direct by helicopter to the M.A.S.H.

These remarks apply principally to Korea and do not apply to units likely to be cut off from a surgical unit for sensory impairment, nor had there been any pain or paræsthesiæ

The relevant facts in his past history were that for some twenty years he had had occasional attacks of "stiff neck" without precipitating cause The usual story was that of a gradual onset of pain in the left neck and shoulder, lasting a few days On two or three occasions the neck was quite stiff during this period, with rotation and inclination, probably to the right

The radiograph (Dr Hugh Davies) showed gross degenerative changes in all the lower cervical intervertebral discs, with osteophytosis on all adjacent body margins Particularly severe changes were present posterolaterally at C5–6 on both sides It proved impossible, owing to the osteophytes to obtain a clear view of the foramina, which were largely obliterated

This patient reported himself completely recovered three months later

Although the usual effect of compression of a cervical root from cervical spondylosis is pain, I have seen other cases in which there has been sudden onset of painless paralysis, comparable in every way with that which may occur from sudden compression of a root by protrusion of a lumbar disc There seems little doubt that some manipulation of the neck during anæsthesia was the determining cause of the root lesion in this case

In the next case there was injury to the cervical spine with no compression of spinal cord or nerve-root

Case 8 —A man, aged 57, had an operation for drainage of an infected right antrum under general anæsthesia, and on coming round complained of severe pain and stiffness of the neck, aggravated by movement As pain and stiffness persisted, radiographs of the cervical spine were taken a fortnight later and showed narrowing of the disc space between the fifth and sixth cervical vertebræ with spur formation on the adjacent anterior margins Next day his neck was manipulated without any anæsthetic by an orthopædic surgeon, with immediate relief of pain on the right side of his neck and some improvement on the left Pain returned, and the manipulation was repeated a week later, with no further improvement When I saw him seven weeks after his operation he still had considerable pain and stiffness

DISCUSSION

From the study of the recent literature and the material here presented the conclusion may be drawn that accidents involving either flexion or hyperextension of the cervical spine may cause injury to an intervertebral disc without fracture or dislocation This may happen when the disc is normal, but is more likely to occur, especially in hyperextension, when there is cervical spondylosis with disc degeneration In the presence of cervical spondylosis sudden compression of the spinal cord may take place with no more cause than what may be regarded as a normal effort or change of posture It may possibly occur spontaneously as the result of a sudden increase of pressure upon a segment of cord in which the circulation has been precariously maintained for some time without symptoms There is nothing in this hypothesis which is revolutionary, for we have recognised for some time that compression of nerve-roots, cervical, lumbar, or first sacral, and more rarely compression of the cauda equina, may happen suddenly from disc protrusion without trauma in the ordinary sense of the word If this be true, manipulation of the cervical spine under anæsthesia with the muscles relaxed, and especially the hyperextension involved in certain operative procedures, of which tonsillectomy and dental extraction may be cited as examples, may be dangerous for a person already suffering from cervical spondylosis Symptoms of this disease existing before operation should certainly be an indication for caution, and in view of the frequency of symptomless cervical spondylosis in persons over the age of 30, it would be well for anæsthetists and surgeons to bear in mind that, deprived of protective spasm, an intervertebral disc, if already diseased, may be torn or caused to protrude by force of no great magnitude

SUMMARY

Recent papers on compression of the spinal cord from cervical spondylosis are considered, with special reference to the traumatic factor in causation

The mechanism of cervical cord injuries is discussed

The coincidence of accidental injury to the spinal cord with pre existing cervical spondylosis is described, with illustrative cases

Two cases are recorded of sudden paralysis in elderly patients, without injury, in the presence of severe cervical spondylosis, the suggestion being made that compression of the cord may occur from this cause in the course of normal movement

Two cases are recorded of quadriplegia following tonsillectomy, with proof in one case of compression of the cord by a prolapsed intervertebral disc

A case is presented in which a lesion of a cervical root immediately followed dental extraction under anæsthesia in a patient with pre existing cervical spondylosis

A case is recorded of severe neck pain following an operation for drainage of an infected antrum in a patient with pre existing cervical spondylosis

It is suggested that manipulation of the head and neck under anæsthesia, and especially manœuvres involving hyperextension, may be not without danger of causing serious symptoms in persons already suffering from cervical spondylosis

I am indebted to Mr D W C Northfield for allowing me to publish the notes of case 6, and to Dr J G Greenfield and Dr Hugh Davies for permission to quote their opinions in the record of case 5 and for their criticism and advice in the preparation of this paper

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PHARMACOLOGY OF M & B. 2050

R Wien D F J Mason
Ph D Lond B Sc Lond
From May & Baker Ltd, Dagenham, Essex

THIS is a preliminary note on the pharmacology of 'M & B 2050,' pentamethylene 1 5 bis(1′-methylpyrrolidinium) di-iodide, a compound devised and synthesised by Libman, Pain, and Slack (1952) We found that this compound possesses high ganglion-blocking activity, about 5 times greater than hexamethonium bromide Its discovery resulted from a wider investigation of compounds of this type, which will be reported elsewhere

Experimental methods have been described previously (Wien and Mason 1951), and in particular the cat's superior cervical ganglion was used for evidence of a blocking effect on sympathetic ganglionic transmission By this method M & B 2050 is about 5 times (ranging from 3 to 6) more potent, and acts for $1^{1}/_{2}$ times longer, than hexamethonium bromide But similar results were observed on the cat's parasympathetic (ciliary) ganglion, thus it did not show a greater selective effect It was, however, less active ($1^{1}/_{2}$ times as active as hexamethonium) on the ganglia mediating the peristaltic reflex of the isolated guineapig's intestine

The compound possessed a specific effect in paralysing ganglionic transmission as shown in the superior cervical ganglion preparation, in which postganglionic excitation or the injection of adrenaline remained fully effective during the complete inhibition of preganglionic excitation Moreover, the bradycardia and fall in blood-pressure on vagal excitation were abolished in the cat under chloralose, whereas the depressor effect of acetylcholine was or gifts. They had the task of consulting an advisory committee, and in the first place the committee would be the Advisory Committee on Medical Research which had links with the Medical Research Council, so that as far as possible overlapping would be avoided. The trustees would be empowered to assist any medical research they thought worthy of help. It would not matter whether it was to be carried out at an establishment connected with the National Health Service, or at a private hospital, a university, or any other organisation.

QUESTION TIME

Salaries of Civil Service Medical Officers

Dr. A. D. D. Broughton asked the Chancellor of the Exchequer why he had not raised the salaries of civil service medical officers to conform with the increase in remuneration granted to general medical practitioners under the Danckwerts award.—Mr. J. A. Boyd-Carpenter, financial secretary to the Treasury, replied: Mr. Justice Danckwerts's award was confined solely to the remuneration of general practitioners in the National Health Service and had no wider application. Dr. Broughton: But does not the Minister agree that these medical officers, who perform their responsible duties very efficiently, have been affected like everyone else by the rise in the cost of living? Will he not reconsider the question of revising their salary scales to bring them into line with their professional colleagues who are practising in other branches of medicine?—Mr. Boyd-Carpenter: Naturally the salaries of Government servants are kept under constant review, but the present scale of salaries of these officers was recommended by the Howitt Committee which reported as recently as Aug. 31, 1951.

Cost of Proprietary Medicines

Dr. Edith Summerskill asked the Minister of Health whether his attention had been drawn to the report of the Comptroller and Auditor-General with regard to the heavy prescribing of expensive proprietary drugs; and what action he proposed to take in order to reduce this expenditure in the future.—Mr. Iain Macleod replied: All doctors have been urged to help to keep this cost down by prescribing standard drugs wherever appropriate and by not prescribing proprietary drugs which are advertised direct to the public —and lists of the latter have been supplied to them. In the last resort it is in the power of the doctors themselves to help most in this considerable problem, and I am sure that we can count on them to do so. For my part, I am considering what further steps can be taken.

Prescriptions for Slimming Tablets

Mrs. Jean Mann asked the Minister what amount was spent in prescriptions in 1950, 1951, and 1952, on slimming tablets; and what researches his department had made to satisfy itself as to the value of these tablets in reducing obesity.—Commander T. D. Galbraith replied: I have no reason to think that doctors are prescribing drugs which are not of value, when taken under medical supervision, in cases where weight reduction is necessary on medical grounds.

Mrs. Mann: Is the Minister aware of a report last week that £400,000 had been spent on slimming tablets?—Commander Galbraith: The drug, 'Dexedrine,' is quite an effective drug for slimming when used under medical supervision, and slimming is not the only purpose for which it is prescribed. Mrs. Mann: Is the Minister aware that the drug cannot be used except under medical supervision, so that his statement is rather superfluous? Is he aware that medical opinion is that the drug does not reduce obesity but merely curbs the appetite? Is not £400,000 an extravagant sum to spend for that purpose?—Commander Galbraith: I have to rely on the medical advice given me, and that is that the drug is effective for slimming.

Pneumoconiosis Research

Mr. S. T. Swingler asked the parliamentary secretary to the Ministry of Works, as representing the Lord President of the Council, what was the present rate of annual expenditure on research into the causes and treatment of pneumoconiosis; how many research units exist; where they are located; and what proposals are under consideration for the extension of this research.—Mr. A. H. E. Molson replied: Current annual expenditure by the Medical Research Council on pneumoconiosis research is estimated at £70,500. The council's pneumoconiosis research unit is situated at Llandough, near Cardiff, South Wales, and cognate research is supported in university departments in Cardiff, Sheffield, London, and Glasgow. These arrangements are additional to those made at Sheffield by the Ministry of Fuel and Power at an annual cost of £47,500 and to the investigations planned by the National Coal Board. Coördination is maintained by a series of expert committees. No immediate extension of Government-sponsored research is under consideration, but any promising new line will be followed.

National Milk Consumption

Mr. I. O. Thomas asked the Minister of Food how far there had been substantial reduction in consumption of milk during 1952, as compared with 1950 and 1951; and what he considered to be the reason for such reduction.—Major Gwilym Lloyd George replied: The national consumption of milk during 1952 was 1546·1 million gallons; during 1951, 1572·9 million gallons; during 1950, 1557·2 million gallons. The decline, which was thus less than 1·0% and 1·7% respectively, was too small to be attributed to any particular reason.

Hospital Building in Scotland

Replying to a question, Commander Galbraith, joint under-secretary of State for Scotland, said that the provisional building programmes submitted by regional hospital boards for 1953 included 98 projects costing more than £10,000 each. All these projects had been approved in principle, and work had already started on 57 of them by the end of 1952.

Toxic Sprays

Sir Ralph Glyn asked the Minister of Agriculture whether he would consider issuing immediate circulars to the county agricultural committees advising that no spraying of weeds or any crops with dinitro-*ortho*-cresol should be carried out without reference to the committees; and whether he would take steps to amend the Agriculture (Poisonous Substances) Act to necessitate obtaining a licence before poisonous sprays could be used on land, in view of the damage being done to insects, birds, and animals as the result of the application of these chemical substances to large tracts of agricultural land; and whether he would set up a committee, not altogether composed of chemists, to report on the results, during 1952, of the spraying of poisons to destroy noxious weeds.—Sir Thomas Dugdale replied: I have no power to require prior notification of spraying, but I am keeping a careful watch on developments. The long-term solution to the problem is the production of equally effective sprays that are not toxic to wild life. Research into this and other aspects is continuing under the supervision of the Agricultural Research Council. I am asking Professor Zuckerman and his Working Party on Precautionary Measures against Toxic Chemicals used in Agriculture to consider the general question of effects on wild life, when they have completed their present sudy of possible risks to the consumer.

Disposal of Anthrax-infected Animals

Replying to a question, Sir Thomas Dugdale said that animals with anthrax were not required to be destroyed. Local authorities were responsible for the safe disposal by burning, chemical treatment, or burying in lime of the carcases of animals which had died of anthrax.

Smoking and Lung Cancer

Squadron-Leader Albert Cooper asked the Minister of Health if he could make a statement on the researches made by his department into cancer of the lung and the possible contributory effect of smoking.—Mr. Macleod replied: My Standing Advisory Committee on Cancer and Radiotherapy have not yet finished their study of the available evidence on this difficult problem.

Births, Marriages, and Deaths

BIRTHS

Evershed.—On Feb. 5, at Liverpool Maternity Hospital, to Elizabeth, wife of Squadron-Leader T. A. Evershed, M.B. R.A.F.—a son.

Gray.—On Feb. 9, at University College Hospital, London, to Jean (née Leader), wife of Dr. Ian Ramsay Gray—a daughter.

Heller.—On Feb. 19, at St. Mary's Hospital, London, to Betty, wife of Dr. Michael Heller—a son (Simon Richard).

Jennett.—On Feb. 20, at Liverpool Maternity Hospital, to Dr. Sheila M. Pope, wife of Mr. W. Bryan Jennett, F.R.C.S.—a son.

the blood-pressure, pulse-rate, and pupil size were determined Change in skin-temperatures indicated alteration in peripheral circulation, and change in skin resistance indicated alteration in the activity of the sweat-glands Paralysis of visual accommodation (shown by inability to read) and dryness of the mouth were noted With the patient fasting the gastric secretion was aspirated completely an hour before, and again shortly before, the drug was given and hourly thereafter

Exact techniques were considered to be less important than identical methods of comparison of each drug with adequate control Once the active drugs were identified, observations were repeated to confirm the results obtained, 328 doses were given during this part of the investigation Subsequently the two most active sympathicolytic drugs were administered to hypertensive patients, and their effects on the blood-pressure and their side-effects were studied

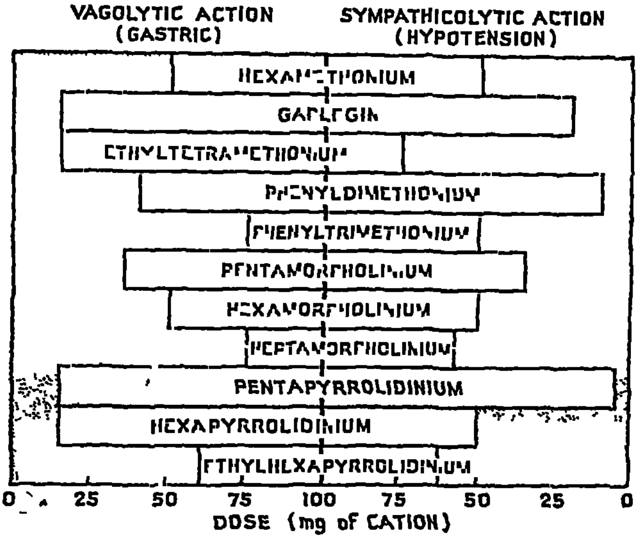

Fig 1—Comparison of vagolytic actions on gastric secretion and sympathicolytic (hypotensive) actions of hexamethonium, gaplegin, and nine new sympathicolytic agents

CLINICAL RESULTS

From the results it was possible to estimate the dose of cation which injected subcutaneously, would definitely lower the blood-pressure of hypertensive patients, and the dose which would produce achlorhydria in the fasting secretion of patients with hyperchlorhydria, in at least 60% of first observations These results are comparable with the actions of hexamethonium in subcutaneous initial doses of 50 mg of cation

The distribution of the activity of these drugs in comparison with hexamethonium and gaplegin is shown in fig 1 Their action in producing mydriasis and an alteration in peripheral circulation when used in hypotensive dosage is shown in fig 2 The effect of these compounds on the heart-rate was similar to that of hexamethonium, a variable production of tachycardia during hypotension Paralysis of visual accommodation and dryness of the mouth were in keeping with the mydriasis recorded The effect on sweating was less than that of hexamethonium in the dosage used No drug affected the respiration-rate or showed any sign of curarising activity

Fig 1 shows that M & B 1950 (phenyldimethonium) and M & B 2050 (pentapyrrolidinium) have the highest sympathicolytic activity Phenyldimethonium has a relatively selective action in depressing the blood-pressure, and pentapyrrolidinium is the most active of the drugs used, having also a high generalised activity The effects of these two drugs were investigated in 15 patients with hypertension, of whom 10 had previously been treated with parenteral and oral hexamethonium The effect of single doses was studied first, in comparison with hexamethonium and control doses of sterile water, with intervals of several days between doses to avoid habituation Fifty subcutaneous doses of each drug were given, varying between 2 5 and 50 mg, and subsequently the effects of fifty oral doses of 25–150 mg of each were recorded The results are presented in the accompanying table

These two drugs produce hypotension when given subcutaneously in a dosage which is from a tenth to a fifth of the amount of hexamethonium required to produce a comparable fall in blood-pressure Pentapyrrolidinium is the more active of the two The hypotension lasted from six to thirty-six hours, excluding the period of recovery of blood-pressure Hexamethonium in single oral doses of 500 mg does not produce hypotension consistently, but single oral doses of these new drugs produced hypotension in 56% of the observations made Hypotension appeared two to four hours after oral dosage and lasted for eight hours or more Both drugs produced side effects in excess of those which followed doses of hexamethonium Pentapyrrolidinium almost invariably produced mydriasis and dryness of the mouth, and occasionally headaches with drowsiness and depression Little difference in their activity was noticed when they were administered to patients who were tolerant to hexamethonium

In subsequent continuous treatment with phenyldimethonium and pentapyrrolidinium in divided subcutaneous doses totalling 50–100 mg daily and divided oral doses totalling 100–150 mg daily, results comparable with our previous experience with hexamethonium were obtained The side effects previously met with tended to persist, but constipation was not troublesome

Severe Hypotension

The application of the new drugs of high activity produced severe hypotension on several occasions Blood-pressure levels of 80/50 mm *Hg* in the recumbent position were well tolerated by normotensive patients, who lost consciousness only if they stood up Hexamethonium produced a rapid symptomless postural faint with moderate tachycardia and a warm skin The postural faint with pentapyrrolidinium was very different It was preceded by nausea and often vomiting Loss of consciousness was slow and accompanied by tachycardia and pallid cold sweating The effects of phenyldimethonium were intermediate between those of hexamethonium and those of pentapyrrolidinium

Severe hypotension was not well tolerated by hypertensive patients Electrocardiography revealed almost

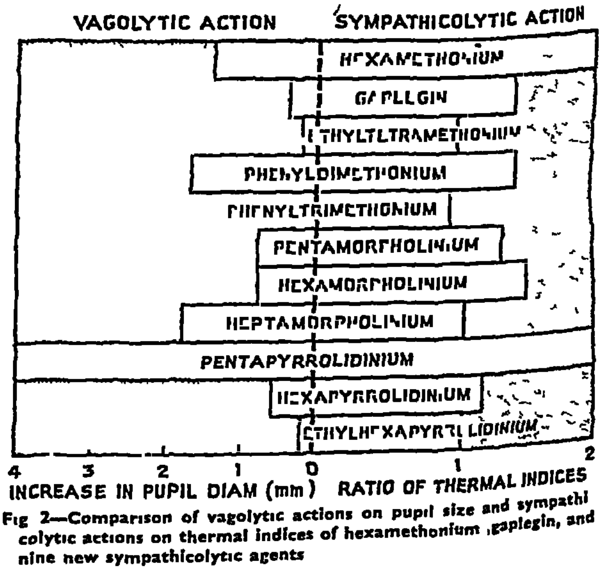

Fig 2—Comparison of vagolytic actions on pupil size and sympathicolytic actions on thermal indices of hexamethonium, gaplegin, and nine new sympathicolytic agents

Notes and News

MALARIA ERADICATION IN MAURITIUS

MALARIA was probably introduced into Mauritius about a hundred years ago; and since then it has existed at a fairly high level, with occasional epidemic peaks in abnormal seasons. It has been carried by *Anopheles funestus*, breeding throughout the year and strongly domestic in habit, and to a slighter degree by *Anopheles gambiæ*, which in Mauritius seems to feed more than usual on animals and to be rather less of a menace than on the African mainland. At a meeting of the Royal Society of Tropical Medicine and Hygiene in London on Feb. 19, Dr. M. A. C. Dowling described the steps taken to rid the island of this disease by means of residual insecticides. D.D.T. and B.H.C. were used; but B.H.C. was abandoned for economic reasons—the brief residual effects would have necessitated several treatments each year. Various preparations of D.D.T. were tried—a solution in kerosene (which was relatively expensive), a suspension of wettable powder, and an oil-bound suspension readily miscible with water.

The results, as the president, Sir Neil Hamilton Fairley, F.R.S., remarked, would have been incredible a decade ago. In children, of whom many thousands were examined, the spleen-rate had been reduced from 34·8% in 1948 to nil, and the parasite-rate from 9·5% to nil. In the people as a whole the number of notified cases of malaria was 105 per 1000 in 1948, and 0·05 in 1952; the general death-rate (all causes) was 27·2 ± 3·37 per 1000 in 1934–48, and 14·8 in 1952; the infant-mortality rate was 150 ± 19·2 in 1934–48, and 83·5 in 1951. *Anopheles funestus* had virtually disappeared, and the same was true of *Aëdes ægypti*, the potential vector of yellow fever. *Anopheles gambiæ*, however, could still be found in new, unsprayed houses and cowsheds; though greatly reduced in numbers, it still bred in the coastal zone, and a larvicidal campaign had therefore been instituted. This outstanding success depended on the fact that the habits of the mosquitoes concerned led them to contact with the insecticidal deposits—as they had led *Anopheles fluviatilis* in India, *Anopheles darlingi* in British Guiana, and *Anopheles sacharovi* in Greece. These mosquitoes had not been repelled or irritated by the insecticide to such an extent that they avoided the lethal doses. The question had arisen whether to continue operations on a maintenance scale, in order to keep down the mosquitoes and malaria to these low figures, or to undertake the relatively much more extensive task of eradicating the last potential vector of malaria. It had been decided not to embark on complete eradication of the mosquitoes, which could not be guaranteed; and a maintenance project, which included permanent anti-malarial works near Port Louis and seasonal house-spraying and larvicidal work, had now been adopted.

In the discussion of this important paper Prof. G. Macdonald remarked on the need to keep a close watch on the parasites, as well as on the mosquitoes, in such circumstances where eradication had not been achieved; for epidemics of malaria could develop with dramatic suddenness. Dr. Fred. L. Soper, of the Rockefeller Foundation, recalled his own extensive experience of *Anopheles gambiæ* in Brazil and Africa, and remarked on its different habits in different places. He thought that eradication from Mauritius was desirable. Sir Gordon Covell also remarked on the different habits of the various vectors of malaria in different areas, which greatly affected the results of spray campaigns.

Mauritius lives on its sugar crop; it is to be hoped that this will be enough to support the population, which is increasing rapidly now that malaria is almost gone. The same problem is facing Ceylon, Cyprus, and other countries where malaria control is suddenly transforming life and economy.

PROBLEM FAMILIES

AT the annual meeting of the Kensington and Paddington Family Service Unit on Feb. 19, the Hon. Denys B. Buckley, the hon. treasurer, said that in 1951–52, with a staff consisting of Mr. David Jones, the secretary, and one male and two female case-workers, 3625 visits were made to families. Of the 29 families dealt with, 16 had been satisfactorily reabled. The total expenditure of the unit had been about £1600. This alone showed the economic value to the community of the unit's work; for a single family consisting of a mother and eight children, when reablement had failed, was evicted from its home in 1951 and admitted to an L.C.C. institution where they stayed for nearly eighteen months at a probable cost to the authority of at least £1500.

Mr. Sidney Miller, the field-work organiser of the unit, said that the main objective of the workers in the organisation was to save not only the very real expense to the community of the break-up of families, but the mass of human misery which this represented. He described two specimen families. In the first, whose ultimate fate was still in the balance, the father, aged 28, was charming but completely irresponsible; he periodically deserted the home, had sold up the furniture while his wife was in hospital having the third child, and occasionally got sent to gaol for larceny. The wife was a good-hearted woman, very dependent on her husband. The second child was a mental defective whom the unit had managed to get into an institution. They had managed to get the husband to let them collect his wages when he was in work; otherwise he drank the money on his way home. Gradually the husband was coming to trust them and to realise he had some responsibility towards his family.

In another family the husband was a temperamental and unsuccessful journalist who had not worked for years, and the wife had been in a mental hospital. They had been saved from eviction with their 6 children. They had been heavily in debt, with the house in chaos and the children not even attending school; but the husband was now working; his wife had gradually been taught to cope better with the household; and they are now carrying on satisfactorily with occasional supervision.

Mr. John Maude, Q.C., said that all felt the vital importance of this work. He knew the appalling results if these families were not set to rights. Were not such families the source of horrifying figures of recidivism and crime? The latest report of the Council of the Central After-Care Association stated that of 1355 male long-term prisoners released into the community since 1949 no less than 42·5% had already been re-convicted. As the association's report said, the trouble with many of these recidivists was that they did not seem to know right from wrong, unless they were at the receiving end. Even some children (and by no means always from poor or broken homes) were apparently incapable of feeling guilt, humility, or gratitude; they were impervious to love and to punishment. It was to be hoped that the study of problem families would shed light on the environmental and hereditary causes of this hard core of incorrigible criminality. Those who had been brought up to treasure Christian values owed their inability to commit crimes to the influence of their parents, who stamped character into them while they were young.

CONFERENCE IN NEW ZEALAND

HOT summer weather greeted the 400 members who enrolled at Auckland for the biennial conference of the New Zealand branch of the British Medical Association, on Feb. 10–13. Mr. Kenneth MacCormick (Auckland) presided; and the delegate from the parent body was Dr. Denis Brinton who spoke on the selection of medical students, on cervical disc lesions, and on cerebral vascular accidents. Mr. John Loewenthal (Sydney) was also an official visitor and spoke on peripheral vascular degeneration, chronic leg ulcer, and kindred topics. Dr. R. D. Lawrence was to have been an official visitor, but transport difficulties delayed his arrival.

University of Sheffield

Dr. Thomas Hanley has been appointed lecturer in medicine; Dr. D. S. Munro lecturer in therapeutics; and Mr. A. Young a part-time clinical teacher in diseases of the ear, nose, and throat.

University of Edinburgh

Prof. Alfred Meyer will deliver the William Ramsay Henderson lecture at the University New Buildings on Tuesday, March 10, at 5 P.M. He will speak on Anatomical Aspects of Neurosurgery in Mental Disorder.

Royal College of Surgeons in Ireland

At the annual Charter Day festival of the college, the honorary fellowship was conferred on Sir Gordon Gordon-Taylor.

Faculty of Radiologists

A postgraduate course will be held by the faculty at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, on Saturday and Sunday, March 21 and 22. Full particulars may be had from the faculty's offices at 45, Lincoln's Inn Fields, W.C.2.

the blood pressure, pulse rate, and pupil size were determined Change in skin-temperatures indicated alteration in peripheral circulation, and change in skin resistance indicated alteration in the activity of the sweat-glands Paralysis of visual accommodation (shown by inability to read) and dryness of the mouth were noted With the patient fasting the gastric secretion was aspirated completely an hour before, and again shortly before, the drug was given and hourly thereafter

Exact techniques were considered to be less important than identical methods of comparison of each drug with adequate control Once the active drugs were identified, observations were repeated to confirm the results obtained; 328 doses were given during this part of the investigation Subsequently the two most active sympathicolytic drugs were administered to hypertensive patients, and their effects on the blood-pressure and their side-effects were studied

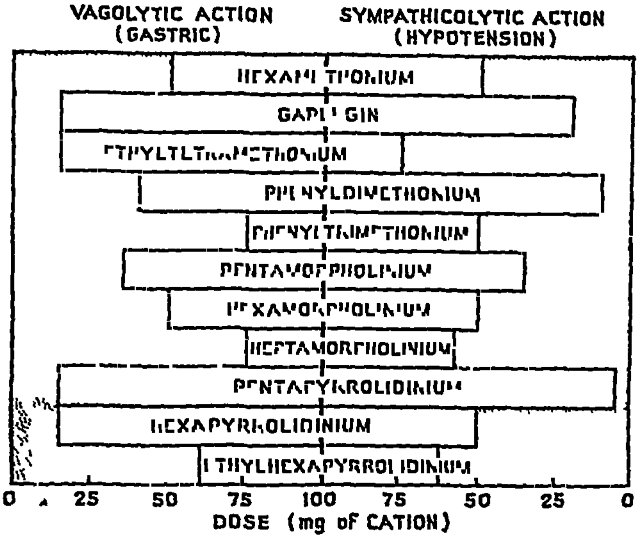

Fig 1—Comparison of vagolytic actions on gastric secretion and sympathicolytic (hypotensive) actions of hexamethonium, gaplegin, and nine new sympathicolytic agents

CLINICAL RESULTS

From the results it was possible to estimate the dose of cation which injected subcutaneously, would definitely lower the blood-pressure of hypertensive patients, and the dose which would produce achlorhydria in the fasting secretion of patients with *hyperchlorhydria, in at least* 60% of first observations These results are comparable with the actions of hexamethonium in subcutaneous initial doses of 50 mg of cation

The distribution of the activity of these drugs in comparison with hexamethonium and gaplegin is shown in fig 1 Their action in producing mydriasis and an alteration in peripheral circulation when used in hypotensive dosage is shown in fig 2 The effect of these compounds on the heart-rate was similar to that of hexamethonium, a variable production of tachycardia during hypotension Paralysis of visual accommodation and dryness of the mouth were in keeping with the mydriasis recorded *The effect on sweating was less than* that of hexamethonium in the dosage used No drug affected the respiration-rate or showed any sign of curarising activity

Fig 1 shows that M & B 1950 (phenyldimethonium) and M & B 2050 (pentapyrrolidinium) have the highest sympathicolytic activity Phenyldimethonium has a relatively selective action in depressing the blood-pressure, and pentapyrrolidinium is the most active of the drugs used having also a high generalised activity The effects of these two drugs were investigated in 15 patients with hypertension, of whom 10 had previously been treated with parenteral and oral hexamethonium

The effect of single doses was studied first, in comparison with hexamethonium and control doses of sterile water with intervals of several days between doses to avoid habituation Fifty subcutaneous doses of each drug were given, varying between 2 5 and 50 mg, and subsequently the effects of *fifty oral doses of 25–150 mg* of each were recorded The results are presented in the accompanying table

These two drugs produce hypotension when given subcutaneously in a dosage which is from a tenth to a fifth of the amount of hexamethonium required to produce a comparable fall in blood-pressure Pentapyrrolidinium is the more active of the two The hypotension lasted from six to thirty six hours, excluding the period of recovery of blood-pressure Hexamethonium in single oral doses of 500 mg does not produce hypotension consistently, but single oral doses of these new drugs produced hypotension in 56% of the observations made Hypotension appeared two to four hours after oral dosage and lasted for eight hours or more Both drugs produced side effects in excess of those which followed doses of hexamethonium Pentapyrrolidinium almost invariably produced mydriasis and dryness of the mouth and occasionally headaches with drowsiness and depression Little difference in their activity was noticed when they were administered to patients who were tolerant to hexamethonium

In subsequent continuous treatment with phenyldimethonium and pentapyrrolidinium in divided subcutaneous doses totalling 50–100 mg daily and divided oral doses totalling 100–150 mg daily, results comparable with our previous experience with hexamethonium were obtained The side-effects previously met with tended to persist, but constipation was not troublesome

Severe Hypotension

The application of the new drugs of high activity produced severe hypotension on several occasions Blood-pressure levels of 80/50 mm Hg in the recumbent position were well tolerated by normotensive patients, who lost *consciousness only* if they stood up Hexamethonium produced a rapid symptomless postural faint with moderate tachycardia and a warm skin The postural faint with pentapyrrolidinium was very different It was preceded by nausea and often vomiting Loss of consciousness was slow and accompanied by tachycardia and pallid cold sweating The effects of phenyldimethonium were intermediate between those of hexamethonium and those of pentapyrrolidinium

Severe hypotension was not well tolerated by hypertensive patients Electrocardiography revealed almost

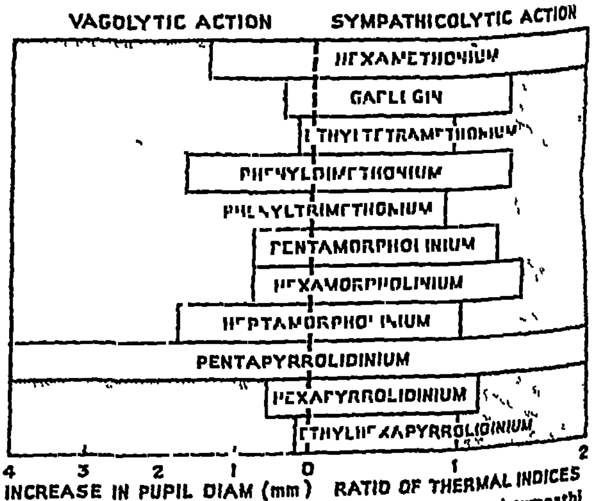

Fig 2—Comparison of vagolytic actions on pupil size and sympathicolytic actions on thermal indices of hexamethonium, gaplegin, and nine new sympathicolytic agents

THE INTERRELATION OF TRAUMA AND CERVICAL SPONDYLOSIS IN COMPRESSION OF THE CERVICAL CORD

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THE frequency of compression of the spinal cord as the result of cervical spondylosis has been brought to light during the past few years in a series of papers recording the clinical history and findings in many cases, with radiological observations, including myelograms, and demonstration of the lesion at operation or post mortem (Spillane and Lloyd 1952, Russell Brain, Northfield, and Wilkinson 1952, Allen 1952, Bedford, Bosanquet, and Russell 1952).

From these and other papers it appears certain that, without any antecedent injury to the head or neck, the spinal cord may be gradually compressed by the protrusion into the vertebral canal of transverse bars or ridges between the bodies of the cervical vertebræ, composed of a bulging or thickened annulus fibrosus and osteophytic overgrowth of the margins of the adjacent vertebræ, and that such compression may occur at more than one level in a single case. In other cases the cervical spondylosis appears to have followed injury to the cervical spine after a long interval, the injury being probably the initial cause of a continuing degenerative and reactive process. In a third group the compression of the spinal cord has immediately followed injury, but radiographs have shown cervical spondylosis at the appropriate level which must have been present before the injury. It is this last group with which this paper is mainly concerned.

MECHANISM OF INJURIES OF CERVICAL CORD

Sudden compression of the cervical cord as the result of severe injury is, of course, a well-known occurrence, but its mechanism is still not fully understood. Barnes (1948), analysing 22 cases of paraplegia in injuries of the cervical spine, concluded that in 15 the cause had been extreme flexion of the spine and in the remainder hyperextension. In the flexion injuries the mechanism of compression of the spinal cord was dislocation in 8 cases, crush fracture of a vertebral body in 4, and acute retropulsion of an intervertebral disc in 3. In this last subgroup there was 1 case in which a radiograph immediately after the injury showed lipping of the anterior margins of the third and fourth cervical vertebræ and narrowing of the disc space, thus indicating disc degeneration before the injury. Here, therefore, is a suggestion that weakening of the annulus by disease might be a predisposing cause of acute spinal-cord compression from flexion injury. Among the 7 hyperextension injuries there was 1 case of dislocation. In all the others there was radiographic evidence of old-standing cervical spondylosis, and "strikingly little evidence of recent vertebral injury." In 2 of these cases post-mortem examinations were made, and in both there was found rupture of the anterior common ligament, in one instance between the third and fourth and in the other between the sixth and seventh cervical vertebræ. There was no dislocation, and the posterior common ligament was intact. Barnes discusses the mechanism of the spinal-cord injury in these cases without any definite conclusion other than that it cannot be due to traction. Taylor and Blackwood (1948) have devoted a paper to paraplegia in hyperextension injuries with normal radiographic appearances, recording a well-documented case with necropsy, showing that the anterior common ligament was ruptured between the sixth and seventh cervical vertebræ, and that the vertebral column had then been torn through by the detachment of the intervertebral disc from the lower surface of the sixth vertebral body. (This was also found by Barnes (1948) in 1 of his cases.) Although the radiograph in this case had shown no abnormality, at necropsy backward angulation of the cervical spine was easily reproduced, with narrowing of the spinal canal, and the conclusion was reached that the spinal cord had been nipped between the postero-inferior border of the body of C6 and the lamina of C7. These workers suggest that in most cases of traumatic cervical paraplegia without radiographic evidence of dislocation or fracture the injury has involved hyperextension, and that the mechanism of the spinal-cord injury has been that described in their case.

ACCIDENTAL INJURY ADDED TO CERVICAL SPONDYLOSIS

The observations and conclusions contained in these two papers indicate that in flexion injuries acute retropulsion of an intervertebral disc may cause compression of the spinal cord, and it may fairly be assumed that this would more readily occur if the annulus were previously weakened by disease, an assumption supported by the radiographic evidence in one of Barnes's cases. In hyperextension injuries the mechanism of spinal-cord injury is such that pre-existing disease of the disc would clearly favour its occurrence, and evidence of such disease was present in 6 of Barnes's 7 cases.

Brain et al. (1952) in a series of 45 cases of spinal-cord compression from cervical spondylosis state that in 8 the symptoms appeared suddenly, caused by traumatic hyperextension of a cervical spine previously the site of spondylosis. The manner of injury, however, is described only in 1 case, and in this it was a fall out of bed with no details to support the hypothesis of hyperextension.

In the following 2 cases there seems little doubt about the manner of the vertebral injury.

Case 1.—A man, aged 50, was thrown from his horse on to his head on soft ground and was concussed, with a brief retrograde and post-traumatic amnesia. There were no facial injuries. On coming to his senses he found himself paralysed in all four limbs, recovery beginning in a few minutes and improving to a point at which, when I examined him three weeks later, he was able to be up and about. He had found that when he flexed his neck he got an electric shock running down into his thighs. He showed wasting of the intrinsic muscles of his left hand and weakness in this distribution and order of severity: intrinsic muscles of left hand, severe; long flexors of fingers, moderate; less of thumb; long extensors left wrist and fingers, moderate to slight. Intrinsics right hand, moderate; long flexors and extensors of right fingers, slight. The reflexes were as follows: biceps and supinator just obtained; triceps both exaggerated; abdominals present and equal; knee and ankle jerks brisk and equal; plantars, right equivocal, left extensor. Sensory examination showed no loss to cotton-wool, and a hyperpathic response to pinprick over right little finger, and left little and ring fingers, extending on both sides along the ulnar border of the hand, on both dorsal and palmar surfaces. Postural sense was defective and two-point discrimination at 0·5 cm. was lost over both little fingers.

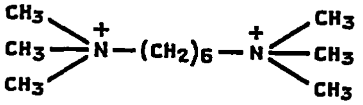
The radiograph showed congenital fusion of the fifth and sixth cervical vertebræ and narrowing of the space between the sixth and seventh vertebræ, with gross anterior and posterior marginal lipping.

This was a flexion injury, and the correspondence between the site of the old disc lesion and the spinal-cord injury suggests that as the result of the two factors, pre-existing cervical spondylosis and recent injury, the cord had been bruised by retropulsion of the disc. This man had had several previous falls with concussion while hunting, but no previous symptoms suggesting compression of spinal cord or nerve-roots.

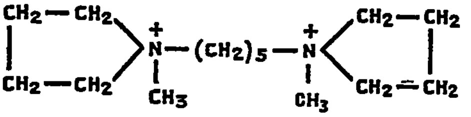
Alstad 1951, Kilpatrick and Smirk 1952) the blood-pressure was again measured by the method recommended by the Committee for the Standardisation of Blood Pressure Readings (1939)

M & B 2050A is compared at all stages with hexamethonium bromide, which was chosen as a reference compound because it has already been the subject of detailed clinical investigations

The structural formulæ are



Hexamethonium (bromide)



Pentamethylene-1 5 bis N-(N methyl pyrrolidinium)
'M & B 2050' is the di-iodide with 47 7% active cation
M & B 2050A is the bitartrate with 44 5% active cation

Preliminary results were obtained with the di-iodide, but these were all repeated more extensively with the bitartrate In the text, therefore, reference is made only to M & B 2050A, the bitartrate

RELATIVE MAGNITUDE OF EQUALLY HYPOTENSIVE DOSES OF M & B 2050A AND HEXAMETHONIUM BROMIDE

In hypertensive patients in the sitting posture an initial subcutaneous dose of 15 mg of hexamethonium bromide ordinarily induces a distinct fall of blood-pressure The corresponding dose of M & B 2050A is 3 0–3 5 mg (figs 1–3) Patients who are more than usually sensitive to hexamethonium bromide are commonly more than usually sensitive to M & B 2050A (fig 3) Insensitivity also, when present, is usually common to the two substances With both substances, as drug toleration develops, larger doses are required to keep the blood-pressure down (see below)

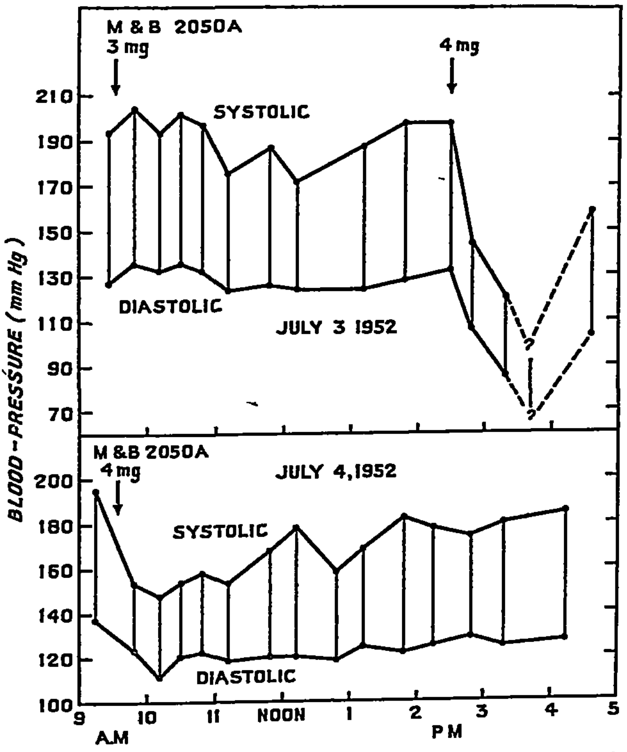


Fig 1—Cumulative effect of two subcutaneous injections of M & B 2050A given at an interval of 5 hours in case 295

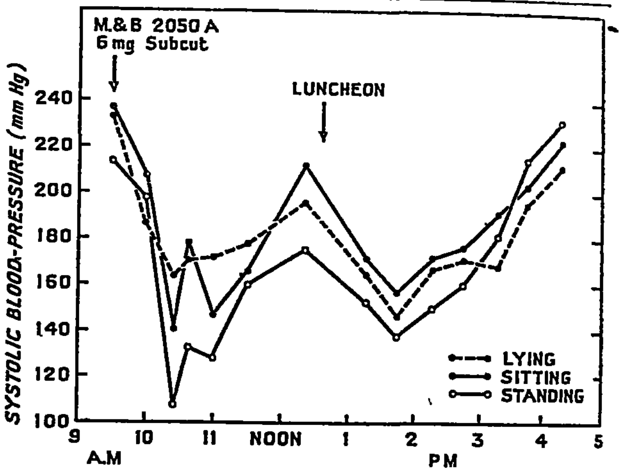


Fig 2—Effect of 6 mg of subcutaneous M & B 2050A on systolic blood pressure in lying, sitting, and standing postures in case 280 Effect on blood pressure of meal given during action of drug is exemplified

An effective oral dose of hexamethonium bitartrate ordinarily lies between 350 and 2100 mg, according to the state of drug toleration, and thrice daily administration before meals, sometimes with an additional dose at bedtime, is the usual routine With M & B 2050A a corresponding fall of blood-pressure follows much smaller doses Significant falls of blood-pressure have been induced by us with as little as 10 mg before meals, but, with less than average sensitivity of the patient to the drug and with the development of toleration, as much as 700 mg has been required for a single dose

Thus, after a few weeks' or months' treatment with M & B 2050A the effective oral doses in eleven patients who had not necessarily acquired a full measure of toleration were 380, 100, 300, 560, 375, 700, 220, 200, 140, 270, and 180 mg In ten patients successfully treated with oral hexamethonium bromide or bitartrate the doses used were 750, 750, 1500, 250, 750, 500, 500, 750, 250, and 1500 mg In fifteen patients who were unable to continue with oral administration the doses of hexamethonium bitartrate required to produce a sufficient fall of blood-pressure were 1000, 2500, 3000, 1000, 2250, 1750, 250, 1000, 1000, 1000, 3000, 1500, 2250, 1000, and 1250 mg These latter doses were all accompanied by side effects sufficient to determine cessation of oral treatment The general impression has been that alimentary side effects, which are the most troublesome consequence of oral administration of hexamethonium bromide or bitartrate, are less prominent when the required dose is comparatively small It was this observation which led us to think that a more active drug such as M & B 2050A, which could be given in a smaller dose, might be better tolerated

M & B 2050A was given by mouth to patients who had either had to stop taking hexamethonium bromide or bitartrate by mouth, because of side-effects, or required doses which it seemed unwise to continue, such as six or seven tablets of hexamethonium bromide (250 mg) or bitartrate (350 mg) before meals Our initial experience includes six such patients, five of whom can take effective oral doses of M & B 2050A with comparatively few side effects Of a further eight patients, not previously tested with oral hexamethonium bitartrate, six could take effective doses of M & B 2050A without important side-effects

The basal blood-pressures of all the patients were determined as described previously (Smirk 1944, Kilpatrick 1948), and with suitable doses of M & B 2050A the blood-pressure fell well below the basal level There is no doubt that M & B 2050A reduces the basal as well as the supplemental pressure As with hexamethonium salts (Smirk and Alstad 1951), the higher a nurse helping to lift a patient, the other in a woman during a severe fit of coughing. In both instances a protruded disc was found at operation. It seems not impossible that, as the result of slow compression by cervical spondylosis, the blood-supply to the anterior half of the spinal cord may be so reduced that a sudden additional protrusion of a disc, or stretching of the cord over a bony spur, in the course of normal movement might cause immediate paraplegia.

INJURY TO CERVICAL SPINE AT OPERATION

What has already been said is by way of preparation for a further question: can damage be done to the cervical spine as the result of manipulation of the head and neck during operations under general anæsthesia, with or without pre-existing cervical spondylosis? This question has already been raised in a court of law, and the following case is one in which Dr. J. G. Greenfield, Dr. Hugh Davies, and I were called to give expert evidence.

Case 5.—The main facts in this case are undisputed, but their medical interpretation is a matter of opinion.

The patient, aged 36, underwent tonsillectomy by dissection under general anæsthesia on the evening of Feb. 1, 1949. During the operation he was in the supine position with his shoulders supported by a sandbag and his head so turned backwards that the surgeon sitting at the head of the table looked directly into his mouth, this position of the head being steadily maintained by means of an apparatus comprising a gag, a metal plate strapped to the trunk, and a metal rod connecting the two, the necessary tension being obtained by a ratchet device. Anæsthesia, operation, and the transportation of the patient from theatre to bed followed routine procedure.

On recovery from the anæsthetic the patient complained of inability to move, and was later found to have the physical signs of a partial transverse lesion of the cord at the fourth cervical segment. From this he made an incomplete recovery, but later he developed symptoms which proved to be due to a sarcoma of the pelvis, from which he died twenty-two months later.

The spinal cord was removed post mortem, when no injury of the vertebral column was noted, and sections were later examined by Dr. Greenfield, who reported an old focus of softening, with secondary cavitation and scarring in the fourth and fifth cervical segments of the spinal cord. This lay for the most part behind the central canal in the anterior part of the dorsal columns and dorsal horns of grey matter, also involving the crossed pyramidal tracts. Dr. Greenfield's report continues: "I have been at some pains to compare the condition of the spinal cord in this case with that in which the paralysis was known to have been due to protrusion of cervical discs, and I have had the opportunity of examining ten such cases. From this examination it appears that the most common position for the softening in cases of protrusion of cervical discs is the same as was found in this case—that is, affecting the inner part of one or both pyramidal tracts, the base of the posterior horn of grey matter, and the anterior part of the posterior columns. Since in the cervical region this part of the spinal cord is the part supplied by the terminal branches of the anterior spinal artery, it is probable that the softening in these cases is due to pressure on the anterior spinal artery by the protruding intervertebral disc."

The symptoms for which the tonsillectomy was performed in this case were intermittent fever with pains in various parts of the body, especially the left shoulder; and because of the shoulder pain the patient's physician had obtained a radiograph of the cervical spine two months before the operation, [illegible]. In these radiographs Dr. Davies observed an alteration in the normal curve of the cervical vertebræ, [illegible] a flattening of the curve as a whole and a slight [illegible] in the [illegible] region. The same abnormality was seen in a film taken shortly after the onset of paralysis. A further radiograph taken fourteen months later showed [illegible] in the anterior common ligament between the fourth and fifth cervical vertebræ.

All that is certain in this case is that at some time while he was under the anæsthetic the patient sustained [illegible] to the spinal cord. The evidence is at least consistent with the probability that the factors concerned were pre-existing degeneration of a disc and a hyperextension injury occurring during the normal procedure of tonsillectomy.

Mr. D. W. C. Northfield has kindly let me see the notes of another case of paraplegia following tonsillectomy with a happier issue.

Case 6.—A previously healthy woman, aged 27, underwent tonsillectomy by dissection on Sept. 19, 1938. When she came round from the anæsthetic she complained of great pain in the shoulders and lower part of the neck, at times excruciating and radiating upwards into the head and neck, and associated with inability to move the head and tenderness over the lower cervical spines. After a few days the pain radiated into the arms and later into the forearms, with tingling in the hands. On Oct. 14 difficulty in micturition was noticed, and thereafter catheterisation was needed from time to time. A day or two later the patient complained of numbness of the legs—she could not feel her knees touching—and soon afterwards weakness of the lower limbs and clumsiness and weakness of the hands so that she could no longer write. The numbness rapidly spread upwards from the lower limbs to the abdomen with a girdle sensation at the lower costal margin. Associated with this was the complaint of diffuse burning pain when the skin of the abdomen was lightly touched.

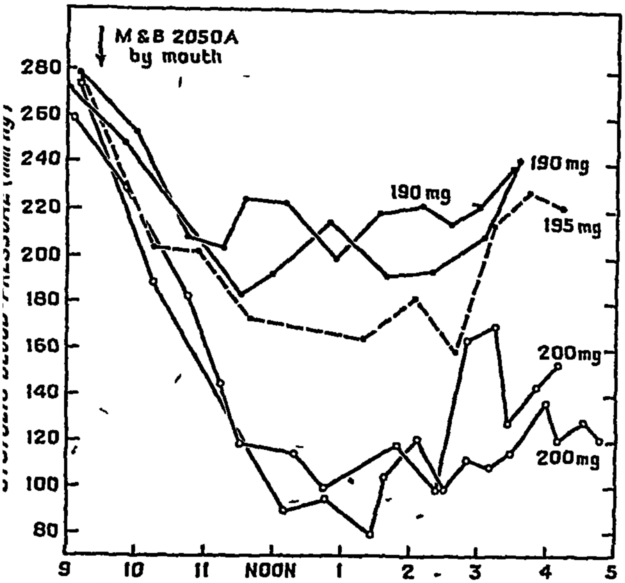
Mr. Northfield's note of his examination on Oct. 21 revealed the following abnormalities. There was tenderness over the lower cervical spines and painful limitation of movement on rotation to the left. On the motor side, flaccidity of all limbs, generalised wasting of the upper limbs with particular wasting of left deltoid muscle, generalised moderate weakness of the upper limbs, including the shoulders, weakness of the trunk (she could not raise herself from the bed), and severe weakness of the lower limbs. She was just able to raise her right leg from the bed, but not her left. All the tendon-reflexes were exaggerated, equally on the two sides, and both plantar responses were extensor. Sensory examination revealed hypalgesia below the fifth cervical level on both sides, with analgesia on the right below the fifth thoracic level. Postural sense was good in the thumb and big toes but impaired in the fingers.

Lumbar puncture showed complete manometric block, and the cerebrospinal fluid contained 1000 mg. of protein. A lateral radiograph of the cervical spine showed no abnormality. Laminectomy a few days later revealed severe compression of the cord from an anteriorly placed swelling opposite the fifth and sixth cervical laminæ, pushing the cord backwards. On palpation this seemed somewhat elastic, and on its being incised a little milky fluid oozed out, after which fragments of tissue were removed, which proved on microscopy to be fibrous tissue. After operation there was slow but steady improvement, and the patient reported by letter in November, 1942, that she was then quite well, married, and with two children.

The story in this case is very different from that of case 5. Although the complaint of neck pain immediately followed the operation, the development of spinal-cord compression was gradual, and what was found at operation appears to have been a retropulsed disc. This was Mr. Northfield's opinion. It seems quite likely that hyperextension, as well as flexion injuries, would cause this to happen. Provided that the force is insufficient to rupture the anterior common ligament, compression of the disc might lead to a tear in the posterior part of the annulus, with subsequent extrusion of the nucleus pulposus. There was no clinical or radiological evidence in this case of pre-existing disease of the disc.

In the following case the sixth cervical nerve-root suffered injury in the course of a dental extraction.

Case 7.—A man, aged 61, had his two lower left pre-molar teeth extracted under nitrous oxide. On recovering from [illegible] he noticed difficulty in putting his left hand into his trouser pocket to get out his handkerchief, and on attempting to [illegible] he found that he could not raise his [illegible]. The weakness improved but was still [illegible] when I saw him three weeks later, and [illegible] weakness and wasting of [illegible] [illegible]. The left biceps and supinator jerks were [illegible], all other reflexes [illegible]. There was [illegible]



ig 4—Effect of M & B 2050A by mouth on systolic blood pressure in case 110, who had a narrow range of therapeutic response, showing need for accuracy in dosage

EFFECT OF MEALS ON HYPOTENSIVE ACTION

With M & B 2050A, as with hexamethonium bromide, pentamethonium bromide, 'M & B 1863,' and 'Ciba 9295,' an additional fall in blood-pressure may occur when a meal is taken in the course of the drug's action Smirk and Alstad 1951) It has been suggested previously that this is due to inability of vascular reflexes to compensate for splanchnic dilatation A larger than average fall following a meal is shown in fig 2, and an average fall in fig 3

EFFECT OF ORAL M & B 2050A BEFORE AND AFTER MEALS

When M & B 2050A is given by mouth after meals, the blood-pressure falls much less than when it is given n water before meals Delay in absorption will explain this The difference is such that a dose of M & B 2050A which is effective when given before a meal may have little action when given afterwards

EFFECT OF POSTURE ON ACTION OF M & B 2050A

As after other methonium salts, the fall of blood-pressure after M & B 2050A s greatest in the standing posture, ntermediate when sitting, and least when lying These differences are considerable The postural element in the fall of blood-pressure seems to be more mportant shortly after the injection han later in the course of action The relative importance of the postural and non-postural falls of blood-pressure seems to be about the same for M & B 2050A figs 2 and 3) and for hexamethonium bromide

EFFECTS OF M & B 2050A ON PULSE-RATE

The effects of M & B 2050A on the pulse-rate are variable Sometimes the rate decreases with fall of blood-pressure, more often it increases In the standing posture the pulse-rate is usually a little higher than it is in the lying posture, presumably because of the lower blood-pressure Changes in heart-rate seldom exceed 20 beats a minute and are ordinarily much less than this, especially if the blood-pressure falls slowly or is maintained at a steady low level

TOLERATION

Administration of M & B 2050A for three or four months produces far less toleration than is seen when hexamethonium bromide, pentamethonium bromide, M & B 1863 or Ciba 9295 is given for a week or even a few days Whether, with M & B 2050A toleration goes on developing, though much more slowly, remains to be discovered

It will be seen (tables IIa and IIb) that toleration develops with repeated injections or oral doses of M & B 2050A The impression is that, as with hexamethonium bromide, the dose required to produce an effective fall of blood-pressure eventually becomes stable and no further dosage increase is needed

CROSS-TOLERATION

Evidence of cross toleration was found in patients already tolerant to hexamethonium bromide when they received a first dose of M & B 2050A The minimum dose of M & B 2050A required to induce a satisfactory fall of blood-pressure was two or three times as great as the minimum effective dose when no other methonium drugs had been given previously (table III) Evidently the previous administration of hexamethonium bromide induces some toleration to M & B 2050A but this is small Similarly sensitivity to injected hexamethonium bromide was largely retained by patients who had received M & B 2050A

Cross-toleration between M & B 1863 and hexamethonium bromide is practically complete (Smirk 1952c and d) Hexamethonium bromide has half the activity per milligramme of M & B 1863, and this relationship is preserved at all stages in the development of drug toleration Hence, if the patient has received only hexamethonium bromide, a corresponding dose of M & B 1863—i e, half the dose of hexamethonium bromide—may be substituted at any time in the knowledge that a corresponding degree of toleration has been acquired also to this other methonium salt

In contrast, it is evident that cross-toleration between hexamethonium bromide and M & B 2050A is incom

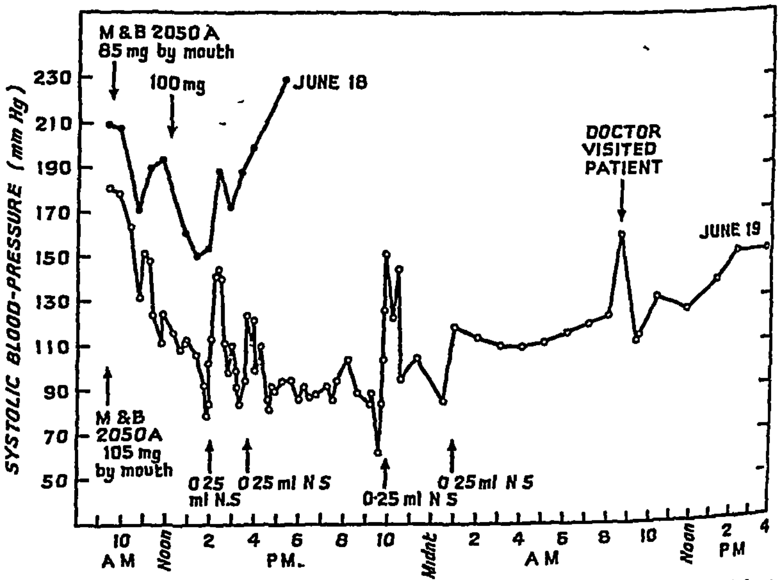


Fig 5—Effect of M & B 2050A by mouth on systolic blood pressure in case 260 Capricious alimentary absorption led in this patient to great day to-day variation in the effect on the blood pressure Although side-effects were absent, the irregular appearance at times of excessive hypotension and at other times of inadequate falls of pressure led to rejection of the oral route. N.S neo-synephrine

unmodified, and the pressor effect of nicotine in the dog was abolished. The absence of an atropine-like action was shown by the lack of effect on the salivary flow induced by carbamylcholine, and in other ways. From this evidence a specific action on ganglia can probably be inferred.

The effect on blood-pressure is very similar to that obtained with hexamethonium, except that the onset is slightly slower and the recovery slightly more prolonged, the hypotension resulting from the release of vascular tone. There was no direct effect on the isolated perfused heart of the cat and the coronary outflow in the dog was unaltered.

M. & B. 2050 is devoid of anticholinesterase, neuromuscular-paralysing, and histamine-liberating properties in doses fully effective in blocking ganglia. Gastric secretion in the dog (chloralose) induced by vagal excitation was inhibited in small doses (0·05 mg. per kg. body-weight) injected intravenously, the flow of juice and acidity being decreased to a greater extent than peptic activity. Toxicity was investigated in various species, and daily subcutaneous injections for 2–4 weeks in rats and guineapigs, of doses far in excess of those pharmacologically effective, had no effect on the growth-rate, blood picture, or bodily health.

SUMMARY

M. & B. 2050 has a type of action similar to that of hexamethonium, with greater potency (5 times) and a longer ($1^1/_2$ times) duration of action. The results reported very briefly here will be described in detail elsewhere.

We wish to thank the directors of May & Baker Ltd. for permission to publish these results.

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NEW SYMPATHICOLYTIC AGENTS

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SINCE the indication by Paton and Zaimis (1948) that the ganglion-blocking action of compounds of the methonium series would have a clinical application, many reports have been published on their use in hypertension. These have been reviewed (*Lancet* 1951, *British Medical Journal* 1951, Turner 1951), and enough time has now elapsed to suggest that with hexamethonium it is possible to modify in some cases the course and prognosis of hypertension with severe symptoms and signs. Campbell et al. (1952), Grimson (1952), and others have reported results of treatment lasting two years or more. It can be concluded that, although hexamethonium has no action on the cause of hypertension, it can modify the hypertension of some patients, giving a variable degree of relief from symptoms and signs.

Meanwhile the search for other hypotensive agents has continued. Study of the actions of the hydrogenated alkaloids of ergot (Rothlin and Cerletti 1949 and others) has been extended. Rankin and Smith (1952) and Smirk (1952b) have examined 'Pendiomide.' Apresoline and [illegible] have been used by Grimson (1952).

Hexamethonium is not an ideal drug for the production of sympathicolysis in the treatment of hypertension.

(1) It produces a generalised ganglion blockade affecting gastro-intestinal activity (Kay and Smith 1950), which may lead to paralytic ileus (Mackey and Shaw 1951, and others). Other actions include inhibition of salivation, paralysis of ocular accommodation, and reduction of sweating, the last having been used in the treatment of hyperhidrosis by Sommerville and McMillan (1952).

(2) It is inconstant in action, there being also an individual variation of response. This variation is increased when hexamethonium is given by mouth. Further, a strong tolerance develops rapidly, making large doses necessary for continuous treatment.

(3) The duration of action of a dose of hexamethonium is normally short, making frequent injections necessary when it is given parenterally. Masini and Rossi (1952) and Smirk (1952a) have used macromolecular substances, such as polyvinylpyrrolidone and dextran, to provide depot injections of hexamethonium salts and thus to prolong their action.

Paton (1951) suggested that it might be possible to obtain ganglion-blocking agents exerting selective action on different parts of the autonomic nervous system. With Graham, we have described results with 'M. & B. 1863' or 'Gaplegin,' a monoethyl homologue of hexamethonium which we found to be of greater activity but without any great specificity of action (Campbell et al. 1952). Smirk (1952b) has confirmed these findings.

Wien and Mason (1953) have examined new compounds prepared by May & Baker Ltd., some of which possess strong ganglion-blocking activity. In view of the known species difference in response to these drugs, we selected nine of them for examination of their actions in man in comparison with hexamethonium and gaplegin.

The new compounds examined are structurally related to hexamethonium. They are :

M. & B. 2074. Butane-1 : 4-bis(diethylmethylammonium hydrogen tartrate) dihydrate.

M. & B. 1950. Phenylethane-p-ω-bis(trimethylammonium dihydrogen phosphate) tetrahydrate.

M. & B. 2034. N.N′-tetramethyl-β-p-aminophenylpropylamine bismethobromide.

M. & B. 2002. Pentamethylene-1 : 5-bis-4′-(4′-methylmorpholinium) dibromide.

M. & B. 1978. Hexamethylene-1 : 6-bis-4′-(4′-methylmorpholinium) di-iodide.

M. & B. 2023. Heptamethylene-1 : 7-bis-4′-(4′-methylmorpholinium) dibromide.

M. & B. 2050 A. Pentamethylene-1 : 5-bis(1′-methylpyrrolidinium) bitartrate.

M. & B. 2024. Hexamethylene-1 : 6-bis-N-(N-methylpyrrolidinium) di-iodide.

M. & B. 2060. Hexamethylene-1 : 6-bis-N-(N-ethylpyrrolidinium) dibromide.

Dosage of these we have expressed in terms of active cation.

METHODS

Grimson et al. (1952) and others have noted that the response of hypertensive patients to the initial dose of hexamethonium may be excessive. Accordingly we decided to investigate the action of drugs with strong hypotensive properties first in patients with normal blood-pressures and subsequently in patients with hypertension, a procedure similar to that of Arnold and Rosenheim (1949) when they examined hexamethonium. As a record of the effect on the gastric secretion was required, which involved repeated swallowing and toleration of Ryle's tubes, 75 patients with duodenal ulceration and hyperchlorhydria without cardiovascular abnormality were selected. Subcutaneous administration was begun with 2·5–5 mg. of cation repeated at short intervals in increasing dosage until a definite effect was observed. To minimise errors due to tolerance or to variations in sensitivity, the same drug was not given again to any patient and the drugs were given in different order. The smallest number of observations made on any drug was ten, but more observations were made on those found to be of interest. Control experiments with injections of sterile water were made in each patient. The effects on

8 to 19 weeks—four of them for 16 weeks or more None of these have had side-effects which warranted interruption of treatment One patient had an episode of diarrhœa and vomiting which, however, did not recur with continued treatment

Using simple 2% aqueous solutions with $^{1}/_{2}$% chlorbutol as an antiseptic we have had satisfactory clinical results similar to those reported previously (Restall and Smirk 1950, Smirk and Alstad 1951) from hexamethonium-bromide injections, but with fewer side effects Injections of M & B 2050A act rather longer than injections of hexamethonium bromide and may need to be separated by 5-hour intervals Even so, the second and third injections of the day may need to be smaller than the first because of the retention of sub-threshold doses Such complications add to the work involved in supervision of the regime In a few patients two injections daily—one at, say, 8 A M and the other at 5 P M —may be sufficient The advantage to the patient of simple aqueous M & B 2050A by injection when compared with injections of hexamethonium bromide is small but probably worth while Preliminary studies suggest, however, that M & B 2050A dissolved in polyvinyl pyrrolidone may have a distinct advantage over earlier methonium preparations used for injection

CLINICAL TRIALS OF M & B 2050A DISSOLVED IN 25% POLYVINYL PYRROLIDONE SOLUTION

Polyvinyl pyrrolidone has been used to delay the absorption of hexamethonium bromide and of M & B 1863 (Smirk 1952a and b) Absorption can be further prolonged by the addition of 1 in 2000 or 1 in 1000 ephedrine hydrochloride to the multidose container The absorption time of the injected drug is increased by the local vasoconstriction at the site of injection, but the doses of ephedrine used have no appreciable effect on the blood-pressure after absorption

By adjusting the concentration of the local vasoconstrictor it is usually possible from a single injection of M & B 2050A in polyvinyl pyrrolidone to obtain a fall of blood-pressure lasting 8–12 or more hours With two injections daily—at, say, 8 A M and 8 P M (or earlier if necessary)—the blood-pressure may be kept low over most of the 24 hours, but the blood-pressure varies with the amount of M & B 2050A in circulation at the time On this régime the blood-pressure in some patients does not seem to rise to serious hypertensive levels unless the M & B 2050A is omitted for one or two days to allow of its elimination

A suitable initial dose is 4 mg , and this is increased by 0 5 mg or 1 0 mg every few days until no further drug toleration takes place

In three patients with papillœdema, retinal improvement occurred more rapidly than has been usual with hexamethonium bromide

CLINICAL TRIALS OF M & B 2050A BY MOUTH

Attempts to control blood-pressure with hexamethonium given by mouth often fail at an early stage, particularly where, because of drug toleration, large doses are needed (Kilpatrick and Smirk 1952) Thus many patients do not show an adequate response when doses as large as 2000 mg of the bromide or bitartrate are administered before a meal, and in some instances, especially where large doses were required, any definite fall in blood-pressure is preceded or accompanied by vomiting, diarrhœa, or other symptoms Other patients could take effective doses of hexamethonium bitartrate for several days or weeks, but side-effects, usually diarrhœa, ultimately made it necessary to stop them

In clinical trials with single oral doses, M & B 2050A has shown a decided advantage over hexamethonium bromide or bitartrate in that a fall of blood-pressure to approximately normal levels can be obtained without toxic reactions in a majority of hypertensive patient., even when these have acquired tolerance Hypotensive symptoms due to excessive fall of blood-pressure are not counted here as toxic reactions, because they can be avoided by decrease of dosage and do not interfere wi continued control over the blood-pressure

The lowest effective oral dose of M & B 2050A wa 10 mg , in a patient who was also unusually sensitive t hexamethonium bromide A reasonable *initial trial do* is 20 mg , but 10 mg is sufficient in patients likely t prove unusually sensitive—e g, the elderly and feebl those who are on a salt poor diet, or who have undergo a sympathectomy

The amount given should be raised by 20 mg dai until an effective dose is attained Further increas of 20 mg daily, or less frequently, will then be require to keep the blood-pressure down as drug toleratio develops Eventually the dose required becomes stabl

Eighteen patients have been treated, fourteen succes fully, for periods ranging from 8 to 14 weeks—ten o them for 13 weeks or more Of the fourteen who we successfully treated without important side effects, si had already been unsuccessfully treated with hexa methonium bromide or bitartrate

Two patients could not be controlled with oral M & B 2050A, and two were doubtful

In one of the doubtful patients (case 340), aged 81, attack of cardiac asthma and breathlessness were much relieved b subcutaneous M & B 2050A A severe attack of diarrhœ followed several days' oral therapy, and it was judge expedient to administer the M & B 2050A by subcutaneou injection in polyvinyl pyrrolidone

In the other two patients, who were accounted failure (cases 110 and 260), the blood pressure could readily b reduced with M & B 2050A and no side effects as ordinaril understood were encountered Unfortunately, even by subcutaneous injection the minimum effective dose was ver close to the dose which led to an excessive fall of blood pressure The absorption of methonium salts from th alimentary tract, even when it is not capricious, is not sufficiently regular to give reproducible blood pressure falls in such patients In both cases the administration of a constant dose, even under comparatively constant alimentary conditions, *gave rise sometimes to an inadequate* fall of blood pressure and at other times to such an excessive fall that the patient had to lie down for the day Oral therapy was therefore impracticable, even though the two patients were free from side effects Both of the patients were well controlled by subcutaneous injection

PRACTICAL DETAILS THE STANDING TEST

The method we have used principally is suitable only for a well-equipped hospital or for an outpatient department or private clinic where patients may be under observation for the whole day, and which they may attend on two or three days a week for about a month At our clinic the responses to hypotensive agents are usually studied by measuring the blood-pressure in the sitting and standing postures half-hourly throughout the day, and it is thus possible to maintain control over the blood pressure while drug toleration is developing, though the effective dose changes from day to day On such a régime, once drug toleration is stable, there is no difficulty in discovering a system of dosage which gives a good measure of blood-pressure control throughout the day and much of the night, even though, for reasons stated above, the two, three, or four daily doses taken before meals may have to be of a different magnitude

Although such a method of objective control over the effects of a hypertensive drug is much to be preferred, sometimes it is impracticable but treatment is still required The following technique for starting treatment with M & B 2050A is applicable to consulting room practice It should, however, be used only by doctors who have gained some familiarity with the drug in cases where the régime has been stabilised in hospital

CHARACTERISTICS OF PHENYLDIMETHONIUM AND PENTAPYRROLIDINIUM COMPARED WITH THOSE OF HEXAMETHONIUM IN SINGLE DOSES

Drug	Minimal effective dose (mg.)		Duration of action (hr.)		Consistency of action		Gastric activity	Mydriasis
	Subcutaneous	Oral	Subcutaneous	Oral	Subcutaneous	Oral		
Hexamethonium ..	50·0	500 +	2–4	?	+ + +	+	+ + +	+
Phenyldimethonium ..	5·0–15·0	25–100	6 +	8 +	+ + +	+ +	+	+ +
Pentapyrrolidinium ..	2·5–10·0	25–100	6 +	8 +	+ + +	+ +	+ +	+ + +

constant changes affecting the ST segment and T waves, which may also be seen in normotensive patients. Hypotensive measures are likely to be dangerous in the presence of coronary arterial disease. No treatment of the severe hypotension is necessary other than rest in bed with the feet raised until the drug's action ends, adrenaline being contra-indicated (Burn 1951).

DISCUSSION

These results indicate that phenyldimethonium and pentapyrrolidinium probably overcome some of the disadvantages of hexamethonium. As regards selectivity of action, their doses which produce hypotension are smaller than those required to affect gastric secretion. Kay and Smith (1950) have shown that the paralysis of vagal ganglia by hexamethonium in hypotensive dosage inhibits the volume and acidity of gastric secretion in hyperchlorhydric patients. Gastric motility is difficult to study, because the concomitant severe hypotension often causes nausea and vomiting, but it is improbable that inhibition of gastric motility can be produced by ganglion-blocking agents in the absence of an action on gastric secretion.

Preliminary observations suggest that constipation is less during continuous oral treatment with these drugs than with hexamethonium, indicating a smaller risk of paralytic ileus. Inhibition of sweating is less, and the incidence of dryness of the mouth is about the same, but mydriasis is more common and more severe with both of the new drugs, and pentapyrrolidinium has been observed to produce sustained mydriasis during continuous treatment.

Both drugs are more consistent in action than hexamethonium when used orally, and single oral doses produce a definite hypotension more often, although comparably with hexamethonium the hypotensive effect may be delayed until several doses have been given. Habituation develops at least equally rapidly—probably more rapidly with pentapyrrolidinium—but a satisfactory reduction of blood-pressure is often obtainable with a daily dosage very much smaller than that of hexamethonium.

The two drugs appear to be effective even after habituation to hexamethonium, and may be sometimes used successfully by mouth in patients who have not responded to oral hexamethonium. The duration of response in parenteral administration is longer, suggesting that frequency of dosage may be reduced compared with hexamethonium; but in continuous parenteral treatment we have found that at least three doses a day are required.

Headache, drowsiness, and depression are unusual side-effects of pentapyrrolidinium, but their incidence and severity have not been such as to necessitate withdrawal of this drug. The high activity of these new drugs requires caution in their administration to avoid severe hypotension.

Fig. 1 shows that M. & B. 2074 (ethyltetramethonium) and M. & B. 2024 (hexapyrrolidinium) act on gastric secretion in a dosage not affecting blood-pressure. Studies of the application of these drugs in the management of hyperchlorhydria are in progress.

SUMMARY

Examination of nine new ganglion-blocking agents has indicated that two of them, phenyldimethonium and pentapyrrolidinium, have a high degree of activity in man in reducing the blood-pressure.

Pentapyrrolidinium is the more active of the two but is less selective in action.

Their action lasts longer than that of hexamethonium, and more consistent results follow oral dosage.

The preliminary results suggest their suitability for examination as therapeutic drugs in the management of hypertension.

We are grateful to Dr. J. Gibson Graham for permission to make this investigation and for his advice and encouragement; to the nurses of this hospital for their coöperation in managing the patients; and Miss K. J. S. Brander for laboratory and documentary assistance. The drugs were supplied by Messrs. May & Baker.

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ACTION OF A NEW METHONIUM COMPOUND IN ARTERIAL HYPERTENSION

PENTAMETHYLENE 1 : 5-BIS-N-(N-METHYL-PYRROLIDINIUM) BITARTRATE (M. & B. 2050A)

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THERE seems to be a fundamental similarity in the pharmacology of many methonium salts whose activity depends on the blocking of sympathetic and parasympathetic ganglia. 'M. & B. 2050A' has been described by Libman et al. (1952), and observations in man (Smirk 1952c) suggested that its use in the treatment of hypertension should be studied further, because, when it is given by mouth, it reduces blood-pressure, without toxicity, much more readily than do hexamethonium salts given by mouth.

METHOD

M. & B. 2050A was administered by subcutaneous injection and by mouth. To maintain uniformity with observations on hexamethonium bromide made in the last three years (Restall and Smirk 1950, Smirk and

2050A may be related to the fact that the patients who gave the best responses to oral hexamethonium salts were usually those who required only small doses

Like hexamethonium bromide, M & B 2050A *gives* rise to postural hypotension in the erect *posture* and leads to an additional fall of blood-pressure after meals The pulse-rate is ordinarily accelerated or little changed

Papillœdema, soft retinal exudates and hæmorrhages, breathlessness, and headaches have diminished sooner on treatment with M & B 2050A than on treatment with hexamethonium salts

Preliminary studies justify extensive therapeutic trials with orally administered M & B 2050A, but the *régime* of administration differs from that found suitable for hexamethonium bromide Where side effects prevent continued oral administration, the M & B 2050A should be dissolved in 25% polyvinyl *pyrrolidone*, to which 1 in 1000 ephedrine hydrochloride is added to slow further the absorption This preparation is injected twice daily with an interval of 10–12 hours between the injections

Thanks are due to Miss B Stanton and Miss B Hoare for technical assistance, and to Miss M Poppelwell for secretarial help The diagrams were prepared by Miss J Rivers I am indebted to Dr R Wien, who sent me a personal communication about the experimental pharmacology of several methonium compounds, and to Messrs May & Baker for generous supplies of these compounds, from which M & B 2050A was chosen for further study The cooperation of the Otago Hospital Board has been much appreciated The expenses of the research were defrayed in part by the Medical Research Council

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COMPRESSED-AIR ILLNESS ON TYNESIDE

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SEVERE effects upon workmen exposed to high atmospheric pressures are nowadays *fortunately* rare, but the sudden onset of serious disability or death from this cause in men in the prime of life is still a matter of grave concern Compulsory notification of compressed-air illness came into force on Jan 1, 1939, and in that year 12 cases were reported The numbers notified in subsequent years are shown in the accompanying table

These yearly notifications must be related to the amount of work at high pressures which is going on at the time, to the number of men at risk, and to the severity of all the incidents reported, but little information about these factors is given in the annual reports of the Chief Inspector of Factories

Civil compressed air work practically ceased in Great Britain during the 1939–45 war, with the result that in 1941–47 only 2 fresh cases of compressed air illness were notified, and 1 death in a man disabled twelve years previously

NOTIFICATIONS OF CAISSON DISEASE

(From Annual Reports 1939–50 of Chief Inspector of Factories),

1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949	1950
12	3*	0	0	1	1†	1	0	0	28	46‡	46

* 1 died
† Died, case dating from 1932
‡ Highest number hitherto recorded

22 of the 28 cases notified in 1948 were reported in the London area, but there were no serious or permanent results The remaining 6 happened in the North of England and include the 2 serious cases resulting in permanent disablement which *are reported here*

In 1949 and 1950 occurred the highest number of notified *cases, 46 in each year These were almost all slight, and there* were no deaths These high figures suggest *an increase in* the amount of compressed air work and the number of men at risk, but part of the increase in 1949 and 1950 may be attributable to more attention being paid *to mild forms of compressed-air disease* since the two severe *cases in* 1948

The effects of high atmospheric pressure are well known, and the textbook descriptions of caisson disease or compressed-air illness are adequate, but in normal times few doctors acquire experience of working conditions or of the disease Unfortunately, compressed air sickness may present as an acute emergency in which a delay of only a few minutes makes the difference between gross damage to the central nervous system and *complete recovery In addition, the treatment* must be given long enough to ensure that recovery is maintained

The 2 cases reported here were seen in the Royal Victoria Infirmary, Newcastle upon Tyne, *within six* months of each other, and both illustrate important *aspects of the environmental control of* work in high pressure

THE TYNE TUNNEL

In 1948 work began on a tunnel under the River Tyne, linking Jarrow on the south bank with Howdon on the north bank. *At Howdon two separate* air locks were installed at the shaft top one, fitted with bench seats, was for the use of workmen, and the *other* was used for tubs and materials

The air locks consisted of two horizontal steel cylinders, 6 ft 3 in in diameter and 21 ft long, at opposite sides of the shaft, opening to the shaft and lift at one end and to the exterior at the other *through* airtight doors in each of which was a small glass window An air inlet valve was fitted inside the lock used for the men so that it could be controlled by them and the rate of compression adjusted The outlet valves *could* be controlled only from the outside, and decompression in the man *lock* was in charge of a lock keeper It was the lock-keeper's responsibility to keep a record of the time workmen spent under pressure, *and of the* pressure used, and to decompress the men according to a fixed schedule *Decompression of the other lock*, used for materials, was not regulated, and men were forbidden *to come out through it*

The method of decompression used conformed to the Provisional Revised *Draft (June*, 1948) of Regulations as to Safety, Health and Welfare in connection with Work of Engineering Construction (Factories Act, 1937) The tables employed were calculated on Haldane's system so that the tissue supersaturation pressure should fall to 18 lb per sq in by the time a man left the lock

This method depends on the principle that it is safe to reduce rapidly the absolute pressure by half in any part of the pressure scale up to about 7 atmospheres, and to continue decompression slowly, the rate depending

CHARACTERISTICS OF PHENYLDIMETHONIUM AND PENTAPYRROLIDINIUM COMPARED WITH THOSE OF HEXAMETHONIUM IN SINGLE DOSES

Drug	Minimal effective dose (mg.)		Duration of action (hr.)		Consistency of action		Gastric activity	Mydriasis
	Subcutaneous	Oral	Subcutaneous	Oral	Subcutaneous	Oral		
Hexamethonium ..	50·0	500 +	2–4	?	+ + +	+	+ + +	+
Phenyldimethonium ..	5·0–15·0	25–100	6 +	8 +	+ + +	+ +	+	+ +
Pentapyrrolidinium ..	2·5–10·0	25–100	6 +	8 +	+ + +	+ +	+ +	+ + +

constant changes affecting the ST segment and T waves, which may also be seen in normotensive patients. Hypotensive measures are likely to be dangerous in the presence of coronary arterial disease. No treatment of the severe hypotension is necessary other than rest in bed with the feet raised until the drug's action ends, adrenaline being contra-indicated (Burn 1951).

DISCUSSION

These results indicate that phenyldimethonium and pentapyrrolidinium probably overcome some of the disadvantages of hexamethonium. As regards selectivity of action, their doses which produce hypotension are smaller than those required to affect gastric secretion. Kay and Smith (1950) have shown that the paralysis of vagal ganglia by hexamethonium in hypotensive dosage inhibits the volume and acidity of gastric secretion in hyperchlorhydric patients. Gastric motility is difficult to study, because the concomitant severe hypotension often causes nausea and vomiting, but it is improbable that inhibition of gastric motility can be produced by ganglion-blocking agents in the absence of an action on gastric secretion.

Preliminary observations suggest that constipation is less during continuous oral treatment with these drugs than with hexamethonium, indicating a smaller risk of paralytic ileus. Inhibition of sweating is less, and the incidence of dryness of the mouth is about the same, but mydriasis is more common and more severe with both of the new drugs, and pentapyrrolidinium has been observed to produce sustained mydriasis during continuous treatment.

Both drugs are more consistent in action than hexamethonium when used orally, and single oral doses produce a definite hypotension more often, although comparably with hexamethonium the hypotensive effect may be delayed until several doses have been given. Habituation develops at least equally rapidly—probably more rapidly with pentapyrrolidinium—but a satisfactory reduction of blood-pressure is often obtainable with a daily dosage very much smaller than that of hexamethonium.

The two drugs appear to be effective even after habituation to hexamethonium, and may be sometimes used successfully by mouth in patients who have not responded to oral hexamethonium. The duration of response in parenteral administration is longer, suggesting that frequency of dosage may be reduced compared with hexamethonium; but in continuous parenteral treatment we have found that at least three doses a day are required.

Headache, drowsiness, and depression are unusual side-effects of pentapyrrolidinium, but their incidence and severity have not been such as to necessitate withdrawal of this drug. The high activity of these new drugs requires caution in their administration to avoid severe hypotension.

Fig. 1 shows that M. & B. 2074 (ethyltetramethonium) and M. & B. 2024 (hexapyrrolidinium) act on gastric secretion in a dosage not affecting blood-pressure. Studies of the application of these drugs in the management of hyperchlorhydria are in progress.

SUMMARY

Examination of nine new ganglion-blocking agents has indicated that two of them, phenyldimethonium and pentapyrrolidinium, have a high degree of activity in man in reducing the blood-pressure.

Pentapyrrolidinium is the more active of the two but is less selective in action.

Their action lasts longer than that of hexamethonium, and more consistent results follow oral dosage.

The preliminary results suggest their suitability for examination as therapeutic drugs in the management of hypertension.

We are grateful to Dr. J. Gibson Graham for permission to make this investigation and for his advice and encouragement; to the nurses of this hospital for their coöperation in managing the patients; and Miss K. J. S. Brander for laboratory and documentary assistance. The drugs were supplied by Messrs. May & Baker.

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ACTION OF A NEW METHONIUM COMPOUND IN ARTERIAL HYPERTENSION

PENTAMETHYLENE 1:5-BIS-N-(N-METHYL-PYRROLIDINIUM) BITARTRATE (M. & B. 2050A)

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There seems to be a fundamental similarity in the pharmacology of many methonium salts whose activity depends on the blocking of sympathetic and parasympathetic ganglia. 'M. & B. 2050A' has been described by Libman et al. (1952), and observations in man (Smirk 1952c) suggested that its use in the treatment of hypertension should be studied further, because, when it is given by mouth, it reduces blood-pressure, without toxicity, much more readily than do hexamethonium salts given by mouth.

METHOD

M. & B. 2050A was administered by subcutaneous injection and by mouth. To maintain uniformity with observations on hexamethonium bromide made in the last three years (Restall and Smirk 1950, Smirk and still complained that they were numb A doctor, not the practitioner who usually supervised the works, was summoned, and advised decompression, which was performed fairly rapidly over perhaps thirty minutes The patient was then sent to his home by ambulance, although he lived on the other side of the river, and after a sleepless night he was admitted next morning to the Royal Victoria Infirmary, Newcastle

On examination he was pale and slightly cyanosed, with cold extremities His pulse was regular but weak, and its rate was 120, his temperature was 97 6°F and blood pressure 90/60 mm Hg His bladder was distended and palpable 2 in above the pubic symphysis There were moist sounds at both lung bases posteriorly Besides paralysis of the legs, there was weakness of the arms, and the lower intercostal muscles appeared to be immobile Sensation was present, and the tendon reflexes were all present and equal in the upper limbs, but there was complete anæsthesia to all stimuli in the legs and in the trunk below the level of the seventh thoracic vertebral spine behind and the third intercostal space in front Above this was an area of hyperæsthesia Abdominal reflexes were just present on the left side and absent on the right On stimulation of the soles of the feet there was flexion withdrawal of both lower limbs and priapism

Treatment and Progress.—A catheter was passed six-hourly and the patient was given carbachol and sulphadimidine as a prophylactic against urinary infection Oxygen therapy by B L B mask was given intermittently Two days after admission he began to have pins and needles in his arms, and a left ankle jerk was obtained Acute bronchitis with pyrexia (100 7°F) developed and was treated with penicillin 1 mega unit daily The extent of sensory loss appeared unaltered The condition of his chest gave rise to some anxiety during the next two weeks, and he had a small hæmoptysis Radiography of the chest revealed a small opacity in the left lower zone, and pyrexia was still present By now the upper limit of anæsthesia was at the level of the fifth intercostal space in front His bladder was functioning automatically, and there was flexion withdrawal on stimulation of the left leg but not of the right

Four weeks after admission he had much improved generally but was becoming spastic, with bilateral extensor responses The upper border of anæsthesia was at the level of the sixth intercostal space in front, and the skin over the buttocks had broken down superficially in three places Sensation now began to return fairly quickly over the abdomen, but discrimination between pinprick and light touch remained poor Physiotherapy was started and exercises to arms and legs were given with the aid of a frame and springs Ten weeks after his mishap he had regained a little voluntary power in his legs, the arms appeared normal, knee and ankle jerks were present, and there were extensor plantar responses with occasional spontaneous extensor spasms in the legs He remained in hospital until August, 1949, nine months after the accident, without any great improvement in the use of his legs, though walking-callipers were of considerable help, and he could get about with the aid of crutches He was still incontinent of urine

DISCUSSION

These two cases, one in an experienced compressed-air worker, the other in a novice, illustrate the fact that compressed air illness, although theoretically preventable, may still occur in a severe and crippling form The events which led up to these incidents raise important points in connection with the preventive measures in use, and with the general medical supervision of compressed air work, which is undertaken sporadically and in different parts of the country

A small incidence of minor bends must be accepted, for, unless exceptionally long decompression times are used, it is impossible to ensure that every man shall be adequately desaturated during decompression, and individual variation in susceptibility seems to be very large If those who are highly susceptible can be weeded out, safety lies in strict observation of the regulations, provided these are physiologically sound and psychologically acceptable As there is clearly a limit to the time which a man will spend in decompressing, because of the monotony, either the period must be short or means must be provided of relieving the tedium

In case 1 it is clear that the accident arose through deliberate disregard of regulations covering decompression The man was experienced but over confident, and he had probably taken similar risks previously without serious consequences The disturbing feature of this story is that it was possible for a man to come out through the "muck" lock, but it is difficult to suggest what steps should have been taken to ensure that this route was not used for anything other than conveying materials Safety on this point must lie in the careful choice of reliable men for the responsible jobs and on a high standard of discipline.

In this man's treatment recompression was begun very soon after the onset of paralysis, and the pressure was increased to an adequate height repeatedly but unsuccessfully

Welham and Blanch (1945), referring to the treatment of decompression sickness following diving operations, emphasise that, where the central nervous system is involved, a long period under pressure is required—e g, twenty-four hours or more They conclude that the commonest mistakes are made when (1) no treatment is given in doubtful cases, (2) recompression after the onset of symptoms is delayed, and (3) in serious cases compression is not maintained for at least twenty four hours They also recommend that the patient should be kept near a compression chamber for twenty-four hours after decompression, in case of urgent need

By these standards this man's treatment in the medical lock was inadequate, he should have spent at least twenty-four hours under pressure when it was seen that the damage was severe enough to paralyse his legs Between leaving Howdon and his admission to hospital next day some deterioration in his condition probably took place

A similar criticism applies to the second case, but this presents a series of unfortunate occurrences, each of which probably contributed to the final result If this man had been recompressed in the man lock as soon as he became ill, serious results would probably have been avoided by decompressing him again at a slower rate It was not thought by the workmen and lock keeper that he had bends but that he had fainted, and the accident was unusual It is evident that the serious nature of the patient's condition was not appreciated until decompression had been completed, when he was taken at once to the medical lock

The time spent in the medical lock under pressure was insufficient, and decompression was dangerously rapid, once more because the seriousness of the case was not appreciated The doctor who was called did not know that, without much delay, he could have examined the patient in the medical lock under pressure, nor did he recognise the disadvantage of sending the patient home to a distance that would much delay his return to the medical lock if an emergency arose In retrospect it is evident that the patient should have been left in the medical lock under pressure for another twenty four hours, after which, failing recovery, he should have been removed to hospital

This man may have been highly susceptible to compressed-air illness, since his symptoms came on although he was being correctly decompressed His previous history of bends, including one apparently severe attack, should have been taken to indicate his unsuitability for the work

SELECTION OF WORKMEN

Suitability for work under high atmospheric pressure is decided by excluding the obese and those not medically levels of casual blood-pressure are usually associated with bigger falls of blood-pressure.

RELATION BETWEEN MAGNITUDES OF EFFECTIVE SUBCUTANEOUS AND ORAL DOSES OF M. & B. 2050A

To make a fair comparison of the activities of orally administered and injected M. & B. 2050A the tests must be made at the same stage in the development of drug toleration. A series of such comparisons is set out in table I. It will be noted that an oral dose sufficient to lower the blood-pressure may be from five to twenty-five times as great as a correspondingly active subcutaneous dose.

COURSE OF FALLS IN BLOOD-PRESSURE WITH SUBCUTANEOUS M. & B. 2050A AND HEXAMETHONIUM BROMIDE

The time taken for the blood-pressure to reach its lowest value after an injection of M. & B. 2050A is similar to that after hexamethonium bromide. Times in minutes compared in the same patients were:

Case no.	13	274	304	253	295	297	291
M. & B. 2050A	26	20	24	37	40	57	25
Hexamethonium bromide..	35	50	32	23	60	60	25

Case no.	283	294	289	284	280	296	276
M. & B. 2050A	35	60	40	65	40	50	40
Hexamethonium bromide..	23	14	30	15	20	90	30

The action of M. & B. 2050A lasts longer than that of hexamethonium bromide. In a series of tests the times in hours were:

Case no.	13	274	304	253	295	297	291
M. & B. 2050A	6	4	$6^1/_2$	5	$5^1/_4$	$4^1/_4$	$6^1/_4$
Hexamethonium bromide..	6	3	$3^3/_4$	4	3	4	$3^3/_4$

Case no.	283	294	289	284	280	296	276
M. & B. 2050A	3	6	6	$5^3/_4$	5	6	4
Hexamethonium bromide..	$2^3/_4$	5	4	$2^1/_2$	$2^1/_2$	6	6

The magnitude of the difference between the duration of action of the two drugs is not fully apparent from the foregoing figures. Even when the action of an injection of M. & B. 2050A appears to be ended, as judged by the blood-pressure, the amount retained in the body may for some hours be enough to influence the response to a subsequent injection. This does *not* happen with hexamethonium bromide, which, in the absence of renal insufficiency, can usually be injected 4-hourly without enhancing its effect; but repetition of an effective dose of M. & B. 2050A within 4 hours ordinarily leads to an exaggerated fall of blood-pressure (fig. 1). If this feature of the action of M. & B. 2050A is overlooked, unpleasant reactions will be encountered both with oral and with subcutaneous doses.

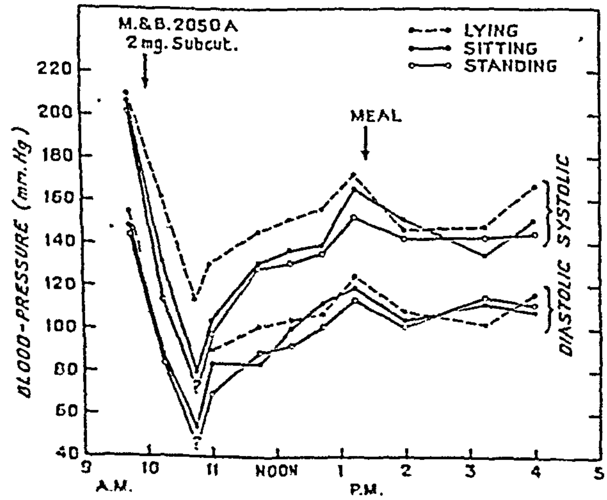

Fig. 3—Effect of 2 mg. of subcutaneous M. & B. 2050A on systolic and diastolic pressures in lying, sitting, and standing postures in case 104. Patient is unusually sensitive to M. & B. 2050A because of previous sympathectomy for hypertension.

TABLE I—COMPARISON OF EFFECTS OF M. & B. 2050A BY ORAL DOSAGE AND SUBCUTANEOUS INJECTION ADMINISTERED AT SAME STAGE IN DEVELOPMENT OF DRUG TOLERATION

Case no.	Subcutaneous injection		By mouth	
	Dose (mg.)	Fall in blood-pressure (mm. Hg)	Dose (mg.)	Fall in blood-pressure (mm. Hg)
13	12	90/40	60	92/54
274	..	..	10	73/22
304	6	98/60	54	92/76
253	5	32/40	26	30/42
220	7	120/62	125	36/36
295	4	40/50	75	38/24
293	4	46/44	115	94/62
291	8	74/62	155	84/60
294	3	22/26	60	52/52
297	4	44/20	140	68/44
60	8	60/12	100	44/32
306	12	60/40	180	100/52
323	4	64/56	50	36/32
328	10	68/70	380	46/36

In a woman aged 52 (case 295), 3 mg. of M. & B. 2050A produced an inadequate fall of blood-pressure, and $4^1/_2$ hours later it was thought reasonable to try an injection of 4 mg. After this, however, the blood-pressure fell to hypotensive levels, the patient felt faint, and the observation had to be interrupted (fig. 1). Next day the first dose given was 4 mg. of M. & B. 2050A which reduced the blood-pressure to the desired extent. It will be seen (fig. 1) that the fall in blood-pressure lasted more than 4 hours, which is rather longer than is usual with hexamethonium bromide.

COURSE OF BLOOD-PRESSURE FALL AFTER ORAL M. & B. 2050A

The duration of the fall in blood-pressure after oral M. & B. 2050A depends largely on the dose. The amount by which the blood-pressure falls is apt to vary when any methonium salt is given by mouth, because absorption from the alimentary tract is somewhat capricious, and because with most patients there is a comparatively narrow margin between the dose which has an inadequate effect and that which has an excessive one. Moreover, the drug may be absorbed in amounts which have no apparent action until a further dose increases the blood concentration above the threshold level. Hence, in one and the same patient, a dose may have comparatively little effect, or only a short-lasting effect, on the blood-pressure, and yet a slightly larger dose may induce a comparatively prolonged fall.

Oral doses of M. & B. 2050A which are taken before meals and are sufficient to reduce the blood-pressure to near normal levels usually have their greatest effect between $1^1/_2$ and 3 hours after being taken. The effect has usually lasted between 6 and 8 hours. The rapid increase in the extent of the blood-pressure fall which may be seen occasionally even with small changes in the dose is shown in fig. 4. Where capricious alimentary absorption is combined with a critical dosage level a bewildering variation of response may be encountered.

In case 260 (fig. 5) a dose of 85 mg., followed within a few hours by 100 mg., of M. & B. 2050A induced a fall of systolic pressure to 150 mm. Hg, some diminution of blood-pressure being apparent for 5 or 6 hours. The administration next day of 105 mg., however, induced a fall to below 70 mm. Hg systolic in the lying posture, the blood-pressure remaining at a comparatively low level for over 24 hours. When the blood-pressure fell to hypotensive levels, an injection of 1% 'Neo-Synephrine' 0·25 ml. raised the blood-pressure. Even when the blood-pressure was about 120 mm. Hg systolic in the lying posture, the visit of a doctor could still produce an emotional rise of blood-pressure of about 35 mm. systolic.

We have usually found that, when a fully effective oral dose of M. & B. 2050A is administered before breakfast, only a very small additional dose is required before lunch to extend the period of activity into the early evening.

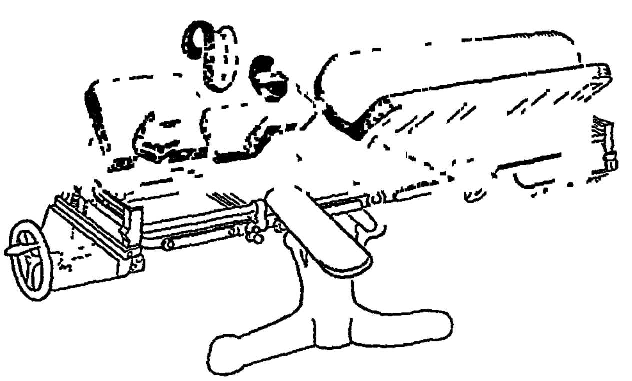

Fig 1—General view of tilting table-top, with upper leaf tilted to 45° to show to best advantage its several components

forcibly brought home to me on several occasions that this is a compromise position which is ideal for neither the abdominal nor the thoracic part of the operation For the former one would like a rather more extended abdominal incision and a supine position of the patient, for the latter a full lateral position of the patient It has therefore been thought worthwhile to design a tilting appliance which can be fitted to an ordinary operating table to overcome these objections It provides firm fixation of the patient, and at the same time allows the amount of tilt of his body to be varied in accordance with the changing demands of the surgeon during the operation, from a normal supine position to one 90° to the horizontal

Many modern operating-tables are, of course, capable of a lateral tilt of 20-30° to one or other side But, if the patient is placed in the supine position on such a table, the back of his left chest remains in contact with the table top when the latter is tilted and it is not therefore made accessible to the surgeon Alternatively, if he is put initially in a true lateral position, as for an orthodox posterolateral thoracotomy, and the table-top is then rotated backwards to the full range allowed, this still leaves him at an angle of 60 or 70° to the horizontal, which is far from ideal for a difficult abdominal dissection What is required is an appliance for rotating the patient's body from 0 to 90°, so as to lift the left hemithorax away from the table and to expose it posteriorly One could have designed an entirely specialised table rather after the fashion of an orthopædic " horse " but allowing a greater range of rotation and equipped with some device for raising and lowering the patient to suit the height of the surgeon One of the most costly parts of an operating-table, however, is the base, with the pump for elevating the top, and it seemed that, if this part of an ordinary operating-table could be used in conjunction with a special tilting top, considerable expense would be saved

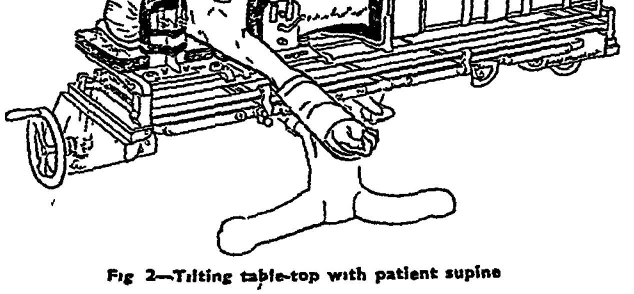

Fig 2—Tilting table-top with patient supine

THE APPARATUS

The tilting appliance which has been designed consists of two leaves of roughly the same length as the top of an operating-table, the upper one being approximately two-thirds, and the lower one half, of its width They are connected by a hinge along one edge The underneath leaf is firmly fastened to the ordinary table top, the edge with the hinge fitting along the right edge of the latter The top leaf, on which the patient rests, supports his head, shoulders, buttocks, and lower limbs, but has a deficiency on its free unhinged edge corresponding to the left half of the thorax and abdomen (fig 1) Naturally, the size of the defect in the upper leaf must be varied according to the size of the patient, if he is to be adequately exposed on the left side and at the same time sufficiently supported at the shoulders and buttocks This has been achieved by dividing the upper leaf into three components—a head piece which also supports the uppermost part of the shoulders, a chest piece corresponding to the right hemithorax and upper part of the abdomen and a main body and leg piece for the buttocks and lower limbs These three slide on an axle at the hinged edge of the leaf so as to increase or diminish the gap corresponding to the back of the left chest Also, to take the patient's weight when he is in the right lateral position and to prevent him from sliding on to the floor, there is a raised support along the right edge of the body and leg piece, and a side chest piece and head piece attached to the corresponding edge of the chest and head components of the upper leaf respectively Finally, to restrain the patient from falling forward when in the lateral position, there is a chest pad pivoting on an adjustable arm extending from the top edge of the side chest piece (figs 2-4) This is arranged to press evenly on the front of the lower end of the sternum without interfering with the incision or embarrassing respiration The side chest and head pieces can be moved in a longitudinal and a transverse axis, so that they are applied to the chest and head at the best sites The arms are accommodated on special rests, the right in an extended position on a flat arm board, the left on an angled arm rest, across the upper chest or neck The latter is borne on an adjustable lever stretching from the top of the side chest piece All the parts of the upper leaf on which the patient presses are well upholstered with thick ' Sorbo ' rubber

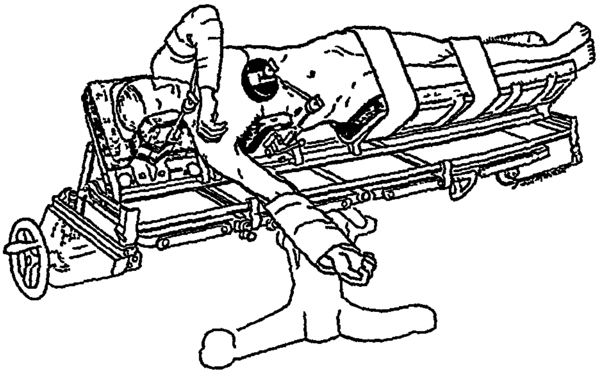

Fig 3—Tilting table-top with patient tilted to 45° Note arm rests and position of front chest piece relative to abdomen

The top leaf is raised by means of triple start bevel gears fixed in apposition at either end of the table One of these gears is mounted at each end of the horizontal shaft with rotating wheel (figs 1 and 2) Its counter part is fitted on a vertical spindle whose opposite end is attached to the under leaf of the table top These vertical spindles are gear cut and carry a box nut, which in turn is attached to an elevating lever whose

TABLE IIa—DEVELOPMENT OF TOLERATION TO HYPOTENSIVE ACTION OF M. & B. 2050A ON REPEATED INJECTION

Case no.	Effect of M. & B. 2050A (subcutaneous) at outset of treatment			Effect of M. & B. 2050A (subcutaneous) after repeated administration		
	Dose (mg.)	Change in blood-pressure (mm. Hg)	Fall (mm. Hg)	Dose (mg.)	Change in blood-pressure (mm. Hg)	Fall (mm. Hg)
304	6	192/118– 72/50	122/68	6	158/96 –118/88	40/8
295	4	198/138–148/112	50/26	4	178/134–132/88	46/46
293	3	244/158–174/132	70/26	4	184/132–138/108	46/24
289	6	272/172–184/136	88/36	9	254/152–174/126	80/26
284	4	178/124–132/88	46/36	12½	202/134–156/112	46/22
228	5½	192/128–138/92	54/36	5	192/138–142/102	50/36
336	29	208/142–138/72	70/70	48	192/128–120/64	72/64
Average	8·2	212/140–141/97	71/43	12·6	194/131–140/98	54/33

TABLE IIb—DEVELOPMENT OF TOLERATION TO HYPOTENSIVE ACTION OF M. & B. 2050A ON REPEATED ORAL ADMINISTRATION

Case no.	Effect of M. & B. 2050A at outset of treatment			Effect of M. & B. 2050A after repeated oral administration		
	Dose (mg.)	Change in blood-pressure (mm. Hg)	Fall (mm. Hg)	Dose (mg.)	Change in blood-pressure (mm. Hg)	Fall (mm. Hg)
13	60	214/132–122/78	92/54	92	208/142–162/124	46/18
274	10	178/ 82–118/64	60/18	10	184/106–122/84	62/22
304	37	196/112–118/64	78/48	72	172/114–142/134	30/–20
220	55	182/128–119/65	63/63	62	208/142–114/86	94/56
293	24	204/138–152/118	52/20	75	200/146–174/128	26/18
60	100	182/112–138/84	44/28	220	184/118–144/90	40/28
306	200	212/132–112/80	100/52	650	192/132–172/102	20/30
309	340	208/132–102/58	106/74	540	190/124–128/98	62/26
321	105	232/148–112/74	120/74	310	234/108–114/62	120/46
297	50	208/108–138/88	70/20	130	224/108–132/84	92/24
Average	98	202/122–123/77	79/45	216	200/124–140/99	60/25

plete. The *initial* effective dose of M. & B. 2050A is usually a fifth of the *initial* effective dose of hexamethonium bromide; but, when toleration has been established and the dose of hexamethonium bromide has increased, the corresponding effective dose of M. & B. 2050A is likely to be less than a tenth, sometimes less than a twentieth, of the toleration dose of hexamethonium bromide. Patients treated with very large doses of hexamethonium bromide or bitartrate orally may have acquired so little cross-toleration to M. & B. 2050A that they show large falls of blood-pressure with small doses of the latter.

Case 68 had comparatively small falls of blood-pressure with 1750 mg. of hexamethonium bitartrate taken by mouth, and on this dose had frequent diarrhœa. She showed much larger blood-pressure falls with initial doses of 15 mg. of M. & B. 2050A by mouth.

Case 162 had inadequate blood-pressure falls, but few side-effects, with doses of 2100 mg. of hexamethonium bitartrate thrice daily. 60 mg. of M. & B. 2050A induced larger blood-pressure falls when given at a stage before drug toleration to M. & B. 2050A had developed.

CLINICAL TRIALS OF SUBCUTANEOUS M. & B. 2050A

Thirty-eight patients each received several subcutaneous injections of M. & B. 2050A sufficient to reduce the blood-pressure to within the normal range. As indicated above the dose of M. & B. 2050A is much less than that of hexamethonium bromide, but symptomatically there has been no great difference in the actions of the two drugs when they are injected subcutaneously. Some patients have gained the impression that symptoms such as dry mouth, blurred vision, constipation, and attacks of diarrhœa are less with M. & B. 2050A; but in a few patients these symptoms are more pronounced.

The blood-pressure can be reduced to normal or near normal throughout the day with M. & B. 2050A, usually without discomfort to the patient. To do this, however, requires adjustment of the dose in terms of careful observations of blood-pressure changes throughout the day. This is even more important than with hexamethonium bromide, because there is an additional difficulty in control of blood-pressure with M. & B. 2050A—namely that, even when the effect of the first dose of the day appears to have worn off, a repetition of this dose tends to produce an excessive action. We think this is due to the retention of sub-threshold doses in the body (fig. 1). Hence in our initial trials each dose given in the course of a day was adjusted in accordance with the response to the previous dose. When this has been done satisfactorily, the patients seem to be more comfortable than on hexamethonium bromide.

Fifteen patients have been on continuous subcutaneous treatment with M. & B. 2050A for periods ranging from

TABLE III—DEVELOPMENT OF CROSS-TOLERATION BETWEEN M. & B. 2050A AND HEXAMETHONIUM BROMIDE

Effect of M. & B. 2050A (subcutaneous) before administration of other methonium salts				Effect of M. & B. 2050A (subcutaneous) after development of toleration to hexamethonium bromide			
Case no.	Dose (mg.)	Change in blood-pressure (mm. Hg)	Fall (mm. Hg)	Case no.	Dose (mg.)	Change in blood-pressure (mm. Hg)	Fall (mm. Hg)
296	4	203/138–112/88	91/50	13	12	228/148–138/108	90/40
280	6	214/150–128/104	86/46	274	5	208/130–124/126	84/4
254	3	208/148–176/132	32/16	297	5	194/128–132/98	62/30
253	4	174/114–132/98	42/16	291	6	218/142–138/92	80/50
304	5	208/142–132/78	76/64	289	6	272/172–184/136	88/36
295	4	198/138–148/112	50/26	276	10	192/132–172/122	20/10
297	5	212/128–112/78	100/50	256	10	176/124–142/108	34/16
292	3	244/158–174/132	70/26	272	6	178/146–110/92	68/54
294	3	176/128–154/102	22/26	49	19	230/146–152/94	78/52
325	4	194/126–130/70	64/56	60	6	178/124–142/98	36/26
328	7½	214/134–144/98	70/36	306	12	212/138–152/98	60/40

vary his operation according to the state of affairs revealed at exploration, and so he is encouraged to adopt a versatile approach to carcinoma of the stomach.

For higher œsophageal growths at or just below the level of the arch of the aorta many surgeons prefer to carry out the resection through the right chest because of the untrammelled access which can be obtained to the œsophagus on this side by division of the vena azygos This necessitates, however, a separate epigastric incision for the preliminary mobilisation of the stomach so that it may later be drawn up into the chest in the thoracic stage of the operation In designing this tilting table-top the requirements of this type of operation have been borne, in mind, and the appliance can be arranged to tilt the patient on his left side The three components of the top leaf can be slid off and refitted so that the head and chest pieces lie at the foot end of the table and the body piece at the head end If the patient is now placed on the table, with his head towards the former tail end, he can be rotated on his left side and the right chest fully exposed posteriorly round to the spinous processes It is necessary, however, to arrange for the gap behind the right hemithorax to be specially long, so as to leave the right chest uncovered posteriorly up to the top of the right shoulder, because with the rather high thoracotomy incision through the bed of the 5th or 6th rib which is used in these cases it is usually necessary to retract the scapula upwards

The patient is placed on the table, and the various components are adjusted He is then tilted on to his left side, and his abdomen and right chest are painted with iodine, and sterile towels are applied Next, the table is flattened for the abdominal exploration and mobilisation of the stomach through a left paramedian or median epigastric incision When this phase has been completed, the patient is tilted into a full lateral position for the right thoracotomy The abdominal incision can be closed at this stage by an assistant if desired or, preferably, kept open till the growth in the œsophagus has been freed and the stomach is due to be drawn up into the right chest The assistant can then help its passage through the diaphragm with a guiding hand, and can ensure that it does not become twisted on its long axis, as happened in one of my earlier cases Finally the epigastric wound is sutured while the anastomosis is proceeding in the chest

Other Operations —Though this appliance was designed primarily for gastro œsophageal surgery, it is of course useful in any operation for which an abdominothoracic approach is required, and also in purely abdominal operations where a tilt of the patient to one or other side can be of assistance Thus, in the left upper abdomen, a difficult splenectomy will be undertaken with greater confidence if the surgeon knows that he can alter the tilt of the patient at will during the operation and extend the incision into the left chest as required The same applies to splenorenal anastomoses In the right upper abdomen the table should be of value for portocaval anastomoses for which an abdominothoracic incision may be required, but I have not yet had the opportunity of using it for this procedure

This tilting appliance has been made to my design by Messrs A L Hawkins & Co , Ltd , of New Cavendish Street, London, W 1

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NORMAL VALUES FOR BLOOD CONSTITUENTS

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IN interpreting a biochemical result, detection of the *abnormal depends on an accurate knowledge of the* normal It is conventional to express normal values for any constituent as a range, but a single range does not provide enough information *Thus, if the range is made* rather narrow, many normal people will have values falling outside it Enlarging the range will cause it to include a higher proportion of normals, but a range which attempted to include all possible normal values would be uselessly large It follows that any range should be quoted with the percentage of normals which it include

NORMAL VALUES OF BLOOD CONSTITUENTS

A simple way of doing this is to give the mean and standard deviation, but these parameters only allow the necessary figures to be calculated when the distribution of results approximates to the symmetrical "normal" form It has been shown (Wootton, King, and Maclean Smith 1951) that this was the case for only about half of the constituents tested, while the remaining distributions were skewed and all except one were fitted with a

NORMAL VALUES FOR BLOOD CONSTITUENTS

—	Lower 1%	Lower 10%	Upper 10%	Upper 1%	Remarks
Whole blood					
Urea (mg per 100 ml)	12	16	35	47	Lognormal
Non protein nitrogen (mg per 100 ml)	25	29	43	51	Lognormal
Uric acid (mg per 100 ml)	0 6	1 6	3 9	4 9	Normal
Creatinine (mg per 100 ml)	0 1	0 1	1 2	2 6	Lognormal
Phosphate (inorganic as P) (mg per 100 ml)	2 0	2 4	3 5	3 9	Normal
Cholesterol (mg per 100 ml)	*115*	*140*	*215*	*265*	*Lognormal*
Glucose (mg per 100 ml)	55	68	96	109	Normal
Chloride (as NaCl) (mg per 100 ml)	*425*	*454*	*526*	*555*	Normal
Serum and plasma					
Sodium (m eq per litre)	133	137	148	152	Normal
Potassium ,, ,,	3 5	3 9	5 0	5 6	Lognormal
Calcium ,, ,,	4 5	4 8	5 4	5 7	Normal
Chloride ,, ,,	99	101	106	108	Normal
CO_2 combining power (m eq per litre)	24	25	29	31	Normal
Total protein (g per 100 ml)	6 3	6 7	7 7	8 2	Normal
Albumin (g per 100 ml)	4 0	4 4	5 3	5 7	Normal
Globulin ,, ,,	1 5	1 9	2 8	3 0	Negative skewness
Fibrin ,, ,,	0 1	0 2	0 4	0 5	Normal
Bilirubin (mg per 100 ml)	0 1	0 1	0 5	0 8	Lognormal
Cholesterol (mg per 100 ml)	*123*	*153*	*260*	*324*	*Lognormal*
Phosphate (inorganic) (mg per 100 ml)	2 4	2 9	4 1	4 5	Normal
Phosphate (ester) (mg per 100 ml)	*0 0*	*0 1*	*0 6*	1 7	Lognormal
Phosphate (total acid *soluble) (mg per 100* ml)	2 7	3 2	4 3	4 7	Normal
Phosphate (lipid) (mg per 100 ml)	7 0	8 3	12 6	14 9	Lognormal
Phosphatase (alkaline) (units)	3 3	4 5	9 5	12 9	Lognormal
Phosphatase (acid) (units)	0 8	1 2	3 1	4 6	Lognormal
Phosphatase (formol stable) (units)	0 0	0 0	2 1	4 1	Lognormal
Amylase (units)	71	91	163	209	Lognormal

The method is based on the use of the standing test, which has been used extensively here in controlling patients treated with hexamethonium bromide. *It is important that, during the trial period and while the drug action is at its height, patients should not go away from their homes or from some place in which they may lie down to counteract any hypotensive symptoms.*

The standing test consists in asking the patient to stand perfectly still for 60 seconds or until symptoms of hypotension develop. The test is made at the time when the maximum drug action is experienced.

With subcutaneous injections of simple aqueous hexamethonium bromide or of M. & B. 2050A the test may be made 30 minutes after the injection; but, if the patient thinks that the drug's action is greatest at some other time, the test may be made then.

With oral administration the test may be made $1^1/_2$ hours after the dose of hexamethonium bitartrate, or $2^1/_2$ hours after that of M. & B. 2050A, or at such time as the maximum effect is noted by the patient.

The patient is told that there is no need to make the test if faintness or weakness on standing, or a need to flop down and rest, is felt spontaneously after most injections. Such symptoms indicate usually that the blood-pressure has fallen to near normal or even to a hypotensive level. Even when no such symptoms arise spontaneously, they are likely to develop as the result of postural hypotension if the patient stands quietly for one minute, provided the dose is at or just above the ideal level. If the patient feels faint or inordinately languid on standing quietly, the sitting or lying posture should be resumed at once. If there is no faintness or other symptom of hypotension, the dose of methonium salt should be raised daily by a small increment until the patient experiences hypotensive symptoms either spontaneously or on the standing test.

The correct dose is the highest dose which just fails to induce hypotensive symptoms, either spontaneously or on the standing test. The adjustment of dosage level is delicate, the final doses being:

3·0–5·0 mg. below "hypotensive symptom-level" with hexamethonium bromide subcutaneously.

1·5–2·5 mg. below "hypotensive symptom-level" with M. & B. 1863 subcutaneously.

0·5 mg. below "hypotensive symptom-level" with M. & B. 2050A subcutaneously.

93–187 mg. below "hypotensive symptom-level" with hexamethonium bitartrate orally.

10–20 mg. below "hypotensive symptom-level" with M. & B. 2050A orally (occasionally with small-dose patients, 2 or 3 mg. of M. & B. 2050A orally may make a significant difference).

The initial doses of the various methonium salts and the dosage increments which have been found suitable are:

	Initial dose (mg.)	*Dose may be raised by increments of* (mg.)
Hexamethonium bromide aqueous, subcutaneously	15	5
Hexamethonium bromide dissolved in 25% polyvinyl pyrrolidone or 20% dextran (molecular weight 20,000–45,000) subcutaneously	20	5–10
M. & B. 2050A aqueous	3	0·5–1·0
M. & B. 2050A dissolved in 25% polyvinyl pyrrolidone with 1 in 1000 ephedrine hydrochloride	4	0·5–1·5
Hexamethonium bitartrate orally ($^1/_4$ tablet)	187	187
M. & B. 2050A orally	20	20

Where the patient is feeble, or over 70, or on a salt-free diet, or has had a sympathectomy, the initial doses and the increments by which doses are increased should be halved. When the response to the drug is controlled by all-day tests, increases of dosage may be somewhat larger.

The aim in most patients is to reduce the trough of the blood-pressure fall to as near normal as is practicable when the patient is in the sitting or the standing posture. We have usually been content with smaller falls of blood-pressure in patients with known coronary disease or with recent cerebral thrombosis. The time of occurrence of hypotensive symptoms, whether spontaneous or induced by the standing test, serves as an indication of the time after a dose when a doctor may arrange to see a patient and to measure the minimum blood-pressure in the standing and sitting postures. It must be remembered that the doctor and his sphygmomanometer are potent blood-pressure-raising stimuli (fig. 5) and the pressure may be above its true level on the occasion of a visit. If, however, the doctor will wait 10 minutes, avoiding conversation with the patient but measuring the blood-pressure at $^1/_2$–1 minute intervals, the emotional reaction will usually pass off, and a better indication will be obtained of the blood-pressure level in an unstimulating environment.

TABLE IV—ORAL DOSES (MG.) OF M. & B. 2050A ON WHICH PATIENTS ARE CONTROLLED AT PRESENT*

Case no. ..	297	293	13	332	306	129	162	60	323	207	309	328	337
Before breakfast	140	250	310	400	680	310	190	270	100	320	610	550	70
Before lunch ..	50	0	150	140	100	60	50	70	0	60	0	30	0
Before 5 o'clock tea	0	0	0	0	140	0	0	0	100	0	0	0	0
9 P.M.	70	175	0	190	0	130	130	250	0	260	270	500	70
11 P.M. ..	0	0	180	0	280	0	0	0	100	0	0	0	0

* Probably a small additional dose of 50–150 mg. before 5 o'clock tea would have been advantageous in most of these patients.

The dose of M. & B. 2050A must be raised at intervals to keep the blood-pressure down as drug toleration develops. It seems that, as with hexamethonium bromide, the dose of M. & B. 2050A finally becomes stable, with the result that no further increase is needed. However, even in patients whose dosage has become stable it has been found advisable to attempt small increases every few weeks or months, retreating to the same dose if the increase causes hypotensive symptoms either spontaneously or on the standing test.

The doses on which our patients on oral M. & B. 2050A are controlled at present are set out in table IV.

The injections of M. & B. 2050A with polyvinyl pyrrolidone 25%, and ephedrine hydrochloride 1 in 1000, are a convenient way of administering the drug. Equal doses are usually administered at intervals of about 12 hours.

We have found it of great value to provide patients with typescript instructions.

SUMMARY

A methonium compound, M. & B. 2050A, exhibits properties significantly different from those of hexamethonium bromide. Initial subcutaneous doses of M. & B. 2050A are about five times as active as initial doses of hexamethonium bromide, and the fall in blood-pressure lasts longer.

With M. & B. 2050A it seems that a good control over the blood-pressure without toxic manifestations can be obtained in a majority of hypertensive patients. In a few patients doses fully adequate to produce hypotension cause extreme mouth dryness, which is only partly relieved by carbachol 0·25 mg. by mouth.

Although control of dosage presents some new problems, M. & B. 2050A should prove superior for oral administration to hexamethonium bromide, pentamethonium bromide, M. & B. 1863, and Ciba 9295, provided that additional side-effects do not make their appearance with continued treatment.

In four months' continued administration toleration and cross-toleration do not develop to the same extent as they do with hexamethonium bromide, pentamethonium bromide, M. & B. 1863, and Ciba 9295.

The oral dose of M. & B. 2050A is much greater than the effective subcutaneous dose, but much smaller than the oral dose of hexamethonium salts. The comparative lack of side-effects during oral administration of M. & B.

RAT-BITE FEVER

REPORT OF A CASE DUE TO ACTINOMYCES MURIS

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RAT-BITE fever has two forms according to whether it arises from infection with *Spirillum minus* or *Actinomyces muris* (*Streptobacillus moniliformis*). Most of the earlier published cases were caused by *S. minus*, but recently an increasing number of cases caused by *A. muris* has been reported.

Infection, with either organism, usually follows the bite of a wild or laboratory rat; but the bite of a mouse, cat, dog, weasel, or squirrel has occasionally produced the fever. Rat-bite fever may also follow other minor injuries associated with any of those animals, and may even occur without a history of trauma or contact with animals. Place and Sutton (1934) reported an interesting outbreak, at the Massachusetts town of Haverhill (now eponymous), of *A. muris* septicæmia which appeared to be milk-borne. In the United States rat-bite fever has been reviewed extensively by Crohn (1915), Bayne-Jones (1931), and Brown and Nunemaker (1942). In England rat-bite fever is less common, and the earliest account of it is that of Horder (1910). Infection with *A. muris* is unusual in both countries, especially in the British Isles, where only 3 cases have been reported in which this organism was isolated (see table).

Early clinical accounts of rat-bite fever emphasised the long incubation period of two or three weeks, relapsing fever, rash, and recurrence of inflammation in the previously healed bite. More recently the variability of this incubation period and the common absence of many of these classical features have been reported, and the occurrence of arthritis often mentioned, particularly with *A. muris* infection, in which it may be a prominent feature and even cause permanent changes in the affected joints.

CASE-RECORD

A robust farm foreman, aged 50, was admitted to Addenbrooke's Hospital under Dr. L. B. Cole on May 28, 1951. A week earlier, on May 21, while destroying a rat's nest, he was bitten at the base of his left thumb. The wound was deep and bled profusely, but he did not dress it after the bleeding stopped; he had often been bitten by rats before. Three days later (May 24) he felt unwell, and the next day he was worse, with rigors. The next two days (May 26 and 27) he was ill in bed with fever, headache, and pain in the limbs. A rash developed on May 27, and he was admitted to hospital the following day.

On admission he appeared ill, with temperature 101°F (see figure) and pulse-rate 112. There was only a small healed puncture wound on the left thenar eminence at the site of the bite, and there were no enlarged axillary lymph nodes. A discrete pink macular rash was sparsely distributed over the whole body, including the palms and soles, and was most profuse about the knees and elbows. There was some tenderness of the joints but no swelling or redness of the skin over them. The spleen was not palpable.

Course

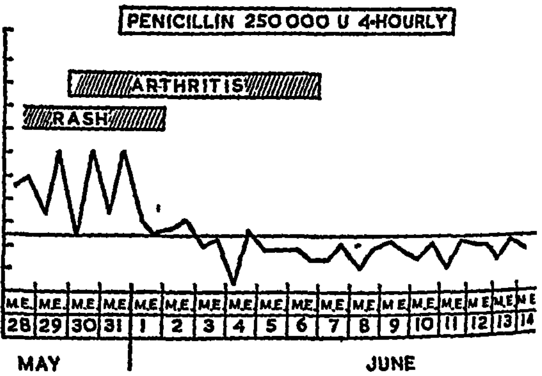
May 29.—The rash was fading, especially on the trunk; condition otherwise unchanged.

May 30.—The rash, at first discrete, had become confluent and blotchy, and was now confined to the skin over the knees, the right elbow and ankle, and the soles of the feet, with pustulation in some places; the left knee was painful and a little swollen.

May 31.—The rash now consisted of large red papules, with some purpuric areas in them. The largest papule, on the right ankle, was 1·8 cm. in diameter, with a pustular centre 0·4 cm. in diameter; the left knee was swollen and painful, and the right elbow painful, especially on movement. Rat-bite fever was diagnosed.

Treatment and Progress

A course of intramuscular penicillin 250,000 units four-hourly was begun at 6 P.M. on May 31. On June 1 the patient felt better. His evening temperature was 98·4°F, his right elbow was no longer painful, and the rash was less conspicuous. On June 2 the rash had completely faded, but the left knee was still tender. All pain and swelling had subsided five days later (June 7). There was no further fever, and the penicillin was stopped on June 11 after 15,750,000 units had been given in eleven days. The patient was discharged home completely well nineteen days after admission, and has remained well since then.



Treatment and symptoms in rat-bite fever

Laboratory Investigations

A white-cell count on May 29 showed 9100 per c.mm. (polymorphs 82%). A Widal reaction on May 29 was negative (titre less than 1 : 20) to *Salmonella typhi* H and O, *S. paratyphi B* H and O, and *Brucella abortus*. Wassermann and Kahn reactions on May 30 were negative. Thick blood films were examined for *S. minus*, which was not found.

Isolation of A. muris

The diagnosis of rat-bite fever was confirmed by culture of this organism from a pustule on the right knee, taken on May 31. A swab from the pustule was inoculated directly on to Loeffler's serum medium; after forty-eight hours there was a plentiful growth of small circular convex trans-

A. MURIS RAT-BITE FEVER IN GREAT BRITAIN

—	Symonds (1943)	Kane (1944)	Lominski et al. (1948)	*Present case*
Sex and age (yr.)	M., adult	M., 15	M., adult	M., 50
Occupation	Rat catcher	Schoolboy	Laboratory attendant	Farm foreman
Place	Belfast	Belfast	Glasgow	England
Source	Wild rat	Wild rat	Hooded laboratory rat	Wild rat
Incubation (days)	13	13	2	3
Local lesion	Slight at first, recurred with indurated lesion and adenitis	Healed quickly, no recurrence	Healing, no recurrence	Healed quickly, no recurrence
Rash	Absent	Absent	Present, but not pustular	Present, pustular in places
Arthritis	Absent	Absent	Right elbow	Right elbow and left knee
Organism	*A. muris* grown from axillary lymph node	*A. muris* isolated on blood-culture	*A. muris* isolated on blood-culture	*A. muris* grown from a pustule
Leucocyte-count	—	Leucopenia, lowest 1300 per c.mm.	Leucocytosis 10,400 per c.mm., polymorphs 85%	9100 per c.mm., polymorphs 80%
Therapy	Sulphanilamide	Penicillin 200,000 units in 2 days	Penicillin 12 million units in 2 days	Penicillin 15,750,000 units in 11 days
Result	Convalescence slow	Rapid recovery	Rapid recovery	Rapid recovery

on the length of the working period and the pressure in use (Boycott et al. 1908). These rates are based on calculations of the varying speed at which nitrogen is carried away from different parts of the body (Haldane and Priestley 1935). The working pressure at this stage of the construction of the tunnels was kept at about 34 lb. per sq. in. according to the state of the tide, which might require the pressure to be raised or lowered a few pounds. Two powerful compressors, later supplemented by other machines, were used to maintain the pressure required.

THE WORKERS AND THEIR SUPERVISION

The firm engaged in this work had had long experience in compressed-air operations; but, as the war had led to the dispersal of trained workers, men had largely to be recruited locally and were not always suitable. Hence there was a big turnover of labour. The experienced men available were mainly from the South of England.

Medical supervision was given by a local general practitioner, who advised on the suitability of men for the work on general grounds—e.g., whether they were physically fit or subject to sinus infection, obesity, or hypertension. He was also on call for any emergency. A first-aid room and an adjacent medical lock for treatment of "bends" were a short distance from the shaft, and two trained orderlies were in charge of this. The medical lock was similar in construction to the man lock but contained a couch. It was entered from outside through a small chamber with airtight doors which allowed a first-aid man or a doctor to get in or out while the lock was in use. At the other end there was a smaller chamber through which food could be passed. The medical lock had a high-pressure air-supply independent of that for the shaft.

TREATMENT OF BENDS

Three recompression methods for the treatment of bends were used at this time, and their relative merits are discussed elsewhere (Medical Research Council 1953). These methods differed in detail, but the principle was to compress the patient to a few pounds above the working pressure in the tunnel, and to keep him at this pressure for ten minutes. If the symptoms were not relieved as soon as this pressure was reached, he was held at it until ten minutes after the disappearance of symptoms. A normal decompression according to the schedule was then carried out as though the exposure to pressure had been for a period greater than four hours.

From the records kept of the use of the medical lock at Howdon the weekly incidence of bends was analysed by a Medical Research Council unit investigating decompression illness. The rate was not unduly high at first, and the works agent confirmed that in his experience the numbers were no greater than usual. Among experienced workers the incidence was about 1·5% of decompressions, and amongst new starters slightly higher. On a few occasions the incidence rose to 3% or 4% of decompressions, but this was probably due to the large turnover of labour and the high proportion of new starters.

CASE-RECORDS

Case 1.—A foreman, aged 45, with considerable experience of compressed-air work, in which he had been employed for about fifteen years, had been working at Howdon for three weeks on alternating weekly day and night shifts. In the course of a shift it was usual for him to enter and to leave the shaft several times; hence he was in high pressure for frequent short periods. At various times in the past he had experienced minor attacks of bends without any serious results. On July 6, 1948, he had spent about two hours underground at a pressure of 34 lb. per sq. in., for which a decompression time of forty minutes is necessary after the first reduction of pressure to about 9 lb. For some reason, however, he wished to see the chief engineer urgently, and, instead of entering the "man lock" to be decompressed in the ordinary way, he came out through the materials or "muck" lock, taking probably only a few minutes.

About a quarter of an hour later his legs became numb and weak, and he had to be assisted to the medical lock, where the pressure was at once raised to 40 lb. per sq. in. Decompression by the method described for bends was attempted five times unsuccessfully. Retention of urine necessitated catheterisation by the works doctor, and the patient was admitted to hospital sixteen hours after the onset of paralysis, when it seemed evident that further compression would not make him any better.

He was well built, bluff, and over-confident, and maintained throughout an optimistic attitude to his illness.

On examination there was paralysis of both legs, and the bladder was distended as far as the umbilicus. The cranial nerves were normal, and the arms and upper part of the trunk appeared unaffected. The abdominal reflexes were absent, and in the lower limbs the tendon-reflexes were brisk and equal and there was left ankle-clonus. In both feet the plantar reflexes were extensor, and sensation to pin-prick was absent in the legs and abdomen up to the umbilicus (T_{10}). Vibration sense was absent in the legs and iliac crests, and he was incontinent of fæces. His pulse-rate was 56 and blood-pressure normal, and there were no abnormal signs in other systems.

Treatment and Progress.—He was catheterised soon after admission, and afterwards eight-hourly by a strictly aseptic technique. He received daily injections of carbachol, and a course of sulphadimidine was given as a prophylactic against urinary infection. By the evening of the day of admission some movement had returned to the left leg and to a very slight degree in the right; and from then on there was a gradual return of power and sensation. It was necessary, however, to continue catheterisation for a further month and finally to leave the catheter in place for 24-hour periods. Slight urethritis was the only complication, but at no time was there any pyrexia.

A month after admission the patient had recovered the use of his legs sufficiently to move about the ward with assistance; but although he had partial control of his bladder he was still incontinent of fæces. His right leg was wasted and relatively weak, coördination of the lower limbs was poor and vibration sense absent, and right patellar clonus and extensor plantar reflexes were still present. A course of Fraenkel's exercises was given, and he was encouraged to use his legs as much as possible. He was discharged six weeks after admission, because he was anxious to return to his home in London. He still had poor coördination of leg movements and a grossly abnormal gait which required the use of crutches. Some fæcal and urinary incontinence remained, and for the latter he wore an absorbent apparatus.

Follow-up.—In July, 1949, a year after the incident, he reported that his condition was much the same, and that defective control of defæcation led to periods of constipation followed by diarrhœa. Urinary incontinence made it necessary to continue wearing the absorbent bag. He was now using a motor-propelled invalid chair. In February, 1953, his condition was much the same.

Case 2.—A fitter's mate, aged 29, had worked for four and a half months at Howdon, which was his first experience of compressed-air work. He had previously been quite healthy, but since starting this work he had experienced two or three minor attacks of bends. On one occasion he said, he had lost the use of his legs for a short time without any residual disability. This incident was either not reported or had little attention paid to it.

On Nov. 11, 1948, he worked a $3\frac{3}{4}$-hour shift at a pressure of 34 lb. per sq. in., and was being decompressed in the man lock together with some other men. At the end of the phase of rapid reduction he complained of numbness about the left elbow and of feeling faint. His companions signalled for decompression to be hastened, and atmospheric pressure was reached in about thirty minutes instead of seventy-six minutes according to the schedule. At first he moved about a little and was thought to be dozing, but on completion of decompression it was evident that he was unconscious.

He was taken immediately to the medical lock and recompressed to 38 lb. per sq. in., with the result that he recovered consciousness. He vomited and moved his legs a little but

Reviews of Books

Essentials of Medical Diagnosis

2nd Ed Lord Horder, M D Lond , F R C P , and A E
Gow, M D Lond , F R C P , consulting physicians,
St Bartholomew's Hospital, London London Cassell
1952 Pp 462 22*s* 6*d*

It is almost 25 years since the first edition of this book appeared Written then for the junior student starting work in the medical wards, it still offers a practical and thorough guide to methods of clinical examination based upon long experience and ripe wisdom Lord Horder and the late Dr Gow have wisely preferred to describe the methods actually employed by the practising physician, rather than to seek some theoretical or academic approach which may be little used They emphasise the need for careful examination of the patient, accurate observation, and detailed search for particular signs which a tentative diagnosis may specially require The student will find all he needs for his daily ward work, but elaborate laboratory techniques have been deliberately omitted

As a basic foundation for clinical diagnosis this book will reward the study and attention of senior as well as junior students It is of convenient size and well indexed

Posture and Pain

Henry O Kendall, director, physical therapy department, Children's Hospital School, Baltimore , Florence
P Kendall, assistant director , Dorothy A Boynton,
physical therapist London Baillière, Tindall, &
Cox 1952 Pp 204 54*s*

In this country the student is taught that the control of posture is primarily a function of the central nervous system, the locomotor apparatus (comprising the bones, joints, and muscles) being the machinery by means of which this function is effected , that those parts of the nervous system responsible (usually referred to for convenience as the postural centres) work by habit, these postural habits being the result of the development of conditioned reflexes , and finally that postural habits can only be altered by re-educational methods designed to develop new ones Postural defects may therefore be the result either of faulty habits of the controlling postural centres, or of mechanical defects in the machinery itself

In any treatise dealing with this subject a consideration of both factors might be expected This work, however, deals exclusively with those postural abnormalities which are the result of defects in the machinery, especially paralysis, and nowhere is there any indication that the central nervous system is also concerned It follows that the methods of treatment advocated consist solely in massage, passive stretchings, and exercises designed to strengthen weak muscles Within these limitations the various deviations from the normal that are encountered in clinical practice are well presented, together with the structural abnormalities that may be associated with them, and the methods of examination by which these factors can be assessed Good photographs and diagrams support the text, and the arguments are logical and convincing The criteria laid down for the normal, the methods advocated for assessing deviations from the normal, and the structural abnormalities that may be associated with such deviations, might well be accepted as standards

Die Angiographie zur Erkennung, Behandlung, und Begutachtung peripherer Durchblutungsstorungen

Dr Med Habil H W Pässler, *chief doctor of the*
Municipal Hospital, Leverkusen Stuttgart Thieme
1952 Pp 115 D.M 29 70

This monograph to some extent belies its title in that it essays to cover the whole field of peripheral vascular disease, including the ætiological, pathological, clinical, and therapeutic features as well as the angiographic As regards radiology the text is lucid and concise and the reproductions of angiograms are really good The clinical descriptions are brief and reasonably accurate, but betray a lack of the sort of physiological background that Sir Thomas Lewis brought to this subject Indeed the bibliography contains no reference to Lewis, although his name is mentioned as an eponymous attachment to the "hot box." Many of the views concerning ætiology and pathology would find little support in this country for instance, Raynaud's disease is attributed to structural changes in autonomic ganglia

Dynamic Psychiatry

Editors Franz Alexander, M D , and Helen Ross
Chicago University Press London Cambridge University Press 1952 Pp 578 75*s*

This volume contains contributions from some of the foremost American psycho-analysts, *from psychiatrists* from a psychologist, and from an anthropologist It is edited by the director of the Institute for Psycho-analysis in Chicago, who himself contributes three chapters, and by his administrative director

The first part of the book is concerned with psycho analytic theoretical concepts The growth of interest in transference phenomena, which has led American analysts increasingly to try innovations in technique, is discussed, and there is a good account of the contrast between Freud's "associative interpretation of dreams and the "problem solving" theories of Maeder Psycho analytic theories of personality development are well outlined by Dr Therese Benedek The second part of the book deals with clinical psychiatry, including the neuroses, acute neurotic reactions, emotional disorders of childhood, the contributions of psycho-analysis to the study of the organic cerebral disorders and the psychoses, and the principles of psychiatric treatment This part of the book is more even, and the chapter on contributions of psycho analysis to the study of the psychoses is especially good The third part of the book examines the influence of psycho analysis on allied fields—psychosomatic medicine, social anthropology, clinical psychology, animal psychology and general current thought

The final chapter gives some idea of the spread of psycho analytic theories in the United States, where 70% of all psycho analysts are teaching in medical schools and hospitals schools for social work, and allied fields The popularisation of Freud's theories, and their apparent acceptance by the U S Army medical authorities, the churches, and Hollywood, is not without its dangers This volume, despite its title is singularly lacking in dynamism, but it gives a useful survey of what looks like becoming—anyhow in America—the new orthodoxy

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Surgical Care *A Handbook of Pre Operative and Post Operative Treatment* (2nd ed London Butterworth 1952 Pp 422 37*s* 6*d*) —The early chapters of Mr Ronald Raven's interesting book are short monographs on the big general problems presented by the surgical patient—shock, hæmorrhage, fluid balance, and the like—and these are admirable The remaining three quarters of the book gives details of the preoperative and postoperative care applied to the various regions of the body, and to the individual operations which are done This is a herculean task for so small a book, and it is inevitable that the author should discuss only the methods he uses himself This is interesting for the widely read surgeon who wants to know how Mr Raven achieves his undoubted success, but is not so valuable for an apprentice, who may be asked to describe alternative methods Such detailed descriptions do not lend themselves to continuous reading, but for the aftercare of more unusual operations the book is a valuable work of reference It ends with short chapters on the specialties

Some Religious Illusions in Art, Literature, and Experience (London Watts 1953 Pp 104 10*s* 6*d*) —The illogical and irrational elements in traditional accounts of Heaven, of immortality, and of Hell, lead Sir Ernest Kennaway, F R S , to dismiss these concepts As one would expect, much learning lies behind his brief essays He seems to take no account, however, of a developing vision, such as he would presumably allow to modern scientists as compared with, say, Heraclitus Explanations satisfying to the Early Church, yet rejected by later thinkers, seem insufficiently explored He would probably have little use for any evidence from the senses, apart from the intellect , but is there nothing true in human life except what can be proved ? Surely he would allow for honest doubt, which has a place in science as in religion ? The subjects of the 19 plates (4 coloured) include a village cricket field and Stonehenge, and reproductions of famous masterpieces of art They aptly illustrate the range and mixture of the interesting text fit on general grounds. Because of the risks inherent in the work it seems desirable also to demand a good standard of intelligence; but this seems to be a counsel of perfection. As the work is hard, and working conditions are bad, workmen of the right degree of physical fitness are difficult to attract, and there is little opportunity for selecting the most intelligent. The men should also be temperamentally suitable and psychologically stable, for some of them may use the medical lock too frequently through undue anxiety over minor aches and pains, due perhaps to causes other than bends.

There seems to be no means of picking out men unduly susceptible to compressed-air sickness other than by recording the effects of actual work on the job, because individual susceptibility varies from day to day and from week to week. It is reasonable, however, to remove a man from this type of work when he is having comparatively frequent incidents following correct decompression. This requires careful recording of all degrees of bends in each workman but has the disadvantage that it depends on the man's own statement that he has had them, for he may conceal an attack if he wishes.

The medical supervision likely to be available for this type of work will usually be the nearest general practitioner who is prepared to give the necessary time to it. As very few practitioners will have had any practical experience in dealing with compressed-air illness, some assistance by a physician familiar with the condition would be an advantage at the start of the work. He would be able to advise the practitioner on the detailed management of mild and severe cases and on the selection of men for the work, and also to stimulate interest in its problems. It should be possible to have a panel of experts in each area, one of whom could be called on in the initial stages of this type of work wherever it was being done. Supervision of the training of orderlies and first-aid men could also be the panel's responsibility.

MANAGEMENT OF SEVERE CASE

Where a patient remains paraplegic after proper decompression, treatment is the same as for other cord injuries causing paraplegia: it is directed to avoiding urinary infection, preventing bedsores, preserving any remaining muscle function, and retraining it. In case 2, where the respiratory muscles were affected, a lung infection had to be treated. When everything has been done to ensure maximum recovery of function of the limbs, rehousing on one floor and provision of invalid chairs may enable the patient to get about with little extra help. An absorbent bag will often be necessary if there is urinary incontinence, and, if defæcation is affected, visits from the district nurse to give enemas every few days will be necessary. Prospects of employment will depend very much on what is available locally and on the degree of recovery taking place in the few years after the accident.

It makes an interesting contrast in prognosis to refer back to a case of compressed-air illness which occurred on Tyneside during the construction of the high-level bridge across the Tyne in 1904:

> An electrician, aged 27, who had been working at a pressure of 25 lb. per sq. in. for four and a half hours, was decompressed in three minutes. Within ten minutes of leaving the caisson he became comatose for about three hours, and when he recovered consciousness his arms and legs were paralysed. The arms recovered in a day, but he was left with a spastic paralysis of his legs. Within three days he developed bedsores and a urinary infection, from which he died sixteen months later.

This was the most severe of 5 cases of the disease seen at the Newcastle Infirmary at this time (Parkin 1904). Sulphonamides and antibiotics, together with improved nursing, have much improved the outlook in these cases.

SUMMARY

Two cases of compressed-air illness, leading to paraplegia and severe disability, are reported. One man was an experienced compressed-air worker, the other a novice, and the differing circumstances in which each accident arose are described. In both cases recompression in the medical lock was not maintained long enough—i.e., for at least twenty-four hours.

As compressed-air work is done sporadically and few practitioners are familiar with the illness, it is suggested that a panel of doctors with experience of the work should be available in each area, to give advice on the selection and medical supervision of the men.

We wish to thank Prof. R. C. Browne for help with this paper; members of the M.R.C. unit investigating decompression sickness for some of the data; and Prof. F. J. Nattrass for permission to publish the cases.

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TILTING TABLE-TOP FOR ABDOMINO-THORACIC APPROACH TO STOMACH AND ŒSOPHAGUS

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The technique of resection of upper gastric and lower œsophageal carcinomata, with restoration of continuity by bringing up the stomach remnant or the jejunum—to establish an œsophagogastrostomy or œsophagojejunostomy in the chest—was conceived independently by Ohsawa (1933) and by Adams and Phemister (1938), and was subsequently popularised in America by Churchill and Sweet (1942) and in this country by Brock (1942), Thompson (1945), Allison (1946), and Tanner (1946). For these operations an entirely transthoracic transdiaphragmatic approach through the left chest was at first often used, but in recent years most surgeons have preferred to prolong the incision into the abdomen to make an abdominothoracic approach. This has the advantage of improving the access to the pyloric end of the stomach, a point of special importance if it is necessary to do a total gastrectomy with closure of the duodenal stump and œsophagojejunostomy. Also, if the abdominal part of this incision is made first, as recommended by Garlock (1946), the surgeon can explore the abdomen with one hand and perhaps reach a decision regarding the unsuitability of the growth for resection without having to inflict on the patient the possible complications of a major thoracotomy. Noland Carter (1947) has listed the various modifications of the abdominothoracic incision that have been advised by different authors.

In making an abdominothoracic incision it is customary to have the patient lying on his right side, with the transverse axis of his body tilted backwards some 15° or more to the vertical (see *Lancet* 1947). Usually this position is achieved by propping the patient up with sandbags, and fixing his left arm in an elevated abducted position above the head. I have found it a matter of some difficulty, particularly in dealing with a well-built person, to secure really stable positioning of the patient in this way. Also I have had it very reviewed by **Davis** and **McDermott**[4] The fear that too small, and therefore ineffective, dosage will favour emergence of resistant strains is well founded, and no doubt partly explains the trend towards ever larger doses, which also have a convenience in reducing the number of injections But if these methods are now proved to produce resistant strains we must work out the right dosage **Gould, Bowie**, and **Cameron** challenge us to think again about how best to use antibiotics This duty may involve us in more quantitative work than we have hitherto accepted as necessary, but we should not regard this as too great a price to pay for keeping our miracle drugs in good working order

Patterns of Disease in Childhood

In the second issue of the new *Australasian Annals of Medicine* Sir **MacFarlane Burnet**, F R S,[5] reviews the physiological and immunological factors underlying the patterns and outcome of infective disease He recognises that the biologist has difficulty in gathering material, because ascertainment and notification are seldom complete the illness may be atypical, or it may be hard to decide when an abortive attack becomes notifiable, or the ratio of subclinical to clinical attacks may vary Moreover, **Burnet** is not content to represent the passage of time on an arithmetical scale, since this conveys no idea of "biological time" Roughly speaking, the rates of bodily processes are inversely proportional to age, and the curve of mortality at different ages from birth to 70 years is symmetrical on a logarithmic scale, with the lowest point between 10 and 12 years This accords with clinical experience, which shows that resistance to severe infection is greatest at about this age whereas it is lowest in the very young and very old if one must have generalised peritonitis, 10 years is the age of choice The steep fall in death-rates up to the age of 10–12 years is also evident in the figures for such diseases as measles, pertussis, diphtheria, mumps, and influenzal meningitis, for some infections, such as influenza and measles, there is afterwards a temporary rise in young adult life **Burnet** concludes that non-specific resistance increases from birth up to 10 or 12 years, that this increasing resistance may be partly overcome by the specific damaging effects of a particular infection (e g, diphtheria in a non-immunised community), and that after adolescence there is diminishing resistance with a secondary peak of mortality from respiratory infection at 25–30 He suggests that the childhood increase in non specific resistance is related to the increasing capacity of the young organism to regulate the control mechanisms of the body in the presence of adverse factors Under favourable circumstances the infant learns, by a series of minor adventures with micro-organisms of low virulence, how to meet the more dangerous infectors encountered in later childhood or adult life Thus the young organism needs a sheltered, but not too sheltered, environment in which to gain immunological experience to fit it for life in a potentially hostile environment

The age-distribution of notifiable infectious diseases is influenced not only by variations with age in the pattern of disease but also by (1) the relation of age to opportunity for infection, (2) the changing ratio with age of clinical to subclinical infections, (3) the influence of past infection in modifying the reaction that produces specific immunity to infection, and (4) the development with age of non-specific immunity Poliomyelitis is never far from **Burnet**'s thoughts, and he illustrates the variations in the age distribution of this disease by referring to epidemics in three different communities In Malta, a crowded urban community normally saturated with poliomyelitis virus, with much subclinical infection in the first three years of life, clinical attacks in the epidemic of 1942–43 were virtually confined to patients below the age of 10 In Melbourne (1937) the number of cases increased for each year of age from 2 to 10 and, though it then fell, there was a significant number of clinical cases in young adults On St Helena (1947), a "virgin soil" community, the peak was in young people aged 10–20 years

Burnet contrasts the different approaches of the medical statistician and the practising doctor in this field, remarking on the unpredictability of the single incident and the regularity of occurrences in the aggregate Surely, however, we may question whether such a comparison gives a fair picture To understand the response of the host to infection at different ages and under different circumstances we need to synthesise many techniques, including that of the practising doctor who is in a position to detect the variation of illness with age There can be no doubt that studies of the natural history of disease and its variation with age, sex, occupation, and genetic inheritance should be one of the chief disciplines of clinical medicine **Spence**[6] has emphasised this in relation to the newborn, and **Thomson**[7] in relation to old people The need is illustrated in the Newcastle morbidity survey, which shows that the real incidence of whooping-cough in the first year of life is three times that notified Another example[8] is the famous family epidemic in which the same pathogenic streptococcus produced in a single household four different clinical illnesses, only one of which would have been notifiable as streptococcal infection The work of **Burnet**[9] himself, and of **McNair Scott**[10] on primary herpetic stomatitis, indicates the need to teach the natural history, as distinct from the topographical description, of infection

Inaccuracy in the Laboratory

Sir **Henry Dale**[11] has pointed out that during the past ten years there has been "a growing use in the clinic of objective physical measurements and chemical analyses", and he has also referred to "the need to control the significance of a large part of medical evidence by statistical methods" His views are being ever more widely accepted, despite the opposition of those who fear the displacement of hard-won clinical experience by the cold logic of the statistician On another page of this issue, Dr **Wootton** and Professor **King** provide a statistical framework for interpreting the results of blood analyses These workers rounded off their study by seeing how far their results are

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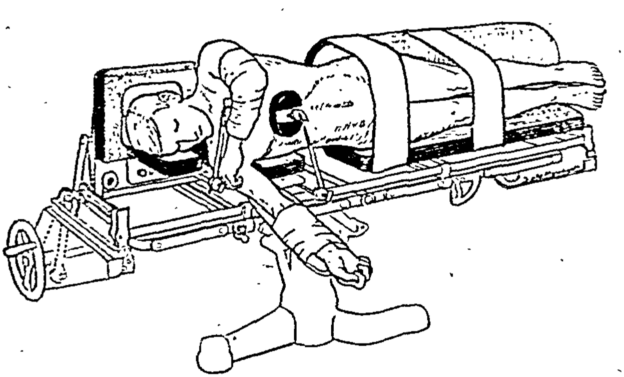

Fig. 4—Tilting table-top with patient tilted to 90° with the horizon.

other end is fixed to the free corner of the upper leaf. As the box nut cannot revolve, rotation of the vertical spindle, produced by winding the wheel on the horizontal shaft, moves the nut up or down on the spindle. This in turn raises or lowers the elevating shaft and the free edge of the upper leaf of the table-top. It is important to note that the attached edge of the upper leaf of the table is fixed to the lower leaf by means of a roller spigot which moves in a grooved bracket so that, while the free edge is being elevated, the hinged edge is gradually dragged towards the opposite side of the table, at which the surgeon is standing (figs. 2–4). The gearing is so arranged that the movement of the table is slow and smooth, and the winding of the wheels calls for little effort.

THE TILTING TOP IN USE

The patient is placed directly on the tilting table-top *without an intervening stretcher canvas.* The three components of the top leaf, which were already roughly adjusted in position to suit the patient's size, are now moved as required to ensure that the tail end of the head piece supports the top of the shoulders, and the head end of the body piece comes to the top of the buttocks (fig. 5). The side chest and head pieces are next adjusted so that the chest and head will be maintained in position during tilting; the former is usually fixed opposite the middle four right ribs for a left abdominothoracic approach. The front chest pad is now attached to the side chest piece in correct position, and the arms are placed on their rests. Finally the pelvic region and legs are fastened to the body piece by webbing belts.

The patient is tilted almost into a full lateral position, and the skin of the abdomen and chest is painted with iodine. Sterile towels are applied, and posteriorly these are fixed close to the midline of the back of the chest and loin, not with towel clips, which might be crushed when the patient is put flat, but by skin stitches. The table-top is now turned down into a full supine or slightly tilted position for starting the operation (figs. 3 and 6). The abdomen is opened usually by a small transverse incision crossing the upper part of the left rectus muscle and abutting on the left costal margin at the 8th or 9th costal cartilage. The operability of the growth is established as far as possible on exploration of the abdomen, and a decision made whether a purely abdominal or an abdominothoracic approach is required; the incision is accordingly prolonged into the right epigastrium or the left chest or both.

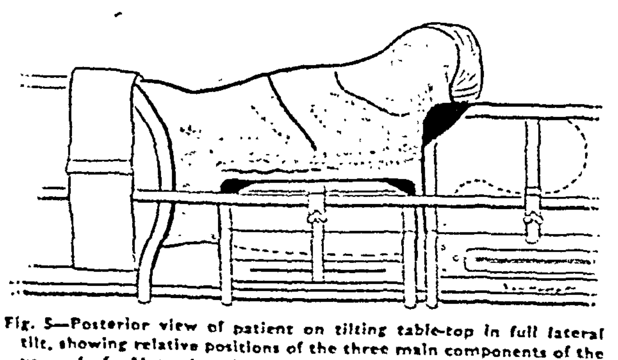

Fig. 5—Posterior view of patient on tilting table-top in full lateral tilt, showing relative positions of the three main components of the upper leaf. Note that the head piece only touches the top of the shoulder, giving free access to the whole of the posterior aspect of the left hemithorax.

If an abdominothoracic total gastrectomy or a resection of cardia and distal œsophagus is to be done, the table is put practically flat for the pyloroduodenal phase of the resection (fig. 2), but this may not be necessary if a proximal gastrectomy only, with preservation of the pyloric part of the stomach, is to be undertaken. After this part of the dissection has been completed, the table-top is turned into a 60 to 90° tilt for the remainder of the operation (figs. 3 and 4). For the final œsophagogastrostomy or œsophagojejunostomy it is best to have the patient in a full lateral position; otherwise the heart overhangs the anastomoses and makes suturing more difficult.

If a purely abdominal total or subtotal gastrectomy is decided on, the ability to tilt the patient is not wasted, because once the duodenum has been divided and closed a 60 or 70° tilt of the patient is ideal for the remaining parts of these operations. The mobilisation of the greater curve of the stomach by division of the short gastric vessels is greatly facilitated because the tilt causes the small gut to gravitate into the right half of the abdomen out of the crevice between the spleen and the stomach. If it is planned to combine with a total gastrectomy the Allison manœuvre of removing the spleen and tail and body of pancreas en bloc with the stomach, the tilt will be of very great assistance; indeed without it the approach to the posterior aspect of the spleen and pancreatic body through a purely abdominal incision may be a matter of some difficulty.

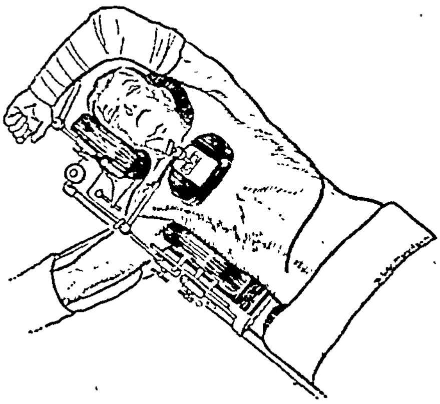

Fig. 6—Position of patient as seen by surgeon for start of laparotomy for gastric carcinoma.

It may, I think, fairly be claimed for this appliance that it helps the surgeon to maintain an eclectic attitude towards the treatment of carcinoma of the stomach which, in the present uncertain state of our knowledge of the relative efficacy of the different types of gastric resection for carcinomata in different parts of the stomach, seems highly desirable. From clinical and radiological examination it is often difficult to determine the precise extent of a growth of the stomach and to decide before operation whether the case can best be treated by a high subtotal gastric resection or by an abdominal total gastrectomy, or whether an abdominothoracic total or proximal partial gastrectomy will be required. As the best position of the patient for these various operations differs somewhat, it may be a source of difficulty and annoyance if the preoperative plan of campaign has to be altered in the light of the findings at laparotomy. With the tilting top, however, the surgeon can readily that ergometrine maleate and ergotamine tartrate are official, and iodoform has been supplanted by more efficient antiseptics It is interesting to see the deletion of a number of preparations introduced only a few years ago, to make way for preparations which represent a further stage of development in the practice of medicine or in the science and art of pharmacy The injection of pituitary (posterior lobe) is replaced by two injections—one of vasopression and one of oxytocin Liquid extract of liver is replaced by the injection of vitamin B_{12} or cyanocobalamin Œstradiol dipropionate, hexœstrol, and œstrone are also deleted, but æthinylœstradiol retains the place it gained in the addendum to the *B.P 1951* Other notable newcomers are aureomycin hydrochloride, bacillus Calmette Guérin vaccine, bentonite, decamethonium iodide, ethyl biscoumacetate, folic acid, helium, injection of dimercaprol, injection of globin insulin, injection of procaine benzylpenicillin, methadone hydrochloride, and phenadoxone hydrochloride

It is easy to justify the deletion of the toxic analgesic, amidopyrine, and that unsatisfactory hypnotic, sulphonal On purely medical grounds, however, it is less easy to account for the disappearance from the *Pharmacopœia* of diamorphine Many surgeons believe that there is a place for diamorphine in the postoperative management of the abdominal case, and something can be said in its favour in the short-term treatment of a patient with an intractable dry cough The danger of addiction to diamorphine is real, but in the United Kingdom this is hardly likely to be so serious as to merit deletion of the drug from the *B P* Perhaps the real reason must be sought in administrative expediency and measures calculated to facilitate the international control of drugs of addiction

The commission are to be congratulated on this new edition, which comes into force on Sept 1

TWINS OF UNEQUAL AGE

In Sydney a 24-year-old woman is reported to have given birth to twin sons at an interval of fifty six days At birth the first weighed 3 lb 10¾ oz and the second 5 lb 14¾ oz, by the time the second was born the first had grown to 6 lb 5¼ oz[1]

Unusual delay in the birth of a second twin has been recorded quite often, especially in the 18th and early 19th centuries when obstetricians were handicapped by the conventions of the period and there was apt to be a lack of scientific accuracy Twins were born to an Irish woman in 1880 with an interval of forty-four days The first was born about a fortnight before it was expected, though small it seemed healthy, but it died in six hours The second was a fine well grown baby who, with the mother, did very well[2] The case was described in 1846 of a Strasbourg woman who bore term infants on April 30 and Sept 17 of the same year, at necropsy she was found to have a single uterus In 1808 a Palermo woman was delivered of term infants eighty-two days apart

Studdiford,[3] who cited these cases, concluded that up to 1936 there had been no convincing record of superfœtation—by his definition, the implantation of a second fertilised ovum in a single uterus already containing a pregnancy of at least one month's duration Many would agree with this view Theoretically, superfœtation is possible only so long as the membranes of the first fœtus have not come in contact with the uterine wall It is therefore not possible after the third month[4] Gaupin,[5] however, claimed a case of superfœtation in a woman delivered on the same day of fœtuses of six and eighteen weeks' development, in his opinion a second fertilisation took place when the original conception was of about twelve weeks' duration A much more usual cause is a double uterus, which may carry a fœtus in each side, as in the case of a woman who gave birth to a fully developed child five and a half months after she had delivered one of seven months In another case of the same type a woman gave birth three months apart to two well-formed fully developed boys[6]

The most engaging recorded case of delay concerns a Birkenhead woman who in 1822, in her fifth pregnancy, was taken in labour at the seventh month of gestation A little girl was born, and as the pains persisted a "veteran accoucheur" was called in to advise The woman stated at the time that she was positive there was another child in her womb, and she there and then booked the accoucheur to attend her again at the end of two months He smiled tolerantly, promising to send her an anodyne, and she quickly returned to her busy household duties Exactly two months from the first birth she was delivered in his presence, and to his astonishment, of another living child The first child survived only a few months, but the other child and the mother were living twenty years after the event[7]

BRAIN CHANGES IN ELECTROCONVULSION THERAPY

Therapeutic trauma to the nervous system has become increasingly fashionable At the periphery percussion and vibration of painful neuromata, and at the centre leucotomy and induced convulsions, have proved sufficiently effective to ensure their continued trial in treatment Their effects, however, are not always entirely beneficial, and the anatomical or physiological changes which mediate the results are often uncertain This is true of therapeutic convulsions, which have been practised in psychiatry for over two decades

Originally given by means of an intravenous convulsant drug such as leptazol, seizures are now almost always electrically induced Moreover, the convulsion is deliberately curtailed or abolished by drugs which block motor impulses either centrally or at the motor neurone junction, so electroconvulsion therapy (E C T) now often consists simply in the passage of a controlled electric current through the brain in such a way as to produce loss of consciousness or narcosis There may be a brief tonic stiffening or myoclonic jerk, but the full grand-mal convulsion which used to be part of the treatment no longer occurs Nevertheless, such treatment may possibly impair cerebral structure and function Consequent memory defects, usually transient, of a type seen in other organic cerebral deteriorations, suggested that repeated E C T might result in organic damage—a possibility that cannot have escaped anyone witnessing the treatment in its more primitive forms Studies of memory and intelligence in patients before and after such treatment have never revealed any striking changes, but the kind of illness in which it is used has of course made assessment difficult

Anatomical studies in animals have yielded conflicting results Petechial hæmorrhages in the brain early after shock have been found fairly constantly, but when the animal is not killed until some days or weeks later no distinct histological changes may be found, though both nerve cell and glial changes have been noted Recently Hartelius[8] has described his observations with E C T in cats He has been at great pains to control both his material and technique and also his histological observations For that reason the changes he has observed, though slight, can be taken as definite He reports ognormal type of curve (Gaddum 1945). This finding ias made it necessary to return to the use of ranges, ind two separate ranges have been calculated for each onstituent. The inner range includes 80% of normal indings and values falling outside this are suspected of ibnormality; the larger range includes 98% of normals, ind a correspondingly greater weight can be attached to values falling outside it.

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[1] *Manchester Guardian* Feb 13, 1953
[2] Carson J C L *Brit med J* 1880, 1 242
[3] Studdiford W E *Amer J Obstet Gynec* 1936, 31, 845
[4] Browne F J Antenatal and Postnatal Care London, 1951 p 171
[5] Gaupin, C E *Amer J Obstet Gynec* 1951, 62, 212
[6] De Lee J B, Greenhill J P Principles and Practice of Obstetrics London 1947, p 420
[7] Vale, J T *Lancet*, 1843 1 577
[8] Hartelius, H *Acta Psychiat Kbh* 1952, suppl no 77

The original work on this subject has been confirmed and extended, and the accompanying table includes all the constituents so far examined. Each value is based on 50–100 analyses done by the methods used in this laboratory (King 1951). The subjects, of either sex, were aged 18–50 and were not known to have any systemic disease. They had fasted for at least four hours before the samples were obtained.

INTER-HOSPITAL DIFFERENCES

To determine whether the table was applicable to other hospitals, it was necessary to examine the agreement shown between different laboratories examining the same specimen. This has been done with two samples. The first was whole blood preserved in acid citrate-glucose solution and containing added streptomycin. It was analysed in 21 laboratories attached to different types of civil and service hospitals. Six commonly determined constituents were requested, but not all the laboratories were able to perform all six analyses. The results are shown in fig. 1, each result being indicated by a dot. The scale has been calculated so that 100 is equivalent to the mean of all the available determinations; thus each individual result is shown as a percentage of the mean.

Since we had no way of deciding what were the true values of the constituents of this sample, the experiment was repeated with the substitution of an accurately prepared solution of inorganic salts. The results, provided by 36 laboratories, are shown in fig. 2, where 100 on the scale represents the theoretical value calculated from a knowledge of the constituents of the solution.

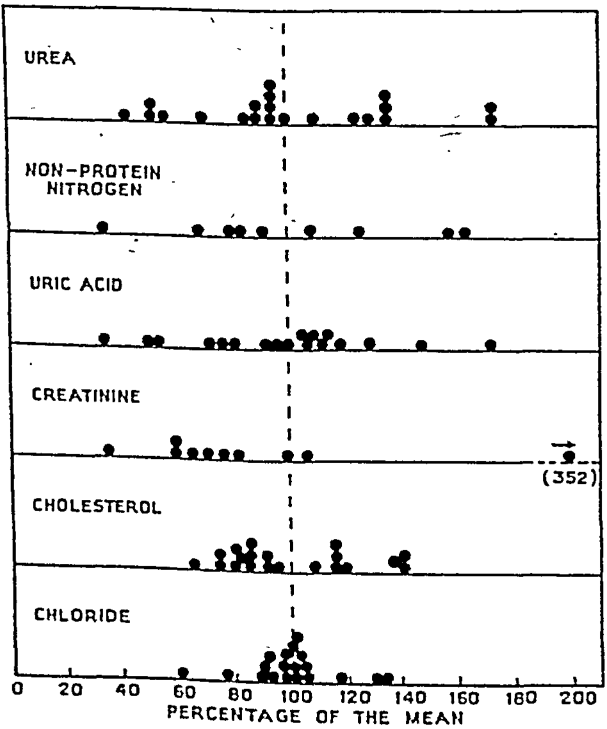

Fig. 1—Results obtained by different laboratories on a single specimen of blood. Each result is represented by a dot, and the scale is arranged so that the mean value of all the laboratories equals 100.

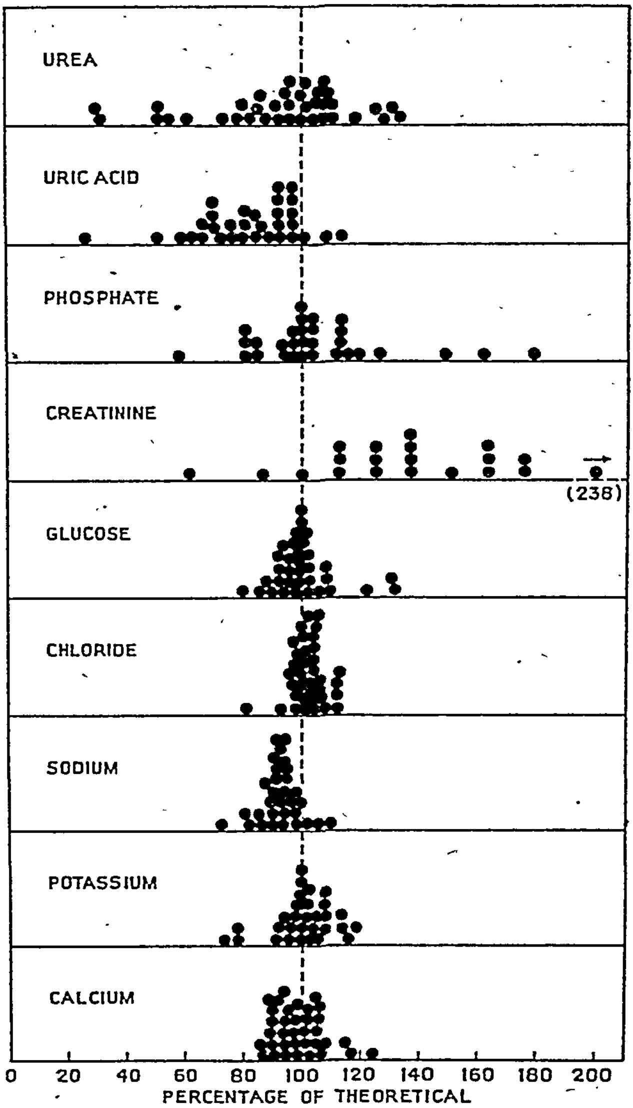

Fig. 2—Results obtained by different laboratories on a prepared solution. The results have been expressed as a percentage of the theoretical value calculated from a knowledge of the composition of the solution.

It is evident that very large disagreement exists between different laboratories. The causes are obscure and need investigation, but it is already clear that the differences are not explained by the use of different analytical methods. Some regular check on laboratory performance would obviously be useful. This can be done within individual laboratories or on area or national basis. We intend to look further into the comparability of results obtained in different laboratories, both in terms of absolute values and proportionality of results, and to investigate the possibility of some system of regular checks. Any laboratory which is willing to participate is invited to communicate with us.

This work was made possible only by the willing coöperation of Prof. R. H. A. Plimmer and the staff of the analytical laboratory; Dr. R. Haslam, Dr. J. Maclean Smith, and Dr. D. Oriel, and Miss D. S Bain, Miss P. Kind, and Miss E. Schmidt also provided valuable assistance. Our thanks are due to the laboratories which undertook the collaborative test.

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of the old Although survival is not the sole criterion of success, no new method is likely to last if it offers a lower survival-rate In the series described by Foster-Carter and his colleagues, 80% of patients with effective pneumothoraces (in that the cavities appeared to have closed) were alive after 8 years, many had had extensive disease, and excluding these the survival-rate was 89% Of patients with no obvious cavities before the pneumothorax was induced 88% survived 8 years, while of those without cavitation who had no initial collapse treatment 89% were still living 8 years afterwards It is against such figures that new methods will eventually be judged

NOISE IN INDUSTRY

AMID the increasing din since 1831, when Fosbroke[1] described deafness in blacksmiths, many occupational hazards to hearing have been identified The latest to be added to the list is the jet engine According to Lieut.-Colonel J E Lett,[2] of the United States Army Air Force School of Aviation Medicine, the noise of such an engine is now the loudest industrial noise, measuring 120–140 decibels This noise has little or no effect on the pilot, who sits ahead of it, but is a serious problem for ground staff and for the personnel of aircraft-carriers Air Vice Marshal E D D Dickson[3] has remarked that a whisper has an intensity of up to 30 decibels, normal conversation, or a quiet motor-car, of 35–55 decibels, the raised voice, or a railway sleeping car, of 60–75 decibels, and a shout of about 100 decibels Any noise of more than 90 decibels' intensity may cause acoustic trauma, and at an intensity of 120 decibels the human ear experiences discomfort The intensity of noise of a jet engine is about 145 decibels

Johnston[4] has investigated the hearing of chippers and riveters, stampers, platers, headers, welders, wormers, and turners (these occupations are listed in descending order of noise level) He found that hearing-loss is very prevalent among them, and in those who had been exposed for more than twenty years the loss was definitely related to noise intensity In addition to the intensity of noises, many factors contribute to acoustic trauma in industry these factors include the total time of exposure, the duration of each exposure, the frequency and volume of the noise, the age of the person exposed, and the presence or absence of previous aural disease Theilgaard[5] suggested that conductive deafness due to middle ear disease afforded some protection to the organ of hearing in noisy surroundings Johnston found in his series of 438 ears in 219 people that 19 ears were the site of active suppuration and 58 ears showed scarring or a dry perforation of the tympanic membrane In 4 cases of otitis media (active or healed) the hearing-loss was 20–40 decibels greater in the unaffected ear than in the affected one, in two of the frequencies commonly attacked by acoustic trauma (2896 and 5792 cycles per second) Thus otitis media may occasionally give some protection to the cochlea for these frequencies Furthermore, he cites a single case of long-standing unilateral meatal occlusion by wax in which the unaffected ear showed a hearing-loss of over 50 decibels in the frequencies 2048, 5792, and 4096 cycles per second, whereas the previously occluded ears showed little or no loss

Long exposure to noise may have other effects According to R M Woodham,[2] administrator of the Daniel and Florence Guggenheim Aviation Safety Centre at Cornell University, it "makes one jittery" and can even break down body tissue, the lung is one part of the body known to be adversely affected by the sound of jet engines Johnston investigated several other subjective effects of noise in industrial workers Tinnitus was common complaint (though rarely present at the time examination), but was always slight and never cause loss of sleep Vertigo was rare Poor concentratio headache, and irritability were usually attributable t dissatisfaction with the nature of the work

Individual susceptibility to noise varies widely, an it is important that a method should be devised whereb susceptibility may be determined before workers ar employed *in one of the noisier industries* Dickso believes that some idea of susceptibility could be gaine from knowing the rate at which hearing recovers afte exposure, for if exposure is stopped, hearing loss ma be reversible in what he calls the "chronic" type o acoustic trauma, which is caused by long continue exposure, *particularly to sounds of high frequency* (th peak-frequency of a jet engine is about 2000 cycles pe second) Grove[6] recommended that every workma engaged *in a job where the noise level exceeds 90 decibel* should have a pre-employment audiogram and b re tested after one week and subsequently at interval Any workman who complains of tinnitus after workin *in a noisy environment should have his hearing re-te ted* Johnston observes that the ideal remedy would be t eliminate injurious noise Improvement in the desig of machines and their mountings has already don much to help, and reduction of reflection and reverbera tion of noise by sound-proofing surfaces and baffle wall has sometimes been effective Failing these measures there remains the "acoustic insulation of the worker' ears" by protective devices A meatal plug, such a cotton-wool impregnated with yellow soft paraffin, ma attenuate noise by 20–30 decibels, it of course reduce hearing for conversation, but some ear "muffs" ar designed to allow the hearing of speech while stil protecting the ear from acoustic trauma Johnston found that of 64 boiler makers 10 wore protective devices i the ears, but in no other trades were they worn at all

TREATMENT OF BREAST CANCER

JUST as the *British Journal of Radiology* last year devoted a supplement to the clinical, pathological, and statistical aspects of cancer of the breast,[7] so the *Acta Radiologica* has published a volume concerned with radiotherapy in cancer of the breast, with special reference to the value of preoperative irradiation as a supplement to radical mastectomy[8]

Cancer of the breast is usually treated by operation combined with radiotherapy In most centres there is an enthusiastic team spirit, which guides the form of the treatment and encourages a systematic follow up Naturally, from time to time treatment is modified in detail, but in general the team pursues some planned scheme, *hoping with the passage of the years to be able* to compare results So far as length of follow up is concerned, comparison is now becoming possible, but the difficulties of comparing the results of one centre with those of another are still very great

Dr Sigvard Kaae poses two questions Do treated patients survive longer than untreated, and are the results of one form of treatment any better than those of another form? *The search for the answer to the first question* brings us to the main stumbling block—we do not know with any accuracy how long women with untreated *cancer of the breast may be expected to survive* Kaae has had to use figures compiled by Greenwood[9] before 1926, covering 651 untreated cases in which survival was lucent colonies, with an entire edge, some colonies being confluent in pairs; microscopically these consisted of chains of rods, and filaments, both of various lengths, with oval and rather more deeply staining moniliform bodies lying mostly terminally or subterminally.

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[2] *New York Times*, Jan 30, 1953
[3] See *Lancet* 1952 ii 967
[4] Johnston C M *Brit J industr Med* 1953, 10, 41
[5] Theilgaard E Thesis Copenhagen 1951

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[7] Cancer of the breast a review By D W SMITHERS P RIGBY JONES, D A G GALTON and P M PAYNE *Brit J Radiol* 1952, suppl no 4
[8] Radiotherapy in Cancer of the Breast By SIGVARD KAAE *Acta radiol Stockh* 1952 suppl no 98
[9] A Report on the Nat … Dr M GREENWOOD Reports on Public … no 33 Ministry of Health London, 19

Cultural characters.—There was no growth on plain agar or on 5% horse-blood agar; the best growth was at 37°C on Loeffler's serum or on 25% horse-serum agar, though growth was scanty on the latter unless the serum had been heated at 56°C for thirty minutes; growth also occurred readily on Dorset's egg medium, though less luxurously than on Loeffler's serum. After two or three days' growth on solid media the colonies became rough and rather granular. Growth also took place readily in 5–10% horse serum-glucose broth, the serum having been heated as described above; in this medium the appearance was that of discrete white particles about 0·2 cm. in diameter, together giving the impression of bread crumbs, while individually they appeared as mulberry-shaped balls of fluff; they were not easily disintegrated by shaking the culture. Growth was not affected by increased carbon dioxide tension. The organism died out easily in culture; it survived five days on solid media, but subculture every forty-eight hours was necessary with the glucose-serum broth-cultures. The organism has survived freeze-drying, and is now stored in this condition.

Microscopical appearance and staining.—In older cultures the moniliform bodies were less conspicuous; with Gram's stain the organism was gram-negative; methylene-blue gave more satisfactory results than did Gram's stain. "L" forms of the organism were not seen.

Biochemical reactions.—Acid, but not gas, was produced within forty-eight hours in serum-peptone water from lactose, sucrose, maltose, and glucose, but not from dulcite, mannite, or salicin.

Agglutination.—It was found impossible to make a stable suspension for agglutination reactions with the patient's serum.

Blood-cultures.—A blood-culture in glucose-broth made on May 30 was sterile after twenty-one days' incubation. A second blood-culture, made on May 31, showed typical "cotton-ball" colonies on top of the layer of blood in glucose-broth forty-eight hours after the culture had been made; these were morphologically typical of the organism in stained films, but it failed to grow on subculture.

DISCUSSION

Arthritis and a pustular rash were prominent features of rat-bite fever in the present case, and, combined with the short incubation period and complete absence of changes in the healed bite, gave a picture considerably different from many classical accounts of rat-bite fever.

Similar variations in the clinical findings are not uncommon, and have led to attempts to differentiate, on clinical grounds, between infection with *S. minus* and with *A. muris* (Allbritten et al. 1940). Rat-bite fever due to the spirillum has been thought to follow the classical pattern, with a long incubation period and recurrence of inflammation in the healed bite, whereas rat-bite fever due to the actinomyces has been supposed to be characterised by a short incubation period (from one to three days), absence of changes in the bite, and arthritis. Fever, sometimes relapsing, is common to both types of infection, but various points of difference have been described in the rash. Brown and Nunemaker (1942) point out that in most cases this differentiation is impossible, many of the clinical features being common to both types of the disease, and subject to considerable variation. Arthritis has, however, rarely been described in naturally occurring rat-bite fever except with *A. muris* infection, and pustulation of the rash also appears to be confined to this form of rat-bite fever. In the absence of these features clinical diagnosis of the causal organism is rarely possible. Comparison of the present case with the 3 cases of rat-bite fever due to *A. muris* in the British Isles (see table) confirms this view, and shows the diversity of the clinical picture in the actinomycetic form of rat-bite fever. The good response of both types to penicillin makes clinical differentiation less important now than in the past.

A. muris, if present, can usually be isolated by blood-culture on suitably enriched media. It has also been isolated from a subcutaneous abscess (Brown and Nunemaker 1942), an infected joint (Place and Sutton 1934), and a lymph-node (Symonds 1943). In the present case the diagnosis was confirmed by isolation of *A. muris* from a pustule in the skin.

The response to penicillin of rat-bite fever due to *A. muris* is usually dramatic, but Sprecher and Copeland (1947) reported a case which did not respond to penicillin but was cured by streptomycin. Sulphonamides are ineffective, and the response to the newer antibiotics has not yet been investigated.

SUMMARY

A case of rat-bite fever due to *Actinomyces muris* is described in which arthritis and a pustular rash were prominent features.

The causal organism was isolated from a pustule in the skin.

The response to penicillin was rapid and complete.

We wish to thank Dr. Leslie Cole for permission to publish this case; Dr. M. H. Gleeson-White for assistance with the laboratory investigation; Dr. R. M. Fry, director of the public-health laboratory, Cambridge, for his help, especially with the freeze-drying of the organism; and Dr. Alan Lyell for his description of the rash.

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Medical Societies

LIVERPOOL MEDICAL INSTITUTION

Retrolental Fibroplasia

At a meeting on Feb. 19, with Dr. R. J. Minnitt, vice-president, in the chair, Dr. J. Berkson spoke on Oxygen, the Premature Baby, and Retrolental Fibroplasia.

Dr. Berkson said that retrolental fibroplasia, a disease which led to blindness, occurred in premature infants, and especially those with birth weights of less than 3 lb. In the last 6 months 51 premature babies had been studied, of whom 3 developed the disease during the investigation. It had been suggested that high oxygen concentrations were concerned in its causation. The arterial blood in the fœtal circulation had a relatively low oxygen content. A premature baby of twenty-eight weeks, had it continued its intra-uterine life, would have had a further twelve weeks of hypoxia. Instead it was usually exposed to 20–90% oxygen in an oxygen tent.

Mr. A. McKie Reid suggested that the hot, humid, and over-oxygenated atmosphere in which he had seen premature babies nursed seemed to bring about an unbalanced development, just as a forced plant becomes etiolated. He drew attention to medicosocial factors which, although they had reduced the incidence of blindness due to phlyctenular disease, tuberculosis, and ophthalmia neonatorum, seemed, by excess of care, to have produced a new disease. He wondered whether the vascular phakomatoses—Sturge-Weber and von Hippel-Lindau syndromes—were related to the vascular type of retrolental fibroplasia. Mr. McKie Reid said that on the whole treatment was ineffective; but he referred to a case of the vascular type which had responded to cortisone given systemically.

Dr. E. Dunsby said that Dr. Berkson had stated that retrolental fibroplasia was unknown in India and Japan. Was this not because both these countries had few, if any, premature-baby units?

Points of View

THE SUPERIOR CLINICAL ACUMEN OF THE OLD PHYSICIANS

A Myth

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M D Lond , M R C P
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REFERENCES are often made to a race of great physicians who flourished some fifty years ago Though lacking such modern aids to diagnosis as radiography, laboratory investigations, and 'scopes and other instruments, they were, we are led to understand, nevertheless able to reach the correct diagnosis in a high proportion of cases solely by their clinical skill at the bedside Their dexterity of touch and their acuity of hearing, sight, and smell, acquired by years of patient training of the senses, were such that they were able to detect—and interpret correctly—subtle physical signs which are beyond the grasp of the comparatively ill developed clinical faculties of the doctors of today

It is now taken for granted that the final diagnostic court of appeal for organic diseases is the pathological or bacteriological evidence Such evidence is often not available, but in a high proportion of serious, and particularly fatal, illnesses it can sooner or later be found But in the days of the great physicians such evidence could rarely be obtained from the living, and when obtained from the dead it was not nearly so complete as it is today It follows that the final court of appeal—at least when the patient was not fatally ill—was the bedside diagnosis When an eminent physician, called down from London, diagnosed the threat of consumption, incipient brain fever, diaphragmatic gout, or strained heart the matter no doubt seemed settled The old physicians, therefore, may have been generally judged to be right when in fact they were wrong And they could afford to be confident in their diagnoses , the present-day physician is constrained, by the possibility of subsequent pathological findings, to be more cautious

THE VALUE OF PHYSICAL SIGNS

The reputation of the old physicians chiefly depended on their ability to discover and interpret physical signs It is sometimes suggested that learning to appreciate many signs, particularly those arising from the chest, is very difficult The beginner, it is said, when examining with the greatest care a case of early pulmonary tuberculosis, may detect nothing wrong Whereas the expert, with the aid of his trained senses of hearing and vision, may be able to find an occasional râle, a slightly prolonged expiratory sound, minor variations in the percussion note, almost imperceptible flattening of one part of the chest, and slight impairment of movement of one side But such inconspicuous signs are hardly significant Variations between the chest appearances of normal people, or in the same individual between different parts of the chest, are surely as great as are those represented by many of these signs They do not justify the diagnosis of pulmonary tuberculosis if the radiograph is normal in every view and the sputum is free of tubercle bacilli , and if there is real evidence of the disease they should not influence the opinion of the state of the chest Similar criticism can be made of other inconspicuous signs, such as slight pallor of an optic disc, an equivocal plantar response on both sides, a "slapping" first heart sound, or an increased area of splenic dullness on percussion If there are other reasons for coming to a diagnosis their aid is not required , if they are alone they justify no diagnosis Trivial deviations from the average can be discovered in any man if they are looked for hard enough

The appreciation of physical signs is, then, not the difficult matter it is sometimes held to be The signs of real value are those which are striking, and which anyone, *provided he seeks for them*, can appreciate

Obvious signs are nevertheless often not discovered, for the simple reason that they have not been sought This may especially happen when they were absent at first but developed later A patient may reveal manifestations suggesting carcinoma of the lung The chest is examined over and over again, repeated radiographs are taken, much sputum is sent to the laboratory, and bronchography and bronchoscopy are performed Yet when in the end all these examinations and investigations have confirmed the presence of a carcinoma no one may have noticed that a hard mass of glands has become palpable above the clavicle—glands which were not present in the earlier stages

Does then the idea that the old physicians were better than the new rest on their superior thoroughness in seeking for signs ? No doubt many modern doctors do not examine their patients with sufficient thoroughness, but hasten instead to employ radiography and other aids to diagnosis But shirking the physical examination cannot always be condemned When a patient has an injured leg it may be possible to demonstrate a fracture by eliciting crepitus between the bone ends This is a far less certain method than is an X-ray photograph and it may be highly unpleasant, and possibly dangerous, for the patient A fair comparison between the old and the modern physicians in their ability to discover signs can only be made when signs are as relevant now as they were in the past Although this comparison is very difficult to draw it may be conceded that the old physicians were superior, because they did not start with the assumption, as many modern doctors do, that special investigations inevitably count for more than clinical examination

The main problem presented by physical signs is their interpretation And this requires two distinct stages first, deciding what is the cause of the sign , and second, deciding whether this cause is responsible for the symptoms A double error of interpretation may even be made with a single sign An apical systolic murmur may be discovered in a patient complaining of palpitation, left mammary pain, rapid beating of the heart, and sighing respiration. The wrong deduction may first be made that the sign is due to mitral regurgitation, and next it may be wrongly concluded that such symptoms are caused by this lesion The first stage of interpretation is undoubtedly important, but more attention should be paid to the second stage Too often is it casually assumed that some lesion is responsible for a patient's symptoms when this is not so , and too often are diagnoses made, right in the sense that the conditions thought to be present are present, but wrong because they do not explain why the patients feel ill

Were the old physicians superior to the new in their ability to interpret physical signs ? On the contrary, it seems that some of them put unjustified interpretation upon signs, particularly on those arising from the chest, for they are often non-specific phenomena which may be due to many different pathological states Many old signs, such as the *tache cerebrale* and Campbell de Morgan's spots, are now known to be valueless And there does not seem to have been in the past a widespread realisation of the existence of the second stage in the interpretation of physical signs

THE RELEVANCE OF SYMPTOMS

Symptoms, other than those obviously due to local causes such as boils, piles, or dental caries or to grave illnesses, are not so easy to interpret as physical signs and the results of special investigations To analyse them successfully, the observer has to possess the ability

THE LANCET

LONDON: SATURDAY, MARCH 7, 1953

Dosage of Antibiotics

CHEMOTHERAPY of bacterial infections has reached a stage where there is need of hard thinking based on accurate observation and critical experiments. Sulphonamides, penicillin, and the deluge of antibiotics came so swiftly after each other, with a succession of triumphs over bacterial diseases, that the period from 1935 to the present day has evoked memories of the golden age of bacteriology between 1880 and 1900, during which new discoveries were announced every few months and were featured in the popular press. In the thirty years after 1900 progress was much slower and much less spectacular, even with the knowledge of wound infection gained during the 1914–18 war and the advances made in the study of virus diseases: but the period was one of consolidation during which a great deal of useful tidying and fundamental thinking was done. Patient research was adding to our information about host-parasite relations, and it seemed that this work, together with more knowledge of epidemiology, would furnish the means whereby we should steadily increase our control over diseases caused by bacteria. Then the dramatic discoveries of the new chemotherapeutic agents suddenly presented us with such unexpected powers that attention was naturally concentrated on their development and use. The brilliant results, however, were won without equivalent advances in our knowledge of the complex relations between host, parasite, and drug. Now that the first excitements are passing we should be taking stock of our position.

Drug-resistant bacteria represent one major problem. What is known about the adaptability of micro-organisms is enough to caution us against any impression that bacterial diseases will soon be swept away: indeed, some anxious thoughts have been given to the possibility that within a measurable period we may be unable to discover new antibacterial chemotherapeutic drugs as quickly as resistant strains of micro-organisms establish themselves in their human and animal hosts. It is well, therefore, that we should be asked to consider whether the appearance of resistant bacteria is being unnecessarily encouraged by current methods of administering antibiotics. In their article two weeks ago[1] Dr. GOULD, Dr. BOWIE, and Dr. CAMERON set out to show that instead of using the large "standard" antibiotic doses we can and should base our dosage in each particular case on an estimate of the sensitivity of the micro-organism in vitro. As it is very difficult to ascertain the concentration of an antibiotic in infected tissue (which cannot be conveniently removed from patients for purposes of analysis) they made their investigation on urinary infections, in which the concentration of drug in contact with the infecting organism can readily be measured and related to the dosage. By ascertaining in each of 17 cases the sensitivity of the infecting organism, the six-hourly volume of urine excreted, and the rate of excretion of the antibiotic, they calculated the six-hourly dose of antibiotic required for treatment. To allow for error and variability in excretion they multiplied this calculated dose by a figure which was 5 for most of their cases but which ranged from 1 to 15. In general this figure (the "enhancement factor") proved to be about twice as high as it need have been; but, even so, they found themselves using quantities of antibiotic which were remarkably small by present standards. For example, in different cases they gave such six-hourly doses of streptomycin as 1, 7, 0·2, 4, 12, 22·5, 3·13, and 16 mg., which may be compared with the usual six-hourly doses of 250–500 mg.; and the doses of penicillin, chloramphenicol, aureomycin, and terramycin which were deduced from the results of their sensitivity tests were also small by present standards. Admittedly there were 3 failures: one patient had multiple infection and gross disease of the bladder, another became infected with proteus after removal of the original organism, and the third had a staphylococcus which persisted. Also, a few patients required a second course of antibiotic. But 14 of the original 17 cases were rendered free of infection and so remained during a follow-up period of from one to six months: and this is a satisfactory result in such a series of urinary infections as GOULD and his colleagues describe. What is striking, however, is their report that resistance to antibiotics did not develop in any of the original species of infecting micro-organisms either during therapy or after therapy. (Some species causing new infections showed resistance to the antibiotics first used, but this, of course, is not a material objection to the argument.) Subcultures of the organisms readily developed resistance in vitro, and 3 of the 17 patients treated outside these trials with the usual standard doses all showed resistant species of organisms.

This work deserves to be repeated and extended if possible to other sites of infection. Any measure that may reduce the incidence of resistant bacterial strains is of fundamental importance; and, besides this, the use of smaller doses, if practicable, would reduce the risk of toxic effects and gross disturbance of the normal bacterial flora, which may lead to moniliasis and other undesirable results. GOULD, BOWIE, and CAMERON may prove to have been fortunate in their choice of urinary infections, since the situation favours both concentration of the antibiotic and prolonged contact with the infecting agent—circumstances that may not be readily attained elsewhere. But whether or not this is so, the points they raise are of great interest. Dominance of the resistant individuals of a bacterial species can, of course, be attributed to causes other than exposure to concentrations of antibiotic above the bactericidal level. For example, EAGLE,[2] [3] who found that certain organisms were killed more rapidly at low than at high concentrations of penicillin, thought that a sustained level of penicillin was probably more effective than the rapidly changing levels resulting from the infrequent injections in high dosage now commonly used. The wide range of host-drug-parasite interactions involved in this problem is well

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[1] Gould, J. C., Bowie, J. H., Cameron, J. D. S. *Lancet*, Feb. 21, 1953, p. 361.

[2] Eagle, H. *Science*, 1948, 107, 44.

[3] Eagle, H. *Ann. intern. Med.* 1948, 28, 260.

DISCUSSION

If my arguments have been sound, the concept of the old physician at the bedside reaching diagnoses with his unaided senses and his clinical acumen, which the modern physician can reach only with the help of elaborate investigations—if even then—belongs, not to history, but to mythology

Perhaps the main reason why this myth arose is to be found in the natural habit of young men of looking up to their elders The impressionable student or resident feels that his Chief clearly knows so much more than he does himself that he may come to accept his word as law In later years he may often be conscious of the profound difficulty of medicine, and realise how frequently he cannot decide what is the matter with patients, or what should be done for them His reason may suggest that his Chiefs were also in similar dilemmas, but it may nevertheless be difficult to get rid of the deep feeling that they *knew*, and that when they pronounced a diagnosis they were right When in his turn he instructs students, he may hand on stories of their *infallibility*, which become part of the folk-lore of the medical school Towards their own contemporaries, on the other hand, men are much more critical They may readily admit that someone they do not know is a genius in a subject of which they know little, but few are conscious that one of their own friends may be a genius in their own subject Jealousy, too, tends to be responsible for the belittlement of contemporaries, but people feel little jealousy towards a distinguished old man, and none at all towards the dead

There is nevertheless some truth in the view that all is not well with modern medicine A common error is the widespread assumption that the results of elaborate investigations are inevitably superior to the clinical evidence, and particularly to the evidence of symptoms A figure derived from the pathological laboratory, or a shadow on a radiographic plate, is too often thought to represent exact truth Investigations are increasingly done routinely, and in medical schools this practice may be excused on the ground that the investigations are desirable for the sake of the students, though hardly necessary for the welfare of the patient Why to give students the impression that the nation's money and the patient's time should be wasted in performing tests which do not help, and may be unpleasant and alarming, is not clear Many doctors apparently never ask themselves the question " whatever the possible results of this investigation, will my opinion be affected ? "

The emphasis wrongly put upon investigations at present is of a piece with the emphasis wrongly put upon many physical signs in the past What is needed now, as it was then, is a proper sense of balance Each patient should be considered as an individual clinical problem Routine history-taking and routine physical examination, according to a standard formula, are just as mistaken as is routine investigation In some cases, such as possible hæmophilia, a searching family history may be most valuable In many others, particularly when there are numerous complaints reaching far into the past, a careful study of the symptoms and of personal relationships may be all-important But when there is one predominant symptom of short duration pointing to an accessible region of the body—as with whitlows, sore throat, and piles—the physical examination is supreme, and the remainder almost or quite valueless And when the symptoms suggest organic disease in a region likely to produce no physical sign, or physical signs of indefinite character—as when pulmonary tuberculosis, enteric fever, and urinary infection are suspect—certain special investigations are clearly indicated

* * *

Although in this paper I have attached the view that the old physicians, by their skill in appreciating and interpreting physical signs, were able to make diagnoses of which we are incapable, it is not my intention to belittle the great advances which many of them made They *discovered* the physical signs and began their study and the assessment of their significance An important reason why we can do better than they did is that we are in the fortunate position of enjoying the fruits of their labours

SUMMARY AND CONCLUSIONS

The belief that the old physicians of fifty years ago were able solely by their skill at the bedside to reach diagnoses which modern clinicians can reach only with the aid of elaborate investigations is examined and dismissed Only in one field—namely the discovery of physical signs—has there possibly been a decline in recent years, and in most other respects there has been an advance Nevertheless a common error of modern medicine is the assumption that the results of special investigations are necessarily superior to the clinical findings, and particularly to the symptoms

The views expressed on the appreciation, discovery, and interpretation of physical signs were previously published elsewhere[2] I wish to thank my father for his help in revision, and Dr C C Thomas for his advice and criticism

Personal Papers

ACUTE RHEUMATOID ARTHRITIS WITH RECOVERY

THE onset of acute rheumatoid arthritis in a man of 59 who had previously enjoyed good health appeared to be determined by a fall forward on to outstretched hands This fall gave rise to feelings of annoyance rather than to sensations of physical pain

The initial disability appeared a few days later, when the middle finger of the left hand started to flex and developed a trigger deformity A week later both shoulders, which up to then had been somewhat stiff, became painful and movements were restricted Thereafter other joints became affected in groups, a process which was spread over four to five months

The patient was off duty for six months At the end of this period he returned to work free from deformity and suffering from no disability other than some loss of power in the muscles This residual weakness was, however, rapidly disappearing as the muscles gained tone in response to exercise

SYMPTOMS

Loss of power was the most striking symptom It came on early in the disease before wasting was apparent, and was clearly not a limitation of movement due to pain Illustrations of this loss of power include inability to push down the bed clothes from the chest or to sustain the weight of even a small cup of tea at the end of an extended arm, inability of the quadriceps to raise the extended leg from the bed, and inability to raise the body to a sitting position in bed without the help of the arms Power was regained in the recovery phase at first very slowly, and later with increasing rapidity as the atrophied muscles recovered bulk

Lethargy was a conspicuous feature and made rest in bed very easy to tolerate

Pain was less tiresome than anticipated It was usually possible to find a comfortable position in which pain disappeared and only started again on movement or when the part became cramped through remaining in the same position too long The most trying discomfort was in the early stage, when the shoulders were the joints chiefly affected and the acromioclavicular ligaments were chiefly involved It was then difficult to find a position of ease, recumbency made the pain worse, and relief was only obtained by sitting a little forward of applicable to other hospitals. They arranged to have samples analysed in different laboratories and compared the results. As with previous comparisons of this sort,[12-14] very disturbing errors emerged. The causes of these errors are not known, but there is no doubt that the present expansion of the laboratory services creates a danger of skilled staff being diluted with inexperienced people; and, of course, an overworked laboratory has little time to spare for checking results.

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[2] Todd J W Rational Medicine Bristol 1949

It may be argued that biological variation is such that superior accuracy is not required for clinical purposes. On the contrary, the very extent of variation from case to case makes it essential that the laboratory shall not add a large chemical scatter. It is easier, however, to state the problem than to suggest a remedy, especially since we do not know the exact causes. Help may be had from control charts—a device borrowed from the engineering industry, applied to analytical chemistry by Wernimont,[15] and already introduced in some clinical laboratories.[16-18] Solutions of known composition are routinely analysed by a person who does not know what result is expected (thus conscious or unconscious bias is avoided). The deviations from the expected result are plotted on a special chart which shows at once when any method has gone "out of control." For most substances this method of checking can be applied by any laboratory; but in the case of hæmoglobin estimation there is a peculiar difficulty in that standard solutions are not readily accessible. To fill this gap, Wootton and King have described the Medical Research Council hæmoglobin standards scheme [19] under which laboratories are periodically sent samples of blood whose hæmoglobin content has been determined by the best known methods. The variety of methods and apparatus used at present for determining hæmoglobin makes a common calibration especially important, and samples have been sent all over the world. It would, of course, be comparatively easy for some central organisation to provide pure standard solutions of other blood constituents. It would be even more useful to supply accurately analysed blood, plasma, or serum; but this would involve employing a reputable analytical laboratory on an arduous and uninteresting task.

Many analytical methods are of uncertain specificity, and the values obtained often depend partly on the method used. The analytical methods committee of the Society of Public Analysts and other Analytical Chemists has compiled a bibliography of standard tentative and recommended or recognised methods of analysis [20]; and the American Association of Clinical Chemists is also preparing a recommended list under the direction of Dr. Miriam Reiner. We are not sure that such prepared lists will persuade people to use standard methods, and, if they do, that such adherence to authority is desirable, since initiative may be stifled; but it does seem that the whole question of laboratory analysis should be reviewed by a body drawn from the interested societies, including the Association of Clinical Pathologists, the Biochemical Society, the Society of Public Analysts, and the new Association of Clinical Biochemists.

Annotations

BRITISH PHARMACOPŒIA, 1953

The publication of the new *British Pharmacopœia* marks the climax of a quinquennium of compilation based on research in many fields. In their introduction the Pharmacopœia Commission pay tribute to the help they have received from their ten subcommittees, from scores of individual experts, and from a large number of government departments at home and abroad; and it is particularly pleasing to note that "a cordial relationship has been maintained with the Committee of Revision of the United States Pharmacopœia." The *B.P.* and its equivalent publications in other countries are so much taken for granted that their importance may be overlooked. The exacting standards laid down for maintaining the purity and potency of therapeutic and diagnostic agents confer an incalculable benefit in terms of prevention and cure of disease. In the United Kingdom the *B.P.* has acquired additional importance under the National Health Service, for it is the principal standard work to which committees look when entrusted with the task of advising doctors and pharmacists on the merits of proprietary preparations.

A new departure is the abandoning of Latin in the main titles of the monographs. This change is welcome as a timely gesture to wholesome trends in the evolution of medical science. Although the writing of prescriptions in good Latin is not in itself objectionable, the practice is redolent of an epoch which was far too tolerant of mumbo-jumbo. The kind of care given to the sick can never be separated from the character of the individual practitioner: to this extent the practice of medicine is an art, but a patient has grounds for uneasiness if his doctor lacks the courage to strip his methods of make-believe and superstition and refuses to adopt plain speech, logic, and scientific principles. But the commission are men of mercy: below the English titles they give the Latin names in full and in the abbreviated form. Those who feel that tradition has been outraged will have to thole it. The busy pharmacist accustomed to locating nutmeg oil as *ol. myrist.* and wool-fat as *adeps lan.* will now need to consult the comprehensive index which includes both the English and the Latin titles—though it is surprising how often the titles in the two languages are closely alike. His jars and bottles will also need relabelling—at any rate if the next generation of pharmacists is going to use them—and here it is perhaps permissible to make a plea for clear block capitals rather than early Gothic script.

There must be many circumstances which may determine the exclusion of a drug or preparation from the *Pharmacopœia*: evidence may have accumulated that the substance is not effective as a therapeutic agent; for one reason or another the preparation may not have found favour in practice; international relationships and the science of economics may also change the face of a pharmacopœia; and, most important of all, exclusion may follow advances in the understanding of disease and the development of new drugs. In the present volume not a few drugs are evidently excluded on the ground that they have been eclipsed by new preparations. Thus acriflavine gives place to proflavine hemisulphate; calcium mandelate can no longer hold its own among the urinary antiseptics; prepared ergot is unnecessary now

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19. Wootton, I. D. P., King, E. J. Paper read to the Association of Clinical Pathologists, October, 1952. See *Lancet*, 1952, ii, 769.
20. Bibliography of Standard Tentative and Recommended or Recognised Methods of Analysis. Cambridge, 1949.

it and the patient has complete freedom of movement with no weight on his feet

Bath—If there is weakness of the muscles of the shoulders and upper arms, there is difficulty in entering and leaving the bath, because the final lowering on entering and the initial lift on leaving are accomplished by these muscles This difficulty can be overcome by entering the bath at the tap end, seizing the rim of the bath between the taps, bracing the feet against this vertical end of the bath, and lowering oneself on extended arms To get out, the process is reversed the feet are braced against the end of the bath, the hands grasp the rim of the bath, and one pulls up to the vertical on extended arms

Special Articles

COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS

EIGHT-YEAR SURVEY

THE *Brompton Hospital Reports* for 1952 contain a long account of an inquiry into the results of collapse and conservative therapy in pulmonary tuberculosis[1] This deals with 1153 patients discharged from Frimley Sanatorium between 1937 and 1942

All patients were followed for at least 8 years, and only 1% were lost from observation The aim of the survey was to show the fate of typical hospital patients treated during that period with and without collapse therapy, in the hope that this would be a useful guide to the treatment of similar patients in the future The radiographic extent of disease on admission to hospital was classified as follows class I, one zone, class II, two or three zones, class III, four or more zones

The expectation of survival in pulmonary tuberculosis is shown to vary inversely with the radiographic extent of the disease It follows that any comparison between two groups of tuberculous patients is valueless unless the extent of disease in the groups is similar For instance, it is useless to compare the gross survival-rates of groups of sputum-positive patients In a group with cavitated disease who had no collapse therapy the gross 8-year survival-rate of those with a positive sputum was 38%, but when patients with no more than three zones involved were considered alone the 8-year survival-rate was 71% Too little attention has been paid to this factor in most accepted classifications of the disease

NO COLLAPSE THERAPY

Of the 955 patients with cavitated disease 256 had no collapse therapy, and 46% survived 8 years Those with advanced disease (class III) had a survival-rate of 33%, but of those in classes I and II 74% survived Extent of disease was a more important factor than size of cavities Of 120 patients with large cavities (2 5 cm or more in diameter) 28% survived 8 years 66 of these patients had sanatorium treatment that included graduated exercise, and 45% were alive and 32% were working at the end of 8 years Of the 113 survivors of the whole group 82% were working and three-quarters had returned to the work they were doing before they became ill.

198 patients had pulmonary tuberculosis without obvious cavitation 130 had no collapse therapy during the first admission, and of these 89% survived 8 years Only 12 patients had extensive disease, their survival-rate was 64% 41 patients were in class I with "minimal" disease, 97% survived 8 years The combined survival-rate for patients in classes I and II was 91%, which may be compared with the rate of 74% for patients with disease of similar extent but with cavities

COLLAPSE THERAPY FOLLOWING RELAPSE

Of 311 patients with cavitated disease who had no collapse therapy during their first period of institutional treatment, 55 later relapsed and were given collapse treatment The majority relapsed during the first 2 years, but relapses continued to take place up to the end of the observation period, there were 4 relapses in the ninth year Of 130 patients without cavities who had no collapse therapy initially, 24 relapsed later and were given collapse treatment

INITIAL COLLAPSE THERAPY

644 patients had some form of collapse therapy as initial treatment (71% had a unilateral pneumothorax and 12% a thoracoplasty), 67% survived for 8 years In patients with disease of the same radiographic extent there was no difference in prognosis whether the disease was unilateral or bilateral The 8-year survival rate of 40 class-I patients was 85%, and of 304 class II patients 80% The survival-rate for classes I and II combined was 81%, which can be compared with the rate of 74% for somewhat similar patients who had no collapse therapy There is more difference among class-III patients of 173 who had no collapse therapy 33% survived 8 years, of 300 who had collapse therapy 50% survived 8 years Those with both extensive disease and large cavities show an even greater difference—23% compared with 47% Collapse therapy did not materially improve the prognosis of patients in any class with a persistently negative sputum 520 were sputum positive and their 8-year survival rate was 64% 337 of these had a negative sputum on discharge, and 79% survived 8 years, 183 still had a positive sputum, and 37% survived 8 years The survival rates of patients in all classes who became sputum-negative were better than those of patients of the same class who had no collapse treatment

Artificial Pneumothorax

Of 457 patients with cavitated disease who had unilateral pneumothorax treatment 69% survived 8 years These 457 patients were divided into three groups according to the type of collapse and the persistence of radiographic evidence of cavitation in the collapsed lung In 92 "*satisfactory*" cases the lung appeared to be completely free from adhesions, either from the start of the pneumothorax or after adhesion section, and the cavities appeared to have closed In 242 "*adherent satisfactory*" cases there were adhesions over the diseased area, but the cavities appeared to close within a year In 113 "*adherent unsatisfactory*" cases adhesions and measurable cavitation persisted, or an empyema had developed, 1 year after induction of the pneumothorax

Analysis of the survival-rates of these three groups yielded several important results 79% of the *satisfactory* group survived 8 years, but so did 82% of the *adherent-satisfactory* group, on the other hand, only 36% of the *adherent-unsatisfactory* group survived A pneumothorax, with or without adhesions, which closed the cavity resulted in a longer survival, whatever the extent of disease, compared with those patients who had no collapse therapy, but an unsatisfactory pneumothorax with a persistent cavity carried a worse prognosis than no collapse therapy at all 155 patients (38%) later required further collapse therapy, but despite this they had a better chance of surviving than similar patients who had no collapse therapy

The pneumothorax was terminated in 348 patients who were observed for an average period of 5 years after the lung re expanded The mortality after deliberate re expansion in the *satisfactory* and *adherent-*

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[1] The Results of Collapse and Conservative Therapy in Pulmonary Tuberculosis By A. F FOSTER CARTER, M MYERS, D L H GODDARD F H YOUNG and B BENJAMIN *Brompton Hospital Reports*, 1952 21, 1 Copies of the *Reports* and (15s) reprints of the article (5s) may be obtained from the Secretary Brompton Hospital London S W 3

changes in vessel walls, some glial proliferation, and chromatolysis in nerve-cells, all of which he regards as potentially reversible. He also found, however, evidence of permanent and irreversible nerve-cell changes—shadow cells and neuronophagia—in a small proportion of cells, mainly in animals given intensive treatment (11–16 shocks) as opposed to a lighter course (4 shocks). Since the cats all had typical grand-mal seizures, the relevance of these observations to modern controlled E.C.T. in man is doubtful. They may, however, reflect the type of cell changes responsible for the memory defects and other clinical features noted with the older methods of treatment. They may also illustrate the possible mechanism of "epileptic deterioration" after repeated grand-mal fits in constitutional epilepsy.

X RAYS FOR SKIN DISEASES

THE value of X rays in the treatment of malignant epitheliomata is undisputed; but there is some difference of opinion about the worth of fractional X-irradiation in the treatment of benign dermatoses. Crissey and Shelley [1] have treated patients with lichen simplex chronicus, lichen planus, psoriasis, nummular eczema, contact dermatitis, and acne vulgaris by X rays in such a way as to compare the state of treated and untreated areas. All patients received 100r weekly (measured in air) for four weeks. Accurately located coned areas, 1·9–6 cm. in diameter, were treated. The cone was placed centrally in groups of lesions, but eccentrically in solitary lesions in order to avoid confusion with spontaneous central involution, which is common with some dermatoses. The response of the treated area was compared with the remainder by a marking system in which 1+ represented perceptible involution, 2+ marked involution, and 3+ a return to clinical normality except for skin pigmentation. For each disease the plus marks of all patients treated were added together and graphically recorded, abscissæ representing the weeks of treatment and ordinates the aggregate of marks. A consistently and significantly greater response was noted in the radiated area than the control area in lichen simplex chronicus (16 patients), lichen planus (5 patients), and psoriasis (16 patients); but in nummular eczema (16 patients), contact dermatitis (40 patients), and acne vulgaris (25 patients) there was a steady progress towards healing in both irradiated and control areas, with a small but discernible difference in favour of the treated areas. For strict control it would have been better if an independent observer had inspected and assessed the results; but barring possible errors of this sort from any unintentional bias, X-ray treatment of certain dermatoses seems to have been vindicated.

But are X rays harmless in the dosage employed by dermatologists? The answer is a firm Yes, according to follow-up studies carried out by Sulzberger et al.,[2] who observed 1000 patients who had received X-ray treatment and 1000 who had not, for various skin conditions, including acne, eczema, psoriasis, skin cancer, and neurodermatitis. These workers divided the irradiated patients into two groups: those who had not received more then 85r units on any one occasion (763 patients), and those who had received irradiations of more than 85r (237 patients). The former group included only 2 patients with sequelæ; both had during their lives been exposed to sunlight more than the average, so it was by no means certain that X-irradiation was entirely or even mainly responsible for the atrophy, telangiectasia, depigmentation, hyperpigmentation, and keratosis that were observed. Of the 761 patients who showed no sequelæ 12 had received a total dosage of 37·5–150r, 618 had received 150–1000r, 130 had received 1000—2000r, and 1 had received more than 2000r. Sulzberger et al conclude that there is no evidence of harmful sequelæ from totals of 1000r or less of X rays applied superficially in the fractional doses and qualities generally employed by dermatologists for benign dermatoses; when total doses of more than 1000r are given it must be expected that 1·5% of patients will exhibit X-ray sequelæ that are relatively mild and of only cosmetic importance. There is no evidence that cancer, X-ray ulcer, or any other dangerous ill effects follow doses adding up to a maximum of 1400r, which some dermatologists today regard as permissible for benign dermatoses.

Of the 237 patients who had received once or on several occasions more than 85r only 26 showed X-ray sequelæ, even though 76 of the 237 had received over 1000r and 5 more than 4000r.

Clearly, sequelæ are to be expected in some patients receiving large X-ray exposures for malignant disease of the skin. Sulzberger and his colleagues conclude that the doses necessary for the cure of cancers and other malignant growths of the skin cause mild sequelæ in about 25% of cases.

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1. Crissey, J. T., Shelley, W. B. *New Engl. J. Med.* 1952, 247, 265.
2. Sulzberger, M. B., Baer, R. L., Borota, A. *Arch. Derm. Syph., Chicago.* 1952, 65, 639.

PROGNOSIS IN TUBERCULOSIS

THE Brompton Hospital Sanatorium at Frimley was opened in 1905. By 1935 Hartley et al.[1] were able to survey 8766 cases which had been treated there; and Professor Bradford Hill [2] has cited their report as an excellent example of the application of statistical methods to this type of clinical research. The analysis by Dr. Foster-Carter and his colleagues,[3] which is summarised on p. 486, maintains the standard; it is an important and timely contribution to the knowledge of pulmonary tuberculosis.

These workers have wisely concentrated on the prognosis of treatment by artificial pneumothorax, about which so much has been written to so little effect. They show convincingly that adhesions in a pneumothorax are not necessarily dangerous to the patient. Rafferty [4] concluded that closure of cavities and failure to find tubercle bacilli in the sputum were not suitable criteria of an adequate pneumothorax; success was to be judged by the freedom of the lung from adhesions. This view has been widely accepted, and in a recent extensive study [5] one of the main conclusions was that "free anatomic collapse should be achieved or the pneumothorax abandoned." The Brompton analysis shows clearly that such a view is not tenable. It establishes beyond reasonable doubt that adhesions have no effect on the prognosis, provided that pulmonary cavities disappear. Foster-Carter and his co-workers claim that the whole conception of what constitutes a satisfactory pneumothorax should be re-examined, and that "many patients have been, and are being, sacrificed to the fetish of free anatomical collapse." Their conclusions, though based on detailed evidence which is presented fully in an appendix, are unlikely to pass unchallenged.

Pneumothorax treatment is now being used much less commonly in this country. It requires years of skilled attention by the physician, and if badly carried out it may be dangerous. Newer methods of treatment, and especially pulmonary resection, may seem to offer a more rapid return to normal life for the patient and less constant anxiety for the doctor, yet there is always a danger that the early spectacular results of new methods may distract attention from the familiar achievements

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In England Now

A Running Commentary by Peripatetic Correspondents

By a merciful provision of Nature most of us can not only stomach but even admire and, if necessary, defend in our own children behaviour which we find insufferable in those of others Thus, palpable greed and selfishness as manifested by the little brute next door are secretly hailed in our own little angel as evidence of healthy appetite and enlightened self-interest That disgusting tantrum in somebody else's little pest is tacitly regarded in our own darling as a sign of splendid determination If at a birthday party or other occasion of goodwill ours bashes another we are sure, despite the absence of all evidence, that his action was prompted by extreme and justifiable provocation Sometimes we parents pose as intelligent persons taking a detached view of our progeny, but however much we may criticise them ourselves and to each other we will seldom brook even the mildest criticism from those outside the family circle—or even within it It is only when our children approach maturity, and we ourselves senescence, that a more objective and less emotional judgment is possible (By that time, of course, any hint of a flaw in their characters can be readily blamed on their schooling or at any rate attributed to the genes on the spouse's side)

At what age do children achieve their peak of social beastliness ? In a series of three cases under the writer's observation it is agreed by the cases themselves that the curve rises steadily up to the age of 8, after which some, though not necessarily much, improvement may occur and continue intermittently till perhaps the age of 20 or 21 After that further improvement is not to be expected , the child has become just one more adult human being—and we all know what they are like

* * *

Once you've done with examinations, there is little to mark the passage of time There are births, marriages, and deaths, of course, but the years slip by so fast that you soon count only the decades Our new colleagues on the senate seem mere schoolboys and we older members feel rather nervous about them

The extramural world has its own rough-and-ready way of dating you Until last year, people who wanted the right time always called me " mate," but, although some still do, the usual title is now " guv'nor " My clothes will not explain the change, for I'm still wearing the same inconspicuous ones as in my " mate " days (Sartorially I have always steered a middle course between the sordid squalor of the physiologist and the meretricious gaudiness of the gynæcologist) A year or so ago I was deep in exposition when a student said " Excuse me, Sir, but my grannie pushed you out in your pram, and she wanted me to tell you " Research proved him right So it cannot be long now before I receive the higher degree of " gaffer "

* * *

A friend of ours who proudly possesses a rather exotic thermocouple buttonholed us the other day It seems he was approached by a psychologically minded colleague whose ambition it was to record the thermal changes engendered in his skin by psychological traumata Our friend was delighted to demonstrate his electronic skill, but was momentarily taken aback to find that he was expected also to supply the psychological traumata " What do you expect me to do ? " he asked doubtfully " Oh, just insult me," said the psychologist, stirring impatiently in his chair, " anything will do " Opportunities of this sort are rare enough in the Welfare State, and our friend was somewhat out of practice He essayed a few tentative remarks on his visitor's physical appearance and dress , the psychologist smiled blandly Warming to his task, he cast aspersions on the psychologist's ancestry and relations , the psychologist crossed his legs and examined the ceiling Finally our friend animadverted on the intimate habits and moral shortcomings of his guest , the skin-temperature went down half a degree and the psychologist stifled a yawn Our friend retreated, baffled, and put the case to the lab man outside, an embittered and disillusioned character of great resource " Ask him to add up a sum," said the lab man, " no psychologist knows any arithmetic " Our friend returned to battle, and found the psychologist examining the thermocouple with ill-disguised contempt " What are seventeen seventeens ? " he demanded fiercely, " quick, now ! " A slow flush mounted to the psychologist's cheeks and his lips trembled " Seventeen seventeens " he repeated weakly, " let me see, let me see " The needle trembled, and shot up , the day was won. Five minutes later the psychologist had called for pen and paper, and finally crept out, a beaten man Our friend understands that his thermocouple will not be needed after all

* * *

One of the curious difficulties facing clinicians that has increased since the war is that so many of their patients speak the minimum of English It is helpful to know the word for the commonest symptom, pain, which is *mal* in French, *dolor* in Spanish, *dolore* in Italian, *schmerz* in German, and *bolli* in Polish This combined with judicious pointing will go far, but for more complex maladies an interpreter is required, and Yugoslavian wardmaids or Polish porters may be invaluable, not to mention other patients Sometimes a patient will bring his own interpreter, such as the one brought by a patient consulting a gynæcological acquaintance of mine, who repeated his questions in English, only much louder One of my patients, who had injured his shoulder, at his second visit produced a tiny note—" My friend write this " It read " To twinge and to push pleace "

* * *

At the medical school here a substantial prefabricated building, known officially as the *Animal House* and colloquially as someone's Folly, provides several species of experimental creature with a home so comfortable that it may strike the outsider as a kind of subhuman Sybaris The monkeys have everything done for them by courteous smiling attendants They dine off sterile plastic plates, inscribed with their names in Simian ideographs , they bathe weekly in water deliciously scented with the product of a well-known cosmetic house , and lately have been able to watch television every evening on a set with a 17-in tube, provided by the B B C as part of its viewer-response scheme The rabbits of course are all Angoras, and have their coats combed and water-waved daily by an expert coiffeuse (who shall blame her if she knits up the combings into twin sets for the export market, and keeps her extra-curricular earnings a secret from P A Y.E ?) As for the rats, a special effort is made to disguise from *them their undeniably humdrum place in life* by conferring upon the most distinguished members of the colony the honorary order of " Hero of the Association of Scientific Workers "

But apart from its domiciliary function the Animal House also serves as a Centre of Research Within it dedicated scientists spark and crackle with ideas like so many Wimshurst machines Though some are grim methodologists and others romantic postulators of the ad hoc, all spend the livelong day in happy pursuit of knowledge for its own sake with never a care for riches or fame, They are well known to harry and cozen Mother Nature into parting with her precious secrets in every available corner of the place, but I had not realised to what extremes they would go until, on a visit last week, I noticed that now even the lavatory has been impressed into service to house a crucial experiment in the biophysics of tadpole *metamorphosis* Will the University Grants Committee please, please help ?

* * *

My favourite patient is full of paranoid ideas, and can be relied upon each evening to record the theft or partial destruction of one of her belongings But it is one of her saving graces that she is an enthusiastic *racing* fan, and just now wherever a conversation begins it always ends at Aintree Yesterday she was admiring a solitary daffodil

She Isn't it beautiful ?
Self Very
She What does it remind you of ?
Self Spring It is not very far off
She Well yes " Wot No Sun " Now that's an old horse, but he knows the course

It would be unfair to keep this tip to myself calculated from the time of onset of the first definite symptom of carcinoma. Ten years later only 4% of these women were alive; whereas of 663 new patients treated at the Radium Centre in Copenhagen from 1931 onwards 18% were alive after ten years, and some slight improvement in this figure may be hoped for in the results for the past decade. Supposing that the comparison is valid, this is no mean achievement.

The second question is also difficult to answer, because the kind of case referred to the various centres differs so greatly. The proportion of operable cases reaching a clinic may range from 43 to 81%; but operability does not necessarily go hand in hand with post-therapeutic survival—a fact which supports the view of Smithers and his colleagues[7,10] that prognosis depends fundamentally on the growth characters of the tumour itself. These growth characters cannot possibly be assessed if radiation treatment is given before operation. Allowing for variations in the type of case, the results of treatment in centres in Scandinavia, this country, and the U.S.A. accord reasonably well with one another. Kaae concludes that "the literature as well as the present studies indicate that the demand for systematic preoperative X-radiation advanced by so many workers is probably not justified."

Despite all the difficulties and fallacies in this sort of investigation, we must persevere in the attempt to compare the results of recognised methods of treatment of cancer of the breast—and indeed of all forms of cancer.

INTESTINAL OBSTRUCTION IN THE NEWBORN

THERE are perhaps two reasons for the interest lately aroused by intestinal obstruction in the newborn. Firstly, modern anæsthesia and supportive measures and a high standard of nursing care have shown how the apparently fragile infant can withstand long and severe operations, provided its oxygenation is assured (indeed the early days of life may be the best time for such operations, when the infant has been prepared for the trauma of birth and needs little food). Secondly, improved control of infectious disease has increased the relative importance of congenital defects as a cause of neonatal deaths.

Ehrenpreis and Sandblom[11] turned a mortality-rate of 75% to a 75% survival-rate in the treatment of duodenal atresia and stenosis by adopting transanastomotic tube-feeding. The development of such techniques suited to the special problems of surgery in the newborn is contributing to the more hopeful outlook for these babies. The account by Gross and Ferguson[12] of the surgical care of premature babies will surprise those unaccustomed to pædiatric surgery; their series includes 29 survivals out of 53 cases of small intestinal obstruction. Jolleys[13] distinguishes four main groups of cases according to the causes: (1) errors of rotation of the midgut loop; (2) atresia of the bowel; (3) neuromuscular dysfunction (typified by Hirschsprung's disease); and (4) meconium ileus, where the lumen of the bowel is plugged by abnormal meconium of astonishing tenacity, generally the result of cystic fibrosis of the pancreas. To these Jolleys[13] adds the rarer causes, such as strangulated hernia, volvulus associated with a persistent Meckel's diverticulum, duplication of the bowel, and annular pancreas. Jolleys does not include the rather mysterious entity, meconium peritonitis, lately discussed by Forshall et al.[14] Many children with this condition present with signs of obstruction: the immediate cause may be atresia or constriction by the bands and sheets of leathery adhesions which abound in a peritoneal cavity generally containing a considerable quantity of light-brown bowel contents. On the other hand, the peritonitis may be present without trace of an original obstruction. Nothing could look less encouraging to the surgeon, yet even here cures are being achieved.[14,15]

Louw,[16] in a review of 79 cases of intestinal atresia admitted to one hospital over a period of 25 years, showed the close connection between mortality and delay in diagnosis. The classical triad of obstruction is vomiting, distension, and absolute constipation. But distension is absent in many high obstructions; and the bowel may act deceptively, for meconium may be passed which appears normal, even to the experienced eye, but comes in fact from below a complete obstruction. Vomiting is the symptom that should arouse suspicions of obstruction. Vomiting of no serious significance is common enough in the neonatal period, but the production of green bile-stained vomit should be regarded as a matter for urgent investigation. Both Jolleys[13] and Louw[16] commend the use of straight radiography of the abdomen; this can be carried out with little disturbance of the infant, and the presence of fluid levels in dilated bowel gives an early diagnosis. Bizarre pictures may be obtained in cases of meconium ileus.[17,18] Radiography may be inconclusive in partial obstruction, but here delay for further investigation is more justifiable. Obstruction of the duodenum above the ampulla of Vater will of course give rise to persistent vomiting without bile staining; and œsophageal occlusion will produce the now well-recognised syndrome of profuse salivation and inhalation of saliva, with bubbling and cyanotic attacks. Persistent vomiting at this age may also arise from cerebral injury at birth or from infection. But either condition may accompany obstruction, and early radiography may be a wise precaution. Occasionally, cretinism can cause sufficient retention of meconium to produce a picture of obstruction.

Jolleys considers certain other investigations which may identify the cause of the obstruction before operation. But, in general, it seems advisable to follow Louw's advice and perform laparotomy as soon as possible after the diagnosis of an obstruction beyond the œsophagus has been made. The lesions are often more complex than the list of underlying causes suggests, and they may be multiple. A wide exploration is therefore necessary to ensure that nothing is missed. There are two exceptions to the need for laparotomy. Most children with neonatal obstruction due to Hirschsprung's disease recover after digital examination of the rectum or after a rectal washout given to confirm a diagnosis of obstruction; and a low imperforate anus can be dealt with from the perineum. In a few babies who show the full picture of obstruction, no obvious cause is found at operation; but some of them will later develop Hirschsprung's disease.

In sum, therefore, the mortality of intestinal obstruction in the newborn could be further reduced by treating all biliary or persistent vomiting as an urgent matter, and by dealing with these babies in units where the nurses and surgeons have a wide experience of this exacting condition. Even in these tiny patients the policy of "look and see" is safer than that of "wait and see."

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10. Smithers, D. W. *Lancet*, 1952, ii, 495.
11. Ehrenpreis, T., Sandblom, P. *Acta chir. scand.* 1949, 98, 404.
12. Gross, R. E., Ferguson, C. C. *Surg. Gynec. Obstet.* 1952, 95, 631.
13. Jolleys, A. *Brit. J. Surg.* 1952, 40, 201.
14. Forshall, I., Hall, E. G., Rickham, P. P. *Ibid*, p. 31.
15. Franklin, A. W., Hosford, J. P. *Brit. med. J.* 1952, ii, 257.
16. Louw, J. H. *S. Afr. J. clin. Sci.* 1952, 3, 109.
17. Neuhauser, E. B. D. *Radiology*, 1946, 46, 319.
18. Zimmer, J. *Acta radiol., Stockh.* 1948, 29, 228.

WE regret to announce the death on March 3 of Dr. MARC DANIELS, a member of the scientific staff of the Medical Research Council, at the age of 46.

THE INDEX and title-page to Vol. II, 1952, which was completed with THE LANCET of Dec. 27, is published with our present issue. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

palms and soles, severe "raindrop" pigmentation, and a few scattered vesicles of dermatitis herpetiformis Despite dimercaprol, paracentesis, supportive measures &c, he died two weeks later An accurate history was impossible to obtain owing to his desperately ill condition and language difficulties, but it seemed that he had been taking Fowler's solution for three or four years and was not attending a dermatological clinic

CASE 3—A woman, aged 38, was admitted to hospital in 1951 complaining of abdominal pain vomiting, anorexia, and pruritus She had attended a dermatological clinic seven years previously, when dermatitis herpetiformis had been diagnosed Subsequently she remained under the care of her own practitioner, receiving Fowler's solution during most of that time On admission she had marked hyperkeratosis of soles and palms, "raindrop" pigmentation, and active dermatitis herpetiformis, the liver edge was just palpable Treatment with dimercaprol and sulphapyridine produced an extraordinary change the hyperkeratosis slowly resolved, and the dermatitis herpetiformis is now completely controlled with 1 g sulphapyridine daily

CASE 4—A man aged 47, was referred to a dermatological department in 1951 suffering from hyperkeratosis of the hands He had advanced hyperkeratosis of hands and feet and "raindrop" pigmentation on the trunk The thickening of his palms was so severe that he could not grip properly, and this interfered with his work He also showed traces of psoriasis vulgaris on the left leg His liver was not palpable He had once been prescribed Fowler's solution at another hospital in 1946 and since that time he had obtained regular supplies from his local chemist without prescription He was treated with dimercaprol and the hyperkeratosis is now considerably improved

CASE 5—An intelligent schoolmaster, aged 65, attended a dermatological clinic in 1952 complaining of hyperkeratosis of the palms and soles He had been treated for these with radiotherapy at another hospital Examination showed classical arsenical keratoses of palms and soles, but no pigmentation, liver enlargement, or evidence of peripheral neuritis He admitted to taking an arsenic mixture for thirty years but had ceased three years ago

The dangers of inorganic arsenic must be realised particularly when given in small doses over a long period, but its value in dermatitis herpetiformis is unquestioned Given over short periods in gradually increasing doses followed by decreasing doses, it controls the disease more rapidly than any other drug except A C T H The itch of this disease has a character and intensity of its own, and patients will often plead for the drug despite warnings concerning its cumulative dangers It is not surprising, therefore, that some of them obtain the drug by various means The only other drug which controls the disease to the same extent is sulphapyridine, usually in quite small doses of 0 5–2 g per day Actually this is a much safer drug to use (in these doses) despite the pharmacologists' warnings of its dangers If sufferers from dermatitis herpetiformis were denied the controlled use of arsenic and sulphapyridine their lot would indeed be unhappy

Manchester G AUCKLAND

SLEEP PARALYSIS

SIR,—Having experienced sleep paralysis for many years, I can confirm the statement in your annotation (Feb 14) that one is quite conscious during an attack, though completely unable to move or speak

I would, however, question your statement that the disorder is "rather rare" When I wrote about sleep paralysis in the *Daily Express* recently, stating that doctors believed it to be rare, I had more than 600 letters from readers claiming they experienced the phenomenon Most of them described it in such vivid detail as to leave me in little doubt that they do so The findings of newspaper circulation research would suggest that such a heavy response means there must be many tens of ousands of people in Britain who experience sleep lysis

The letters made it clear that many people, though thoroughly frightened by their experiences, do not report them to their doctors for fear of looking foolish or being disbelieved

CHAPMAN PINCHER
Medical correspondent

Daily Express, London, E C 4

PAID SICK-LEAVE

SIR,—In your annotation you quote the analysis by Buzzard and Shaw of two years' experience of this scheme, which shows that sickness absence has doubled since its introduction The conclusion would seem to be obvious—namely, that if you pay people as much or more when not at work, they will be reluctant to return to work

There are exceptions, of course, but, in general, human beings do not feel that work is a pleasurable activity but rather an unpleasant necessity of existence Do you therefore urge the immediate abolition of such ridiculous sick-leave schemes? Not at all The general practitioner must persuade, cajole, and implore the worker to return to work Should he fail, for one moment only, to display the most exquisite tact in this thankless task, the worker will change his doctor There is always one doctor in any town who is known to give certificates on demand In my experience in general practice, the danger of a sick person returning to work too soon is negligible, except in the case of professional men and housewives These classes do not in any case benefit from paid-sick-leave schemes

Bridlington P D H CHAPMAN

SIR,—Your annotation last week on sick pay performs invaluable service in attracting the attention of those doctors who, like myself, do not normally read the *British Journal of Industrial Medicine*

Possibly the most important factor in the successful operation of a scheme for paid sick-leave is accurate certification, which demands thorough examination, which may be difficult under conditions of general practice

One of my duties is to see employees who are off work for more than 4 weeks Immediately on receiving a request to attend for examination, a proportion of them return to work Is this purely coincidental?

Judging by reports in the local press, there is much suspicion that sick-pay schemes operated in this area by local authorities are being abused, particularly those affecting building workers I do not know whether similar circumstances operate throughout the country In the case of building workers, the scheme provides great food for thought, for it began in 1951 and covered employment that was traditionally "casual" Under this scheme an employee enjoys up to 6 weeks' sick pay after 6 months' employment, with the usual provisions At the same time this agreement does not affect building workers employed by private firms Under their agreement they have no sick pay, but enjoy a guaranteed minimum week, as did council employees until the new agreement came into force

In those trades in which there is a shortage of labour this produced an invidious position, for when it was found that payment could not be made for loss of work owing to bad weather, employees left the council for private builders, even though they lost the benefit of sick pay Subsequently, there seems to have been a rise in minor illnesses amongst council employees during periods of bad weather

Another important factor in sick-pay schemes is the example set by some workers If one man is successful in obtaining benefit, although justified, others may feel aggrieved or tend to follow his example These difficulties cannot be entirely resolved by either purely medical or purely lay considerations, as the following examples may show

As work on one site was nearly completed, the foreman gave verbal notice to some labourers Before seeing the last to appreciate the feelings of others, who may be stupid, unable to express themselves and describe their sensations, or even wilfully misleading. Yet the symptoms can be supremely important in diagnosis. Anginal pain, for example, may be the only definite manifestation of coronary-artery disease, and is often far more valuable than the other findings.

When symptoms are unaccompanied by other evidence of disease, there is a modern tendency to consider them imaginary or neurotic. This last conclusion may often be true, though the reason for reaching it should not be the absence of evidence of bodily disease but the discovery of positive evidence of psychological disorder and the demonstration of how the symptoms are due to this disorder. Formerly such symptoms were often wrongly attributed to disorder of the organ where they arose; and this practice is still far from dead. The old physicians often ascribed palpitation, aching in the precordial region, sighing respiration, fatigue and giddiness (which in reality appear to be bound up with temperamental upsets and unrelated to disease of the heart) to heart strain, disordered action of the heart, tired heart, and, with even less justification, to valvular heart disease, especially when a systolic murmur happened to be present. Sir Thomas Lewis after the first world war gave the classical description of the enormous scale of this error in relation to soldiers.

In the field of interpreting symptoms unaccompanied by other findings, therefore, the old physicians were not superior, and were probably much inferior, to the new. If now symptoms are sometimes wrongly minimised, in the past they were often wrongly ascribed to fanciful pathological causes.

WHAT IS A CORRECT DIAGNOSIS ?

I concluded elsewhere [1] that it is wrong to assume that it is usually possible to make a pathological diagnosis. Apart from the patients with somatic symptoms of psychological origin, a high proportion of complaints, especially pains in the limbs and back, headache, and much dyspepsia, cannot yet be related to pathological states. Moreover, when the symptoms have some pathological basis, a bald pathological label does not represent their whole cause; the state of mind must also be taken into consideration, particularly when the lesion is chronic and comparatively benign. A hallux valgus does not wholly explain pain in the foot on walking; and the end-results of the treatment of this condition are determined by the patient's temperament as well as by the severity of the lesion and the nature of the operation.

In olden days the proportion of disorders without a known pathological basis was higher than it is today. Yet the reputation of the old physicians does not rest upon their ability to recognise and classify conditions of this kind; nor did they seem to lay great stress on the importance of psychological factors even when some pathological state was present. On the contrary, the stories of their prowess are mostly about their ability to diagnose gross, and especially fatal, pathological lesions.

Leaving considerations of this kind aside (which means ignoring a high proportion of diagnostic problems) and viewing diagnosis solely as a process of identifying some gross pathological lesion, it must be asked what is, in any particular circumstance, a correct diagnosis ? It cannot be disputed that the most searching clinical examination by the most brilliant diagnostician may not reveal sufficient data to reach a confident conclusion. Later developments may provide an answer, but until then the diagnosis should be tentative. A patient may have fever lacking any special characteristics such as those of malaria, no physical signs, and no symptoms save the general ones of fever. Clearly there are numerous possibilities, including enteric fever, brucellosis, Hodgkin's disease, pyelitis, infective endocarditis, and various kinds of septicæmia. A physician may make an inspired guess that one of these conditions is present, and, if subsequent developments confirm his guess, his feat may appear most impressive. Although he turned out to be right, his diagnosis was in reality wrong because it was formed on insufficient grounds. The correct provisional diagnosis here was the bald "pyrexia of undetermined origin." A similar conclusion can be reached of many other diagnostic problems, such as the "acute abdomen" and the chest possibly the seat of malignant disease.

Often, therefore, a definite diagnosis is unjustified, and the best diagnostic statement is provided by a review of the various conditions which could explain all the available data; though often it will also be sound to conclude that some condition is highly probable, others are possible, others improbable, and others conceivable. The reputation of many of the old physicians does not depend on their reaching cautious conclusions of this kind, but on their dogmatic statements that the diagnosis is such and such a disease.

It should also be remembered that diagnosis is not an end in itself, but a means to providing treatment or making prognoses. In the last century specific medical treatment hardly existed, and until towards the end of it there was little effective surgery. It was perhaps because of this that diagnosis came to be considered so supremely important, since the physician was almost impotent to do anything but diagnose. And there then existed a host of futile or dangerous remedies persisting from a more ignorant epoch, and the physician who was a therapeutic nihilist as regards these remedies was clearly superior to his less critical colleague who still continued to use them. Now we have such a large number of highly effective, and often life-saving, drugs and so many excellent surgical procedures that the old doctrine which emphasised the importance of making an accurate diagnosis before giving treatment is far from universally applicable. For example, some patients with undiagnosed high fever should be treated blindly, especially when malignant tertian malaria is a possibility, for the failure to discover parasites in the peripheral blood proves nothing, the untreated disease is often fatal, and the specific drugs for malaria are highly effective and can do no harm to those without malaria. The desperately ill patient with swinging fever may rightly be given penicillin while undiagnosed. And a reasonable suspicion of amœbic hepatitis justifies the giving of emetine. Indeed, the possible presence of a potentially fatal disease, or a disease liable to cause permanent sequelæ, which cannot certainly be excluded and is susceptible to some specific remedy, provides sufficient reason for giving that remedy while the diagnosis is still in doubt. Moreover, the study of the remedy's effect can itself often be diagnostic. The failure of fever to respond to quinine provides virtual proof that malaria is not the cause of fever.

A physician cannot, then, be judged, as the old physicians often seem to have been judged, solely by his ability to reach precise diagnoses, for the following reasons:

(1) In a high proportion of cases no pathological diagnosis can be made.

(2) When a pathological lesion, especially if chronic and benign, is related to the symptoms, the mere identification of this lesion does not make a complete diagnosis, since the state of mind, which is partly responsible for the symptoms, must also be considered.

(3) When a patient clearly has organic disease there are often insufficient data to reach a precise diagnosis, and the best diagnostic statement is represented, not by a guess at a likely diagnosis, but by a review of the various possibilities.

(4) Diagnosis is not an end in itself, but the means to an end. It is often right to give treatment when diagnosis is but tentative and the effect of treatment may itself be diagnostic.

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1. Todd, J. W. *Lancet*, 1952, ii, 1235.

seems that the only satisfactory form of exercise tolerance test is to walk The patient is concerned with the alleviation of the symptoms which interfere with his daily life, and the test must produce those symptoms under conditions as nearly natural as possible The more severe the test the more difficult it is to demonstrate an improvement a patient whose condition improves to the stage of having no pain on the level may easily experience pain on climbing stairs or a steep hill

In an exercise tolerance test the rate at which the work is done has a profound effect on the amount of work which can be performed One of the main purposes in developing the "claudicometer" was to measure the variations in distance walked at a constant speed Assessment of exercise tolerance of patients with arterial disease is difficult enough without introducing extra variables

Criteria

The accumulation of muscle metabolites at the commencement of exercise is rapid, even in the individual with a normal blood supply In the patient with a diminished blood supply the accumulation of metabolites will cross the pain threshold before a stabilisation level is reached—hence the intermittent claudication The measure of the deficiency is shown by the stabilisation level and by the ability of the patient to continue after the onset of pain, rather than by the time or distance at which the pain first appears

Statistical Analysis

Arguments about the correct form of statistical treatment for a given set of clinical data are interminable, and we do not propose to enter into them We would point out, however, that dilution with insignificant data will render any type of analysis meaningless Where both time and distance are variables in an exercise tolerance test the results are hard to interpret An increase in a patient's walking distance from 50 yards to 100 yards—a 100% improvement—will not produce a satisfied patient A reduction of an athlete's time for 100 yards from 10 seconds to 9 5 seconds—a 5% improvement—will make headlines

The use of vitamin E in arterial disease will be a controversial subject for a long time to come, and any contribution to the subject, from whatever angle, is extremely valuable

A M BOYD
A HALL RATCLIFFE
K BLOOR

University Department of Surgery,
Manchester Royal Infirmary

SIR,—We have just seen the report by Dr Hamilton and his colleagues Before this study Hamilton and Wilson [1] had demonstrated that there was no case for any other agent now in use against intermittent claudication

The question that arises is Can any vasodilator ever be found that will survive the rigours of the "double blind" test? How lucky that liver extract induced a rise of reticulocytes in the blood! Could it have been demonstrated to be useful for addisonian anæmia by a clinical method analogous to Hamilton and Wilson's? We have encountered an exemplary controlled study on the use of nitroglycerin in angina in which that drug was proven valueless! How would one demonstrate the value of irradiation for carcinoma by such a standard? We think insulin was fortunate to be open to test by blood-sugar levels Could it have survived the "double blind" test on the clinical features of diabetes alone? Remember that when blood-sugar studies demonstrated the efficacy of insulin in the hyperglycæmia of diabetes they took no account of its inadequacy for the vascular half of the disease So much depends on the criteria selected

All studies having pain as an end-point are open to serious criticism—except one kind of pain, "rest pain" No subjective factors can induce a man to awaken from sound sleep complaining of severe leg pain, and obviously such patients are far-advanced cases—further advanced than the patients who complain of leg pain only on exertion If patients with rest pain in the legs can be relieved—and we have often seen alpha-tocopherol accomplish this—the presumption would be strong that the same agent can do at least as well in milder cases

Patients with intermittent claudication often have irreversibly sclerotic vessels or other chronic obstructions of the arterial supply to the legs [2] An improved collateral circulation, improved local oxygen utilisation, and local vasodilatation should help them Only alpha tocopherol can meet all these demands at once Ten groups of workers contend that it does

WILFRID E SHUTE
EVAN V SHUTE

Shute Institute,
London Canada

PROVINCIAL MEDICAL JOURNALISM

SIR,—Following the kind remarks about the *University of Leeds Medical Journal* made by Dr Brockbank in his article of Feb 28, I should like to draw attention to the fact that we are now able to announce that our subscription has been reduced from 1 guinea to 15s 6d per annum

HUGH GARLAND
Editor *University of Leeds Medical Journal*

Leeds, 1

POLIOMYELITIS IN DENMARK

SIR,—Having recently visited the Blegdam Hospital in Copenhagen to study the treatment of respiratory paralysis in poliomyelitis, we have read with great interest last week's letter from Dr Kelleher and Dr Sellick No-one who has seen the work in Copenhagen can fail to be impressed with it, and we agree that it is now a matter of urgency in this country to review our own methods of treatment

The tracheotomy and bag-ventilation technique is reasonably simple, and the apparatus, in comparison with tank and cuirass respirators, is cheap, easily stored and mobile it is familiar to every anæsthetist The operation of tracheotomy, performed over a bronchoscope or endotracheal tube, is in our experience very simple by comparison with the stab-tracheotomy well known in fever hospitals We were most impressed by the ease with which nurses in Copenhagen could pass catheters through the tracheotomy tubes to suck out large amounts of mucus from their patients' bronchi Nevertheless, we regard it as advantageous for a unit treating poliomyelitis by this method to be linked with a thoracic surgical unit

We have equipped two beds at Fazakerley Hospital with complete bag ventilation equipment this includes cylinders of 50% nitrogen-oxygen mixture and suction pumps We are now training doctors and nurses in the technique by using a "dummy" lung, and we hope to enrol and train a reserve of medical students

Our main difficulty is the supply of the nitrogen oxygen mixture this is not a standard mixture in this country, and until cases of respiratory paralysis require treatment there is no demand for it It is therefore not practicable to have large numbers of cylinders throughout the country standing by and out of circulation Another difficulty is the supply of electric suction-pumps This is less serious, and cheap water pumps attached to wash basin taps would probably prove adequate in most cases with one or two more powerful pumps available for emergencies

The possibility of producing a "mechanical student" to squeeze the bag must also be tackled One machine was on trial in Copenhagen, and we hope soon to produce a cheap, simple, and effective machine here The place of tank and cuirass respirators in the future treatment of poliomyelitis cannot be assessed the cuirass, at least seems still to be indispensable We recently produced in our hospital workshops, a cuirass which, if not elegant, was highly efficient It is surely not beyond British industry to produce a first class cuirass respirator upright with the elbows supported. Pain, if present, was always more severe at night.

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[1] Hamilton M Wilson, G M *Quart J Med* 1952, 21, 169

[2] Boyd A M Ratcliffe A H Jepson R P James, G W H *J Bone Jt Surg* 1949, 31B 325

Stiffness, when it occurred independently of pain and as a result of effort or of too long maintenance of one position, responded quickly to exercise or to light massage.

Areas of superficial hyperæsthesia.—Patches of skin became unduly sensitive from time to time. The sensation was similar to the tender scalp so often associated with an attack of influenza.

PATHOLOGY

The only noteworthy feature was an initial rise of the erythrocyte-sedimentation rate to 46 mm. in 1 hour. At the conclusion of the attack six months later a reading of 6 mm. in 1 hour was obtained.

TREATMENT

Before the patient diagnosed his condition he went to a spa in the hope of a quick cure. His optimism was unrewarded, and painful experience suggests that this form of treatment is unsuitable in the early stages of acute rheumatoid arthritis.

The diagnosis having been established by wiser minds, it was decided, after a consideration of the possible merits of cortisone and gold, to rely on a prolonged course of salicylates combined with complete rest in bed. This treatment was continued with minor interruptions for five months. The interruptions in this treatment were due to the trial of penicillin and chloramphenicol, and for test purposes or because the digestion was upset.

Except for one period of ten days during which soluble aspirin was tried, the preparation used was a sodium-salicylate mixture. Until the terminal phase of the illness the dosage was never less than gr. 180 daily (gr. 30 four-hourly), and for considerable periods gr. 240 daily (gr. 40 four-hourly) was required.

The aspirin experiment was not a success. The dosage—gr. 12$^{1}/_{2}$ four-hourly—did not control the symptoms, and the mixture caused severe localised epigastric pain, which remained for some days after the mixture was discontinued.

Penicillin was used as an umbrella to cover minor precautionary dental extractions. The penicillin seemed to have no influence on the arthritis.

Chloramphenicol used at a later stage seemed to have no immediate influence on the rheumatoid arthritis. Its use was followed by an attack of "thrush" and evidence of riboflavine deficiency. The "thrush," which affected the fauces, gave rise to an unexpectedly severe feeling of malaise. A week after this intercurrent infection had subsided there was much improvement in the main complaint.

CONVALESCENCE

The patient was subject to rheumatic twinges, and stiffness was much more easily incurred than normally by effort or by remaining in one position; but muscular power increased rapidly and was regarded as evidence of recovery.

SOME OBSERVATIONS

Sodium-salicylate Medication

Mixtures are commonly flavoured with syrup of orange. This flavouring, though palatable to start with, becomes nauseating later. The addition of gentian then gets over this difficulty.

There seems to be a "critical dose" of this preparation. Above this dose the joints are free and pain is absent, whereas below this dose pain is present and movements are limited. Possibly the critical dose for some patients in the acute phase may be as high as gr. 300–360 daily. The margin between adequate and inadequate dosage is small—about gr. 5.

Whether salicylates cure rheumatoid arthritis may be a matter for argument, but in adequate dosage they seem to prevent the development of permanent deformities and other disabilities. As an instance of this, on one occasion during the illness all medicines had to be omitted for some days because of severe dyspepsia which had resulted from taking soluble aspirin. During this medicine-free interval considerable ulnar deviation of the left hand, accompanied by fusiform swelling of the interphalangeal joints, speedily developed. These deformities cleared up completely within forty hours after the resumption of treatment with sodium salicylate gr. 40 four-hourly. Further, after an illness lasting five months the patient was left with no residual deformity or disability.

Side-effects of the salicylates were as follows:

Deafness was severe, and more annoying to visitors than to the patient because the latter always shouted at the former. There seemed to be a maximum of deafness after which it did not increase with increased dosage.

Gastro-intestinal symptoms included mild flatulence as an early symptom and slight diarrhœa as a late one.

Saturation with salicylates required forty-eight hours' medication. Partial desaturation was shown by return of the pain twenty-four hours after stopping the mixture, and full desaturation by complete return of the hearing forty-eight hours later.

Sweating was not so prominent a feature as anticipated; it became less noticeable as time went on.

If salicylates are effective because they encourage the secretion of cortisone it is noteworthy that large quantities can be taken without cortisone side-effects becoming apparent.

No evidence of hæmorrhage into any ductless gland was observed.

It was noteworthy that, when for any reason the course of salicylates was interrupted, an occasional dose of aspirin or of 'Veganin' was of very little use in alleviating symptoms.

Vitamins.—The importance of vitamins in the treatment of rheumatoid arthritis has been emphasised, and every effort was made to ingest vitamins in adequate quantities. All preparations tried, however, gave rise to violent indigestion; and, since it was considered essential that salicylates should be continued at all costs, vitamin preparations were abandoned lest the ensuing dyspepsia should prevent the assimilation of the salicylates. In the event failure to take extra vitamins did not prejudice recovery.

Iron and liver therapy.—Neither of these medicaments was indicated, because red-cell counts and hæmoglobin levels remained high throughout the illness.

Physical medicine.—Electrical therapy of one kind and another was of only quite transitory value. Light massage was definitely very helpful; it relieved stiffness and was very soothing. An hour's massage twice daily was not found too fatiguing.

NURSING POINTS

New Zealand lift.—This method of lifting a patient up the bed was unfamiliar. It is comfortable for the patient and imposes far less strain on the nurses than the method generally in use in this country. In this lift the two nurses stand facing each other across the bed *behind* the patient—i.e., between the patient's back and the head of the bed. The patient then leans forward and raises his arms slightly from the sides of his chest. The nurse on the right side then inserts the point of her right shoulder into the patient's right axilla while her right hand travels forward to a position under the patient's right knee. The nurse on the left side places the point of her left shoulder into the back of the patient's left axilla and passes her left hand forward to meet her partner's right hand under the patient's knees. With this method the patient's weight is borne by the nurses' backs without strain. There are the further advantages that the patient is lifted higher off the bed and that, since each nurse has a hand free, a bedpan or an air-ring can be easily inserted.

Bed-cradle.—This accessory is often inserted with its long axis parallel with the long axis of the bed. If it is inserted tranversely with one side tucked under the end of the mattress, the bed-clothes can be arranged over relative low morbidity and mortality in this age-group from tuberculosis, and surely the removal of these undiagnosed infectious patients will in the long run achieve greater protection of the child than is likely to result from B C G vaccination at earlier ages

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CHARLES J STEWART

CONGENITAL DEFECTS FROM MATERNAL RUBELLA

SIR,—I would support Dr Dudley Baker's objections (Feb 21) to the deliberate spreading of german measles amongst schoolgirls Further, the complications of german measles include encephalitis, is it right deliberately to infect children, especially without parental consent, when it is impossible to forecast the risk ?

E D IRVINE
Exeter
Medical Officer of Health

ISONIAZID IN MURINE LEPROSY

SIR,—Dr Goulding, Professor Robson, and Dr Rees in their preliminary communication last week report that isoniazid is active against *Mycobacterium lepræ murium* injected into the cornea of mice They emphasise that this conclusion is based on the result of a single experiment, but observations made by us *in mice infected* intravenously with this organism support their findings In fact, we submitted a report, entitled The Activity of Isonicotinic acid hydrazide in Murine Leprosy, to you for publication in November, 1952, but this was rejected on the grounds of being too experimental to justify giving space to it, and it has now been published elsewhere [1] We showed that isoniazid almost completely suppressed the disease which became widespread, including the skin, in untreated mice

Goulding and his colleagues also emphasise that the value of using this murine strain for forecasting the activity of drugs in human disease is doubtful We, too, stressed this, but pointed out that as there was available at least one group of drugs, the sulphones, that was active in man it should be possible to settle this question by treating some of the infected mice with a sulphone Goulding et al included oral 'Sulphetrone' in their experiment, but this drug may not be a satisfactory control when given by this route because very little is absorbed from the intestinal tract and its oral activity in man depends upon a breakdown to 4 4'-diaminodiphenyl sulphone (D D S), and the extent of the breakdown is variable In our experiment, however, we compared the activity of isoniazid not only with that of sulphetrone but also with those of D D S , and of streptomycin and the thiosemicarbazone, T B 1/698 Our results with the sulphones were, however, similar to those of Goulding et al , for neither drug had significant effect upon the disease , but equally important was the finding that streptomycin was almost as active as isoniazid, and even the thiosemicarbazone had some effect, for not only was the number of organisms in the various tissues reduced but the distribution of the lesions in the liver was altered

In view of the widespread use of the sulphones in human leprosy, as compared with the relatively rare use of streptomycin and the thiosemicarbazone, our results might be interpreted as indicating that the murine strain is more closely related to the tubercle bacillus than to the bacillus of Hansen Published reports, however, suggest that these drugs may in fact be more active than the sulphones in the treatment of leprosy, and that their restriction is more on account of high toxicity and cost than lack of activity In consequence we are by no means certain that the test is of no value for forecasting antileprotic activity of drugs.

We, too, like Goulding and his colleagues felt that th activity shown by isoniazid against the murine strai should encourage further inquiries into the value of the drug in the treatment of human disease These workers regard the [illegible] clinical report by Low as strongly [illegible] oniazid will prove of litt value, but there are other reports [3] [4] which are le discouraging

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MARGARET BARNETT
S R M BUSHBY

HALLUX VALGUS

SIR,—I hasten to follow in the footsteps of Dr Boo (Feb 21) in deprecating the defeatist tone of yo leader (Feb 14) on hallux valgus

In 1951 a chiropodist, Mr Charles A Pratt, publish a very useful and pungent little book, *Your Childre Feet*, in which he dealt briefly, clearly, and vigorously wi the effects of bad shoes on the health of the feet Yo present attitude is all the more strange in view of yo approving comments [5] on the book

> "It is surprising with what complacency the authorit and the public accept the fact that four people out of eve five have foot defects severe enough to interfere with the comfort and efficiency It is perhaps not so well realis that the great majority of these defects arise during childho and are largely preventable Though it lies within t power of the authorities to effect the remedies, they w never act except under the pressure of public opinion "

The truth of these remarks was well illustrated by t extremely unsatisfactory and evasive reply given the Minister of Health to the following question on Jan by Mr R C D Jenkins

> "In view of the very high incidence of acquired fo deformity in children, will the Minister of Health give cle guidance to parents by issuing a 'seal of approval' th manufacturers, under licence, could emboss on their footwea to show that it complied with the Minister's requirements fro the point of view of foot health ? "

The Minister answered "I think that, although difficult over material and manufacture during the war and immed ately post war years have created difficulty, sufficient well co structed shoes in an adequate variety of sizes and shapes fit the feet of the great majority of children are now availab but finding shoes to fit the small minority of children wi abnormally shaped feet is still a difficulty With regard the 'seal of approval,' I favour the idea in principle but, view of the fact that the boot and shoe trade have ma considerable efforts in recent years to produce footwear whi meets health requirements, I would prefer to see a marki similar to a seal of approval agreed upon by the trade its rather than enforced by a Government department "

This is, of course, a travesty of the facts, which a quite plain In only a few relatively expensive bran is it possible to buy shoes at all which fit the natur shape of the feet , and even these are mostly availab only for the younger children and teen agers in a ve limited range of sizes It is quite misleading to imp that the difficulty is confined to fitting "the sma minority of children with abnormally shaped feet " O the contrary, most shoes will only "fit" children wi hallux valgus We may all agree that there are intrins factors in the ætiology of hallux valgus (e g , malnutritio poor constitution, faulty habits, lack of exercise), b surely it is self evident that if feet are splinted for t greater part of waking life in a valgus toe positio (as they are in the majority of shoes), then hallux valg at least tends to result Furthermore no convincin evidence exists of any substantial incidence of hallu valgus in unshod populations

"Research" is not the primary need, nor are elaborat plans for training new shoe fitters What is imperati

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[1] Bushby, S R M Barnett M *Leprosy Rev* 1953 24, 18

[2] Lowe, J *Lancet* 1952 ii 1012

[3] Gil D E T *Rev Leprol , Font* 1952 3 21

[4] Latapi F , Rubio, J B Report to American Society of Tropic Medicine *Chem Engng News* 1952 30 4968

[5] *Lancet*, 1951, i, 1421

satisfactory groups combined was 7%. 45 patients had adhesions together with "atelectasis" of part of the collapsed lung, but no persisting cavities. 80% survived 8 years—almost the same survival-rate as those with a free lung. Nor was there any difference in the incidence of effusions and empyemas. Previous reports of the ill effects of atelectasis were not therefore confirmed.

Influence of adhesions.—There is a widespread belief that adhesions in a pneumothorax are always a danger to the patient. This can be tested by comparing the *satisfactory* and *adherent-satisfactory* groups.

57 patients with two or three zones involved had a *satisfactory* pneumothorax; 82% survived 8 years. But 92% of 141 similar patients with adhesions but no cavities survived for the same period. The "sputum-conversion" rate was almost the same in the two groups (80% and 85%). 37% of the *satisfactory* group required further collapse treatment; but only 30% of the *adherent-satisfactory* group. 25% of those with a free lung required later collapse therapy for a previously clear contralateral lung; but this was necessary in only 11% of those with adhesions but no cavity. Persistent effusions were found in 36% of the *satisfactory* group and 35% of the *adherent-satisfactory* pneumothoraces; the frequency of empyemas was 14% and 9%. The 5-year survival-rate after deliberate termination was 91% in the *satisfactory* pneumothoraces and 94% in the *adherent-satisfactory* group. In these two groups there was no significant difference between the 8-year survival-rates of those patients who had few adhesions, numerous adhesions, or a free lung. The conclusion is that closure of cavities, and not absence of adhesions, is the major factor determining the prognosis and is the key to successful pneumothorax treatment.

Of 62 patients with non-cavitated disease who had unilateral pneumothoraces, 87% survived 8 years. Only 15 had free lungs—a number too small to justify a separate statistical analysis.

Other Forms of Collapse Therapy

Altogether 77 patients were treated by thoracoplasty, and 65% of those who survived operation lived for 8 years. The results in the whole group were statistically inferior to those of an *adherent-satisfactory* pneumothorax. But among the 36 patients whose sputum became negative after operation, the 8-year survival-rate was 91%. Of 38 who had simultaneous bilateral pneumothoraces, 55% survived 8 years; and of 29 who had extrapleural pneumothoraces 66% survived 8 years.

CONCLUSION

This survey of 1153 patients with pulmonary tuberculosis who were treated at Frimley Sanatorium and were followed for at least 8 years shows that the expectation of survival is inversely proportional to the extent of the disease, regardless of other factors. The closure of cavities, and not the presence of adhesions, is the key to successful pneumothorax treatment.

SUCCESSION TO VACANT PRACTICES

A LETTER[1] from the Ministry of Health to executive councils sets out some changes in the provisions governing the succession to a vacant practice by a partner and imposes certain restrictions on the acquisition of vacant practice premises.

Succession by a Partner

The letter points out that partnerships have occasionally been formed between an established single-handed doctor, who intends or is expected shortly to retire, and another doctor, apparently with the object of enabling the latter to succeed to what is essentially a single-handed practice. Such an arrangement defeats the intention of the regulations by which the executive council and the medical practices committee in consultation are required to select doctors for single-handed vacant practices.

> "In order to meet this situation, the Medical Practices Committee, in agreement with the Department and the General Medical Services Committee of the British Medical Association, will not, unless there are special circumstances, accept one partner as a logical successor to another partner who has died or resigned, if the partners have not been in active practice together for about a year. It is realised that there will often be good reasons for an exception being made. A genuine partnership might, for instance, have been formed and then terminated soon afterwards by the sudden death of the original partner, or his resignation because of unexpected illness . . . . The Committee will give sympathetic consideration to such cases."

Acquisition of Vacant Premises

Sometimes a doctor selected for a vacant practice has to face competition from another doctor who has secured the premises from which the practice was previously conducted. To help the selected doctor to establish himself and to buy the premises if he wishes, new provisions are to be inserted in the terms of service.

> "The effect of these provisions is, in short, that the successor to a vacant practice will have a month in which to decide whether to accept an offer of the practice premises. The month will date from the day when the successor is advised that there has been no appeal against his appointment or, where there has been an appeal, from the date when the decision of the Minister has been issued. The terms of the offer will have to be approved by the Medical Practices Committee which, following the necessary inquiries, will act as expeditiously as possible. Where, therefore, the premises are to be offered to the successor, in order to allow sufficient time for the Committee to obtain a valuation the owner (or his representative) should forthwith be advised to apply to the Committee for the necessary certificate. If the successor does not want the premises, or if he fails to accept the offer within a month, the premises can then be used by any other doctor. If no offer of the premises is made, they cannot be used by any other doctor for a practice within the Health Service during a period of twelve months from the date of the successor's appointment, except with the consent of the Executive Council or, on appeal, of the Medical Practices Committee."

Public Health

Influenza

THE weekly total of deaths from influenza in the 160 great towns of England and Wales decreased in the week ended Feb. 21 for the first time since the epidemic began in early January. There were 521 deaths, compared with 530, 446, and 313 in the three preceding weeks. In the London and South-eastern region 201 people died—73 less than in the week ended Feb. 14. In the northern half of the country there was a slight increase in deaths from influenza. Of those who died, 404 were aged 65 or over. Reports from medical officers of health indicate that the epidemic in the south is subsiding gradually rather than abruptly. For the week ended Feb. 24 the Ministry of National Insurance reported a decline in the total number of claims for sickness benefit; all regions showed at least a slight reduction in claims received. In the London area the Emergency Bed Service was able to find beds for 86·5% of the cases referred to it in the week ended March 2. The white warning has been withdrawn.

In the United States reports from various parts of the country indicate that the epidemic is now subsiding. The disease has been most widespread in the central and southern States. It has generally been a mild infection due to an A-prime virus; the illness rarely lasted more than a few days, and complications were uncommon.

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[1] E.C.L. 11/53. Feb. 25, 1953.

in cor pulmonale has been confirmed in catheterisation studies where the right ventricular filling pressure has been shown to fall considerably after such an injection [6] It would be most interesting to hear other physicians' opinions concerning venesection and digitalis in this condition

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K W DONALD

GONORRHŒA IN ANCIENT ROME

SIR,—It is surprising that one so highly critical of tradition as Dr Vertue, who dismisses the generally accepted interpretation of Celsus's chapter on venereal diseases with a simple "I believe it is wrong," should take the reports of antiquity about "seminal flux" at their *face* value The mere fact that we still, in deference to Galen, refer to this disease as *gon*orrhœa should have preserved him from such a naïve error

Classical medicine is full of references to these seminal discharges, which are described as cold by Aretæus, as occurring without sexual excitement or imaginings by Celsus, and as biting and burning in character by Hippocrates Has Dr Vertue ever come across a case of seminal flux which polluted the patient lying and sitting as described in *Leviticus*, continuing day and night (Galen) ?

His acceptance of the orthodox translation of piles for *mariscæ* is equally uncritical. Admittedly, piles rhymes with smiles, and in lay terms any anal excrescence might be referred to as a pile, but this tells us nothing of the nature of the lesion *Marisca* is a kind of fig, and the term *ficosus* is used by Martial to designate persons with figlike excrescences round the anus

De familia ficosa
Ficosa est uxor, ficosus est ipse maritus
filia ficosa est, et gener atque nepos
nec dispensator, nec villicus, *ulcere turpi*
nec rigidus fossor, sed nec arator eget

Are we to assume that Martial is alluding to an epidemic of hæmorrhoids on this unfortunate estate ? Or is it not more reasonable to infer the contagious nature of these figs from the above epigram ? Whether tumid or humid the correct translation in medical terms of Juvenal's *marisca* must remain an open question

It would be impossible to give in this column all the references to gonorrhœa in antiquity, but by starting with R A Fraser's monograph on gonorrhœa (H Kimpton, 1923) and working his way backwards, Dr Vertue would soon be convinced that, even in the absence of bacteriological proof, there can be no reasonable doubt that gonorrhœa was a common and well-known though badly understood disease in ancient Rome

Edinburgh

ERICH GEIRINGER

WATERHOUSE-FRIDERICHSEN SYNDROME TREATED WITH CORTISONE

SIR,—Dr Haynes describes (Jan 17) how a man, aged 47, considered to show the Waterhouse-Friderichsen syndrome, died in *convulsions seven hours after* a dose of 100 mg of cortisone and four hours after 20,000 units of intrathecal penicillin

Dr Haynes attributes the convulsions to the cortisone, and of course he may be right Alternatively he may be a little precipitate, as indeed I think he is He should remember that no convulsions occurred in the two cases described by Nelson and Goldstein [7] or in the case described by Newman [8] when much larger doses were used, and they occurred in only one of the cases described by us [9] Here they were clearly due to the cortical hæmorrhages, long recognised as hazards of meningococcal meningitis *Incidentally it is a pity that Dr Hay* does not record the post-mortem findings, if an examination was made, or the effects of the cortisone on th patient's blood-pressure

One other point seems to require clarification W do not recommend the use of cortisone "in meningitis, but solely to combat collapse—the essential feature the Waterhouse Friderichsen *syndrome* Furthermore, would be prepared to advocate its trial in any fulmina *infection in which collapse occurs—for example,* so cases of hypertoxic diphtheria

From the scanty evidence av [illegible] to infer that death, so usual in the Waterhous Friderichsen syndrome, is due to temporary adren exhaustion, resulting in the shortage of some compon for which cortisone seems to compensate The sa may apply to other infections, and indeed, in line wi Selye's hypothesis, to shock produced by any form "stress"

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Isleworth

G E BREE

KWASHIORKOR

SIR,—Your leading article [1] *stated that this conditio* as defined by Brock and Autret,[2] is a distinct clinic entity Although these authors have produced muc useful information, their definition of kwashiorkor somewhat arbitrary and impracticable It is based o "a fundamental group of five signs," and "any clinic *syndrome which includes these five characteristics* an occurs in Africa, can undoubtedly be called kwashiorkor *Of these five basic criteria, alterations* in skin and ha pigmentation are singled out for special attention Th authors are apparently not prepared to include in th syndrome cases without these pigmentary changes The state, for instance, that the term kwashiorkor cann be applied to the malnutrition syndrome, formerl prevalent among white children in Europe and th United States of America, which Czerny named *Mehl ährschaden* "If used in this way, the term loses i etymological meaning," *they say,* because white childre show comparatively little alteration of skin and ha pigmentation when they are malnourished Clearl Brock and Autret attribute pathognomonic significan to changes in the skin and hair which may or may n occur in malnourished children, and this is done f etymological reasons

Cicely Williams, who introduced the word kwashiork *into* medical terminology, pointed out recently[3] tha this narrow application of the term excludes early case suffering from the ill effects of a poor diet She prepared to diagnose *the* syndrome in infants "wit slight swelling of the dorsum of the foot, or with unac countable peevishness, or with failure to gain weight, in the absenc [illegible] changes I tried to show in an earlier [illegible] on the presence o pigmentary changes in the diagnosis of kwashiorko automatically excludes infants weaned on a water pa diet at, or shortly after, birth, because at this age suc a diet usually kills so rapidly that pigmentary chang *have no time to develop*

It seems to me that the definition given in the W H O publication, however correct etymologically, can be o little value to those interested in the ill effects of bad diet To insist on pigmentary changes creates syndrome as artificial as that of "infantile pellagra," in which the dermatoses become the sine qua non o diagnosis, or "nutritional œdema" in which the water logging of the tissues becomes the all important sign

It is now accepted nearly everywhere that kwashiorko can be caused by faulty diet alone—i e, in the absence

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[6] Ferrer, M I Harvey, R M, Cathcart R F Webster C A, Richards D W, Cournand, A *Circulation* 1950 1, 161
[7] Nelson J Goldstein N *J Amer med Ass* 1951, 146, 1193
[8] Newman, L R *Ibid*, p 1229
[9] Breen, G E Emond R T D, Walley R V *Lancet*, 1952, i 1140

[1] *Lancet* 1952 ii, 1070
[2] Brock, J F Autret M Kwashiorkor in Africa W H O Monograph Series no 8 Geneva, 1952
[3] Williams, C D *Brit med J* 1952 ii 1360
[4] Kahn, E *Lancet*, 1952 ii 588

Letters to the Editor

DEATHS IN THE FOG

SIR,—Analyses of the effects of the December fog by Dr. Logan, in his article of Feb. 14, and by Dr. J. A. Scott, in his report[1] to the L.C.C. public-health committee, have been based on a comparison of the number of deaths during the week of fog with the normal number of deaths expected at the same time of year. On this basis they have shown a great excess, amounting to 4000 deaths in the London area.

Dr. Abercrombie (Jan. 31) has presented graphs of the applications for urgent admission to hospital made to the Emergency Bed Service at this time. These applications provide a valuable index of the amount of urgent sickness, and, as he shows, the periodic rises are largely due to outbreaks of respiratory disease. I have since been allowed, through the kindness of Mr. R. Peers, to study the more detailed originals of these graphs, which throw considerable doubt on the validity of the comparison of the fog week with a normal week at this time of year.

Demands for admission started to increase in a normal and irregular manner in September, and by Nov. 23 the "moving" weekly total had reached 1070. On that date the shape of the curve altered radically and abruptly, a completely steady and progressive multiplication of demands occurred and by Dec. 5 the moving weekly total had reached 1470. Judged by all past experience of the service, this represented an acute epidemic, and such a demand had only been experienced once before in the history of the service—during the influenza outbreak of January, 1951, when it exceeded this figure for three weeks.

It was only on Dec. 5 that the fog started and at a time when sickness was already exceptional; it does not therefore seem reasonable to assume that all or even the greater part of the deaths which occurred during the ensuing week were attributable to the fog.

The fog, however, had a considerable effect on demands for admission: they had been increasing at a completely regular rate for the previous fortnight, but this rate accelerated on the day the fog started and continued at this higher value for the succeeding five days, when it slowed down. The peak of demands for admission occurred on Dec. 12, three days after the end of the fog, and thereafter the demand rapidly declined.

It would seem from these figures that the fog caused considerable morbidity, but that this came as an addition to an epidemic occurrence with only one recent precedent, and which may well have been responsible for a part of the mortality of which you have published analyses.

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London School of Hygiene and
Tropical Medicine.
G. MACDONALD.

ARSENIC

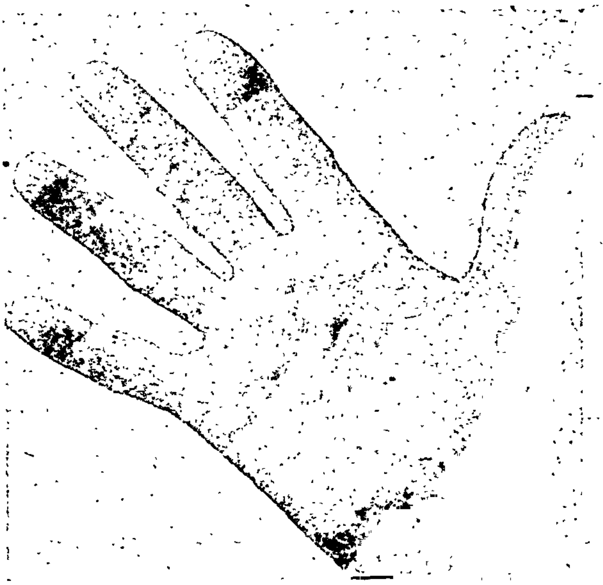
SIR,—The article by Dr. Wade and Dr. Frazer (Feb. 7) describing a case of toxipathic hepatitis due to arsenic, raises some points of interest and several of importance.

Hyperkeratosis occurs on both palms and soles, and occasionally on the backs of the hands and fingers as well. It is diffusely spread over the whole of the palms, soles, and flexor surface of the fingers, and in addition there may be localised nodules of hyperkeratosis in these areas and on the backs of the hands. These localised tumours are called arsenical keratoses and may become malignant. Epitheliomata of basal-cell type may also develop later on the trunk without pre-existing keratoses. In the case described no mention is made of the presence or absence of hyperkeratosis on the soles—an important point when trying to decide whether the palmar hyperkeratosis was due to arsenic. It is of interest, too, that this palmar hyperkeratosis was unchanged after treatment with dimercaprol. In my experience the hyperkeratosis due to arsenic lessens considerably, but the pigmentation remains unchanged. I would suggest that this palmar hyperkeratosis was occupational.

Pigmentation.—The illustration does not bear out the statement in the text that the patient had "raindrop" pigmentation. It should be remembered that dermatitis herpetiformis itself causes pigmentation of the skin in the areas where the vesicles appear, and as the vesicles are usually scattered over the body in groups the pigmentation follows this pattern. Fig. 1 in the article shows this well. "Raindrop" pigmentation on the other hand is a diffuse pigmentation over the whole body, maximal on the trunk and neck with depigmented "raindrops" giving the impression that a shower of rain has washed out the pigment where the drops fell. The "raindrops" are therefore white on a brown background, not brown on a white background. The figure shows only pigmentation of dermatitis herpetiformis, not of arsenic.

Hepatitis.—The liver enlargement would appear to be the only undisputed clinical sign of arsenic poisoning in this case. It therefore seems that the diagnosis rests mainly on this finding, combined of course with the history and subsequent course.

It should not be assumed from one case that the evil effects of inorganic arsenic are largely due to uncontrolled administration of the drug in dermatological clinics. I would suggest that, in fact, awareness of the effects of arsenic is greatest in these clinics, and that the dermatologist is most often responsible for diagnosing chronic arsenic poisoning.



Arsenical keratoses on hand.

The following cases have been seen recently in a dermatologist's practice.

CASE 1.—A man, aged 32, was referred to a surgeon by his own practitioner in 1950 suffering from gangrene of the right second toe. On admission to hospital it was noticed that his trunk was pigmented. Examination showed hyperkeratosis of palms and soles, arsenical keratoses (see accompanying figure), intense "raindrop" pigmentation of the trunk, and traces of dermatitis herpetiformis. His liver was not palpable, and there were no signs or symptoms of neuritis. He gave a history of the onset of an irritable vesicular rash soon after joining the Army in 1941. He was invalided out in 1942 with a diagnosis of dermatitis herpetiformis. Since then he had remained entirely under the care of his own practitioner and received Fowler's solution uninterruptedly till his admission to hospital. After treatment with dimercaprol his toe was amputated, but he died suddenly three weeks later.

CASE 2.—A Pole, aged 25, was admitted as an emergency to a medical ward suffering from wasting, ascites, and pain in the limbs. His liver edge was palpable two fingerbreadths below the umbilicus; he had marked hyperkeratosis of the their own ambulance service, and it was the practice for a nurse trained in infectious diseases to admit the patient from his place of removal The possibility of cross-infection was thus largely removed, as information gained and observations made often prevented admission to a ward when there had been contact with a second infection Under the present system, in this area, it has been known for more than one patient notified as having the same disease, but not residing in the same house, to be admitted in the same ambulance In this way the possibility of cross-infection has arisen, for on several occasions the final diagnoses for the patients in question have been very different One of your correspondents last week commented on the ever-widening range and academic nature of the subjects in the syllabus of the General Nursing Council I feel that the insight into social conditions which the nurse gained from her ambulance duties was worth more to her, both as nurse and citizen, than many of the proposed theoretical teachings

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[1] See *Lancet*, Feb. 7, 1953, p. 288.

I sincerely trust that the attention which has been given to this question may arrest the policy of the General Nursing Council and prove to its members that our concern lies not only in the loss of status which our hospitals will suffer, but in the retrogression which will ensue in the cause of public health

Moxley Hospital,
Wednesbury,
Staffs

M W CURTIN
Matron

TOPICAL APPLICATION OF HISTAMINE ANTAGONISTS

SIR,—Your leading article of Jan 17 prompts me to report on a small but carefully controlled series of cases treated in a dermatological outpatient department with phenindamine hydrogen tartrate ('Thephorin') ointment

25 cases were selected, all in the neurodermatosis group (lichen simplex chronicus, pruritus ani et vulvæ, prurigo) The symptoms had been present in most cases for over a year Information was being sought purely as to whether a chronic localised pruritus could be controlled in this way It was considered that the treatment of any acute or subacute eczematous process with a cream of this type was theoretically unsound

Two ointments were used—one contained thephorin and the other the base only (both supplied by Roche Products Ltd) These were labelled "ointment no 1," and "ointment no 2" The physician himself was unaware as to which preparation was being used (a check being kept in the dispensary only), and the patients were not informed that any sort of experiment was being carried out No other treatment was given The cases were observed for a period varying from three to seventeen weeks

The results were as follows

Ointment	*Total no of cases*	*Cured*	*Substantially improved*	*Initial symptomatic relief not maintained*	*No change*	*Aggravated*
Thephorin	15	3 (*20%*)	3 (*20%*)	4 (*27%*)	3 (*20%*)	2 (*13%*)
Base only	10	1 (*10%*)	2 (*20%*)	2 (*20%*)	4 (*40%*)	1 (*10%*)

This experiment had unfortunately to be discontinued before enough cases had been observed for statistical purposes The following points, however, seem to emerge.

1 Anti histamine substances locally applied do seem to have an antipruritic effect comparable to that of the alkaloids, and may enable the patient to stop scratching and thus allow the skin to return to normal

2 This symptomatic control is not generally maintained for more than a few weeks, after which the ointment has very little effect

3 Sensitisation reactions (similar to those seen with the alkaloids) do occur, generally after 3–4 weeks on the treatment It is therefore unwise (or at any rate useless) to persist with this type of treatment for much longer than a month

4 *Many bland emollients, carefully applied, may be ju* as effective This would account for the temporary contr of symptoms in the first month in 50% of the cases where the base only was used

As your leading article points out, in the neuroderm toses pruritus is often produced in the first place emotional conflict, and therefore resolution of the psyc logical situation is essential before permanent cure be expected Nevertheless, relief, especially if obtai early enough, may prevent that irreversible damage the skin which so easily converts a temporary functio ailment into an uncontrollable organic disease It wo seem that antipruritic ointments (like superficial X therapy) are of limited value when used for this purp

Royal Naval Hospital,
Portsmouth

RONALD SCOTT

Medicine and the Law

Selly Oak Hospital Inquiry

Mrs Greaves, aged 57, died in Selly Oak Hospi last October Her right side became paralysed so 20 years ago, she had been bedridden and unable speak ever since, she was being cared for in the wome ward for the chronic sick Her death followed fracti of her femur as she was being lowered into her b after having been brought back from her bath in wheel-chair In reporting his evidence of the necrop when before the coroner, Prof J M Webster ma allegations of "bad nursing" and "bad doctoring" the hospital

The Minister of Health called for a full report on case and on the validity of the charges, and the B mingham Regional Hospital Board set up a commit of inquiry The chairman was Mr Paul Sandlands, Q recorder of Birmingham, a barrister of over 50 yea standing Other members included Dr R E Tunbrid professor of medicine at Leeds University, Miss O Copeland, matron of St George's Hospital, Rothw near Leeds, and Mr C D Langley, the borough coro of Wolverhampton The committee's report decla all Professor Webster's charges to be unfounded a exonerates the hospital staff from any lack of prop care and skill

The allegations of "bad doctoring" were four fir a failure to treat the patient's constipation, second, failure to deal with the ascending genito urinary inf tion, third, a failure to report the discovery of abdominal swelling, and fourth, a failure to send sample of urine for analysis The detailed findings a the evidence on these four points are too long to set o here There was no report of constipation to the doctor the patient was taking no solids and, according to t nurses' reports, was passing fæces The genito urina condition was secondary to the treatment of the fractu and the comfort of the patient A test of the ur would have been normal ward routine but would ha served no useful purpose in her condition Profess Webster considered that the fracture of the femur w not pathological or spontaneous but was caused trauma which might have been due to some involunta act of a nurse, Dr J F Brailsford, radiologist, ga evidence in support of this view The committee conclusion is that the fracture was due to no fault the hospital staff but was probably due to the fall or turning over of the paralysed limb as the patie was being put into bed Professor Webster, who soug to establish a shortage of bedpans at the hospital, ha described the constipation as "shocking", he foun an impacted mass of fæces Medical witnesses at th inquiry said that an enema strong enough to mo such a mass would have done more harm than go and might have killed the patient from shock ian concerned, he was called away to take a telephone call. ater this man told him he wanted to report sick. In the ian's defence it should be stated that he had been off sick rithout pay in previous years for duodenal ulcer. Had his ymptoms been delayed by a matter of minutes, he would ot have received the 7 weeks' pay (6 weeks' sick, 1 week's otice) that he was given.

In another case the foreman was dissatisfied with the work f a man he was trying out as a joiner's labourer, and told im he would revert to his previous job of general labourer. The man immediately went sick, and later produced a medical ertificate for "lumbago," although on subsequent examination by me his symptoms were possibly those of a mild ibrositis in the shoulder. His own doctor said that he was ompletely unaware of these circumstances when issuing the ertificate.

Employees do not perhaps sufficiently appreciate that there must be an economic limit to sick pay, and, if the load becomes too heavy, the employer would probably try to stop these benefits in negotiating a later agreement —with consequent hardship to genuine cases.

Finally, there is another aspect to sickness. The conscientious and sensitive man may well suffer pangs of conscience when he is up and about during convalescence, feeling that he should be back at work. He may feel that lay people regard him as a shirker. Although there are admitted difficulties, it seems that not enough is being done to provide temporary light duties that would enable him to return earlier.

M.O.H.

A SURGICAL POLICY FOR PEPTIC ULCER

SIR,—I hope that in answering his one criticism I shall not seem ungrateful to Professor Wells for the generous remarks in his letter of Feb. 21.

Our use of self-assessment questionnaires was not in place of interviews, for all but very few now inaccessible patients were seen regularly and all possible symptoms sought for and discussed. The questionnaires were used in addition only to allow comparison between the results of two different surgical policies (our own and another), for we felt that only by standardising our method of assessment in this way could we claim to have eliminated our own bias. The method is not ideal, but we are still at a loss for a more valid one and would welcome further suggestions.

London, W.1. H. DAINTREE JOHNSON.

THE ANKLE BLOW-OUT SYNDROME

SIR,—I would in no way wish to detract from the valuable contribution which Mr. Cockett and Mr. Elgan Jones (Jan. 3) have made in directing the limelight once again upon the surgical "Cinderella" of leg ulcers. But from their paper one infers that the anatomical sites of the main perforating veins of the leg have not been well recognised in the past.

In 1931 the late Mr. W. Turner Warwick, surgeon to the Middlesex Hospital, described the site of these veins accurately.[1] Though from his dissections he concluded that they more often communicated with the long saphenous vein, he was aware of the posterior perforating communications mentioned in Gay's Lettsomian lecture of 1867, and he ascribed ulceration to incompetence of these veins.

At that time Turner Warwick was treating ulcers by injection of the incompetent perforating vessels. He came to realise during the ensuing eighteen years the superiority of operative treatment, and it is unfortunate that his untimely death prevented the revision of his book. In this he intended to include his teaching of the last few years, which was that the success of surgery in the ulcerous or non-ulcerous leg depended on the identification and excision of as many "T-junctions" as possible.

It may be added that the experience of those conducting the Middlesex Hospital varicose-vein clinic has led us to believe that obdurate ulcers are usually a problem of fibrous tissue versus blood-supply, and excision is often therefore the most necessary part of the treatment when conservative measures have failed.

London, W.1. JOHN FERGUSON.

VITAMIN E AND INTERMITTENT CLAUDICATION

SIR,—The suggestion made by Dr. Hamilton and his colleagues (Feb. 21) that the widespread use of vitamin E is due to our publications is extremely flattering. But we cannot accept this as true of a substance which is "of no value in the treatment of intermittent claudication."

It is extremely difficult to criticise this report with regard to the statements which are made. We feel that the experimental work as described, using these criteria and the same form of statistical analysis, will always produce an equivocal result. Before commenting on this paper we would like to make our own position clear. We do not, and never did, regard vitamin E as a "wonder drug," but we feel that there have been worth-while clinical results in a sufficient number of cases to justify its use.

In our opinion vitamin E has two effects in the treatment of arterial disease: firstly, in those cases where a minor improvement in the condition makes a great deal of difference in the patient's ability to carry on his normal daily life; secondly, in slowing down the progress of the disease and therefore increasing the patient's expectation of life. The latter statement will, we feel, be borne out when we are in a position to make a report on a minimum of 1000 patients observed over a period of five years.

We would like to make the following observations on the report of Dr. Hamilton and his co-workers:

Selection of Patients

There appears to have been no attempt to determine the underlying clinical condition. Where there has been a secondary thrombosis of the femoral or popliteal arteries during the six-month period preceding treatment, the patient's exercise tolerance is extremely labile and such patients must be excluded from the experiment. The variation observed is such that it cannot be covered by any form of statistical analysis—the differential calculus cannot replace the differential diagnosis.

Clinical Grading

We agree that by our own standards the clinical grading will vary with the severity of the exercise-tolerance test. On the less severe test of the "claudicometer" we have shown that the improvement of the grade-III patient is too slight to be assessed If the test employed shows a patient to be grade III—even though he may be grade II by our standards—he will be equally difficult to assess by that test, and should be excluded. More than half the patients on which this report is made fall into grade III on the test used.

Duration of Treatment

In our experience it is impossible to assess the effect of vitamin E less than three months from the start of treatment; and we feel that the period of observation should be at least six months, with continuous treatment.

Method of Assessment

Obviously intermittent claudication must be assessed by some form of exercise-tolerance test. Various mechanical devices have been produced with the idea of exercising the patient under controlled conditions and measuring the amount of work done. Simmons[1] devised a treadle system: Kissin et al.[2]—and later Hamilton and Wilson[3]—have described a simple method of making the patient climb up and down steps at a known rate. Unfortunately, whatever the scientific merits of exercise devices, they have in general one serious drawback: the patient gets the pain when walking and it

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[1] Turner Warwick, W. The Rational Treatment of Varicose Veins and Varicocele. London, 1931.

[1] Simmons, H. T. *Lancet*, 1936, i, 73.
[2] Kissin, M., Stein, J. J., Adleman, R. J. *Angiology*, 1950, 1, 141.
[3] Hamilton, M., Wilson, G. M. *Quart. J. Med.* 1952, 21, 169.

Obituary

LOUIS LEISLER GREIG

K.B E, C V O, M B Glasg

Sir Louis Greig, who died on March 1 at the age of 72, first entered Court circles through his care for the health of the late King in early manhood, and he remained the counsellor and friend of the Royal Family even after his retirement from his official appointment

The son of David Greig of Glasgow and Fife, he was educated at Merchiston Castle in Edinburgh and at Glasgow University Both at school and university he won renown as a games player, and from 1906 to 1908 he was a memorable Scottish half-back He graduated M B in 1905, and the following year he joined the medical service of the Royal Navy In 1908 he was appointed surgeon to the Royal Naval College at Osborne, and while holding this post he first came to know Prince Edward and Prince Albert when they were serving there as cadets During the 1914–18 war he was for a time held as prisoner-of-war, and on his release he was appointed to H M S *Malaya* in which Prince Albert (later King George VI) was serving The Prince's health at that time was not robust, and his parents came to place much reliance on Greig's counsel and care During these years of doctor-patient relationship the patient and doctor's regard for each other grew, and in 1920 Greig was appointed comptroller to the Duke of York Though in 1923, after the Duke's marriage, Greig retired from the royal service he remained formally attached to the Court as a gentleman usher in ordinary to King George V, and in 1932 he was appointed deputy ranger of Richmond Park, where he lived in the 18th-century Thatched Lodge He was appointed K B E in 1932

During the late war he served as personal air secretary to Sir Archibald Sinclair (now Lord Thurso), who was then Secretary of State for Air The many interests which made up Greig's life are reflected by the varied honorary appointments he held He was a governor of Westminster Hospital, chairman of the Not Forgotten Association and of the All England Lawn Tennis Club, and a former deputy lieutenant of the City of London He also gave much of his time and energy to the National Playing Fields movement

He married in 1916 Miss Phyllis Scrimgeour, who survives him with a son and two daughters

ARTHUR HERBERT NORRIS

C B E, M C, M R C S

Dr Arthur Norris, formerly chief inspector of the Children's Branch of the Home Office, died on Feb 20 at the age of 77

He was educated at Ellesmere, Shropshire, Manchester University, and St Thomas's Hospital He qualified in 1906, and in the spring of 1914, after holding various hospital and public-health appointments, he became the first full-time medical inspector of reformatory and industrial schools at the Home Office Five years earlier he had joined the 1st battalion of the Manchester Regiment, and by the end of August, 1914, he reached Egypt He served with the unit in Gallipoli and France as medical officer until 1917, when he was released to return to his post in the Home Office, to investigate the health conditions in the reformatories The tuberculosis morbidity-rate was then high, and the standard of health of the children was a cause of concern A few months later he became chief inspector, the only doctor to hold the appointment, and immediately he made his influence felt He had a great love for children, a real understanding of their needs, and a great desire to help them He possessed the gift of inspiring others, and he was able to bring out the best in all those with whom he came in contact The old reformatories and industrial schools, which in 1919 contained over 23,000 children, began to be known as Home Office schools, and with the change in name there was a change in atmosphere and purpose No longer were the children occupied in hard tasks, instead, attention was given to their educational needs

Already there was growing up around Norris tha small body of inspectors, both lay and medical, m and women, of whom he was to be such an inspirin leader In 1923 the first report of the Children's Branch of the Home Office was published, and publ interest began to be aroused An exhibition at Centr Hall, Westminster, of the crafts being taught a made the public aware of the more liberal régime develo ing in the schools It is not, therefore, surprising th by 1927 a Departmental Committee was considering t treatment of the young offender, and that in 1933 t Children and Young Persons Act came into force, f Dr Norris was not only able to arouse the enthusia of those working with the children, but he possess that more subtle quality of knowing how to coöpera with those working for the children As an inspect he was able to bring back to the Home Office such viv pictures of conditions in the schools, and such vit stories of the children, that all connected with the wo were inspired to seek ways by which progress could b made

As the years went by his influence was felt over widening field Voluntary organisations sought h advice Religious bodies found him understandin of their difficulties and welcomed his counsel At th end of his official career war again broke out, and his la task before retiring in 1940 was to supervise the evacu tion of many of the approved schools He settled i Dawlish and, as a major in the Home Guard, worke full-time for two years as adjutant to a battalio His interest in children, especially in those depriv of a normal home life, did not diminish in retirement He became a member of the council of the Nation Children's Home, a coopted member of the children committee of the Devon County Council, and a manag of five approved schools in the West of England N long ago he became a manager of the secondary moder school in Dawlish, and by frequent visits he soon kne the children as he had known the children in the approve schools in earlier years

The work of the Children's Department of the Hom Office has increased greatly since the Children Act 1948, and the inspectorate has grown considerabl But Dr Norris's influence persists and his name is hel in affectionate remembrance

D M

Dr HAROLD BALME

Dr John Kershaw, who as chief of the rehabilitatio unit in the United Nations secretariat in 1951–52 wa one of Dr H Balme's closest professional colleagues i the last phase of his work, writes

“Dr Balme joined U N as a consultant at an age whe most men are retiring from active professional work. U N an its specialised agencies had all been finding themselve engaged on problems of rehabilitation of the handicapped and it was necessary to integrate their separate activitie into a coördinated whole As chairman of the joint workin party of U N and the Agencies, Balme, with his experienc and personality, was the perfect catalyst, and the grea measure of unity achieved between 1950 and 1952 was largel due to him In the more active task of expert adviser t some of the less highly developed countries he combined realistic outlook with unbounded enthusiasm and severa U N projects which are now in operation owe much of thei success to him

‘The work was exacting and probably hastened his death but he never spared himself Even those working with him did not always realise that he sometimes came straight to the conference table from a sick bed to which he would return as soon as the meeting adjourned I have, at hi request, taken difficult problems to him in a hospital ward and found him as alert and helpful as if he were well and in his office The report on a Coordinated International Programme for the Rehabilitation of the Handicapped, which was presented to the U N Social Committee last year and which is likely to form the basis of future developments in this field, was largely Balme's work, and in its fulfilment he will have a fitting memorial ”

Dr F S Cooksey, who found working with Harold Balme an inspiration and a pleasure, writes

“He was a dynamic personality a clear thinker, and a stimulating teacher Whether as lecturer or chairman of

We feel, Sir, that this problem must be tackled on a national scale. The central supply of cylinders and pumps, and the production of a "mechanical student" and a cuirass respirator are all matters which cannot be economically dealt with on a local basis. The organisation of the service itself should, we feel, be national. We suggest that an energetic committee should at once be formed so that plans can be perfected before the poliomyelitis season is on us.

In conclusion, we should like to express our gratitude to Professor Lassen, Dr. Neukirch, Dr. Ibsen, and their colleagues for their great kindness to us in Copenhagen, and for the time they devoted to us when they could ill afford it. We are also grateful to Dr. Lloyd Hughes and the Liverpool Regional Hospital Board, who sponsored our visit to Denmark.

Fazakerley Group of Hospitals,
Liverpool.

A. B. CHRISTIE
J. R. ESPLEN.

CHILD-WELFARE CLINICS

SIR,—As an officer of a local authority, I am somewhat amused by Dr. Charlotte Naish's impression (Feb. 28) that a clinic, when it has outlived its usefulness, can be maintained as it is a vested interest. Dr. Naish may be assured that local authorities, who have to raise rates, would be only too pleased to encourage some abatement.

In this context, however, no such arrangement is necessary. My earlier letter (Feb. 21) referred to infant-welfare centres (sometimes called "well-baby clinics"). For each district these meet for one session a week. They are held in two types of premises: (a) clinics; and (b) hired rooms, usually church halls. Clinic premises are used for many other purposes, such as minor ailment, specialist, health education, antenatal, and dental clinics. Accordingly there will be no need to turn them into occupational centres or mother-and-baby homes if they cease to be used for one session a week, or even more, for the purposes of an infant-welfare centre. A local authority has no vested interest in church halls, which are only used for one session a week. Accordingly, the question of resisting the disappearance of these centres again does not arise.

Ilford, Essex.

I. GORDON
Area Medical Officer.

ANÆSTHESIA IN WHOOPING-COUGH

SIR,—The happy experiences described by Dr. Naji (Jan. 17) will not, I hope, encourage the use of general anæsthesia in whooping-cough. I would like to temper his enthusiasm by an account of an unfortunate experience.

A 5-year-old male child, in his 4th week of whooping-cough of moderate severity, developed central, colicky abdominal pain and vomiting. Marked tenderness and guarding were elicited in the right iliac fossa, where the vague outline of a mass could be felt. A surgical consultant agreed that an immediate laparotomy was indicated. The anæsthetist, with whom the type of anæsthesia was carefully discussed, suggested a gas-oxygen-ether sequence.

After uneventful induction, the abdomen was entered through a right paramedian incision, which provided adequate exposure. The appendix, which was readily accessible, was found enveloped in acutely inflamed omentum. Palpation of the appendix showed it to be unduly hard and thickened; and in a rapid search of neighbouring lymph-glands a mass of hard glands was palpated in the retroperitoneal tissues. It was therefore considered wise to limit the operation to appendicectomy, and without any technical difficulties this was completed. After the peritoneum had been closed, 35 minutes after the start of the operation, the anæsthetist announced that the heart-beat had suddenly ceased. There had been no indication throughout the period of anæsthesia of any respiratory or circulatory embarrassment; an adequate airway through an intratracheal tube had been maintained all along. Despite cardiac massage through the abdominal opening, artificial respiration, &c., for 45 minutes, resuscitation could not be effected.

Post-mortem examination the next day showed the myocardium to be pale and flabby, the seat of severe toxic myocarditis presumably due to whooping-cough. The retroperitoneal lymph-glands were heavily involved with lymphosarcoma, and the appendix showed the same infiltration with an acute inflammatory lesion superimposed.

It was reasonable to deduce that the type and extent of the surgical procedure in itself did not explain the death on the table; nor could it be said that nitrous oxide, oxygen, and ether with intratracheal intubation was not the anæsthesia of choice. The unsuspected presence and severity of whooping-cough myocarditis was the factor responsible.

Johannesburg.

ISAAC FREED.

DETERGENTS

SIR,—Your timely warning (Feb. 21) about the domestic use of detergents is of considerable interest not only to dermatologists but also to industrial medical officers and general practitioners. Undoubtedly there is an increasing number of patients who say definitely that they can date their dermatitis from the time they started to use detergents.

In industry, as a general rule, we are prepared to meet cutaneous risks from all types of chemicals and skin sensitisers by the intelligent use of barrier creams, which will protect practically all workers. We have not had a case of dermatitis for some years from any of our canteens or maintenance departments, where detergents are in daily use and barrier creams are provided. One notes with considerable surprise that none of the makers of detergents advise the user of the quantity which should be used for any specific purpose. It may well be that detergents are being used too liberally. This may account for the relatively large increase in the number of cases of dermatitis.

London, N.5.

L. B. BOURNE
Senior Medical Officer,
A. C. Cossor Ltd.

B.C.G.

SIR,—Your leading article of Feb. 21 states that "B.C.G. vaccination in this country has rightly been judged as a matter for planning and strict control; but there now seem good reasons for lessening control; while preserving the general plan of campaign."

Before the vaccine is released for general use it is essential to consider certain other aspects. Tuberculin matriculation in the hands of Gedde-Dahl [1] in Norway and Tattersall et al.[2] in this country is proving a valuable method of discovering patients suffering from infectious tuberculosis. By tuberculin testing groups of people at regular intervals and noting the converters, they are able to pin-point the source of infection.

The need for such methods is shown by the failure of present case-finding methods to discover infectious patients until late in the course of the disease and after death. Doctors' patients with symptoms, hospital patients, contacts of patients suffering from tuberculosis, and mass X-ray examinations provide the bulk of new cases of tuberculosis; but they are insufficient. Last year in this area with a mixed urban and rural population of 250,000, 12 cases were notified after death—5 as the result of post-mortem examinations requested by the coroner. It is impossible to say how many more went to their graves having disseminated the disease widely.

None of the existing medical services can be blamed for having missed these cases. One method of dealing with this problem is the observation of tuberculin matriculation of school-children at the time of entry and at the intermediate and school-leaving medical examinations, combined with an intensive search for the source of infection. This would mean leaving the child unvaccinated with B.C.G. till the age of leaving school. All things considered this is a small price to pay, because of the

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1. Gedde-Dahl, T. *Amer. J. Hyg.* 1952, 56, 139. See *Lancet*, 1952, ii, 922.
2. MacDougall, I. A., Maklall, J. R., Tattersall, W. H. *Brit. med. J.* Jan. 10, 1953, p. 61.

National Fund for Poliomyelitis Research

Speaking at a dinner held at the Mansion House, London, on March 2 to inaugurate this fund, Sir Russell Brain, P R C P, said that research into poliomyelitis had reached a stage at which a rapid expansion might lead to a great advance Over £2500 was raised at the dinner for the fund, whose aims were lately described in our columns (Feb 7, p 301)

Goat's Milk

Arrangements have been completed between the National Milk Testing Service and the Sussex County Goat Club for samples of goat's milk to be tested for cleanliness and keeping quality Names and addresses of suppliers of goat's milk can be obtained from the British Goat Society, Diss, Norfolk

Medical Art Exhibition in Paris

The 25th Salon des Médecins, Dentistes, Pharmaciens, et Vétérinaires will be held at the Musée d'Art Moderne in Paris, from March 29 to April 11 Members of these professions are invited to send their paintings or sculptures to this exhibition All works submitted should be sent immediately to the transport agents Messrs Davis Turner & Co, 4, Lower Belgrave Street, London, S W 1, who will forward them to Paris

Northern Ireland Health Ministry

Dr J T Johnston, medical officer in the ministry, has been promoted to be a senior medical officer in succession to Dr L D I Graham, who will retire this month after nearly thirty years' service with departments of the Northern Ireland government

World Health

The World Federation of United Nations Associations is holding a seminar on this subject in Geneva from May 4 to 15 during the World Health Assembly Applications may be sent through a U.N association or directly to the federation's offices 1, Avenue de la Paix, Geneva, or 19, Avenue Kléber Paris, XVI

Care of the Aged Sick in Bristol

A subcommittee of the Bristol local medical comm… has been examining the treatment and care of the eld… chronic sick in Bristol A report has now been publish… and copies may be had, price 2*s* 6*d* post free, from th… secretary of the committee, 7, *The Dell*, Westbury on Try… Bristol, 9

Register of Chiropodists

The Board of Registration of Medical Auxiliaries h… now published the 1952 register of chiropodists Co… may be had from the secretary of the board, B M A Ho… Tavistock Square, London, W C 1

Ophthalmological Society of the United Kingdom

At the 17th International Congress of Ophthalmolog… be held in New York next year, a new edition of the *In…* will be issued under the title *Index Ophthalmologicu…* the Ophthalmological Society has been asked to prepare section covering Great Britain. Any ophthalmologi… is not a member of the society or of the Faculty of Opht… mologists, and who wishes to be included in this index asked to send his name and address to the hon secretary the society, 45, Lincoln's Inn Fields, London, W C 2 be… March 31

European Association against Poliomyelitis

The next general assembly of the association is to be h… at Copenhagen on Saturday, April 25 The program… includes a symposium on the Treatment of Poliomyel… Complications at the Acute Stage, and there will also free discussions on methods of diagnosis and on the u… gamma-globulin and vaccination The secretary general the association may be addressed at 130, rue de Linth… Brussels, Belgium

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SERVICE —In the week ended last Mon… acute cases numbered 1302 The propor… The white warning has been withdrawn

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Diary of the Week

MARCH 8 TO 14

Monday, 9th

UNIVERSITY OF LONDON
5 15 P M (Bedford College, Regent's Park, N W 1) Prof S Bergstrom (Lund) Intestinal Absorption of Fats (First of two lectures)
INSTITUTE OF PSYCHIATRY Maudsley Hospital, Denmark Hill, S E 5
5 30 P M Dr E Stengel Lecture demonstration
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W 1
8 30 P M Dr E R Cullinan Some Disorders of the Liver and Bile (Second of three Lettsomian lectures)
UNIVERSITY OF EDINBURGH
5 P M (New Buildings, Teviot Place) Dr Pierre Mallet Guy (Lyons) Manometric and Radiographic Control of Biliary Surgery

Tuesday, 10th

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
8 P M *Section of Psychiatry* Dr D W Kay Anorexia Nervosa
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street W C 2
5 30 P M Dr R G Cochrane Leprosy
WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane W 1
5 30 P M Dr T Rowland Hill Neurological demonstration
CHELSEA CLINICAL SOCIETY
8 30 P M (South Kensington Hotel 41, Queen's Gate Terrace S W 7) Mr W V Gibson Sir Hugh Griffiths Medical Aspects of Road Accidents
MANCHESTER MEDICAL SOCIETY
5 P M *Section of Surgery* (University of Manchester) Mr A V Cooke Laparotomy
UNIVERSITY OF EDINBURGH
5 P M (University New Buildings) Prof Alfred Meyer Anatomical Aspects of Neurosurgery in Mental Disorder (William Ramsay Henderson lecture)

Wednesday, 11th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields, W C 2
3 45 P M Mr V E Negus Protection of Respiratory Tract (Erasmus Wilson demonstration)
ROYAL SOCIETY OF MEDICINE
4 30 P M *Section of Physical Medicine.* Prof K M Walthard (Geneva) Modern Procedure of Electrodiagnosis and Electrotherapy
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W 1
3 30 P M Dr W Clunie Harvey Food Hygiene
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Cochrane Histopathology of Leprosy
INSTITUTE OF UROLOGY, St Paul's Hospital, Endell Street, W…
5 P M Dr A H Harkness Non
LONDON ASSOCIATION OF THE MEDI
8 30 P M (Royal Free Hospital … Street, W C 1) Miss Diana Beck Management of … Injuries in General Practice (Presidential address)
MANCHESTER MEDICAL SOCIETY
4 30 P M *Section of Pathology* Prof R E Glover, F R C V … Virus Diseases in Animals

Thursday, 12th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr J B Wyman Use of Pentamethonium and He… methonium Salts in Major Surgery
UNIVERS…
5 15 P … r Bergstrom Formation… (Second of two lectures)
UNIVERSI… C 1
4 45 P … F R S Chemical Aspect… our lectures)
ROYAL SOCIETY OF MEDICINE
5 P M *Section of Ophthalmology* Dr Peter Beattie Oc… Troubles of Dr Johnson and Mr Pepys Miss … Savory Later Results of Perforating Eye Injuries
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Childr… Great Ormond Street, W C 1
5 P M Dr R E Hope Simpson Epidemiological Research … Children under Fifteen Years of Age
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Pathology of Mycotic Infection
ROYAL ARMY MEDICAL COLLEGE, Millbank, S W 1
5 P M Mr R Llewelyn Davies, A R I B A Modern Trend… Hospital Architecture
ST GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corn… S W 1
5 P M Dr Desmond Curran Psychiatry demonstration
ALFRED ADI…
8 P M (1 … Dr Donald Blair, Dr … Re… Three Difficult Cases Tr… by …
LIVERP…
8 P … 114 Mount Pleasant Liverpool … Antarctic Observations of Co… Hygiene and Forensic Medici… se of Concomitant Endometr… Adenocarcinoma with Squamous Metaplasia and En… metrial and Tubal Tuberculosis
UNIVERSITY OF ST ANDREWS
5 P M (Medical School, Small's Wynd, Dundee) Sir Jam… Spence Methods of Clinical Teaching

Friday, 13th

INSTITUTE OF DERMATOLOGY
5 30 P M Dr Cochrane Leprosy
UNIVERSITY OF OXFORD
NOON (Department of Human Anatomy) Prof G W Corn… (Baltimore) Application of Scientific Methods to Stu… of Sex and Reproduction

s action to ensure that proper and cheap shoes exist to be fitted.

We can of course appreciate the difficulties of the shoe trade. The drastic re-lasting required would cost very large sums, and the public might not like the look of the new shoes. A physiologically designed shoe does look bizarre to eyes accustomed to the present conventional shape with a curved inner border. It is the duty of the Minister of Health to take the necessary steps—popular or otherwise—even if powerful interests are thereby antagonised.

London, W.8.   GEOFFREY G. SHERRIFF.

ACUTE RESPIRATORY INSUFFICIENCY

SIR,—I have read your excellent leading article of Feb. 21 with great interest, and would like to make a few comments.

Firstly, with regard to oxygen therapy, I feel that your article has, unintentionally, left the impression that some of those workers who have studied and described carbon dioxide narcosis have suggested that for this reason oxygen should not be used in cor pulmonale. Further, readers may have gathered the impression that the prevention of carbon dioxide narcosis presented such great difficulties that it was probably best to turn a blind eye to the not very well defined dangers of severe gaseous acidosis.

No-one, as far as I know, has recommended that oxygen therapy should not be given to patients who are dying of anoxæmia, because of the possibility of carbon dioxide narcosis. The dangers of extreme carbon dioxide retention are very real indeed, and the fact that patients with cor pulmonale are already gravely ill makes it even more imperative that the slightest adverse factor must be scrupulously controlled. The dehydration and electrolyte disturbances that killed many patients after severe hæmatemesis were not appreciated for many years because there was always " a reasonable cause of death " to lean on. In this department we have evolved a standard procedure which we have used for the last three years, by which oxygen therapy can be safely given in all cases without the dangers of severe carbon dioxide retention.

Since I wrote in these columns in 1949,[1] suggesting that the coma and rise of pressure of cerebrospinal fluid reported by Davies and MacKinnon[2] after oxygen administration to cases of cor pulmonale was not due to oxygen poisoning, as they thought, but to underventilation and resultant carbon dioxide intoxication with cerebral vasodilation, our concepts and experience have expanded considerably. Although it was then pointed out that the main respiratory stimulus in these patients appeared to be anoxæmia and that when this was relieved ventilation fell considerably, it was not possible to state why these patients did, in fact, fail to respond to the powerful respiratory stimulation of increased carbon dioxide tensions and H ion concentration. There are, however, important clues to this problem. Marshall and Rosenfeld[3] showed that when the respiration of animals was greatly depressed by anæsthetics the limited ventilation appeared to be almost entirely maintained by the anoxæmic stimulus, and that the administration of oxygen caused a further reduction of respiratory volumes with retention of carbon dioxide. Further, Schmidt[4] showed that the administration of carbon dioxide to dogs with respiratory depression due to morphine and heroin actually reduced their minute volume and in some cases precipitated complete and permanent respiratory failure. Ivy[5] et al. gave 5% carbon dioxide to animals with developing respiratory failure due to anoxia and showed a progressive decrease of response to this gas and in some cases even further respiratory depression. In other animals carbon dioxide appeared to precipitate circulatory failure as well.

Such experiments cannot be performed on man, but it would appear reasonable to make the following conclusions. Firstly, in partial respiratory failure caused by anoxæmia or drugs there appears to be a stage where there is still a ventilatory response to anoxæmia, but no longer to increased carbon dioxide tensions or raised H ion concentrations. Secondly, the patients who underventilate in oxygen and develop carbon dioxide narcosis are in partial respiratory failure due to their recent severe anoxæmia, and it is for this reason that they do not respond normally to endogenous carbon dioxide. Thirdly, to allow too great a rise of body carbon dioxide tension may cause not only unconsciousness but further medullary depression. It is generally accepted that all drugs and substances that cause unconsciousness will in greater dosage cause medullary failure, and there is no reason to think that carbon dioxide is an exception.

How can such considerations help in the administration of oxygen to patients who are dangerously anoxæmic? It is our experience that patients with extreme arterial anoxæmia (55–30% saturation) are in the greatest danger of carbon dioxide retention when breathing oxygen. This is to be expected as it is at such levels that respiratory depression occurs. The patients who develop such levels of anoxæmia are almost always those with an acute infection and respiratory obstruction superimposed on chronic lung disease. The raised arterial carbon dioxide which can be demonstrated in these patients before oxygen therapy is often due partly to previous carbon dioxide retention and partly to developing respiratory failure. If there is not severe anoxæmia or carbon dioxide retention then the risk of carbon dioxide narcosis in oxygen is negligible, as respiratory depression will not be present. It is therefore most important to know the degree of anoxæmia when the patient is admitted. Variable polycythæmia and peripheral circulation makes the degree of cyanosis a most unreliable guide to the degree of anoxæmia, particularly when such important issues are at stake.

For these reasons arterial puncture is resorted to in all cases. This investigation is never allowed to delay the administration of oxygen. In all patients with severe anoxæmia and carbon dioxide retention, carbon dioxide narcosis from administration of oxygen is to be expected. In such cases the tent is rolled up for 10 minutes in every hour. The patient responds to the transient anoxæmia by vigorous ventilation and removal of carbon dioxide, and becomes less drowsy and more alert. This short period of anoxæmia has never given rise to any anxiety. It is hardly practical to consider such heroic measures as mechanical and electrophrenic respiration in these gravely ill patients when nature has still left us with one valuable physiological remedy. We find that as the benefits of oxygen and other therapy become apparent the patient needs less and less " blowing off " periods, as his respiratory behaviour becomes more normal. The sisters and nursing staff show great skill in this procedure and watch out for drowsiness, coma, and twitchings with a hawk-like eye. It is a rewarding experience to hear a sister tell the medical attendant that she has rolled up the tent a little more often as the patient was underventilating and drowsy.

Finally, we find that brisk venesection in patients with cor pulmonale, gross venous congestion, hypervolæmia, and polycythæmia is one of the most dramatically effective therapeutic procedures at our disposal. We also find that intravenous digoxin often causes a visible fall of venous pressure during the next half-hour. This improvement of right ventricular function with digoxin

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1. Donald, K. W. *Lancet*, 1949, ii, 1056.
2. Davies, C. E., MacKinnon, J. *Ibid.* p. 883.
3. Marshall, E. K. jun., Rosenfeld, M. *J. Pharmacol.* 1936, 57, 437.
4. Schmidt, O. *Proc. Soc. exp. Biol., N.Y.* 1924, 21, 264.
5. Ivy, J. H., Grodins, F. S., Adler, H. F., Snapp, E. F. *J. Aviat. Med.* 1947, 18, 577.

Medical School of London only 2 out of 110 with all types of pneumonia had Q fever (Crofton et al 1951) But these are selected samples which include a high proportion of patients from London or other urban areas where Q fever might be less common

Since Q-fever antibodies persist for many years after infection, an estimate of past infection in a community can be made by testing sera from a representative number of healthy individuals

The study by Bell et al (1950) on the prevalence of Q fever in Southern California is based on this method and involved a survey of nearly 10,000 people The over all rate in Los Angeles was 1 36%, indicating previous infection in some 50,000 persons, but in this city the dairy industry is somewhat unusually situated within the urban area The rate varied from 10 7% in households which drank raw milk to 0 9% in those which did not and from 5 9% in employees in meat-packing plants to 1 2% in aircraft factories In Northern California, Clark et al (1951) found that 3 5% of people in an endemic area had Q-fever antibody compared with 0 5% and 0 9% respectively in two non endemic areas

A similar survey has now been carried out in Britain through the kindness of members of the National Blood Transfusion Service, tests for Q-fever antibody were performed on numbers of sera from blood donors The main purpose of this inquiry was to compare the prevalence of Q fever in two different areas, rather than to attempt an assessment of the morbidity due to Q fever at any one time

The third part of the paper considers the possible sources of infection and reports investigations on Q fever in cattle from Kent, Devon, and East Anglia, and attempts to isolate *R burneti* from ticks

Sporadic Cases of Q Fever

From January, 1948, to October, 1949, complement-fixation tests for Q-fever antibodies were performed at Cambridge, but upon sera from a limited number of patients only and mainly from those with atypical pneumonia Since October, 1949, however, these tests have been carried out in much larger numbers at Colindale on sera sent for diagnosis to the Virus Reference Laboratory from all patients with respiratory illness

The technique of the tests and the preparation of antigen has been described in previous communications (Stoker 1949, 1950, Marmion et al 1951) A diagnosis of Q fever was made (*a*) when there was a fourfold (or greater) rise in antibody titre during the illness, or (*b*) when an antibody titre of 1 64 or higher was found after an illness clinically resembling Q fever Attempts to isolate the organism have rarely been made in humans, and in no case has the diagnosis depended upon this Most of the patients were seen by us personally, for the remainder, data were kindly supplied by the patient's doctor, the local public-health authorities, or by members of the Public Health Laboratory Service

GENERAL FEATURES

Altogether, 117 cases of Q fever were diagnosed with dates of onset between Jan 31, 1948, and Jan 31, 1952 This total included 48 patients involved in three explosive outbreaks, leaving 69 sporadic cases (Of the 8 cases at the Royal Cancer Hospital (Harman 1949), 4 have been included as sporadic cases) Of these 69 patients, 58 were males and only 11 females This preponderance of males might be due to a greater risk of infection, but in the Canterbury outbreak (Harvey et al 1951) the proportion of males infected was significantly higher than the proportion of males in the population at risk

The age distribution of 66 of the patients is shown in fig 1 61 (92%) of the 66 patients were between 20 and 60 years old—i e, of working age In this series Q fever is obviously rare both in childhood and in old age, and this might be due to lack of exposure to infection The age-distribution of the small number of female patients is not significantly different from that of the males

In 31 of the 69 cases diagnosis was based on a fourfold or greater rise in serum-antibody level In 37 the specimens were taken too late to show a rise, but after their illness they had antibody titres of 1 64 or higher The remaining case was diagnosed at necropsy and on indirect evidence (Marmion and Stoker 1950) 4 of the patients with Q fever died, giving a mortality-rate of 5 8% in the sporadic cases or 3 4% in all cases

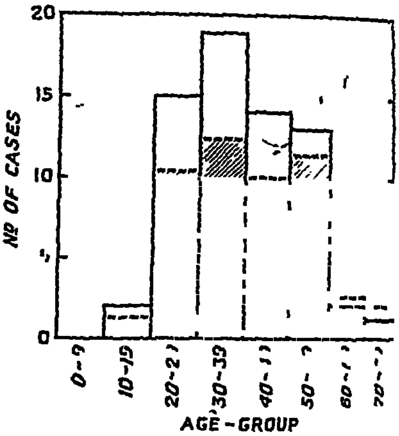

Fig 1—Age-distribution of 66 sporadic cases of Q fever The continuous line shows the actual numbers of cases, the broken line shows numbers corrected for total population in each age-group—i e, cases per 5 million population

CLINICAL FEATURES

It was not possible to analyse the clinical findings in detail because they were supplied by a large number of different observers, but certain general conclusions are possible and a few unusual cases are described in more detail

The attack was typical of Q fever in 61 of the 69 patients Of these, 43 were first diagnosed as suffering from pneumonia, usually virus pneumonia or primary atypical pneumonia, and the remaining 18 patients had febrile illnesses without evidence of pulmonary involvement In 17 of these typical illnesses, which were not treated by aureomycin, chloramphenicol, or terramycin, the fever lasted for from five to twenty days with a mean duration of rather less than nine days Records of X-ray examination of the chest were available in 30 cases, and of these 25 showed evidence of pneumonia and 5 were normal Most of the patients with typical attacks convalesced rapidly when the fever had subsided, but 5 patients suffered from a general malaise and debility lasting up to two months and a further 3 patients had relapses Some patients received aureomycin or chloramphenicol, and these drugs were usually effective, but it was not possible to assess their value in this series

The severity of illness varied greatly from a mild fever and headache, lasting two or three days, to a severe pneumonia with high fever, intense headache, photophobia, and intermittent delirium often lasting several weeks If the signs of pneumonia were not obvious at

TABLE I—SUMMARY OF FATAL CASES OF Q FEVER

Case	Occupation	Age	Clinical diagnosis	Duration of illness before death	Cause of death discovered at necropsy
1	Retired tailor	78	Pneumonia	11 days	Pneumonia
2	Insurance agent	45	Pneumonia	23 days	Pulmonary infarction
3	Cobbler	58	Pneumonia	110 days	Sudden death, no necropsy, ? vascular catastrophe
4	Labourer	37	Subacute bacterial endocarditis	Unknown but more than 6 months	Pulmonary infarction (mitral stenosis and bronchopneumonia)

of tropical diseases or similar non-dietary factors. The time is therefore ripe to discard more or less arbitrary arrays of criteria in defining kwashiorkor. Instead of studying the phenomena associated with depigmentation, or with œdema, or with dermatoses, we would do better to explore the natural history of the disease produced by a defective diet—and in infancy this is almost universally a pap diet containing little or no milk. With this approach we would note at once that some cases do indeed conform with the criteria mentioned in the W.H.O. publication, but that many others, as shown above, do not. We would also see that the pigmentary changes become less easily recognisable the whiter the skin of the race to which the individual belongs, and that in children of European descent a "muddy" complexion is often a sign of malnutrition. Apart from pigmentary peculiarities, the manifestations of dietary deficiencies would be the same in dark and white races. In fact, variations in the clinical picture of the disease produced by a difference in diet, race, climatic conditions, age, sex, &c., would be no more important than variations in the clinical picture of malaria or typhoid fever.

The use of paps of poor nutritional value for the weaning of infants is world wide. Fifty years ago pap malnutrition was one of the most common disabilities of infancy in Europe and the U.S.A. The reasons were widespread poverty, difficulty in obtaining fresh milk in the towns, and the belief that the casein of cow's milk was harmful to young babies. The disease picture resulting from diets containing little or no milk and consisting mainly of cereals was then referred to as infantile malnutrition, hypothrepsia, *Mehlnährschaden*, *Bilanzstörung*, dystrophy, &c. After a study of the relevant literature, I have been unable to discover any basic differences between these syndromes and kwashiorkor.

The first effective treatment of infantile malnutrition was presented by Finkelstein in 1907 in the form of his famous "protein milk." It should not be forgotten that it took from 1933 to 1948 to rediscover this treatment for a condition which had in the meantime changed its name to kwashiorkor. It seems doubtful whether it is wise to retain the term kwashiorkor to denote a malnutrition syndrome. The word could be used more satisfactorily to signify pigmentary changes of skin and hair which are potential signs of malnutrition in dark-skinned races.

Baragwanath Hospital,
Johannesburg, South Africa.

E. KAHN
Senior Pædiatrician.

STANDARDISED SENNA

SIR,—In an annotation last year[1] you discussed standardised senna, with particular reference to the methods developed by Fairbairn and others for assaying preparations of senna. We have made some clinical tests on a new standardised and stabilised preparation of senna marketed under the name 'Senokot.' In this preparation the powdered pericarp of the senna pod is incorporated in a palatable base of cocoa, malt, and sugar, and made up as granules, which are pleasant and easy to take in a dose of $1^{1}/_{2}$–2 teaspoonfuls.

The preparation was given to 101 inpatients with constipation, and good responses were obtained in 93. Those who did not respond were patients with chronic constipation which was resistant to other drugs. Senokot was effective in 4 patients who did not respond to other commonly used purgatives. Severe griping occurred in 3 patients after the higher dose. More recently we have found that, in 25 patients, experimental tablets of senokot were effective on 65 occasions.

We are grateful to Westminster Laboratories Ltd. for supplies of senokot.

The Middlesex Hospital,
London, W.1.

P. FLINTAN
G. D. WEEDEN.

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[1] *Lancet*, 1952, i, 655.

REGISTRATION OF FEVER NURSES

SIR,—I congratulate the correspondents who have so ably put the case for the continuation of the Fever Register. Every argument put by your contributors is logical and full of plain common sense.

Does the General Nursing Council seriously believe that, because of the pronounced decrease in diphtheria and the temporary decline in the virulence of scarlet fever, dangerous communicable diseases are on the way out?

One has only to study the archaic syllabus for fever training which continues to be issued by the General Nursing Council to realise that that body is out of touch with reality. In it, diphtheria and scarlet fever continue to hold pride of place; and encephalitis lethargica, which has possibly not occurred in this country for many years, is included. Smallpox, which not more than 1 nurse in 500 is likely to have to nurse, has prominence. But not a word about the acute bacterial food-poisoning groups (apart from enteric fever), the bacillary dysenteries, or the acute and dangerous gastro-enteritis of infants. Even the epidemic prevalence of poliomyelitis does not seem to have caused the council to think of including it in the nurse's training.

The council may also have overlooked the report of the recent poliomyelitis conflagration in Copenhagen, where more than 3000 cases were admitted to the municipal contagious diseases' hospital in a few months. A similar case-incidence in greater London could produce about 20,000 cases.

If the Council persists in its attitude and persuades the Minister of Health to agree, then Dr. Macrae's suggestion to establish a certificate of training, dissociated from the General Nursing Council, must—and I am sure will—receive warm support from every public-health authority in the country.

Western Hospital,
London, S.W.6.

W. HOWLETT KELLEHER.

SIR,—As matron of a busy infectious-disease training-school of just over 100 beds I am concerned that should the Fever Register be closed the services which we provide for the community will be sorely endangered.

Like other centres we have noted the increased incidence of infectious disease in the post-war years. Since 1947 we have nursed an epidemic of smallpox, an epidemic of poliomyelitis (1950) during which 208 acute cases were admitted in three months, and an epidemic of diphtheria (1951) when in six months 133 cases were confirmed of which 7 proved fatal. The day-to-day admissions are no less eventful, providing a wide range of experience in all types of infectious-disease nursing.

I have been fortunate in being able to maintain an adequate number of trained staff and a steady flow of student-nurse recruits, but I am certain that these numbers will decline when the incentive of a qualifying examination is removed. The closure of the Fever Register will indirectly remove a source of student nurses from entry to the general hospitals, since many girls choose to take their fever certificate as a test of suitability for the profession; in so doing they gain experience in medical nursing which makes them an asset to the general hospital which they ultimately enter. The practice of secondment of nursing staff from a parent hospital to the special hospital is one which I deprecate not only because little experience can be gained in such a short time, but also because no nurse can be expected to hold a simultaneous loyalty to two hospitals—loyalty to the hospital considerably affects the quality of a nurse's work.

There is one sphere in which the trained infectious-disease nurse is already sorely missed, and where I feel her complete absence will be a menace to public health. Before 1948 most infectious-disease hospitals maintained

TABLE II—POSSIBLE SOURCES OF INFECTION IN 69 CASES OF Q FEVER

Exposed to sources of Q fever		46 (67%)
Direct occupational exposure	20 (29% of total)	
Visits to or residence near farms, animal product factories, &c	22 (32% of total)	
Regular consumption of raw milk	28 (41% of total)	
Infected in France and not investigated further		3 (4%)
No obvious source of infection		20 (29%)

Seasonal Prevalence

Fig 3 shows the distribution of sporadic cases and outbreaks by months between January, 1948, and January, 1952 The disease seems to be more common in the summer, for 46 of the sporadic cases occurred in the months of April to September inclusive, compared with 21 between October and March All three explosive outbreaks occurred in the summer months

Source of Infection

Occupational exposure—Q fever is often regarded as an occupational disease of slaughterhouse workers and farmers, but the occupations of the patients in this series do little to confirm this at first sight

Industrial workers	13	Lorry drivers	4
Clerical workers	10	General labourers	3
Housewives	9	Retired people	3
Agricultural workers (including veterinary surgeons)	8	Furriers	2
		Bookmaker	1
		Hairdresser	1
Medical practitioners	8	Cobbler	1
Members of the Armed Forces	5	Publican	1

There are a few obvious exceptions, for example, one patient was a traveller for a firm of agricultural engineers and was a regular visitor to one farm where he was taught to milk cows which were later shown to be infected with *R burneti* A veterinary surgeon and his trainee assistant both developed Q fever three weeks after they had manually removed the placentas of two cows in an endemic area Sometimes the risk was less obvious, for example, one lorry-driver worked near an offal factory and another delivered to a wharf near a chemical works which used animal products Altogether, 20 out of 66 patients had occupations which might have exposed them to infection with *R burneti*

Contact with sources of infection—22 patients (32%) could have been infected through living near a source of Q fever 12 lived at or near a dairy farm or had spent a holiday on a farm a few weeks before their illness The remaining 10 cases developed in a small area in north Kent between October, 1949, and November, 1950 None of these patients lived near farms, and their respective occupations were builder, boiler-maker, lorry-driver, glass-works foreman, colour sprayer, dockyard labourer, crane driver, checker at a glass works, section manager at a pottery, and housewife, none of which suggested contact with a source of Q fever Moreover, the patients were all supplied with pasteurised milk from various sources But 7 of the patients lived in one small industrial town, 2 more went to work in the town each day, and 1 passed through this town daily on the way to his work

In the centre of the town there was a large glue and chemical works, which was supplied with offal, bones, condemned meat and whole carcases, usually of cows or sheep These were collected from Kent and Sussex, but some bones had come from abroad None of the patients with Q fever were employed at this factory, but one of them often fished in a creek which divided the two sections of the glue works, 2 worked in an adjoining glass works, 2 on an adjoining wharf, and 2 in a pottery 200 yards from the glue works 2 more patients lived within a quarter of a mile of the glue works, and the remaining patient passed close to it every day on his way to work There had been no illnesses suggestive of Q fever among employees of the glue works itself, but most of them had worked there for many years and might have been immune We hope to make a more intensive investigation of the locality in due course, but it seems probable that this group of patients were infected by the animal material at the glue works They have been considered as a group of infections due to residence rather than occupation, although 3 of them did not actually live in the area

Milk supply

28 patients (41%) drank unpasteurised milk, and the supply to 20 of them was investigated Q-fever organisms were found in the milk supplied to 10 patients, and 4 more received milk from herds with serological evidence of Q fever 6 patients received raw milk in which there was no evidence of infection

Many people who drink raw milk also live or work on farms, so it is difficult to assess the evidence that Q fever can be contracted from an infected milk supply

TABLE III—PREVALENCE OF Q FEVER ANTIBODIES IN SERA FROM BLOOD DONORS AT VARIOUS CENTRES IN ENGLAND AND WALES

—	Total tested	No positive at titre of 1 10	% positive at titre of 1 10
Northern England			
Chesterfield (Derbyshire)	57	2	3·5
Swallownest („)	60	3	5·0
Alfreton („)	93	6	6·4
Wombwell (West Riding)	50	—	—
Newcastle (co Durham)	188	2	1·1
Swinton (North Riding)	57	—	—
Total for Northern England	505	13	2·6
Midlands			
Birmingham (Warwickshire)	39	—	—
Wales			
Wrexham (Denbighshire)	148	6	4·0
Carnarvon (Carns)	50		
Pwllheli („)		—	—
Bangor („)	44	1	2·0
Flint (Flintshire)	59	—	—
Newtown (Montgomeryshire)	58	1	1·7
Llandilo (Carms)	49	—	—
Cardiff (Glamorgan)	49	—	—
Milford Haven (Pembrokeshire)	32	1	3·0
Total for Wales	489	9	1·85
East Anglia			
Beccles (E Suffolk)	79	1	1·3
Debenham („)	39	—	—
Eye („)	96	—	—
Framlingham („)	54	2	3·7
Ipswich („)	188	5	2·7
Halesworth („)	72	—	—
Lowestoft („)	42	—	—
Stowmarket („)	200	1	1·5
)	61	—	—
lk)	47	—	—
	221	—	—
	60	—	—
Fakenham („)	41	—	—
Hunstanton („)	48	—	—
Wymondham („)	34	—	—
Kings Lynn („)	37	—	—
Peterborough (Northants)	49	—	—
Huntingdon (Hunts)	50	—	—
Total for East Anglia	1418	11	0·78
Southern England			
Sherborne (Dorset)	49	4	8·0
Blandford („)			
South east England			
Ashford (Kent)	279	7	2·5
Canterbury („)	266	8	3·0
Dartford („)	78	—	—
Deal („)	301	6	2·0
Herne Bay („)	167	13	7·8
Hawkhurst („)	68	2	2·9
Sittingbourne („)	179	4	2·2
Whitstable („)	158	1	1·9
East Grinstead (Sussex)	116	3	2·5
Hastings („)	343	12	3·5
Total for South east England	1956	58	2·96
Grand Total	4456	95	2·13%

Professor Webster declined to use the word "negligence," with its forensic implications, when he spoke of "bad doctoring" and "bad nursing." The committee considered that the allegations, in the ordinary sense of the words, could hardly mean anything else. However that may be, they thought it "most regrettable" that the epithet "bad" was employed. There had been no act which tended to the patient's disadvantage.

The hospital board has adopted the report and findings and has sent a copy to the Ministry. It was evidently a full and patient inquiry, and, although one dissatisfied critic has spoken of the report as mere "white-washing," the public will probably be satisfied that the truth has been elicited, notwithstanding the inevitable tendency to wonder how it is that doctors can so violently differ.

Parliament

Transfer of Medical Functions of Ministry of Pensions

In the House of Commons on Feb. 26, the Prime Minister announced that it was proposed to amalgamate the Ministry of Pensions with the Ministry of National Insurance for the award and payment of war pensions and allowances. The new ministry would be known as the Ministry of Pensions and National Insurance. The medical treatment undertaken by the Ministry of Pensions (including the management of hospitals and the supply of artificial limbs, surgical appliances, and invalid vehicles) would be transferred in England and Wales to the Ministry of Health and, in Scotland, to the Department of Health for Scotland. The greatest care would be taken to ensure that war pensioners and their dependants were not in any way adversely affected by these changes. An additional Parliamentary Secretary would be appointed to the new Ministry of Pensions and National Insurance to look after the pensions and allowances of war pensioners. The Central Advisory Committee on war pensions would continue to function.

So far as medical treatment was concerned, such special facilities as war pensioners at present enjoyed would be fully safeguarded and, in addition, the Minister of Health and the Secretary of State for Scotland would be able to call on the facilities of the whole National Health Service to ensure that the necessary treatment of war pensioners was given by the hospital best able to provide it. Arrangements would be made, in consultation with the Government of Northern Ireland, to meet the requirements of war pensioners resident in Northern Ireland.

Abortion Bill

In the House of Commons on Feb. 27, Mr. Joseph Reeves moved the second reading of the Abortion Bill.[1] As this measure was the third order of business for the day, it was only reached about a minute before four o'clock, which on Friday is the hour of the adjournment. Mr. Reeves had time, however, to explain that it was not the object of the promoters to extend the practice of abortion, but to confine abortion to cases where in the view of competent medical practitioners it was in the interest of the mother's health, and for the prevention of injury in her body. In such cases unmistakable authority should be given to the medical profession to act in the interests of the patient. Under the present law, Mr. Reeves pointed out, a great deal of uncertainty prevailed, although some judgments had seemed to provide protection for qualified practitioners performing operations in the interests of the mother.

Because there appeared to be some uncertainty as to the interpretation of clause 1 (*a*) of the Bill, Mr. Reeves said that the promoters were prepared to accept a redrafting to ensure that the term "person" referred to a registered medical practitioner.

Pharmacy Bill

In the House of Commons on Feb. 27, Mr. John Hall moved the second reading of this Bill.[2] Mr. Hugh Linstead, speaking as Secretary of the Pharmaceutical Society, welcomed the Bill as an amending measure which he hoped would be the precursor to the consolidation of the Pharmacy Acts. The Bill was read a second time and committed to a Standing Committee.

QUESTION TIME

Flour and the National Diet

Mr. Beresford Craddock asked the Minister of Food what undertakings he had received on the types of flour which will be produced when controls on cereals are removed; and how far these undertakings would preserve the present nutritional contribution of flour to the national diet.—Major Gwilym Lloyd George replied: As stated in the white-paper,[1] the removal of cereal controls will involve the removal of the present restrictions on the types of flour which may be produced. National flour of the present 80% extraction will, however, continue to be produced and loaves made from this flour will be available at a subsidised price wherever bread is sold. Such flour, as well as flours of higher extraction, contains the three so-called token nutrients—i.e., iron, vitamin B_1, and nicotinic acid—in quantities which conform to the levels recommended in 1945 after a most careful inquiry by the Conference on the Post-War Loaf (Cmd. 6701). Flours of lower extraction than 80% lose a proportion of these three token nutrients in the course of the further refining process. Provision will therefore be made by Order for the restoration of these nutrients to the levels recommended by the Conference, and for the inclusion of the calcium carbonate which is already added to national flour. My medical and scientific advisers, after reviewing the amounts of these various nutrients in the present diet, are satisfied that such measures will ensure the maintenance of existing nutritional standards; but should any future investigations indicate the desirability of further supplementation, I shall naturally be prepared to reconsider the matter.

Hospital Building in Scotland

In answer to a question, Mr. James Stuart, Secretary of State for Scotland, said that the total value of the 57 building projects submitted by regional hospital boards in Scotland which had been approved and started was about £2,450,000, of which £800,000 was due to be spent during 1953. The total value of the 41 other projects which had been approved in principle was about £1,700,000. He hoped that regional boards would be able to start most of these during 1953, but resources could not be made available to carry out more than about £300,000 of work on them during the year.

Protection of Miners against Tetanus

Replying to Dr. Barnett Stross, Mr. Geoffrey Lloyd, Minister of Fuel and Power, said that the small number of fatal cases of tetanus among miners—not more than one or two per year—suggested that the first-aid treatment of injuries at mines had provided reasonably effective protection against infection with the disease. Recently, however, the National Coal Board gave instructions that when a man was injured at a colliery where the risk of infection with tetanus was likely to be present and was sent to hospital, the staff of the colliery medical or first-aid room must notify the hospital accordingly.

Woodberry Down Health Centre

Dr. Santo Jeger asked the Minister of Health whether he had filled the vacancies in the medical appointments to the Woodberry Down Health Centre; and what were the reasons for the delay.—Miss M. P. Hornsby-Smith replied: Local doctors have been asked which of them would wish to practise from the centre, but the abnormal calls on their time recently have delayed them in meeting to consider the matter. It is hoped they will do so shortly.

Aureomycin Supplies in Hospitals

Replying to a question Mr. Iain Macleod, Minister of Health, said that he was satisfied that the supply of aureomycin available to hospitals was sufficient. There was no restriction on the quantities supplied to hospitals, although there had recently been some delay in delivery of bulk aureomycin which was imported for packaging in this country.

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[1] See *Lancet*, Jan. 10, 1953, p. 101.
[2] *Ibid*, Feb. 21, 1953, p. 355.

[1] Decontrol of Cereals and Feeding stuffs. Cmd. 8745. H.M. Stationery Office, 1953. Pp. 4. 3*d*.

he believed that human infection was due to inhalation of dried tick excreta from the hides of cattle, or occasionally to the bite of the tick itself But although several species of ticks in different parts of the world have been found to harbour Q-fever organisms, and although they may help to maintain infection in animals, there is in fact little evidence that they play an important part in the infection of man The excretion of rickettsiæ by the cattle, sheep, and goats themselves is certainly enough to account for the great majority of human infections

COWS

The first outbreak of Q fever identified in Britain quickly led to the discovery of infected cows which were excreting rickettsiæ in their milk This discovery resulted in a study of Q fever in cattle and perhaps to the neglect of other possibly important sources of infection such as sheep and goats Cattle have been studied in Kent and Devon, where human infections are relatively common, and in East Anglia, including Bedfordshire and Hertfordshire, where Q fever in man is rare In these areas, infection in cattle has been identified by tests for Q-fever complement-fixing antibody in the sera from individual animals or by isolation of the organism from the milk Those sera which fixed complement with Q fever antigen were also tested with normal egg antigen or typhus antigen to control the specificity of the reaction For isolation of the rickettsiæ, specimens of milk from one or more herds of cows were sent to Cambridge in containers with ordinary ice or frozen with solid carbon dioxide 2 ml quantities were inoculated into pairs of guineapigs, which were caged with uninoculated guineapigs as controls A fourfold rise in Q fever complement-fixing antibody in the guineapig serum after five to six weeks was taken to indicate the presence of rickettsiæ in the original inoculum Occasionally mice inoculated with 0 25 ml were used instead of guineapigs, either because the latter were not available or because they succumbed to bacteria in the milk Cattle in Kent, Suffolk, and Norfolk were also investigated by examination of sera from guineapigs inoculated with milk at public-health laboratories for routine biological tests When milk pooled from several herds was found to contain Q-fever organisms, samples from the constituent herds were then tested separately

Table IV shows the results of this investigation It will be seen that infection of cattle is much commoner in Devon and Kent than it is in East Anglia Only 7 herds out of 823 in East Anglia were excreting Q-fever organisms (0 85%), compared with 11 out of 185 in Devon and Kent (6 0%) The over all prevalence (1 75%) is low because of the large numbers from areas of low prevalence The same difference is shown in the few areas where tests for Q-fever antibody in bovine sera were carried out No positive cattle were found out of 170 in Suffolk and Hertfordshire, but there were 17 out of 489 (3 5%) in Devon 2 of these 17 cows with high serum-antibody titres (1 160) were also found to be excreting organisms in the milk, but they have not been included in the results of the main milk survey The significance of this geographical distribution of infection, both in man and cows is discussed below

TABLE IV—PREVALENCE OF Q FEVER IN COWS

County	No of herds whose milk was tested	No with *R burneti* in milk	% of herds excreting *R burneti*	No of cows tested for Q-fever serum anti body	No of cows with Q-fever anti body	% of cows with Q fever anti-body
Cambridgeshire and Isle of Ely	22	0	—	—	—	—
Norfolk	49	0	—	—	—	—
Suffolk	435	2	0 46	18	0	—
Bedfordshire	184	4	2 1	—	—	—
Hertfordshire	133	1	1 3	152	0	—
Devon	74	2	2 7	489	17	3 5
Kent	111	9	8 2	—	—	—
Total	1008	18	1 78	659	17	2 46

SHEEP

There is no convenient way of assessing the prevalence of infection in sheep, except by testing sera from individual animals for Q-fever antibody Specimens have so far been collected from 51 sheep at slaughterhouses in North Kent but none contained Q-fever antibody Goats have not been investigated at all

TICKS

None of the patients with Q fever remembered being bitten by a tick, but the peculiar distribution of tick species in this country raised the possibility that they were responsible for infection in cattle and sheep

Ixodes ricinus (the sheep tick) and some other members of this genus are widely distributed throughout the British Isles Little is known of other ticks, but they appear to be rare except in two areas, Kent and Devon Nuttall and Warburton (1915) mention *Hæmaphysalis cinnabarina* var *punctata* occurring on Romney and Lydd Marshes, and the occurrence of this tick on the Kent marshes, to the exclusion of the ixodes species, has been confirmed by various entomologists and later by us personally In Devon *Ixodes ricinus* is common enough, but *Dermacentor reticulatus* is also found The first isolations of *R burneti* from ticks in Australia and the U S A were made from *Hæmaphysalis humerosa* and *Dermacentor andersoni* respectively, and therefore the occurrence of these genera in the very areas of England where Q fever may be most common called for investigation

In Devon, with the guidance and help of Mr Geoffrey Vickers of Exeter College, ticks were collected by "flagging" Although *Ixodes ricinus* was much more abundant than *Dermacentor reticulatus*, a few of the latter were also collected Ticks in Kent were also collected by flagging on the north Kent marshes and engorged ticks were collected from lambs by shepherds No ticks other than *Hæmaphysalis cinnabarina* were identified in Kent Finally large batches of *Ixodes ricinus* were kindly sent from Cumberland by Mr G B S Heath and from Scotland by Dr J A Campbell

Isolation of Q-fever organisms from batches of different species of ticks was attempted by injection of extracts into guineapigs or mice in the same way as in the examination of m[illegible] Altogether 23 batches were tested, comprising 15 [illegible] about 700 *Hæmaphysalis cinnabarina* and about 1800 *Ixodes ricinus* (856 from Devon and the remainder from Cumberland or Scotland) No Q fever organisms were found in any of the batches of *Ixodes ricinus* or *Dermacentor reticulatus* but one batch of *Hæmaphysalis cinnabarina*, collected by flagging in north Kent, produced Q fever antibodies in one of two guineapigs, and another batch collected from sheep in a different part of north Kent produced antibodies in two out of five mice Unfortunately, reinoculation of the stored remains of these batches failed to stimulate antibody production This failure to repeat the results of the first experiments might be due to the greater dilution of the remains or to loss of infectivity through storage (at −20°C) but until these results can be confirmed they must be regarded as doubtful

DISCUSSION

These investigations suggest that over 2% of healthy adults tested have been infected with *R burneti*, but this figure does not necessarily represent the rate of infection for the whole country Only a small number of people mmittee he appeared to have complete mastery of his bject, but behind his confident delivery lay hours of pains-king preparation and rehearsal. He was a deeply religious an who gave expression to his convictions by his own ample of kindliness, self-control even under the most ying circumstances, and devoted work in the service of ankind. Although he set the highest standards for himself e was an excellent mixer and a jolly companion on all ccasions. A visit to a hospital or rehabilitation centre with im always left memories of an enjoyable trip, new friend-hips made, and something worth while achieved either by eeing new developments or by kindly advice as to how some ifficulty might be overcome.

"Harold Balme appeared robust and far younger than his ears. Few of the many who met him in his extensive travels s adviser on rehabilitation to the United Nations realised hat such an energetic and hard-working man was well ver seventy. Yet his looks belied him, for he suffered with a number of serious illnesses in his latter years. It was ypical of his indomitable spirit that even when suffering evere pain from his fatal illness he carried on with the study ourse on rehabilitation which he planned and directed in Sweden, Finland, and Denmark in the autumn of last year."

Births, Marriages, and Deaths

BIRTHS

CRAWSHAW.—On Feb. 21, to Barbara, wife of Mr. G. R. Crawshaw, F.R.C.S., of Johannesburg—a son.

HARE.—On Feb. 23, at Elizabeth Garrett Anderson Maternity Home, Belsize Park, London, to Mary (née Bridges), wife of Dr. Patrick Hare—a son.

PRICE.—On Feb. 23, at Frimley Hospital, Surrey, to Mary (née Brill), wife of Dr. Douglas J. Price—a son.

Appointments

BELL, J. H., M.D. Glasg., D.P.H., D.I.H.: appointed factory doctor, Glasgow East, Lanarkshire.

BERNARD, R. McF., M.B. Aberd., M.R.C.O.G.: asst. obstetrician and gynæcologist (consultant), Aberdeen special and general hospitals.

CASIMIR, C. L., M.B. Lond., D.P.M.: psychiatrist, Sutton child-guidance clinic.

DAVIDSON, L. D., M.B. Aberd., D.A.: anæsthetist, Aberdeen special and general hospitals.

JOHNSTON, N. G., M.B. St. And., D.A.: consultant anæsthetist, Sedgefield H.M.C. group.

McFARLAN, A. M., M.A. Camb., M.B. Edin.: epidemiologist for tuberculosis (senior M.O.), public-health department, Bristol.

SKEOCH, THOMAS, L.R.C.P.E.: consultant pathologist, Middlesbrough area laboratory service.

East Anglian Regional Hospital Board:

BREWER, D. J., M.B. Lond.: medical registrar, Foxhall Hospital, Ipswich.

CIMA, P. H., M.B. Lond.: medical registrar, North Cambridgeshire and Clarkson Hospital, Wisbech.

CREAMER, ALICE, M.B. N.U.I., D.P.H., D.P.M.: registrar in psychiatry, Fulbourn Mental Hospital and psychiatric department, Addenbrooke's Hospital, Cambridge.

LINDSAY, ROBERT, M.B. Glasg.: anæsthetic registrar, Norfolk and Norwich Hospital.

LITTLEJOHN, JOHN, L.R.C.P.E.: registrar in psychiatry, Fulbourn Mental Hospital.

NOEL, P. R. B., M.B. Lond.: medical registrar, East Suffolk and Ipswich Hospital and Ipswich Borough General Hospital.

Manchester Regional Hospital Board:

COLOHAN, A. B., M.B. Belf.: tuberculosis physician and M.O. in charge of M.M.R. unit, Chorley.

COOPER, J. A. L., M.R.C.S., D.A.: consultant anæsthetist, Preston and Chorley hospitals.

DA CUNHA, F. A. L., M.B. Camb., M.R.C.O.G.: asst. consultant obstetrician and gynæcologist, Oldham and Ashton hospitals.

FISHER, HILDEGARDE, L.R.C.P.E., D.P.M.: asst. psychiatrist, Lancaster Moor Hospital.

GEAKE, M. R., M.B. Camb., M.R.C.P.: consultant chest physician, Preston and Chorley hospital centre.

GILL, N. W., M.B. Lond., F.R.C.S.: surgeon, South Manchester hospitals.

JOLLEYS, AMBROSE, M.D. Lpool, F.R.C.S.: consultant pædiatric surgeon, Royal Manchester Children's and Booth Hall hospitals.

McCARTHY, T. F., M.D. Wales, M.R.C.P.E.: asst. physician, Nab Top Sanatorium, Marple.

MUDIE, I. S., M.B. St. And., D.T.M. & H.: tuberculosis physician, Mid Cheshire and Crewe areas.

RANKIN, N. F., M.B. Lond.: asst. pathologist, Bury and Rossendale hospital centre.

SEVILLE, R. H., M.D. Leeds, M.R.C.P.: consultant dermatologist, Lancaster, Barrow and Blackpool hospital centres.

Notes and News

EARLY DIAGNOSIS OF CANCER

THE British Empire Cancer Campaign has prepared a short pamphlet setting out the symptoms and signs that are of greatest value in detecting the presence of malignant disease in its early stages. With the approval and help of the British Medical Association, the pamphlet is now being distributed to general practitioners. It is published with the authority of the campaign's scientific advisory committee, under the chairmanship of Lord Horder. Its purpose is to remind doctors of the need not only to consider a diagnosis of cancer, but to accept the responsibility for excluding it by all possible means. The pamphlet skilfully summarises the features that should arouse suspicion in a particular case, and lays emphasis on the danger of concluding that the lesion is benign because of the absence of certain symptoms or signs, which may only appear when cure is impossible.

The Campaign is anxious to sound the opinion of as many doctors as possible before deciding on its policy in the matter of teaching the public more about cancer. In a letter accompanying the pamphlet, therefore, practitioners are being asked the question: Do you consider that the launching of a scheme of lay educational propaganda on cancer (by pamphlet, lectures, films, &c.) would be of assistance in securing the earlier diagnosis of cancer, and thereby improving the chances of a cure'?

TROPICAL DISEASES BULLETIN

WITH the January issue this year the *Tropical Diseases Bulletin*[1] issued by the Bureau of Hygiene and Tropical Diseases, reached the start of its fiftieth volume. In that issue Mr. R. L. Sheppard recalls that the *Bulletin* sprang, in 1912, from the *Sleeping Sickness Bulletin*, which the bureau began to publish in 1908, and from the *Kala Azar Bulletin*, which first appeared in 1911. The bureau, now directed by Dr. Charles Wilcocks, also issues the *Bulletin of Hygiene*.

University of Cambridge

At recent examinations the following were successful:

M.Chir.—C. G. Attenborough, M. T. Pheils, P. G. Somerville, J. P. Stephens.

Queen's University, Belfast

At recent examinations the following were successful:

M.D.—J. F. Breach, F. D. Honneyman, W. A. Norris (by examination); * D. T. Gilchrist, D. T. Glass, S. H. S. Love, E. A. Murphy, * D. A. R. Orr, G. U. Thomas, * I. D. Thompson, Irene M. Thompson (by thesis).

* With commendation.

Nuffield Gerontological Research Fellowship

The Nuffield Foundation, as part of its programme for the care of old people, is offering a fellowship of professorial status for research on the scientific aspects of ageing, or alternatively one or more fellowships of less senior status.

The fellowship, which may be tenable at any university in the United Kingdom, will be open to men and women usually not more than 45 years of age. The value of the senior award will be not less than £2000 p.a. If a less senior worker is appointed the value will be £1000–1500 p.a.

Applications must be sent by June 1 to the secretary of the Foundation, Nuffield Lodge, Regent's Park, London, N.W.1. Further particulars will be found in our advertisement columns.

Representation on Hospital Management Committees

On Feb. 9 the chairman of the North-west Metropolitan Regional Hospital Board reported that he had received from Willesden Borough Council a deputation which claimed that the council was a health authority and as such was entitled to have members on management committees. The board resolved to advise the borough council that it could not undertake that members should be appointed to a management committee solely on the ground of their membership of a particular body, but to suggest that it might approach Middlesex County Council with a request to that body to include among its nominations names submitted by the borough council. Mr Fred Messer pointed out that the board was compelled by statute to consult 8 bodies on the appointment of members to management committees; but the number consulted had risen to 33. On Mr. Messer's suggestion the board agreed to consider reducing this number.

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[1] Issued monthly by the Bureau of Hygiene and Tropical Diseases, Keppel Street, London, W.C.1. Annual subscription 70s.

Dr. Robert Heilig Library
S. M. S. Medical College
JAIPUR

Summary

Excluding outbreaks, 69 sporadic cases of Q fever have been identified in Britain since the disease was first discovered here in 1948, 58 of these had typical clinical attacks, usually resembling atypical pneumonia, and 4 patients died during the infection, 2 with pulmonary infarction, 1 of whom may have had chronic Q fever

32 patients were infected in Kent, and the remainder in places scattered over England and Wales, except for 3 who were infected abroad Two-thirds of the patients gave a history of exposure to known sources of Q fever

Of 4407 normal blood donors in England and Wales, 91 (2 13%) showed serological evidence of previous infection with Q fever The rates in different areas varied from 2 96% in south-east England to 0 8% in East Anglia This suggests that the cases actually diagnosed represent only a small proportion of the total

Examination of the milk from 1031 herds of cattle showed that 8 2% of the herds in Kent were excreting *Rickettsia burneti* in the milk, compared with 2 7% in Devon and 0 85% in East Anglia

The prevalence, distribution, and importance of Q fever in Britain, both in man and animals, are discussed in the light of these findings

A great many people have helped us in this investigation, but we can mention only a few by name We are particularly indebted to Mr R Petch, assistant in charge of the laboratory at Sheppey General Hospital, for epidemiological and laboratory work, and to Mr Geoffrey Vickers, of University College, Exeter, for his help with the collection of ticks We are grateful to the doctors in charge of the patients with Q fever, and especially to Dr D H Mills, of the Willesborough Hospital, Ashford, Dr J W Fawcett, of the Postgraduate Medical School of London, Dr P B Newcomb and Dr M E Sidaway, of the Hackney Hospital, London, and Dr J M Wingfield of the Royal Devon and Exeter Hospital Our thanks are also due to the medical officers of health and their staffs and the sanitary inspectors who helped us, especially those at Canterbury, Herne Bay, Whitstable, Deal, Folkstone, Ashford Crowborough, Gillingham, Sittingbourne, Ipswich, Oxford, Exeter, and Swansea We are much indebted to Dr W d'A Maycock and to the directors of the blood-transfusion centres and their staffs at Sutton, Cambridge, Sheffield, Liverpool, Cardiff, and Birmingham, and particularly to Miss B E Dodd at the South London Blood Transfusion Centre, Sutton Help has also been given us by the directors and staff of the Public Health Service Laboratories at Maidstone, Taunton, Cardiff, Ipswich, Wakefield, Oxford, and Conway, by Dr I B Morris and Dr G B Forbes, of the Kent and Canterbury Hospital, and by Dr H G Close, of West Hill Hospital, Dartford Sir Thomas Dalling kindly arranged for cows to be bled by veterinary surgeons of the Ministry of Agriculture, and we are very grateful to Mr A J Beeson, M R C V S, and Mr J Stewart, M R C V S of Maidstone In our own laboratories valuable technical assistance has been given by Miss Z Page and Mr P Phipps, and secretarial assistance by Miss F Callaby and Miss M Coad Finally, we are much indebted to Prof H R Dean and Dr G S Wilson for their unfailing support, and to Dr F O MacCallum, director of the Virus Reference Laboratory at Colindale, for his helpful advice and encouragement

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BACTERIOPHAGE TYPING OF STRAINS O STAPHYLOCOCCUS AUREUS FROM VARIOUS SOURCES

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With
LYNETTE M DOWSETT
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A ROUTINE method for the identification of strains *Staphylococcus aureus* by means of bacteriophages w described by Wilson and Atkinson in 1945 and has s been used in the investigation of numerous outbrea especially of food-poisoning and hospital cross infect and in studies of the source of infection in whitlows a other septic lesions For interpreting such studies so knowledge of the frequency of various phage "types of staphylococci in the normal population would be great assistance Unfortunately, however, the set o phages in use at present gives pattern reactions rath than truly type-specific reactions, that is, one staphyl coccus may be lysed by several different phage, an each of these phages may enter into a number of differen patterns on different strains These patterns are to numerous, and overlap too much, for it to be practicab to regard particular patterns as characterising "types and in practice therefore we report the results of typi as a "bacteriophage pattern" (Williams and Rippo 1952)

The bacteriophage patterns fall into three large grou that can be reasonably easily defined and have be referred to in the past as the 3A, 6/47, and 52 group Since these groups correspond broadly to the serologic types defined by Cowan (1939) it has been suggested that they should be given the same numbers (Wahl an Fouace 1952)

For this paper we have classified 1349 independen strains of *Staph aureus* which were sent to us for identi fication during three years and which were tested by th bacteriophage method. We have compared the frequenc of the three groups among strains from carrier sites i healthy persons and from various different lesions.

METHODS

A detailed account of the typing technique and discussion of the interpretation of the results has bee given elsewhere (Williams and Rippon 1952), and ther is therefore no need here to give more than a brie summary.

The staphylococci under test are grown for *four hours* i nutrient broth, some of the broth is then spread over th surface of an agar plate and allowed to dry for thirty to sixt minutes Small drops (about 0 01 ml) of 24 different bacterio

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Q FEVER IN GREAT BRITAIN

AN ANALYSIS OF 69 SPORADIC CASES, WITH A STUDY OF THE PREVALENCE OF INFECTION IN HUMANS AND COWS

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WHEN Derrick (1937) first noticed an illness amongst Brisbane abattoir workers he called it, with due caution, Q (query) fever, and for some years it was looked on as an obscure illness localised to Brisbane and the neighbouring countryside. The organism responsible, a rickettsia, received some attention in academic circles, but although an identical organism was found in ticks in the U.S.A., and some laboratory workers became infected, few imagined that Q fever would prove to be a natural and widespread disease of the Northern Hemisphere. The first sign came in 1944 when outbreaks of atypical pneumonia amongst Allied and Axis troops in Italy and Greece were identified as Q fever (Robbins and Ragan 1946). The disease was identified in Panama at about the same time (Cheney and Geib 1946), shortly afterwards in Texas (Topping et al. 1947), and then in California (Shepard and Huebner 1948). In subsequent years Q fever was found in many countries of Europe, North Africa, and the Middle East—in fact almost everywhere that a search has been made.

Although suspicion may be aroused by its epidemiological behaviour, Q fever is difficult to distinguish clinically from many other fevers, and especially from the primary atypical pneumonia of unknown ætiology. Descriptions of a large number of cases have already been published, and these have been summarised by Harman (1949). Clinical and more often radiological evidence of pulmonary involvement is found in the majority of cases, and the only points which may help to distinguish Q fever from primary atypical pneumonia are the sudden onset and the headache out of all proportion to the fever. Diagnosis ultimately rests on the laboratory, and for this reason Derrick's original discovery of the disease was made at an opportune time, for it came at the beginning of a period of great technical advance in the laboratory study of viral and rickettsial diseases and particularly in their diagnosis by serological means. This has encouraged the study of Q fever in man and has also led to an intensive and remarkably fruitful investigation of the sources of infection, but little progress has yet been made in prevention or control.

Although the causative agent has been isolated from the blood, sputum, and urine of patients with Q fever, case-to-case transmission in man is rare (and for this reason it is not necessary to isolate patients or contacts). Despite the fact that this is a rickettsial disease, arthropods seem to play little part in its spread to man; for although some ticks carry the Q-fever organism, *Rickettsia burneti*, they are very rarely responsible for human infection. The principal sources of human infection are now known to be cattle, sheep, and goats, all of which may, though apparently well, excrete the organism in the fæces, urine, milk, placenta, and fœtal membranes, so that humans are probably infected either by inhaling dust contaminated with these excreta or by drinking infected milk. The organism is remarkably hardy, and the conditions used in pasteurisation are only at the borderline of safety (Huebner et al. 1949, Marmion et al. 1951, Lennette et al. 1952). It also resists many disinfectants and can persist in dust for long periods in normal ranges of temperature and humidity. Perhaps for this reason Q fever is not limited to those whose residence, occupation, or habits bring them into direct contact with cattle, sheep, or goats, or their products.

Q FEVER IN BRITAIN

Soon after Stoker (1949) had found serological evidence of Q fever in Britain, *R. burneti* was isolated by MacCallum et al. (1949) during an outbreak at the Royal Cancer Hospital, London; the clinical features of this outbreak have been described by Harman (1949) and the epidemiological findings by Marmion and Stoker (1950). The outbreak, which involved a nurse, two pathologists, and a mortuary attendant, followed the death and post-mortem examination of an elderly man with pneumonia, in whose lungs rickettsia-like organisms were later demonstrated (Whittick 1950). This man was presumably infected at his home in a town in north-east Kent before admission to hospital. His wife was found to have serological evidence of Q fever, and investigations showed that *R. burneti* was present in the milk-supply.

Some of the cows supplying this milk and some of the workers on the dairy farm had serological evidence of past infection, and so had 13 out of 83 healthy blood donors from the town. At the Royal Cancer Hospital two other members of the staff developed Q fever the following month, but they had had no connection with the first cases and were found to have been infected while on holiday in Devon at a farm where cattle showed serological evidence of infection with *R. burneti*. All this stimulated a more intensive search for Q fever both in man and animals, particularly in Kent and Devon, and before long Harvey et al. (1951) described a larger outbreak involving 28 out of 204 staff and students at the Canterbury School of Art. Although the source of infection of this outbreak was not identified with certainty, contaminated straw from a packing-case which was opened nineteen days earlier may have been responsible. Finally, a third outbreak occurred on a farm in south Kent in September, 1951 (Stoker and Thompson 1953).

But these explosive outbreaks represent only one aspect of Q fever in man, and in Britain isolated cases are more numerous though less spectacular. The first part of this paper deals with those which have been identified at Cambridge or Colindale from January, 1948, to January, 1952, excluding the three outbreaks already referred to.

The second part of the paper describes the prevalence of previous infection in healthy adults. Because the final diagnosis of Q fever depends on a retrospective laboratory test, one would expect the illnesses actually identified as Q fever to represent but a small proportion of the total number which occur, except perhaps in areas where Q fever is known to be endemic and where local practitioners are well aware of it. The true prevalence of Q fever is hard to assess: judging by specimens received at the Virus Reference Laboratory, Colindale, it accounts for 9% of cases of atypical pneumonia (compared with influenza which causes 8%, and psittacosis 1%) and 5% of pyrexias of unknown origin (Virus Reference Laboratory 1953). Among patients at the Postgraduate strains from beat lesions were received from Dr J Marks, of Cardiff, who has already shown that these lesions often result from self-infection (Atkins and Marks 1952) The strains from boils were received from many sources, including hospital outpatient departments, in cases where strains were also received from the patient's nose, the pair were usually the same type (Valentine and Hall-Smith 1952, Overton 1952) It is probable that the infection in whitlows also arises from self-infection (see Williams and Miles 1949), and the same may be largely true of otitis and mastoiditis, although the rather large proportion of group-III strains, which predominate in hospital infections, suggests that some cases may have arisen as a result of cross-infection

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† In receipt of a grant from the Agricultural Research Council.

Miscellaneous Infections, Osteomyelitis, and Bacteræmia (table II, rows 11 and 12)

This group of infections is separated because it was usually impossible, on the information available to us, to distinguish infections that probably arose in hospital, and so may have resulted from cross infection, from those that probably arose outside hospital It will be shown below that strains of group III are very commonly transmitted in hospitals, and about 30% of the strains from the infections of rows 11 and 12 were group III, this is intermediate between the frequency in boils, whitlows, &c, already shown to resemble the normal nasal flora (22 4% group III) and the recognised hospital infections (55 7% group III)

Hospital Infections (table II, rows 13–15)

During the period over which these strains were collected, almost all epidemics of hospital infection were due to penicillin-resistant staphylococci which, as is well recognised (Barber and Whitehead 1949, and below), are most commonly strains of group III and less often of group I In fact, almost all the typable strains from epidemics fell into one or other of these groups, with no fewer than 68 2% of the total into group III The group distribution of the staphylococci from "sporadic" hospital infections did not differ significantly from that of the epidemic strains

Pemphigus and Other Neonatal Infections (table II, row 16)

Staphylococci from cases of pemphigus and other neonatal infections, which are usually hospital infections, were predominantly group-III, but there were more group-I than in other hospital infections

Pneumonia (table II, rows 17–19)

During the influenza epidemic of 1949, we were sent a number of staphylococci from cases of pneumonia complicating the acute infection, and we noted an apparent predominance of strains of group I We therefore requested bacteriologists investigating cases of influenzal pneumonia to send us strains of staphylococci, together with notes on the patients' clinical state and the results of any virus studies From the clinical notes it seemed that a group of very acute or fulminating cases could be separated from the remainder of the acute pneumonias, even though in both these groups the pneumonia appeared clinically to complicate an attack of virus influenza Staphylococci were also received from a further group of patients who had not had an acute attack of pneumonia Of the 34 strains from fulminating cases, no fewer than 56% were group I, while the corresponding percentages for the other acute, and the non-acute, pneumonias were 27 and 21 respectively The latter two frequencies were approximately the same as in the normal nasal staphylococci

It was not possible to show the same association of group-I strains with a fatal termination of the illness, nor was there a predominance of group I in patients from

TABLE II—FREQUENCY OF STAPHYLOCOCCI OF DIFFERENT PHAGE GROUPS FROM VARIOUS SOURCES

	—	No tested		Percentage									
				Group I (52)		Group II (3A)		Group III (6/47)		Unclassified		No lysis by phages used at routine test dilution	
1	Nose, normal persons, miscellaneous	252		21 8		13 1		17 5		5 6		42 0	
2	,, ,, mothers and babies	104		29 8		17 3		21 2		2 9		28 8	
3	, ,, total		356		24 2		14 3		18 5		4 8		38 [illegible]
4	Fæces of normal persons	96		8 3		11 5		28 1		2 1		50 0	
5	Perianal swabs normal persons	23		8 7		4 4		39 1		4 4		43 4	
6	Fæces and perianal swabs total		119		8 4		10 1		30 3		2 5		48 [illegible]
7	Boils whitlows, &c	77		39 0		20 8		18 2		10 4		11 7	
8	Beat lesions	25		28 0		24 0		12 0		0		36 0	
9	Otitis, mastoiditis	54		22 2		13 0		33 3		5 6		25 9	
10	Total		156		31 4		18 6		22 4		7 1		20 5
11	Miscellaneous superficial skin infections		117		15 4		11 1		35 9		4 3		33 3
12	Osteomyelitis bacteræmia, &c		46		19 5		23 9		28 3		4 4		23 9
13	Hospital cross infection, recognised epidemics	22		9 1		0		68 2		9 1		13 6	
14	Sporadic infections	118		15 3		5 1		53 3		5 1		21 2	
15	Total		140		14 3		4 3		55 7		5 7		20 0
16	Pemphigus and other neonatal infections sporadic and epidemic		178		28 1		8 4		38 8		4 5		20 2
17	Pneumonia, fulminating		34		55 9		14 7		8 8		14 7		5 9
18	, acute		84		27 4		14 3		25 0		0		33 3
19	,, other		38		21 1		10 5		39 5		2 6		26 3
20	Food poisoning grade A	40		0		0		87 5		0		12 5	
21	, , B	41		2 4		2 4		78 2		2 4		14 6	
22	Total		81		1 2		1 2		82 8		1 2		13·6
23	Grand total		1349		21 7		11 8		33 0		4 5		29 0

Tests for the significance of apparent differences between the distributions from various sources were made after combining the "unclassified" column with the 'no lysis' column

Comparison between rows	χ^2	D F	P
3 and 6	8 944	3	<0 05
3 and 10	10 990	3	<0 02
3 and 10, on group I, II, and III only	0 087	2	>0 95
10 and 13	13 054	3	<0 01
13 and 17	11 707	3	<0 01
16 and 17	13 690	3	<0 01

rst the clinical picture sometimes suggested a cerebral ondition, and 1 patient presented with severe dysarthria nd ataxia. 4 patients had hæmoptyses during their llnesses.

ATYPICAL CASES

8 cases could not be classed as typical Q fever. Of these, 1 was a permanently bedridden and very old lady from whom it was impossible to get a reliable history, but her husband had just died of Q fever, and her serum showed a high titre of Q-fever antibodies (Marmion and Stoker 1950). Another patient, with pre-existing valvular disease of the heart, had a stroke during her attack of Q fever, and a third patient died from a carcinoma of the lung. A fourth patient already suffered from extensive pulmonary fibrosis and emphysema, and superadded Q fever caused a severe exacerbation. The remaining 4 patients with Q fever died, and these cases are described below and summarised in table

Case 1.—A retired tailor, aged 78, was a patient in the Royal Cancer Hospital, and his illness has already been described by Harman (1949). He died eleven days after the onset of a pneumonia which on indirect evidence was shown to be Q fever. The post-mortem findings have been described by Whittick (1950).

Case 2.—An insurance agent, aged 45, became ill with fever, anorexia, and malaise on April 1, 1950. Despite administration of penicillin, these symptoms continued, and on April 11 he developed a pain in the right side of the chest, aggravated by breathing but not accompanied by a cough. On the following day, when admitted to the Kent and Canterbury Hospital, he was very weak and ill. Slight clubbing of the fingers was noticed, the bases of both lungs were dull, and there was a pleural rub in the right axilla. On April 15 the temperature started to fall and he felt better. Radiography on this day showed what was thought to be a resolving pneumonia of the right lung. Over the next few days his condition improved and the temperature fell to normal; but on April 23 he suddenly became cyanosed and died. Necropsy was performed by Dr. I. B. Morris, who found a massive pulmonary infarct. A specimen of serum taken shortly before death showed a Q-fever antibody titre of 1 : 1024.

Case 3.—A cobbler, aged 58, developed headache, fever, cough, and pain in the chest on Oct. 21, 1950. He was admitted to the Royal Devon and Exeter Hospital on Nov. 1 with a pneumonia which was confirmed by X-ray examination. Specimens of serum showed a titre of Q-fever antibodies rising from 1 : 16 to 1 : 64. His condition soon improved, but after discharge he had recurrent attacks of fever, cough, and pleuritic pain which continued until late in January, 1951, when he died quite suddenly while sitting in his chair at home. No post-mortem examination was performed, but a vascular accident was the most probable cause of death.

Case 4.—A general labourer, aged 37, gave an unreliable history, but he had apparently been ill repeatedly since 1941 with fever, pain in the chest, and breathlessness on exertion. He had been in several London hospitals during this period and was told that he had valvular disease of the heart. It was not possible to distinguish a definite attack of pneumonia, but he was in hospital with "pleurisy" in 1946. From May, 1951, until his death in December, 1951, he was in hospital almost continuously (the Royal Free Hospital and then Hackney Hospital), except for short intervals when he discharged himself. He had obvious valvular disease, he was often in heart-failure, and he had bouts of fever and occasional embolic phenomena. All this suggested subacute bacterial endocarditis, but repeated blood-cultures were negative. Q-fever antibodies were found in a titre of 1 : 1024 on June 7, 1951, and this high level was maintained for six months until the last specimen taken a few days before death.

He died suddenly on Dec. 13, 1951, and necropsy showed a pulmonary infarct on the right side, patchy consolidation of the left lung, and mitral stenosis with right-sided failure, but no evidence of subacute bacterial endocarditis. Attempts to isolate *R. burneti* during life from the sternal marrow, liver, and urine, and after death from the lungs, liver, spleen, brain, and bone-marrow, were all unsuccessful. The persistently high titre of Q-fever antibodies certainly suggests active Q fever, but the part played by the rickettsiæ in this illness is difficult to assess. This case will be discussed in conjunction with other published accounts of long-standing and fatal Q fever.

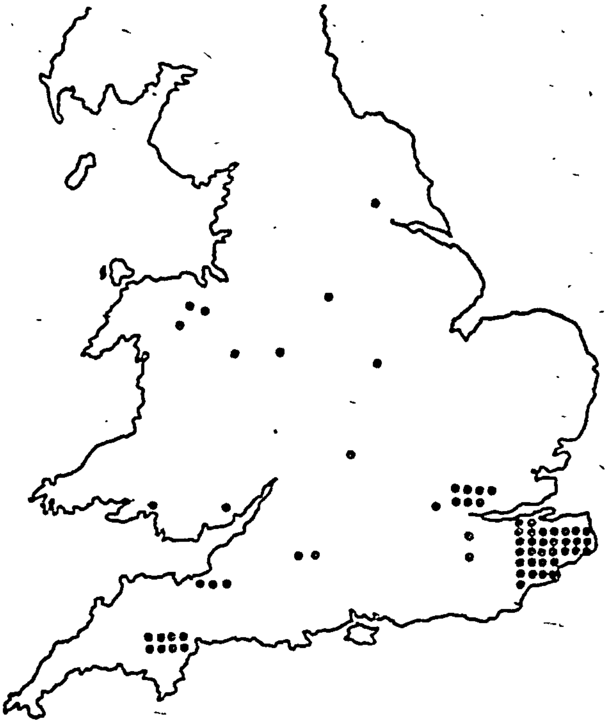

Fig. 2—Geographical distribution of 66 cases of Q fever in England and Wales.

EPIDEMIOLOGICAL FEATURES

Geographical Distribution of Cases

The distribution of sporadic cases by site of infection is shown in fig. 2. The cases are distributed over a wide area of England and Wales, and the concentration in the southern half of England might well be due to the location of the Virus Reference Laboratory at Colindale, London. Almost half the sporadic infections (48%) occurred in Kent, but it is not known how much this was influenced by the chance identification of the first cases in Kent and the more active search which followed in this county. It should be noted that the position of Cambridge has also led to a wide search in East Anglia, but no clinical cases have yet been found in this part of England.

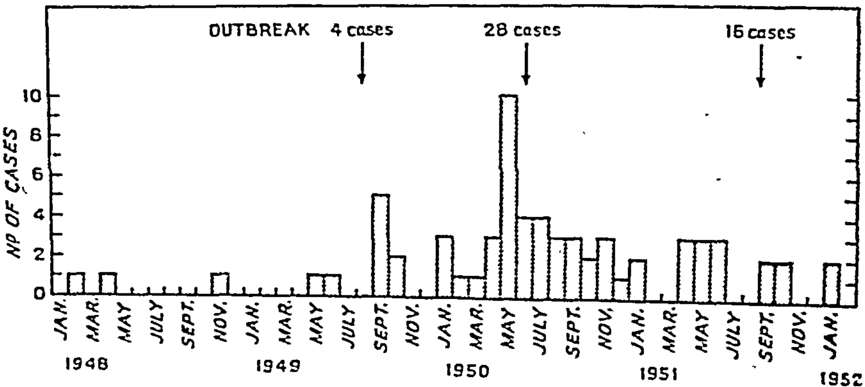

Fig. 3—Monthly prevalence of sporadic cases of Q fever from January, 1948, to January, 1952. Outbreaks, with the number of cases in each, are shown by arrows.

Appendix

Since the work described in this paper was completed the set of phages used for routine typing has been altered somewhat The following phages are now used as a "basic" set

Group I 29, 44, 52, 52A, 79
Group II 3A, 3B, 3C, 55
Group III 6, 7, 42D, 42E, 47, 53, 54, 70, 73, 75, 77

If no reactions are obtained with the diluted phages and it is necessary to define the strain further, it is then tested with these 20 basic phages undiluted, and with a further 18 phages which are used at their routine test dilution in four pools as follows

Pool A 31B, 42F 47A, 52B
Pool B 31, 44A, 51, 69, 71
Pool C 57, 58, 75A 75B, 76, 78
Pool D 42B, 42C, 47B, 47C

When the phages of the undiluted set give reactions, these are reported, whether the pool phages lyse or not The pool phage reactions are only investigated further if the undiluted filtrates give no lysis

If no lysis is obtained with the undiluted basic set, or with the pool phages, the pools, and the following additional phages, are applied undiluted 29A, 53A, 47D, 72, 74, 31A

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BACTERIOPHAGE TYPING OF STRAINS OF STAPHYLOCOCCI ISOLATED IN AUSTRALIA

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BACTERIOPHAGE typing of coagulase-positive staphylococci (Wilson and Atkinson 1945) has been in use in this laboratory since October, 1948 Recently Williams and Rippon (1952) have published a detailed account of the technique used at the Staphylococcal Reference Laboratory, Colindale As far as possible, the same technique and phages have been employed here

Williams et al (1953) have analysed the results of typing 1349 strains examined between January, 1949, and December, 1951 They divide the "phage patterns" found in typing into three broad groups—I (52), II (3A), and III (6/47)—which correspond to the serological groups defined by Cowan (1939)

A similar analysis has been made of the results obtained in our laboratory over a similar period

MATERIAL

The strains of staphylococci examined were isolated between October, 1948, and June, 1952 Most of them were obtained from patients attending the Royal Prince Alfred Hospital, Sydney Strains from sporadic neonatal infections, however, came from six different hospitals—four in the Sydney metropolitan area, one in Melbourne, and one a country hospital in Victoria Two series of strains from nasal carriers were obtained from blood donors at the New South Wales Blood Transfusion Service, one series in March, 1949, and a second in March, 1951 Strains were also obtained from nasal carriers among the nursing and medical staff of the hospital

TABLE I—FREQUENCY OF PENICILLIN SENSITIVE STRAINS OF STAPHYLOCOCCI OF DIFFERENT PHAGE GROUPS FROM VARIOUS SOURCES

Source	Number	Percentage				
		Group I (52)	Group II (3A)	Group III (6/47)	Unclassified	No lysis
Noses of normal persons	387	19 2	19 9	26 9	4 7	29 3
Throats of normal persons	102	17 7	19 6	28 4	5 9	28 4
Conjunctivæ	69	18 8	16	23 2	5 8	36 2
Sputa	40	22 5	12 5	27 5	7 5	30
Otitis and mastoiditis	117	18 8	22 2	23 1	4 3	31·6
Urines	100	17	17	25	5	36
Skin infections including boils and carbuncles	333	24 9	30	20 4	4 7	20
Deep infections, osteomyelitis, abscesses, bacteræmia	59	17	44 1	18 6	5	15 3
Wound and burn infections	76	19 8	21	23 7	6 5	29
Miscellaneous pyogenic infections	241	21 6	28 4	22 4	6 3	21 3
Sporadic neonatal infections	54	9 3	14 8	46 3	0	29 4
Total	1580					

Our material therefore differs from that of Williams et al. in that most of it is derived from the inhabitants of a particular metropolitan area, and furthermore much of it comes from inpatients and outpatients of one particular hospital We have available, however, the records of penicillin sensitivity tests of all the strains Since it has been shown (Barber and Whitehead 1949, Rountree and Thomson 1949, Rountree, Barbour, and Thomson 1951) that the majority of staphylococcal hospital cross-infections are due to penicillin resistant strains, the material has been divided into penicillin sensitive and penicillin-resistant strains and the frequency distributions of the phage groups in the two series will be discussed separately The penicillin-sensitive series should give a picture of the frequency distributions in carriers who have not been admitted to hospital and in patients with infections acquired outside hospitals, while the penicillin-resistant strains should reflect the frequency distribution within the hospital environment

Not more than one strain from any individual is included in the material, except in a few cases where strains of different phage pattern were obtained on different occasions

RESULTS OF TYPING PENICILLIN-SENSITIVE STRAINS

Table I gives the frequency distributions of 1578 penicillin-sensitive strains expressed as percentages of the strains from each source that fell into groups I, II, or III, were unclassifiable, or were not lysed by any of the phages in the usual test dilution

Normal Carriers

Nasal carriers —These strains were obtained from normal persons at the blood-transfusion service, from patients on first admission to hospital for the treatment of non-staphylococcal illnesses, and from trainee nurses on first entering the hospital. They came, therefore, from a fairly random sample of the general population 4% of the strains were penicillin-resistant and have been included in the penicillin-resistant series The omission of these strains, which all belonged to group III, will have only a slight effect on the percentages

Throats —Most of these strains came from children swabbed on admission to hospital and from trainee nurses either on entry into the hospital or before entering the operating-theatres or maternity hospital The frequency distribution is similar to that found in the nasal carriers

Conjunctival —These strains came from patients swabbed on admission to the ophthalmological wards for surgical treatment There was a slightly higher propor

13 of the cases in this series, however, there was no ovious source of infection other than the milk-supply. or example, an Admiralty draughtsman, aged 37, lived Gillingham, away from any obvious source of Q fever, ad travelled to London daily by train. The milk-upply to his home was pasteurised. In July, 1950, he nd his family went to stay with friends who lived in a own in north-east Kent, away from any known direct ource of infection, but supplied with raw milk from a erd with Q fever. Three weeks after his return to illingham, he had a severe attack of Q fever.

A group of 4 cases in a neighbouring town also illustrate this point. A housewife, an insurance agent, a etired soldier, and a medical practitioner developed Q ever at various times in 1949 and 1950. None of them ived near or had visited an obvious source of Q fever, nd, except perhaps the doctor, none of them were ccupationally exposed. It was found that they were all upplied from the same dairy with raw milk, for which the doctor in particular had an unquenchable thirst. On investigation, Q-fever organisms were repeatedly found in the milk from one of the herds supplying this dairy.

The results of these investigations into the source of infection are summarised in table II, which shows that two-thirds of the patients had been exposed to known sources of Q fever.

Survey of Blood Donors

A survey for Q-fever antibody in specimens of sera rom healthy persons was carried out to determine the proportion who had been infected in the past. Specific complement-fixing antibodies are known to persist for many years after Q fever, and, provided adequate controls are included, there is little risk of false positive reactions with normal sera. It was thought that this method would give a much more accurate comparison of the prevalence of Q fever in different areas than is afforded by the identification of clinical cases.

The method is of course open to some criticism. In the first place it does not distinguish between clinical and subclinical infections, which in different outbreaks have numbered from a quarter to three times the total of clinically ill persons. Secondly, blood donors are not a random sample of the population; for example, they are usually between the ages of 20 and 60 and therefore more liable at least to clinical Q fever than children and old persons (fig. 1). Finally, there is no way of knowing how long ago infections took place. But these limitations only make it difficult to assess the actual morbidity due to Q fever at a given time. They do not affect the validity of the method for comparing the prevalence of infections in different localities.

An earlier investigation of 127 sera from venereal-disease centres and antenatal clinics in Canterbury and Whitstable had shown Q-fever complement-fixing antibodies in titres from 1 : 8 to 1 : 64 in 10 specimens (7·9%). A survey was then planned with the coöperation of the National Blood Transfusion Service. East Anglia and south-east England were chosen for a preliminary study because, judging from numbers of clinical cases, these seemed to be areas of low and high endemicity respectively. Nevertheless, some other areas were also investigated to obtain additional evidence of Q fever in localities where a few clinical cases had occurred.

METHOD

Serum from blood donors was sent to Cambridge from the regional transfusion centres in South London, Cambridge, Bristol, Birmingham, Cardiff, Liverpool, and Sheffield. Samples were obtained after bleeding donors in various towns and villages in each area, but serum from donors in large industrial cities (except Birmingham) was not included.

On arrival at Cambridge, the serum was stored at −20°C until tested. After inactivation at 56°C for 30 minutes, complement-fixation tests were carried out on the diluted serum with the technique previously described, using typhus antigen to control the specificity of the test. Sera which reacted with Q-fever antigen, but not typhus antigen, at a dilution of 1 : 10 or higher were considered to be positive.

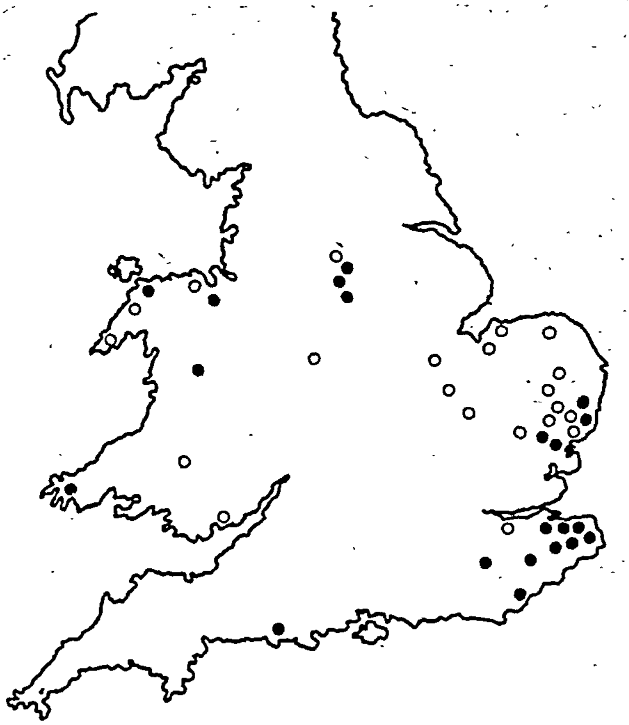

Fig. 4—Results of survey of blood donors. Closed circles indicate centres where some of the donors showed evidence of previous infection with R. Burneti; at centres marked with open circles none of the donors tested showed evidence of infection (see table III).

RESULTS

The results of this survey (table III and fig. 4) show that 95 of 4456 blood donors (2·13%) had serological evidence of previous infection with *R. burneti*. It is at once apparent that the proportion of individuals in Kent with antibodies is considerably higher than in East Anglia. Only 11 of 1418 sera from East Anglia contained Q-fever antibodies (0·78%), as against 58 out of 1956 from south-east England (2·96%), and this difference shows high statistical significance ($\chi^2 = 18{\cdot}8$, $p < 0{\cdot}001$). It should also be noted that most of the positive sera in East Anglia came from a limited area in East Suffolk. Excluding East Suffolk, no positive donors were found amongst 587 tested from the remainder of East Anglia. Some of the towns in Kent—for example, Herne Bay—had a very high proportion of positives, and the only group in Kent which were all negative came from Dartford, which is on the outskirts of London.

Sources of Infection

So far as we know at present, Q fever in man is derived directly or indirectly from cattle, sheep, or goats.

Derrick's original patients in Brisbane were chiefly slaughterhouse workers handling cows, and the importance of contact with these animals has been amply confirmed by Beck et al. (1949) in California. In Northern California, which differs greatly from Southern California both in climate and agricultural economy, Lennette et al. (1949) have shown that most human infections are derived from sheep and goats. Reservoirs of infection in these animals have also been discovered by Blanc et al. (1947) and Caminopetros (1948) in the Mediterranean region. In Australia, Derrick (1944) found ticks (*Hæmaphysalis humerosa*) to be naturally infected, and

England This may be merely because our series of strains is more restricted in origin than the English ones It is apparent however that, up to the present, the great majority of penicillin-resistant strains examined here have belonged to group III

SUMMARY

The results of bacteriophage typing of 3150 strains of *Staphylococcus pyogenes* are described, the strains being divided into penicillin-sensitive and penicillin-resistant

The general pattern of frequency distribution of the various phage groups is similar to that found in England However, among normal nasal carriers of penicillin-sensitive strains there was a slightly higher incidence of group-III strains in Australia, and in skin lesions such as boils and in deep infections caused by penicillin-sensitive strains there was a predominance of group-II strains

Group-III strains comprised 66–80% of the penicillin-resistant strains

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THE TREATMENT OF CEREBRAL GLIOMAS WITH 24-MILLION-VOLT X RAYS

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ONE of the main problems of radiotherapy in malignant disease is that of delivering a high dose to the tumour while giving as little as possible to the surrounding healthy tissues This is particularly important in the treatment of deep seated tumours Since, in general, the penetration of X rays increases with the voltage at which they are produced, there has been a tendency towards the use of higher potentials in treatment. It is difficult to achieve potentials greater than 1 or 2 million volts (MeV) by conventional methods, but use may be made of high-energy machines designed primarily for nuclear physics (*Brown Boveri Mitt* 1951, Garrison et al 1952, Harvey et al 1951, Johns et al 1949, Laughlin 1951, Laughlin et al 1951a and b, Metropolitan-Vickers Electrical Co, L publ no 7905/5, *Rontgen-Institut der Univers* Zürich 1951)

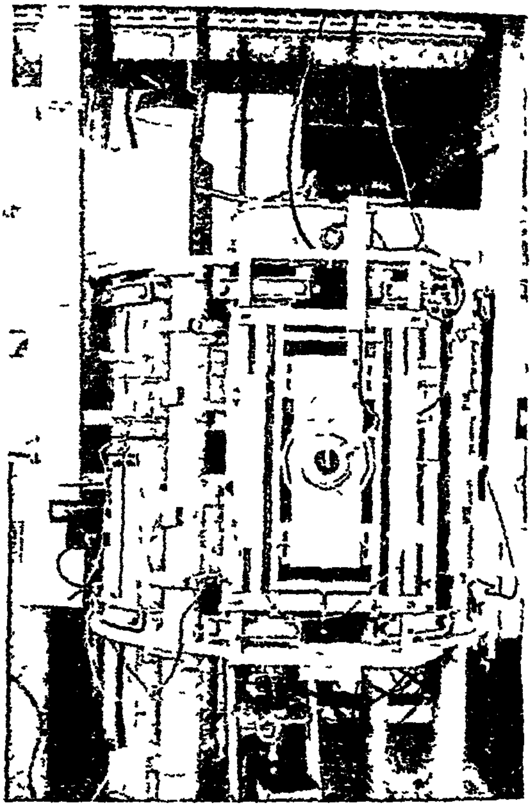

Fig 1—24-MeV electron-synchrotron viewed looking directly into beam through the beam-direction back pointer

It appeared, from a knowledge of the properties X rays produced at 20–30 MeV, that important techn advantages might be gained by their application in clin practice This order of potential is conveniently provid in an electron-synchrotron, and we were fortunate that the Medical Research Council made such an inst ment available to the Royal Cancer Hospital during summer of 1949 A description of the installation already appeared (*Nature* 1949) and may be consult for detail The accelerator (fig 1) was installed investigate further the physical properties of X ra produced at 20–30 MeV, to study the biological effe of the radiations, and to investigate its potentialities a therapeutic instrument for the treatment of patie with cancer

DOSIMETRY

In the use of any new source of high energy ionis radiation the main problems are bound to be those dosimetry and protection Methods of dosimetry w therefore studied (Mayneord and Martin 1950) appeared that, though there are fundamental theoreti difficulties, yet in practice, by suitable modification existing methods of measurement, reliable and significa estimates of dose could be made Using somewhat ar trary defining conditions, we have, in the interests continuity of clinical practice, used in most instances t unit of dose (the rontgen) normally employed

Isodose distribution measurements for a number fields have been made in a water phantom, thus enabli three-dimensional studies of proposed clinical treatme to be made in advance These studies bring clearly light one of the main technical advantages of hig energy X rays—i e, the relatively low surface absorptio of energy The dose is a maximum at a depth of 3 5 c for X rays produced at 24 MeV, the potential most used by us (fig. 2) The prediction, on physical ground re tested outside the two main areas (Kent and East Anglia) which were chosen for comparison because they differed greatly in the numbers of clinical cases. In fact, a greater proportion of specimens were tested from Kent, and this may well have influenced the total. evertheless, infection seems to be fairly widespread in an, for evidence of infection was found in most areas tested, except parts of East Anglia. In various towns of south-east England the rate was uniformly high, and the over-all figure of 2·96% must represent a very large number of cases of Q fever even after allowing for subclinical infections. In their serological survey in Southern California, Bell et al. (1950) found that 1·36% of the inhabitants of Los Angeles showed evidence of previous infection, and this is considerably lower than our figure for south-east England; but exact comparison is not possible because a different complement-fixation technique was used. The technique used by Clark et al. (1951), however, closely resembled that used in our laboratory, and the prevalence-rate of 3·5% which these workers found in an endemic area of Northern California can be compared with the figure of 2·96% in south-east England.

Attention has already been drawn to the difficulty of estimating the morbidity due to Q fever at any one time from these figures; but if one supposes one-third of the population of Kent to be insusceptible and also unsampled, being children or old people, there would be some 30,000 persons in Kent with evidence of previous infection. Assuming that antibodies are detectable for ten years, 3000 fresh infections a year might be expected, of which at least 1000 might be clinically ill. During 1950 and 1951, in an intensive search, we only identified 9 cases including the outbreaks. There must therefore be a large number of undiagnosed infections, which is not surprising with such an indefinite clinical picture.

The clinically typical cases in this series call for no further comment, except that the severity of illness and the ensuing debility in some older patients were at variance with the common conception of Q fever as a minor and harmless incident. It is really the ill-defined and atypical case of Q fever which needs consideration and further investigation, and a question of some interest is whether Q fever can occur in a chronic form, either as a primary condition or as a complication of some other disease. Clark et al. (1951) found that 30 of the 180 patients in their series had febrile illnesses lasting more than twenty-eight days, and there is an indication from the series of patients described by Beck et al. (1949), and also from our own material, that Q fever may occasionally be superimposed on some other unrelated condition, thereby intensifying the patient's illness.

Dr. R. J. Huebner of the National Institutes of Health, Bethesda, U.S.A., has kindly sent further details of a possible chronic case of Q fever mentioned by Beck et al. (1949), and also of 1 other case.

The first of these patients, a man aged 52, had had five years' illness with recurrent fever, and he eventually died with paralysis and coma. Necropsy revealed massive cerebral hæmorrhage, bronchopneumonia, and a fibrosed mitral valve with vegetations. *R. burneti* was isolated from various organs. A serological test done three months before death was positive for Q fever and indicated that infection with *R. burneti* preceded the final illness by at least three months.

The second patient, a woman aged 30, who had a previous history of rheumatic fever, had an illness resembling subacute bacterial endocarditis after an attack of Q fever. During her year's illness numerous blood-cultures were negative for bacteria, and penicillin produced no improvement. *R. burneti* was isolated from both blood and urine almost a year after the original attack of Q fever.

The real significance of these observations cannot be judged until more evidence is available, but Dr. Huebner's cases, considered in conjunction with the atypical ones in our series, 2 of which had cardiac disease, suggest that it may be necessary to enlarge our clinical conception of Q fever and not to confine laboratory tests to patients with pneumonia and fever. As a working hypothesis, it might be suggested that patients with a cardiac abnormality may be abnormally liable to chronic infection with *R. burneti*, or even that this organism, like some other rickettsiæ, may occasionally cause lesions in the vascular system, giving rise, for example, to endocarditis, cerebral hæmorrhage, and embolic phenomena.

A history of exposure to sources of Q fever through occupation, residence, or the consumption of raw milk was obtained in two-thirds of the cases, but the significance of this finding cannot be properly assessed without knowing the proportion of uninfected individuals who are similarly exposed. Beck et al. (1949) obtained histories of exposure in a similar proportion of sporadic cases in Southern California, but the raw-milk drinkers were rather commoner in our series. There seems little doubt that cattle form a major reservoir of infection in this country. Milk from over 8% of herds in Kent was found to contain *R. burneti*, and, perhaps significantly, the organism was even more frequent (being found in half the supplies tested) in the milk-supplies to patients who were not exposed to infection by virtue of their occupation or place of residence. But despite the presence of the organisms in the milk, and the fact that 41% of the patients drank raw milk, it is not at all clear that this is an important method of infection of man. Fonseca et al. (1949) gave *R. burneti* in food to 11 human volunteers, but they all remained well and only 2 developed antibodies. It has already been pointed out that people who drink raw milk often live on farms and are exposed to infection by other routes. Nevertheless, there were several patients in our series for whom the consumption of raw infected milk seemed to be the only possible method of infection.

No reservoir of Q fever other than cattle has yet been found in Britain, but it seems quite possible that sheep and goats are also infected in this country as they are in other parts of the world. A wider survey of Q fever in cattle and other animals in Britain is being carried out at the Central Veterinary Laboratory at Weybridge,‡ and we hope to link this with further work on the distribution of human infections. The possible rôle of ticks in the transmission of Q fever among animals in the British Isles also merits further study.

Judging by the two main areas studied, Q fever is unevenly distributed in England. The high prevalence among the inhabitants of south-east England compared with those of East Anglia was first suspected from the relative numbers of clinical cases and was confirmed by the serological survey of healthy blood donors. The prevalence of Q fever in cattle also seems to be a good deal lower in East Anglia, but there are still large areas, particularly in Norfolk, where the animals have not yet been adequately sampled. The cause of this uneven distribution has still to be identified. It might be connected with the distribution of ticks, with the density of human or animal population, or even with an infection recently imported but not yet widespread.

No method of controlling Q fever in domestic animals has yet been found. Giving aureomycin to cattle is ineffective, and the use of vaccines, although promising, is in an early stage (Luoto et al. 1952). Even if a means of protecting animals is eventually discovered, it may be difficult to interest farmers in the eradication of an infection which does no harm to their stock. Meanwhile, we may be thankful that in man the disease is often mild, chemotherapy is generally effective, and chronic forms and fatalities are rare. But prevention of the disease is an *uncertain* business to which the "Query" must still apply.

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‡ Since this paper was submitted for publication Slavin (1952) has published the results of a wider survey of herds in Great Britain. 192 (5·7%) of 3374 herd milks tested contained *R. burneti*, giving over-all positive rates of 6·9% in England, 2·0% in Wales, and 0·8% in Scotland. Infection was also shown in goats.

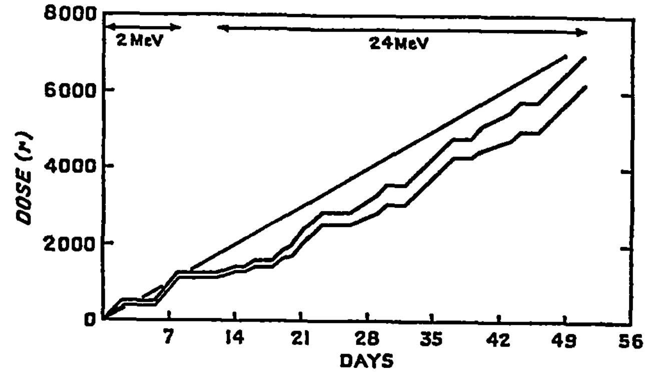

Fig 4—Estimated maximum and minimum tumour doses in case 3 (see fig 3) plotted on a dose time chart showing the tumour dose prescribed as a straight line

restricted the volume of clinical work possible It was decided that a series of patients with cerebral gliomas should be selected for the first trial This group (see table) was chosen for three reasons (1) we wished to irradiate through bone to explore the advantage of lack of differential absorption obtainable with this quality radiation, (2) we preferred a group of patients with a rather bad prognosis (so that no-one would be deprived of a chance of recovery with an established treatment method) yet one which would provide some prospect of a sufficient degree of localisation of the disease to give the new treatment a fair test, and (3) we were limited by the apparatus to the selection of a part of the body which could be placed accurately in the path of a horizontal beam of small size A further limitation within this selected group was imposed by the fact that the patients would have to be kept still during treatment for an hour or more each day The patients treated have therefore of necessity been a carefully selected few within one special group

The first clinical trial following preliminary physical and biological experiments started on May 17, 1950 This report deals with what was done for the first ten patients with cerebral gliomas treated and what has happened to them up to the end of 1952, two and a half years after the first treatment started So far all but one of these patients are alive, having suffered little disability and no permanent epilation

TREATMENT PLAN

The plan of treatment adopted was to attempt to give a tumour dose of 7000r in seven weeks to the smallest volume of tissue consistent with an attempt to include the whole of the estimated extent of the tumour An example of an estimated dose distribution for a four-field technique is shown in fig 3 and the same patient's dose chart in fig 4 The dose was arbitrarily chosen to be on the high side of what experience suggested might be adequate without, at least to the comparatively small volumes concerned, being of the order likely to lead to necrosis if given in one continuous course and not repeated at any future date The accurately located small-volume treatment method was adopted in accordance with a treatment policy (the policy of a limited objective) in vogue for some years in the radiotherapy department of the Royal Cancer Hospital for patients with malignant tumours at several different sites Good palliation, which is often the aim, may be obtained with high dose small-volume local treatment even when this does not quite cover all limits of tumour spread In the few fortunate patients in whom the whole tumour is adequately irradiated a really effective treatment and long survival may be possible which might not have been so if those same patients had received wide field treatment Such a small volume treatment depends for success on a detailed study of each patient with the object of defining as accurately as possible the volume of tissue most likely to contain the whole tumour Patients with brain tumours form a suitable and interesting group for study with such accurate tumour localisation and small-volume treatment

CLINICAL RESULTS

No general reactions have so far been noted in this group of patients treated at 24 MeV, and at no time have any patients complained of any discomfort attributable to the treatment The long treatment times have proved more tedious to the staff than to the patients, who have found the apparatus impressive and the care and attention to detail in planning and positioning gratifying The variation in blood counts has been no more than is often observed from day to day in normal people The local reactions have been far less than we have observed in patients having similar tumour doses at lower voltages Epilation has occurred at an energy absorption equivalent to about 1800–2000r, and a faint skin erythema has been noted in some patients The hair has grown again in all the patients within four months, the only comment being made by one young woman who was delighted to find that her new growth of hair was wavy instead of straight (fig 5)

The period of observation since treatment in a highly selected small group of patients such as this is far too short to allow us to do more than to say that the early response is better than we have observed before in similar patients This communication must be regarded purely as a preliminary report on a new method of radiotherapy applied to a few patients with intracranial gliomas who were carefully selected for their ability to cooperate during treatment Automatically those with the more malignant tumours and the gravely ill patients have been excluded from this form of therapy, because of their inability to cooperate, and patients with an obviously short expectation of life have not been subjected to this form of irradiation

The ten selected patients consist of three with tumours demonstrated by ventriculography but not confirmed by biopsy, making the type unknown, two with astrocytomas of malignancy grade I (Mayo Clinic classification), four with astrocytomas grade II, and one with

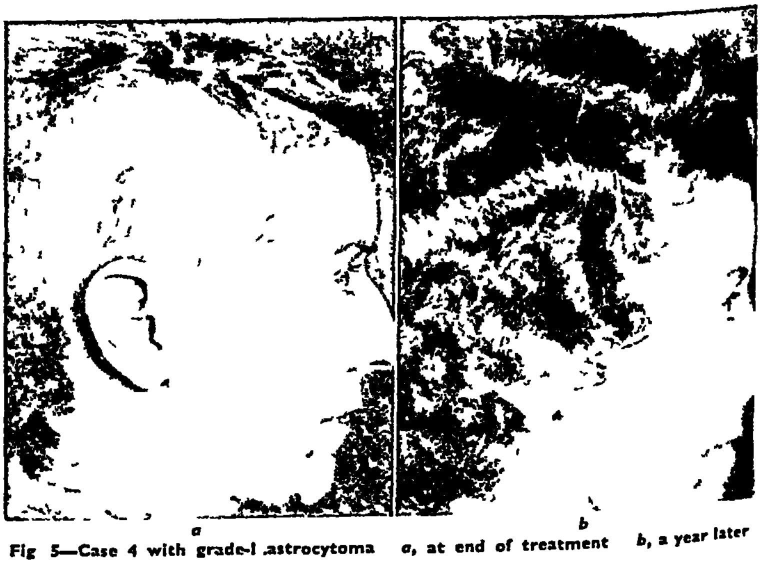
a b

Fig 5—Case 4 with grade-I astrocytoma a, at end of treatment b, a year later

phage filtrates, and pools of several filtrates (see appendix) are then applied to the culture, and, after these have dried, the plates are incubated at 30°C overnight. Plaques of lysis can then be seen in the areas corresponding to the phages to which the strain is susceptible.

INTERPRETATION OF RESULTS

Some 50–80% of coagulase-positive staphylococci are lysed by one or more of the phages in our set used at their routine test dilution, and most of them are lysed by more than one phage to give a "pattern" of lysis. The "bacteriophage pattern" that is reported is a list of the phages that produce strong lysis of the staphylococcus.

The bacteriophages are designated by numbers given according to their order of isolation; adapted phages have a letter suffixed (e.g., 52A). Since many of the phages isolated have proved unsatisfactory, the set in routine use is not numbered continuously. The phages entering into patterns in the three groups referred to above, and a number of representative patterns, are given in table I. Group II (the "3A group") is very clearly defined, and its phages are practically never encountered in patterns with phages of another group; groups I (52 group) and III (6/47 group) are rather less well defined, and some phages, such as 7, 47C, and 42E, form patterns with the characteristic phages of each of these two groups.

TABLE I—PHAGE PATTERNS DEFINING THE THREE GROUPS OF STAPHYLOCOCCI

Group	Phages characteristic of the group	Common phage patterns
I	52, 52A; 29, 29A, 31, 31A, 44, 44A; *69*[*]	52A, 52/52A, 29/52, 29/31/44/52 +,[†] 44/44A
II	3A, 3B, 3C, 51; *55, 71*	3A, 3C, 3B/3C, 3C/51, 3A/3B/3C/51
III	6, 7,[‡] 42B, 42D, 42E,[‡] 47, 47B, 47C,[‡] 53, 54; *31B, 42F, 47D, 52B, 53A, 58, 70,*[‡] *73, 75, 75A, 75B, 76, 77, 78*	6/47 +; 6/7/47/53/54 +, 7/47/53/54 +, 42D, 42E, 7 +, 53/54
Unclassified	42C, 47A; *57, 72, 74*	7/42C/42E/52/52A/54 +, 3A/7/54 +

[*] Phages given in italics have been introduced since the earlier report (Williams and Rippon 1952).

[†] ' + ' sign indicates that other weak reactions are frequently present.

[‡] Phages 7, 42E, 47C, and 70 may enter into patterns with phages of group I.

The fact that a staphylococcus is not lysed by any phage in a routine test may be due to the fact that our typing set does not contain any phage to which it is susceptible. In some cases, however, it may be that the staphylococcus is more than ordinarily resistant to the action of the phages, and such staphylococci may sometimes be lysed by more concentrated phage filtrates. Although the lytic pattern may be more complex, strains typed in this way can usually be classified into the three groups in the same way as those typed by the use of the diluted filtrates; in the present paper they are included among the untypable strains, because not all untypable strains were tested with undiluted filtrates.

For the purpose of this report we have classified the staphylococci into the three broad groups. It must not, however, be concluded that all the strains in any one of these groups are of the same "type" or are thought to have a common source. In our previous report (Williams and Rippon 1952) we compared the patterns given by sets of strains from one site on the assumption that these sets were all derived from a single source. On this basis we showed that many differences in phage patterns are stable, and we gave tentative rules for deciding when two strains were likely or not to come from a single source. The finer classification achieved in this way is used in epidemiological investigations and was applied in the present work where indicated. Thus a statement that two or more strains were of the same "type" or "pattern" means that they were more certainly the same than is indicated merely by their falling into one group.

MATERIAL

The staphylococci considered here, all of which were coagulase-positive, were examined in the period January, 1949, to December, 1951. Most of them were sent to us by various public-health laboratories or hospital laboratories that were investigating particular epidemiological or other problems. In addition, strains from cases of postinfluenzal pneumonia were kindly sent in response to our request by many pathologists and in especially large numbers by Prof. C. H. Stuart-Harris of Sheffield; and many of the strains from the noses and fæces of normal persons were collected at Norwich.

All the staphylococci included in the analysis were from independent sources; that is, no more than one strain was included from any one person, and no more than one strain of any one type was included from one outbreak of infection.

RESULTS

Table II shows the percentage of the strains from each source, or group of sources, that fell into groups I, II, or III, were unclassifiable because of the complexity of their phage pattern, or were not susceptible to any phage at the routine test dilution. In each case where two or more rows have been added together to give a subtotal, a χ^2 test has shown that the group-distributions in the rows do not differ significantly.

Normal Subjects (table II, rows 1–6)

The subjects were either normal healthy persons or were persons with non-staphylococcal illness swabbed very shortly after admission to an isolation hospital. The babies in row 2 were aged 1–12 months and were swabbed at welfare clinics; some had been born at home and some in one of three maternity hospitals in Nottingham.

About 60% of the nasal staphylococci were typable; group-I strains were the commonest (24%) with group-III and group-II strains forming 19% and 14% respectively. The strains from fæces and perianal swabs, on the other hand, though less often typable, showed a significant excess of group III (30%) and deficit of group I (8%); there was no significant difference in the distribution of the groups between the fæcal and perianal strains.

The relation of nasal and fæcal carriage was further explored in the records of 362 persons from whom we had nasal and perianal swabs, and fæces. 86 of the 362 carried *Staph. aureus* in the nose, and 28 (32·6%) of these yielded *Staph. aureus* from fæces or perianal swab or both; of the 276 persons with no staphylococci in the nose, only 25 (9·1%) had staphylococci in fæces or perianal swabs—a highly significant difference. Moreover persons yielding staphylococci from nose and fæces or perianal swab usually (24 of 28) yielded strains of the same pattern from both sites. The excess of fæcal carriers of group-III strains was not, however, due to any greater ability of nasal carriers of this group to infect their fæces, since, in the small number tested, nasal carriers of group-II strains were just as frequently fæcal carriers:

Nasal carriers of group—	*No. of nasal carriers*	*No. of carriers with same type in fæces or perianal swabs*
I	19	2
II	17	6
III	18	7
Unclassified	3	1
Not typable	29	8

The excess of fæcal carriers of group-III strains came, in fact, from the persons who were not nasal carriers. Whatever the reason for it, the relative frequency of this group in normal fæces gains interest because of the group's association with food-poisoning (see below).

Minor Septic Lesions (table II, rows 7–10)

The group distributions of staphylococci from cases of boils, whitlows, acute and chronic otitis, and mastoiditis and from beat lesions in miners, did not differ among themselves, and only differed from the strains from normal noses in that more of them were typable. The

CAT-SCRATCH DISEASE

THE INTRADERMAL TEST IN CONTROLS

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We report here the results of intradermal testing of 40 controls with the antigen of cat scratch disease

ANTIGEN

The antigen was prepared from a young woman, aged 21, who had first been sent to the hospital by her family doctor, Dr C H R Read, with a widespread papular eruption, possibly papular urticaria Six weeks later the doctor sent her to the hospital again with a month's history of subacute lymphadenitis in the left axilla This lymphadenitis had been followed by the development of an ulcerated cutaneous nodule on the dorsum of the left hand The patient had been treated with penicillin and chloramphenicol without response The lymph-gland swelling gave the clinical impression of being too indolent for one due to the common septic organisms, and pain was relatively slight, on the other hand, the swelling came up too quickly for tuberculosis No other lesions appeared, and the clinical characteristics of the adenitis suggested cat-scratch disease, agreeing well with the account given by Daniels and MacMurray (1951) The patient was shown at a clinical meeting of St John's Hospital Dermatological Society on April 24, 1952 This patient kept a cat

A cat scratch antigen for intradermal testing was therefore obtained This antigen had been prepared from a case of cat-scratch fever which had been under the care of Prof Alan Moncrieff at the Hospital for Sick Children, and was reported in detail by Cox (1952) Pus from a gland was diluted 1 in 10, heated for two hours at 60°C, and again for a further hour next day at the same temperature The antigen thus prepared was used for testing our patient and gave a positive reaction

Eight weeks after the onset of the adenitis the axillary gland became fluctuant and was excised The histology of this gland was kindly reported on by Dr A C Thackray as follows

> "Section of the lymph gland shows, in addition to reactive hyperplasia and periglandular fibrosis, numerous rounded, oval, or stellate foci of structureless necrosis surrounded by epithelioid cells with very occasional giant cells There are small numbers of lymphocytes and occasional plasma cells and polymorphonuclears scattered throughout the lesions The appearances correspond to those of cat scratch fever"

These appearances are very like those described as the "final stage" by Mollaret et al (1951a)

The gland was bacteriologically examined by Prof F R Selbie, who reported as follows

> "*Pus from gland*
> Direct film of pus moderate number of pus cells, profuse amorphous debris, no organisms seen, no acid fast organisms seen
> Culture sterile Cultures for *Mycobacterium tuberculosis* sterile Guineapig inoculation no evidence of tuberculous or other infection"

Professor Selbie next prepared an antigen as follows pus from the specimen was heated for an hour at 60°C on three successive days and then tested for sterility The pus was then diluted 1 in 5 with saline solution and put into ampoules in 0 2 ml amounts

The patient was tested with this antigen and gave a positive reaction exactly similar to that given with the antigen obtained from the Hospital for Sick Children To confirm the specificity of the antigen a test dose was sent to Dr Elspeth Campbell Dr Campbell was the case reported by Campbell and Wheaton (1952) and kindly undertook to test herself Dr Campbell reported

> "A reaction appeared on the second day, and was at its height on the third day, when there was a firm red papule 0 6 cm in diameter, with a rim of erythema The erythema faded next day, but the papule persists and is now (tenth day) 0 4 cm in diameter"

CONTROLS

The antigen was next used for intradermal testing of 40 patients attending the skin department For this we selected patients who gave a history of having kept a cat at some time during their lives but gave no history suggesting cat scratch disease They suffered from a variety of skin disorders, none showed any clinical signs suggesting cat-scratch disease All were adults, 25 were women and 15 men

RESULTS

37 of these patients *gave* no reaction to the antigen, and 3 showed a positive reaction exactly resembling *that obtained in the original patient* The *details* of these positive reactors are as follows

Case 1 —A man, aged 43, with relapsing eczema and peptic ulceration had previously had furunculosis of face and neck, *acute* paronychia of foot, morbilli, varicella, pertussis, and mumps He had worked as a fireman, a car body builder, and a taxi driver He had kept a cat for many years, and at times, dogs, chickens, a tortoise, and goldfish

Case 2 —A *man, aged* 44, with *perineal* pruritus, had previously had peptic ulceration, cervical furunculosis, pilonidal sinus, chronic sinusitis, morbilli, and varicella His occupation was *manual, and more recently* secretarial, work in a bacon warehouse He had kept cats until ten years ago, and sometimes dogs

Case 3 —A man, aged 43, with psoriasis, had previously had appendicitis, bilateral axillary *furunculosis*, morbilli, varicella, pertussis, scarlet fever, and mumps He had worked as a baker's roundsman, a milkman, and a fishmonger He had kept a cat for many years and, at times, rabbits, chickens, and budgerigars

Specificity

Since Willcox (1952) suggested that non specific reactions may occur with the antigens of the lymphogranuloma inguinale/psittacosis group, these four positive reactors were further intradermally tested with the antigens of lymphogranuloma inguinale ('Lygranum'), classical psittacosis, and pigeon psittacosis (supplied by the Central Public Health Laboratory) All these reactions were negative

Positive Reaction

The positive reaction obtained in all our cases was a very firm intradermal papule *0 5–1 0* cm in *diameter*, as described by Daniels and MacMurray (1951), but without the surrounding erythema which *they mention* This positive papule appeared within forty eight hours and lasted with little change for six *to eight* weeks The papule *from the* original patient was excised and found to consist histologically *of a zone of* round celled infiltration surrounding the vessels in the upper part of the cutis

DISCUSSION

Mollaret et al (1950) regard the intradermal test in this disease as specific and state that "very numerous" controls gave negative reactions However, in view of the clinical nature of cat scratch disease, and the case *with which it may* be confused with other types of lymph gland enlargement, it seems likely that a good many *cases, particularly* mild ones, will *go* undiagnosed It seems likely, too, that a positive intradermal reaction whom influenza virus had been isolated, or who had shown a rising titre in serological tests. The investigation was complicated by the facts that death was not always due solely to the influenzal pneumonia, and that in fatal cases no serological investigation was possible.

Food-poisoning (*table II, rows 20–22*)

The association of staphylococci of the 6/47 (III) group with food-poisoning has been noted previously (Allison 1949). For the purposes of table II we have classified the food-poisoning outbreaks as "grade A" when staphylococci of one phage type were isolated from the incriminated food and from one or more of the victims, and "grade B" when they were isolated from one or other of these sources but not both; in either case there had to be strong supporting epidemiological evidence that the staphylococci were responsible for the illness. In 35 (87·5%) of the 40 outbreaks in which the data were most complete, the staphylococci fell into group III, and in the remaining 5 they were untypable with the routine phages. Of the 41 less well documented outbreaks, 1 was apparently due to a group-I, 1 to a group-II, and 1 to an unclassifiable staphylococcus; but 78% were due to group-III strains. In view of the widespread interest in staphylococcal food-poisoning we have set out in detail the phage patterns of the staphylococci from the 40 grade-A outbreaks (table III).

TABLE III—PHAGE PATTERNS OF STAPHYLOCOCCI ISOLATED IN WELL-AUTHENTICATED FOOD-POISONING OUTBREAKS (1950–51)

Phage patterns	No. of outbreaks due to strains with each pattern
7 + ...	5
42E	4
6/47/53/54 + ; 6/47 + ...	3
6/54 + ; 42D ; 47/54 + ; 53 + ...	2
6/7/47/47C/53/54 + ; 6/7/47/53 + ; 6/7/47/54 +; 6/47/47C/53 + ; 6/47/47B/53/54 + ; 6/47/53 ; 6/47B/53/54 + ; 7/47/53 weak ; 47 ; 47/53/54 ; 53/54 + ; 54 + ...	1
No lysis	5

It is clear that food-poisoning in Britain is, at most, rarely due to staphylococci of groups I or II. Some food-poisoning strains isolated in other countries have also proved to fall into group III; but one or two strains have fallen into other groups, and a world-wide association of group III with food-poisoning should not be assumed without further investigation. It is important also to remember that there is as yet no evidence of the proportion of strains of group III that produce the enterotoxin; hence a strain cannot be assumed to be a food-poisoning strain because by phage typing it belongs to group III.

PENICILLIN SENSITIVITY AND TYPE

In the great majority of cases we have no record of the penicillin sensitivity of strains sent to us for typing; and, except in the investigation of normal persons at Norwich, we have not determined the sensitivity ourselves. But since the reason for typing was, in many cases, the fact that an outbreak of hospital infection had occurred, and since such outbreaks are nowadays almost always due to strains resistant to, at least, penicillin, our material is naturally biased by the inclusion of an undue proportion of resistant strains.

Of the strains from the nose of normal persons, an average of 22·6% were penicillin-resistant, with a maximum of 34·8% in group III (table IV); in the whole collection the percentage of group-III strains that were resistant was much higher, and group III also formed the bulk of the total resistant strains; a substantial proportion of the resistant strains, however, also fell into group I.

DISCUSSION

We have already emphasised that we regard the present method for typing staphylococci as more valuable for the elucidation of particular epidemics than for establishing a general and stable classification of staphylococci (Williams and Rippon 1952). Used as we have used it here, as a way of recognising three broad groups, it gives no more information than Cowan's serological typing method. But, so far as we are aware, no comparable figures for the frequency of particular serological types in staphylococci from various sources are available.

TABLE IV—FREQUENCY OF PENICILLIN-RESISTANT STAPHYLOCOCCI IN THE VARIOUS GROUPS

—	Collection of strains from nose of normal persons			All strains for which information was available		
	No. of strains	% penicillin-resistant in group	% of total resistant strains falling into group	No. of strains	% penicillin-resistant group	% of total resistant strains falling into group
I (52) ..	25	16·0	17·4	64	32·8	13·0
II (3A) ..	12	25·0	13·0	35	31·4	6·2
III (6/47) ..	23	34·8	34·8	109	79·8	53·6
Unclassified .	4	0	0	14	28·6	2·5
Untypable ..	40	20·0	34·8	95	42·2	24·7
Total ..	104	22·6	100·0	317	51·4	100·0

With two exceptions, no particular staphylococcal type appears to be unduly common in any disease. The first exception is the excess of group-I strains in the lung and sputum of patients with fulminating staphylococcal pneumonia following influenza. We have no explanation for this observation, but since the excess was observed in strains from a variety of sources, and in two different influenza epidemics, we believe it to be real (see also Stuart-Harris et al. 1950). Not all the strains associated with the fulminating disease were penicillin-resistant.

The second exception is food-poisoning, which, in Britain, appears to be due almost exclusively to strains of group III. It is of some interest that the same group is commonest in the fæces of normal persons.

We have not observed the preponderance of group-II strains in furunculosis noted by Rountree (1953), but possibly such a preponderance was masked in our material by a number of patients cross-infected in hospital.

Our admittedly incomplete results on the type distribution of penicillin-resistant strains amplify the earlier results of Barber and Whitehead (1949) in demonstrating the frequency with which strains of group III are resistant, but they also show that resistant strains are now not so uncommon in groups I and II.

SUMMARY

By means of bacteriophage typing, 1349 strains of *Staphylococcus aureus* from normal persons and from patients with various forms of staphylococcal infection were classified into three broad groups.

The three groups correspond to, and are numbered in the same way as, the three groups recognised by serological typing.

Fulminating pneumonia complicating influenza was very commonly due to staphylococci of group I; food-poisoning was almost always due to strains of group III.

The group distribution of staphylococci from boils, whitlows, &c., and from cases of otitis was the same as that from the nose of normal persons; strains from lesions infected in hospital were commonly of group III, owing to the frequency with which strains of this group are penicillin-resistant. Strains of group III were also more common in the fæces than in the nose of normal persons.

We are very grateful to all those who have sent staphylococci in response to our requests, and particularly to Prof. C. H. Stuart-Harris for numerous strains and clinical details from patients with pneumonia. We are also grateful to Dr. J. Overton for permission to quote his results.

tonic saline foot baths or whole tub baths at a moderate temperature, with salt added, do nothing but good Keeping these feet dry merely means that the patient keeps them dirty and increases the risk of infection extending under scabs and crusts Even the frankly gangrenous toes and heels greatly benefit by saline baths twice or thrice daily There is not very great danger of releasing the organisms from the mummified tissues Those on the surface will be washed away, and the clean foot and healthy skin resist infection better Half strength eusol is used as a moist dressing and has superseded any local use of antibiotics There has been no skin sensitivity, and entry of external infection is prevented Neither elaborate heat cradles nor exposure to cold temperatures were used Control of residual œdema by crêpe or elastic web bandages improves the local circulation and hastens healing Mersalyl need not be omitted in œdema due to cardiac failure

RESULTS

In every case there was a good immediate response The characteristic swollen, red, and shiny toe, with a triangular area of lymphangitis and œdema on the dorsum of the foot and possibly a smaller and more localised fluctuating area on the plantar aspect at the base of the toe, subsided in forty eight hours or less Pain due to tension was correspondingly lost The rate of healing depends on the rapid elimination of infection, adequate blood supply, and the parallel improvement in the diabetic control Recurrences, amputations, and deaths are bound to occur in a series of patients of this age group and with so high an incidence of arteriosclerosis and hypertension If, however, recurrent infections are treated immediately they may be controlled, and on humanitarian grounds to postpone the date of mid-thigh amputation in advanced life, provided that the patient is free from pain, is a very real advantage It has been shown that second, third, and fourth courses of terramycin are as efficacious as the first We have met no evidence of resistance The organisms isolated have been staphylococci, streptococci, coliform, and proteus bacilli In-vitro sensitivity tests often proved confusing and in practice unnecessary because terramycin appears to have a more potent effect in the body

In a personal communication Dr E H Rynearson and Dr N W Barker, of the Mayo Clinic, confirm the sometimes dramatic effect of terramycin and aureomycin in diabetics with occlusive arterial disease where penicillin and other antibiotics have failed They also state that they have met with little gastro intestinal disturbance—which corresponds with our experience

In the past one has hesitated to use an expensive drug for rather minor infections, but it seems to be a true economy to control such infections in diabetics as early as possible

CONCLUSIONS AND SUMMARY

The advantages of using terramycin in a diabetic outpatient department are

Administration is easy by mouth in a capsule or a tablet, or in drops for children Hence there is no need for visits by the district nurse to give injections

Toxicity seems to be low, and vomiting and diarrhœa uncommon Hence there is little risk of disturbing the diabetic control, and no change of diet is required

Infections associated with diabetes are often mixed Terramycin, with its wide range of activity, is a suitable means of getting a rapid effect

Sensitivity tests seem rarely necessary Indeed they have sometimes been misleading

In the series of foot infections treated swelling and pain subsided very rapidly, with conspicuous improvement in forty-eight hours Only a simple routine of rest and good hygiene was required When relapse occurred it was due to arteriosclerosis, but by keeping the infection controlled conservative treatment was possible, thus prolonging the patient's term of activity Operation may be avoided, or an operation which is relatively limited may be planned at the time of election, either without further antibiotic treatment or with another covering course Development of resistance of the micro organism to the antibiotic was not observed

My thanks are due to the surgeons of the Leicester Royal Infirmary who have operated on some of these patients, and in particular to Donald McGavin, F R C S, whose unfailing visits to the diabetic foot clinic have given us great encouragement I owe much to E J Fitchett, PH C, who has taken great care in recording dosage and in loyally guarding the supply of terramycin for the purpose for which it was given by Chas Pfizer Ltd, of New York

MAINTENANCE OF THE TRENDELENBURG POSITION BY SKIN FRICTION

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The unexpected interest aroused by a short letter (Hewer 1952) on the Trendelenburg position, commenting on an article by Howkins (1952), has made it clear that many gynæcologists and anæsthetists are dissatisfied with orthodox methods of obtaining a head down slope, and it was felt that a short résumé of this subject might be helpful

First, it is clear that, if a patient is to be kept in a 40° Trendelenburg slope, some method of traction or pressure must be applied to some area of the body It is possible to use traction on the ankles, but orthopædic surgeons are not in favour of this, owing to the strain imposed on the knee-joints and hip-joints in the presence of complete muscular relaxation Pressure can be applied to the shoulder girdle by padded rests, but, however carefully these are adjusted, brachial plexus palsy can develop and congestion and œdema

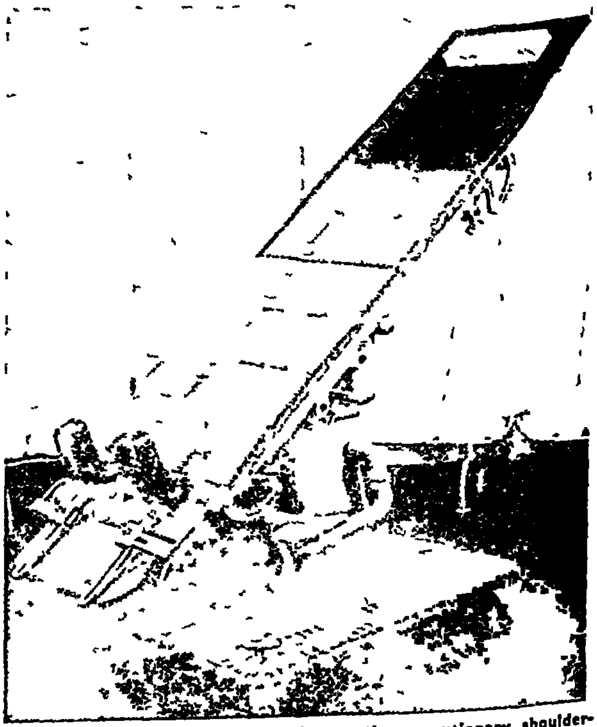

Fig 1—Ribbed mattress in position, with precautionary shoulder-rests and ankle-pad

tion of non-typable strains in this series than in the series from noses and throats.

Sputa.—These strains were isolated on routine examination of a variety of specimens. There was no evidence of staphylococcal pneumonia in these patients.

Pathological Material

Otitis and mastoiditis.—117 penicillin-sensitive strains were isolated from patients admitted to hospital with infections of the ear. The frequency distribution of the phage groups was similar to that found in normal carriers.

Urines.—The frequency distribution of 100 strains isolated from urines is similar to that found in the conjunctival strains. Not all these strains can be regarded as causing urinary-tract infection; some of them will be contaminants introduced during the taking of the specimen.

Skin infections.—These strains were isolated from a variety of skin lesions including varicose ulcers, sycosis barbæ, dermatitis, boils, and carbuncles. There is a higher incidence of group-II strains in this series than in normal carriers. 45 strains were obtained from patients suffering from boils. 5 of these were penicillin-resistant and belonged to group III. The frequency distributions of the remaining 40 penicillin-sensitive strains was:

Group I	12	(*30%*)
Group II	20	(*50%*)
Group III	4	(*10%*)
Not classifiable	2	(*10%*)
Not lysed	2	

It is apparent therefore that typable strains comprised the great majority of strains isolated from those lesions definitely attributable to staphylococcal infection and that there is a preponderance of group-II strains as the causal organisms in furunculosis.

Deep infections.—These comprise 59 strains isolated from blood-cultures, osteomyelitis, and abscesses. In this series the incidence of group-II strains is 44·1% and there were fewer non-typable strains than in the normal carriers. Comparison of the frequency distribution of this series with that from normal nasal carriers shows a highly significant difference, $\chi^2=17{\cdot}43$, d/f=3, $P<0{\cdot}01$. Of 39 strains from abscesses, 20 belonged to group II, as did 6 of 12 strains from osteomyelitis.

Wound and burn infections.—There were 76 cases from which penicillin-sensitive strains were obtained. The frequency distribution of the phage groups is similar to that found in normal carriers, suggesting that these infections may have been autogenous.

Miscellaneous pyogenic infections.—This series comprises strains from pus whose exact source is unknown. The frequency distribution resembles that found in the series from skin infections.

TABLE II—FREQUENCY OF PENICILLIN-RESISTANT STRAINS OF STAPHYLOCOCCI OF DIFFERENT PHAGE GROUPS FROM VARIOUS SOURCES

Source	Number	Percentage				
		Group I (52)	Group II (3A)	Group III (6/47)	Unclassified	No lysis
Noses of hospital staff	273	2·5	0·5	78·7	6·2	12·1
Throats of hospital staff	107	8·4	0	66·4	9·3	15·9
Conjunctivæ	35	0	0	89	5·7	14·3
Sputa	76	9·2	1·3	68·4	2·6	15·5
Otitis and mastoiditis	72	8·3	2·8	70·8	5·6	12·5
Urines	150	8·7	0·6	69·3	6	15·4
Skin infections, including boils and carbuncles	174	8·7	3·4	73	3·4	11·3
Deep infections, osteomyelitis, abscesses, bacteræmia	66	7·6	0	78·7	4·6	9·1
Wound and burn infections	332	7·5	1·5	78·3	4·2	8·5
Miscellaneous pyogenic infections	251	5·6	0·5	75·3	5·6	13
Sporadic neonatal infections	56	5·4	0	73·1	5·4	16·1
Total	1572					

Sporadic neonatal infections.—As already stated, these strains came from six different hospitals. They were isolated from cases of conjunctivitis, umbilical sepsis, and miscellaneous skin infections. No outbreaks of clinical pemphigus were investigated during the period under review. There is a striking predominance of group-III strains in this series.

RESULTS OF TYPING PENICILLIN-RESISTANT STRAINS

Table II gives the frequency distribution of 1572 penicillin-resistant strains, arranged under the same headings as the strains in table I. Inspection of the table shows the great predominance of group-III strains: from 66·4 to 80% of the strains in the various series belong to this group. There are fewer non-typable strains among these strains and one noteworthy feature is the absence from some series, and very low incidence in others, of group-II strains. The penicillin-resistant strains reflect the fact that, in this particular hospital, strains of group III are the organisms predominantly responsible for cross-infection. It should be emphasised that many variations in phage pattern are included in the broad group-III (6/47) classification.

During the period under review, strains of staphylococci isolated from fourteen separate outbreaks of wound infection were obtained from five other hospitals. All these strains were penicillin-resistant; 10 of the 14 phage patterns found belonged to group III, 2 belonged to group II, and 2 were not typable. In Australia therefore the predominance of group III in wound infections is not confined to one hospital.

DISCUSSION

The frequency distributions of the penicillin-sensitive strains showed no significant differences between the series from normal carriers, from sputa, from urines, and from surgical wounds and burns; which suggests that when staphylococci are recovered from urines, ears, and wound surfaces their presence may be correlated with the carrier state of the patient and is not necessarily associated with an infectious process of which they are the causal organisms. However, in the case of frankly staphylococcal lesions, there was a difference in the distribution of the phage groups and a larger proportion of typable strains. There was thus a suggestion that a proportion of the non-typable strains isolated from carriers may not be highly virulent.

No particular group of staphylococci could be associated with any particular type of lesion. There was, however, a predominance of group-II strains in boils, abscesses, and osteomyelitis which were caused by penicillin-sensitive strains.

Comparison of the Australian results with those of Williams et al. (1953) shows many points of similarity and a few differences. A larger proportion of our strains was typable. This may be due to the more homogeneous nature of our material or may indicate slight differences in the method of recording the typing results. Since in only a proportion of their strains were penicillin-sensitivity results available, it may not be legitimate to compare their figures with those obtained here for penicillin-sensitive strains. Nevertheless, the general pattern of distribution in the series of normal carriers was similar. There is, however, a higher incidence of group-III strains obtained from nasal carriers in Australia, 26·9% compared with 18·5% in England ($\chi^2=8{\cdot}39$, d/f=1, $P<0{\cdot}01$). Since a number of penicillin-resistant strains of this group isolated from non-hospitalised nasal carriers were omitted from the calculations, the true incidence of group-III strains was slightly greater than shown in table I, and the difference between the two countries becomes even larger.

With regard to the penicillin-resistant strains, a higher incidence of group-I and group-II strains was found in patient's neck As the table is tilted, the corrugations on the under surface of the pads interlock with those on the mattress, and it has been found in practice that the patient does not slip even with the maximum tilt available on the standard Allen & Hanburys table The lumbar pad has the additional advantage of minimising postoperative backache, an observation emphasised by the late Sir Charles Gordon-Watson

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THE URINE IN SEVEN CASES OF CHRONIC COR PULMONALE

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CONGESTIVE heart-failure in chronic lung disease results from anoxia (or, rather, hypoxia) and pulmonary hypertension According to the relative importance of the two factors, cases of chronic cor pulmonale may be divided into two groups, the anoxic and the obstructive (McMichael 1948)

Anoxic pulmonary heart-failure is usually due to emphysema with an exacerbation of chronic bronchitis, pulmonary hypertension is present, but with recovery from failure the pulmonary arterial pressure is normal or only slightly raised (Cournand 1950, Mounsey et al 1952) The cardiac output is usually increased (McMichael and Sharpey-Schafer 1944), except in the terminal low-output stage (Howarth et al 1947)

In *obstructive (or hypertensive) pulmonary heart disease* pulmonary hypertension is irreversible and the cardiac output in failure tends to be low or normal (Taquini et al 1947, 1948, Cournand 1950, Harvey et al 1951) These cases of "low-output" failure result from primary obstructive changes in the pulmonary arterial system or from major structural changes in the lungs, such as fibrosis Thus it has been found that patients with pulmonary fibrosis and only moderate emphysema may have pulmonary hypertension in the absence of congestive failure (Bloomfield et al 1946, Cournand 1947) In bronchiectasis enlargement of the bronchial arteries, with an increase in the anastomoses with the pulmonary arterial system, is a possible factor in the production of pulmonary hypertension (Liebow et al 1949)

I report here the urinary findings in seven cases of congestive heart-failure due to chronic lung disease All the patients had cyanosis, œdema, hepatomegaly, sinus rhythm, and clinical or radiological evidence of cardiac enlargement The superficial neck veins were visibly distended above the level of the sternal angle in all except case 1

FINDINGS

Emphysema and Bronchitis

In cases 1–5 congestive heart-failure was due to emphysema and exacerbation of chronic bronchitis These patients either died (cases 1, 3, and 4) or showed complete recovery from failure (cases 2 and 5)

The urine was apparently normal in all these cases, except for transient albuminuria in case 5, during a period of circulatory collapse with coma, which resulted from the administration of sodium pentobarbitone ('Nembutal') gr 3 Severe oliguria was not a feature, and the urine was usually straw-coloured and dilute (the specific gravity often being about 1 010) In cases 2 and 5 the reaction was sometimes alkaline The blood-urea level was below 40 mg per 100 ml in three patients on whom this investigation was made during the time that a full pulse volume and other signs of a hyperkinetic circulation were present A preterminal blood urea level of more than 100 mg per 100 ml was found in cases 1 and 3 The findings are shown in more detail in table I

Emphysema, Bronchiectasis, and Pulmonary Fibrosis

In cases 6 and 7 bronchiectasis and pulmonary fibrosis were present in addition to emphysema The œdema and hepatomegaly disappeared with treatment but the patients remained in a state of chronic heart failure, considerable cardiac enlargement persisting and regular mercurial injections being required to prevent fluid retention and systemic venous congestion

In case 6 cyanosis was slight and the pulse volume small, the urinary output was low, the blood urea level raised, and the urine always acid, usually amber, and concentrated, and contained albumin, leucocyte and red cells In case 7 albuminuria occurred intermittently The findings in these cases are shown in more detail in table II

DISCUSSION

According to Fishberg (1940) the urine in congestive heart-failure commonly contains albumin, leucocytes red cells, and hyaline, granular, and epithelial casts The other characteristic features are stated to be oliguria high specific gravity (1 025–1 035), acid reaction, and dark colour, the last-named being due more to increased excretion of urinary pigments than to high concentration The blood non-protein nitrogen increases only when oliguria becomes extreme (about 500 ml daily) With the polyuria of improvement the urine becomes dilute and loses its dark colour, but albuminuria sometimes persists longer.

White (1947) considers albuminuria, leucocytes, red cells, and granular casts to be almost constant findings, but regards hyaline casts as less characteristic, whereas Lewis (1942) and Wood (1950) mention the occurrence only of albumin, hyaline casts, and red cells

I have not been able to find any published account of the urinary findings in congestive heart-failure due to pulmonary disease In the present series only case 6 showed persistent oliguria, a raised blood urea level, and the "typical" urinary findings of congestive heart failure Since this patient had bronchiectasis, radiological evidence of pulmonary fibrosis, a small pulse volume, only slight cyanosis, and considerable cardiac enlargement, after œdema and hepatomegaly had disappeared with treatment, it seems likely that he had the hypertensive type of pulmonary heart disease with a low or normal cardiac output during failure Intermittent albuminuria occurred in the other patient with bronchiectasis and pulmonary fibrosis, and transient albuminuria occurred in case 5 during a period of circulatory collapse and coma A high preterminal blood-urea level was found in cases 1 and 3

These findings suggest that severe oliguria, with a raised blood-urea level, albuminuria, and the other urinary abnormalities, is not characteristic of congestive heart-failure due to pulmonary disease when there is a high cardiac output In heart-failure in thyrotoxicosi the urinary volume may remain almost normal (Fishberg 1940)

The great deterioration which followed the administration of sodium pentobarbitone in case 5 may indicate that barbiturates, like morphine, are dangerous in some cases of severe emphysema

SUMMARY AND CONCLUSIONS

The urinary findings in seven cases of chronic cor pulmonale are described

In six cases the urine was usually dilute and was either normal or free from any persistent abnormality In the remaining case the "typical" urinary changes of congestive heart failure were present Certain clinical features indicate that this patient had "low output" failure of low effect on the surface compared to that at a depth is confirmed by the clinical findings (see below).

Another advantage arises from the fact that the absorption of high-energy quanta in the materials of the body is determined almost solely by their density. The absorption in bone is therefore relatively less compared to that in soft tissues, than it is at lower energies of about 200 kV.

Another advantage is that the total energy absorbed in the body (integral dose) during treatment is less, per unit dose given to the tumour, with high-energy radiation than with radiation at lower energies. Owing to the natural canalisation of the primary beam at these high energies the rest of the patient can be more easily shielded, and in practice we are well below the significant levels of whole-body effects from radiation outside the direct beam. This canalisation also makes the protection of staff easier. Nevertheless, elaborate protective measures are still required.

Our monitoring shows that the amounts of radiation received by staff are extremely small (mean dose about 0·02r per week), less than that often obtained with conventional X-ray machines. Electron-synchrotrons emit low-frequency sound, but by careful acoustic study and precaution the intensity has been reduced to a level at which, far from being an irritant, some patients have fallen asleep during treatment and others have approved of the evidence that something is happening!

BEAM COLLIMATION

While natural canalisation is physically an asset in treatment it creates technical difficulties in providing a limitation on field size obtainable in practice. At high energies considerable thickness (about 20 cm.) of protective materials is required for adequate collimation, and these heavy materials have to be aligned with high accuracy. Recently a new collimating system has been designed and constructed embodying kinematic mounting, optical projection devices, and interlock to ensure that the correct field size is being used. The collimation has in fact proved one of the most troublesome and expensive technical developments required.

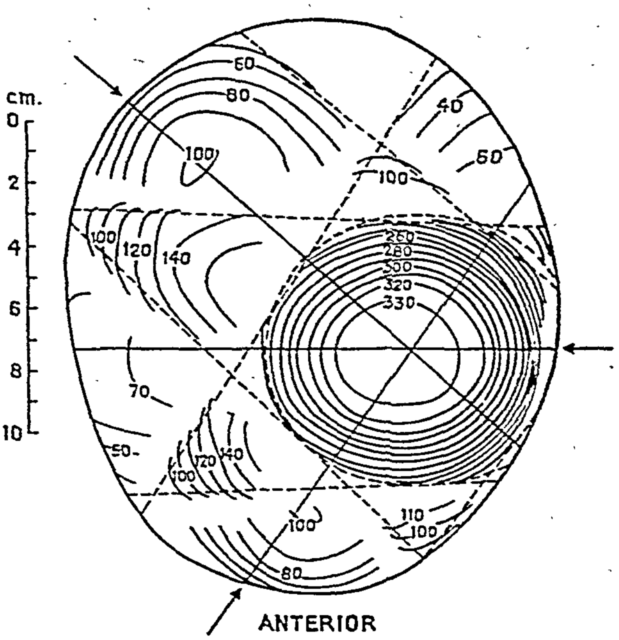

Fig. 3—Estimated distribution of dose in four 8 cm. diameter circle fields in case 3 treated at 24 MeV. Dotted circle represents the edge of the beam from the field which is angled out of the plane selected.

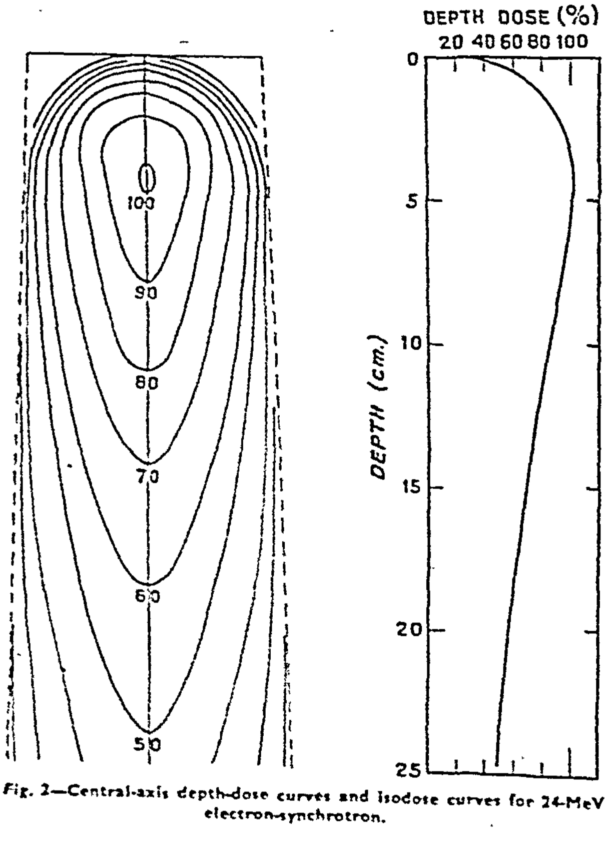

Fig. 2—Central-axis depth-dose curves and isodose curves for 24-MeV electron-synchrotron.

BIOLOGICAL ACTION

At the beginning of the investigations it was known that in addition to the normal methods of interaction of quanta and matter, at very high energies nuclear interactions can also take place, but their magnitude and biological significance were unknown. Preliminary investigations were therefore undertaken to measure the fraction of the energy absorbed in tissues associated with these nuclear effects. It appears that they do not account for more than 1% of the total energy absorbed; but, in so far as they involve the emission of high-energy neutrons and protons of possibly high biological efficiency, more detailed studies are in progress. In collaboration with Dr. F. G. Spear, of the Strangeways Research Laboratory, Cambridge, biological experiments have been made on cell division in vitro, on the processes of differentiation in the chick embryo, and on mouse tumours. Some of the effects are reminiscent of the biological effects of neutrons and protons. Otherwise the effects of the pulsed radiations from the synchrotron are qualitatively and quantitively similar to those seen after a comparable but rather smaller dose of gamma rays (Spear 1951).

An interesting sidelight is the easily observable, but biologically insignificant, artificial radioactivity of the patient, arising from the photo-disintegration of the oxygen and carbon atoms in the tissues (Mayneord, Martin, and Layne 1949).

Experiments on drosophila fly and on bean roots support the view that there is no great fundamental difference in biological efficiency between X rays produced at 24 MeV and those produced at the more usual therapeutic potentials. Such advantages as exist in the therapeutic use of these radiations arise rather from the superior distribution of absorbed energy in the tissues than from any fundamental difference in the nature of the biological actions.

SELECTION OF CLINICAL MATERIAL

The fixed beam and low output (about 5r per min. at 1 metre) limited the choice of patients and severely

Medical Societies

ROYAL SOCIETY OF MEDICINE

Pregnancy Toxæmia

The meeting on *Pregnancy Toxæmia*, held by the society's section of obstetrics and gynæcology on Feb. 27, with Mr A. C. Palmer, president of the section, in the chair, fell into two parts. There was first a discussion on the prevention of toxæmia by diet and weight control, and then an account of attempts to stay the course of established toxæmia by reducing the body's sodium content with ion exchange resins, or by lowering the hypertension with hexamethonium.

Dr R. H. J. Hamlin described the campaign at the Women's Hospital, Sydney, which in the four years 1948–51 had eliminated eclampsia. From 1936 to 1947 there were 106 cases of eclampsia among 36,700 booked patients; in 1947 they were seeing 1 eclampsia every three weeks, and in this year 2 eclamptics died. This was in spite of the usual antenatal care and of treatment commonly involving induction of premature labour and the provision of special rooms for the mothers and expensive premature-baby units. Between 1947 and the end of 1951 a further 18,000 booked patients were admitted, and the eclampsia-rate began to drop, until in 1951 with 7000 admissions there were no cases at all, and few instances of extreme prematurity. The combined neonatal and stillbirth rates had been reduced from 25 per 1000 live births in 1947 to 11.9 per 1000—a reduction which represented a saving in fœtal life at the rate of 50 babies per year. No cæsarean sections were required, and patients with albuminuria regarded as toxæmic were down to 84, as against 418 in 1946. This success had been achieved by ensuring that patients attended regularly for antenatal care, by giving them a carefully designed set of lectures on diet which emphasised a high-protein high-vitamin intake, with little carbohydrate and about 2100 calories in all, and by asking them to watch their weights and limit their weekly gain to $^1/_2$–$^3/_4$ lb. At the same time careful watch was kept for the earliest signs of approaching toxæmia. Earlier records showed that before 1947 at least 10 eclamptics had no record of albuminuria before their first fit. When the urines of toxæmic women were frequently tested, albumin was absent from some specimens. Again, one patient in 1949 went into eclampsia five days after her blood-pressure was noted as 120/70 mm. Hg, which was no higher than it had been in early pregnancy. Hypertension was usually a late sign, a slight diastolic rise being often noticeable at the thirty-fourth week, and a raised systolic pressure with or without albuminuria, at the thirty-seventh. A much more helpful sign was œdema of the fingers, which was noticed in the thirty-first week of pregnancy in those who were hypertensive by the thirty-seventh week. In 1950 a study of two years' results showed that young primiparous patients who were later to become toxæmic nearly all gained too much weight (defined as over 8 lb.) between the twentieth and thirtieth weeks. This emphasised the importance of weight control in mid pregnancy, the use of salt-restricted diets, and twice weekly examination if the weight began to rise too quickly. It was important, if eclampsia was to be eliminated, for toxæmia to be recognised and treated before the hypertensive phase was reached.

Dr G. I. M. Swyer quoted some preliminary figures which did not support the view that rapidly increasing weight between the twentieth and thirtieth weeks heralded toxæmia. In an experiment at University College Hospital a group of primiparous women on an 1800 calorie diet were being compared with a control group on free diet. The average weight-gain of 90 dieted patients was 10.64 lb., compared with 11.91 in 94 controls. In 20 patients who were admitted for toxæmia, the average gain was 12.58 lb. and in others who remained fit, 11.15 lb. But averages did not tell the whole story, for in this fit group the greatest individual gain was 25.62 lb., while in the toxæmics the lowest gain was 3.8 lb. Moreover, the mean gain of the 12 dieted patients admitted for toxæmia was 10.63 lb.—the same as in all the dieted patients.

Prof. W. C. W. Nixon said that of course they had no evidence in this experiment that the women had kept to their diets. The results were disappointing, but dieting in pregnancy was unduly neglected in this country, and if it did no more than reduce maternal obesity mothers would be grateful.

In reply, Dr Hamlin said that he did not claim that his prognostic sign of toxæmia held for more than 25% of multiparæ, or for women with essential hypertension or those over the age of 30. But he was convinced that 90% of young primiparæ who gained more than 8 lb. in any ten-week period before the thirtieth week would get toxæmia.

Dr H. M. Carey discussed the use of ion exchange resins, taking his stand on the view that the toxin in "toxæmia" was excess sodium. By using the isotope dilution method he determined the total body sodium on the day after admission and on the ninth postpartum day. Even mild cases of pre-eclampsia showed excess sodium retention which was not always associated with a corresponding gain in weight. Evidence from the work of other investigators was presented suggesting that this salt retention was due to endocrine influences. Dr Carey outlined the physiological mechanisms underlying the development of the pre-eclamptic signs of œdema, hypertension, albuminuria, and eclamptic fits, and he emphasised the significant contribution made by excess sodium to their development. Salt depletion, produced by bed rest, low salt diet, and ion-exchange resins, was thus a rational approach to the control of pre-eclampsia. Diets were unpalatable if the salt content was reduced below 2 g., but the addition of up to 100 g. of resin a day would convert a low salt diet into what was virtually a *true salt free diet*. Ammonium resin was given for two to three days and then the potassium resin was used. Both types of resin increased the loss of sodium in the fæces, while the ammonium resin also produced an acidosis which increased the urinary loss of sodium during the first forty eight hours. The potassium resin increased the absorption of potassium and allowed the correction of the acidosis, when this was no longer fulfilling any useful purpose. Ion exchange resins were only effective in pre-eclampsia when combined with bed rest and a true low-salt diet. Dr Carey demonstrated examples where this combination had been used with safety to prolong for up to four weeks, pre-eclamptic pregnancies which had failed to respond to routine treatment. In this way the need for cæsarean section and the danger of prematurity, with its attendant neonatal mortality, had been reduced.

Dr N. F. Morris reported a series of 26 patients, all with severe hypertension (over 180/100), who had not responded after a week of inpatient treatment, and who had therefore been given hexamethonium in an effort to prolong the pregnancy. They were selected for this treatment if their blood-pressures dropped adequately after a test dose. In general those with essential hypertension responded much better than those with pre-eclamptic toxæmia, suggesting that different hypertensive mechanisms were at work in the two conditions. Oral dosage began at 250 mg. eight hourly and to overcome rising resistance this had to be increased rapidly to 3–7 g. daily. The response seemed to vary from day to day, perhaps because absorption was variable. Alternatively, 50–100 mg. was given intramuscularly every three to six hours. In several cases treatment could not be continued for very long because of intra-uterine fœtal death, premature onset of labour, and failure to maintain

PATIENTS WITH CEREBRAL GLIOMAS TREATED WITH 24-MeV X-RAYS

Case no.		Sex	Age (yr.)	Grade	Site	Surgical intervention	Survival to date (mos.)	Degree of disability	
								Before treatment	December, 1952
Histologically verified astrocytoma	4	F	33	I	Temporal	Biopsy	17	Severe	Slight (optic atrophy)
	5	F	59	I	Temporoparietal	Biopsy	15	Severe	Slight (optic atrophy)
	2	M	40	II	Frontal	Lobectomy	20	Severe	Severe
	9	M	52	II	Parietal	Part removal	6	Moderate	None
	10	M	34	II	Frontal	Part removal	3	Severe	None
	1	M	49	II	Parietal	Biopsy	30	Moderate	None
	3	F	34	III	Parietal	Part removal	18	Moderate	Slight (occasional petit mal)
Not verified histologically	6	F	44	..	Temporal	Biopsy (inadequate)	14	Severe	Moderate
	7	M	29	..	Para-ventricular	None	9	Severe	Severe (optic atrophy)
	8	M	39	..	Thalamic	Torkildsen	Died after 4	Complete	Dead

an astrocytoma of grade-III malignancy. The last patient had nine years' history of fits and four months' history suggesting raised intracranial pressure. In the one case of fairly high-grade malignancy the clinical impression gained is that of a slowly growing tumour which had perhaps only recently undergone more rapid growth. All the cases of verified tumour therefore fall into the category of the less malignant gliomas, which certainly have a longer life history than the tumours of malignancy grades III and IV.

An expectation of life of from many months to several years is known to exist in tumours of grade I and II malignancy after surgical intervention alone or without treatment of any sort; hence it is impossible, from the small series of cases presented here, to be certain of the effect of 24-MeV radiation on these tumours. Nevertheless the fact that nine out of ten patients are alive, many of them well and working, encourages us to hope that this therapy has had a good effect. So far as immediate palliation is concerned, there is no doubt of its success or of its advantages over any method of radiotherapy we have yet seen for patients with such tumours. ymptoms have been relieved without adding to patients' iscomfort during treatment and without detracting from heir appearance afterwards.

The particulars of the patients are given below, and the effects of treatment are summarised in the accompanying table.

CASE 1.—A man, aged 49, with a right temporoparietal astrocytoma, grade II, and eighteen months' history of fits, started treatment on May 31, 1950. He was well and working in October, 1952, two years and five months after treatment.

CASE 2.—A man, aged 40, with a right frontotemporal astrocytoma, grade II, and seven months' history of headache and vomiting, started treatment on April 12, 1951. He was well and working till October, 1952, a year and six months after treatment; in December, 1952, he was alive with recurrence.

CASE 3.—A woman, aged 34, with a left frontotemporal astrocytoma, grade III, nine years' history of fits, and five months' history of headache and vomiting, started treatment on June 7, 1951. She was well in December, 1952, a year and six months after treatment.

CASE 4.—A woman, aged 33, with a right temporal astrocytoma, grade I, two years' history of giddiness, and two months' history of headache and vomiting, started treatment on July 17, 1951. She was well and doing full-time housework in December, 1952, a year and five months after treatment.

CASE 5.—A woman, aged 59, with a right temporo-parieto-occipital astrocytoma, grade I, with two years' history of visual hallucinations, and recent pain and tingling in her left face and arm, started treatment on Aug. 8, 1951. She was alive and well in November, 1952, a year and three months after treatment.

CASE 6.—A woman, aged 44, with a left frontotemporal tumour (piece removed for biopsy inadequate), two years' history of headache, and six weeks' history of pain and involuntary movement of the arm, started treatment on Aug. 8, 1951. In October, 1952, she had some complaints, but no abnormal physical signs were found, a year and two months after treatment.

CASE 7.—A man, aged 29, with a right anterior para-ventricular tumour (no histological examination), twenty years' history of petit mal, five months' impairment of vision, and recent headache, started treatment on Feb. 8, 1952. In November, 1952, he was in poor condition, and had poor vision nine months after treatment.

CASE 8.—A man, aged 39, with a right thalamic tumour (no histological examination), five months' history of headache and drowsiness, and recent diplopia, impaired vision, and unsteadiness, started treatment on Feb. 28, 1952. He died on July 12, five months after treatment.

CASE 9.—A man, aged 52, with a left parietal astrocytoma, grade II, seven months' history of jacksonian attacks, and six weeks' history of headache, started treatment on June 24, 1952. In December, six months after treatment, he was well, except that his right leg tired before his left.

CASE 10.—A man, aged 34, with a right frontal astrocytoma, grade II, had it excised in June, 1951. He had increasingly frequent fits since January, 1952, and three weeks' history of headaches and progressive hemiparesis. He started treatment on Sept. 3, 1952. In October, 1952, a month after treatment, he had slight residual weakness of arm only; by December he had no disability.

SUMMARY

An account is given of the first clinical experiment in this country in the treatment of patients with malignant disease—in this series cerebral gliomas—with 24-million-volt X rays. The first ten cases treated since the experiment started in May, 1950, are described, with results up to December, 1952.

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shock therapy, and "psychosurgery" The book is illustrated by humorous sketches, excellent in themselves, but striking an incongruous note in what is, after all, a serious work

World-Atlas of Epidemic Diseases

Part I Editor Dr ERNST RODENWALDT, Heidelberg Sponsored by the Bureau of Medicine and Surgery, Navy Department, Washington D C Hamburg Falk 1952 Pp 122, with 52 maps

THIS magnificent tome, with a land area of 266 square inches and a loose-leaf geomorphology, will handsomely furnish any epidemiologist's office whether it will as handsomely furnish his mind is more questionable Its unusual parentage—by the Bureau of Medicine and Surgery of the U S Navy Department out of Heidelberg—is no doubt responsible both for the combination of lavishness and detail and for the unevenness in the choice and presentation of the material—which suggests the work of a collection of players brought together for a benefit match rather than that of a trained team

Hirsch's *Handbook of Historical and Geographical Pathology*, of 1881, and its successor, the *Atlas of Epidemic Diseases*, edited by Heinz Zeiss (which was limited to areas of military importance), may fairly claim for Germany the parentage of geomedicine This new essay, to be followed by subsequent volumes, covers 16 diseases with a series of 33 maps and brief introductions, together with 5 meteorological and 2 population maps of Europe and "basic" maps covering the whole world in 12 regions The epidemic maps cover Europe only, except for 4 global maps and 5 restricted to Germany or Central Europe It is admitted in the preface that the statistics for some of the diseases chosen represent merely the distribution of research workers and laboratories, yet more maps seem to be devoted to these diseases than to those for which the recorded incidence varies less from the actual Thus there are 5 maps on bacterial dysentery, 4 on infectious hepatitis, and 2 on paratyphoid C compared to 2 only on typhus The spread of cholera in the epidemic of 1863–68 is well shown, as is the spread of tularæmia across Europe quite recently, though the attempt to include diagrammatically the various insect vectors—problematical in any case—as well as the animal complicates the map unduly

Professor Rodenwaldt's introduction explains the objectives and limits of cartographical presentation of disease, but its English version is hard going

It is open to question whether stricter limitation of the maps to a single country or, on the other hand, a more completely international approach, such as is found in the publications of the World Health Organisation, might not have been more profitable, but at the least this atlas is welcome as a demonstration of the possibilities of the graphic recording of epidemic disease on maps

Chemical Induction of Cancer

GEORGE WOLF, B SC, D PHIL, assistant professor, University of Illinois London Cassell 1952 Pp 250 17*s* 6*d*

Dr Wolf, with the aid of some 300 structural formulæ, has achieved a remarkable feat of compression of the literature on the chemical induction of cancer His book is divided into ten main sections, dealing with structure and activity, biological aspects of tumour induction, test methods, theories of the mode of action of carcinogens, biogenetic relationships, metabolism of carcinogenic hydrocarbons, carcinogenic azo compounds, carcinogenic aromatic amines and derivatives, some chemical carcinogens, inhibition of tumour growth, and possibilities of tumour chemotherapy It should appeal particularly to those already engaged in this field of research Investigators are liable to be immersed in their own special lines of work, and thus to lose contact with neighbouring studies which were once familiar to them Dr Wolf's book should stimulate their memories and will probably set many checking half-forgotten ideas which have been suppressed or distorted to fit in with convenient conceptions But the public to whom the book is primarily addressed—medical and general scientific readers—will find most of it too technical Condensation does not necessarily render material of this kind more assimilable, or smooth away its complexity In dealing with controversial issues Dr Wolf takes up a modest attitude of philosophical detachment and impartiality, but however much readers may admire his sober handling of attractive but as yet unproven hypotheses, they will remain unsatisfied Though several thousand papers have now been published on the chemical induction of cancer little success has yet attended attempts to elucidate this breathlessly interesting transformation

Surgery of Pancreatic Neoplasms

RODNEY SMITH, M S Lond, F R C S, surgeon, St George's Hospital, London Edinburgh E & S Livingstone 1953 Pp 168 35*s*

Mr Smith's essay was awarded the Jacksonian prize of the Royal College of Surgeons for 1951 He reviews the history of the subject, and it is remarkable to realise in what a short time an operation which was thought to be unjustifiable has become technically possible—indeed almost simple—and regularly and safely carried out This has been achieved by improved methods of anæsthesia, by the ability to deal more effectively with shock, by the use of antibiotics, and by taking to heart lessons obtained from the physiology of patients undergoing operations The method of operating—the handicraft—had been worked out long before With greatly increased experience, the knowledge of when to operate and what to do has crystallised The whole subject is here beautifully presented with abundant illustrations All general surgeons would do well to read this book for few can have a really extensive experience of the subject Here they will find the possibilities, successes and disappointments they are likely to meet

Associated Measurements

M H QUENOUILLE, M A, Yale University New York Academic Press London Butterworths Scientific Publications 1952 Pp 242 35*s*

ALTHOUGH not primarily concerned with the mathematical justification of the procedures described, this is not a book for beginners but rather a useful addition to standard texts Association between quantitative and qualitative characteristics has long been a favourite field for biometricians, and the author has concentrated here a very useful array of techniques applicable to the study of correlation between measurements Some are traditional, more are of recent development The first section, which deals with graphical methods in testing statistical significance, will be particularly useful to medical research-workers who need rapid, simple, yet quite efficient tests of correlation and trend Numerical methods of measuring association are clearly set down, and much attention is given to the curvilinear relationships so often seen in practice Without pretending that the methods suggested are either final or perfect, Mr Quenouille indicates ways of tackling problems in the analysis of time series, and concludes by a discussion of multivariate analysis This section, though a trifle brief, does give a balanced view of techniques such as discriminant function analysis and factor analysis and illustrates their potential value by worked out practical examples

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How to Use a Medical Library (2nd ed London Heinemann Medical Books 1952 Pp 44 5*s*)—In this handy little paper covered booklet Mr L T Morton, A L A, introduces the novice to the guides (such as the Surgeon General's catalogue) to published medical books and articles, the chief medical libraries of the British Isles, the most important medical bibliographies, and the medical abstracting services This edition has been completely rewritten since the book first appeared in 1934

Textbook of Clinical Pathology (4th ed London Baillière, Tindall, & Cox 1952 Pp 1060 68*s* 6*d*)—A new editor, Dr S E Miller, medical director of the United States Public Health Service, has taken charge since the last edition, and he has completely redesigned the book Three new chapters have appeared—on immunological tests, the assay of chemotherapeutic and antibiotic agents, and the diagnosis of viral and rickettsial disease The sections on hæmatology, blood chemistry, and syphilis serology have been rewritten The contributors are all at pains to help in the selection of the appropriate test and in the interpretation of the laboratory report—an emphasis which both clinicians and students will welcome would last for some years, and that for these reasons positive reactions are to be expected in a proportion of controls, particularly in people who keep cats. We believe that the results of our testing confirm this supposition and indicate that undiagnosed or possibly subclinical infections are not very unusual among cat-lovers in this country.

Mollaret et al. (1951b) advance evidence for including cat-scratch disease in the lymphogranuloma-inguinale/psittacosis group of virus infections; they recognise however, that in their cases intradermal reactions for lymphogranuloma inguinale and psittacosis were negative. Campbell and Wheaton (1952) found the same, and our observations confirm this.

These results appear to indicate that the intradermal reaction with cat-scratch disease antigen is specific. Positive reactions should, however, be interpreted with care; they may be obtained in apparently normal people, presumably as a result of previous undiagnosed infection, and are therefore of limited value in the diagnosis of an actual present illness.

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THE USE OF TERRAMYCIN IN INFECTIONS IN DIABETICS

WITH SPECIAL REFERENCE TO GANGRENE

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IN the ten months ended last November, terramycin was used in our department in the treatment of 70 diabetic patients with intercurrent infections. Several patients had recurrences, after a long interval, and some had two concurrent conditions on which the effect of the antibiotic was observed, thus bringing the total number of treated incidents to 93 (table I). There was little selection of cases, because so long as terramycin was available it was used in preference to any other antibiotic for infections of the feet.

It is very difficult to assess improvement or cure, because cases differ greatly and there are no criteria for comparison. Also it has been difficult to time the response to treatment in outpatients; for many of them are brought by ambulance from the country, and daily attendance is out of the question. When possible the patient was seen in forty-eight hours and again at the end of a week. In many cases it was impossible to isolate the infecting organism, because the skin-surface was intact. However, staphylococci of various strains, aerobic and anaerobic β-hæmolytic streptococci, coliform bacilli, *Pseudomonas pyocyanea*, Friedländer's bacillus, diphtheroids, and sometimes a mixture of these organisms, were often found to be more sensitive clinically than the laboratory tests indicated.

TABLE I—CONDITIONS TREATED WITH TERRAMYCIN

Condition	No. of cases	Results			
		Excellent	Good	Fair	Poor
Infections of feet	50	32	14	2	2
Infections of fingers	4	3	1	..	..
Postoperative wound infection, excluding amputation of toes	5	4	1	..	..
Thrombophlebitis following intravenous drip therapy ..	3	3	..	..	..
Urinary infection	6	5	..	..	1
Carbuncles, boils, and other skin infections ..	14	13	1	..	..
Respiratory-tract infection ..	6	6	..	..	..
Preoperative preparation for resection of colon ..	1	1	..	..	..
Panophthalmitis	1	..	..	..	1
Acute arthritis of mid-tarsal joint	1	..	..	..	1
Herpes zoster	1	..	..	..	1
Osteomyelitis of femur ..	1	..	1	..	..
Total	93	67	18	2	6

The dose of terramycin used was 0·5 g. six-hourly until it was found that 0·5 g. three times a day with, or directly after, meals was equally effective and more convenient for outpatients. Only 1 patient was given as much as 3 g. a day. The total dose ranged from 4 g. to an exceptional one of 46·5 g. for the one condition. The average total dose used was about 10 g. No terramycin was used in local application. It was used intravenously in 1 patient only.

There were 11 cases of diarrhœa in 93 treatments. In 1 case diarrhœa was severe; and in 1 other there was associated vomiting, but this usually ceased as soon as terramycin was withheld, and it bore no relation to the daily or total dosage. Vitamin-B complex was not given in these short courses of treatment.

TABLE II—INFECTIONS OF FEET

Age-group (yr.)	No. of cases	Duration of diabetes	No. of cases
80–90	3	Less than 1 yr.	9
70–80	22	1–5 ,,	14
60–70	19	5–10 ,,	7
50–60	5	10–20 ,,	17
40–50	0	More than 20 ,,	3
30–40	0		
20–30	1		

INFECTIONS OF FEET

This group includes simple infections and pregangrenous and frankly gangrenous conditions as the types of infection merge one into the other. Whether arterial occlusion is advanced or not, the common factor of infection can and should be vigorously treated from the earliest moment. There were 50 cases (table II) in 43 patients, of whom 7 were treated twice for two different foot conditions after an interval of weeks or months. In this group there were 34 women and 16 men. Associated deformity was present in 11 women and 2 men, and this high proportion of women may be partly explained by the traumatic effect of the footwear worn by the women. Hypertension was present in 74% of these cases, 40% having a systolic pressure of over 200 mm. Hg.

Pain was present in 25 patients, absent in 11, and unrecorded in 14, which indicates that it was not characteristic. Diabetic control was good in 36, variable in 7, and poor in 7 cases. About 40% of our patients had received previous antibiotic therapy, sometimes in unknown quantities at home and sometimes in full courses under controlled hospital supervision.

Terramycin was given to 33 outpatients, 11 inpatients, and 6 patients who were treated first in the outpatient department to clean up a foot, and then, when a bed became available, admitted for the operation of election. A second course of terramycin was given in some instances but was unnecessary in others. By these methods economy in hospital beds was effected.

ANCILLARY TREATMENT

No change was made in the routine ancillary treatment. Sufficient rest in bed with the limb horizontal is most certainly essential where the circulation is poor. For most patients this can be arranged at home: hyper-the presence of Gram positive organisms on culture", the organisms are not specified In these cases, however, cultures of sputum rarely contain no gram-positive organisms at all, and thus penicillin therapy would be indicated almost always in chronic bronchitis or bronchiectasis where the sputum is purulent Yet experience has shown that only some cases are benefited by penicillin, administered either by inhalation or by intramuscular injection BARACH and his colleagues report that penicillin by inhalation caused 'marked or moderate" improvement in 58 out of 70 cases of bronchiectasis, 46 out of 50 cases of chronic bronchitis without clinical evidence of bronchospasm, and 97 out of 200 cases of chronic bronchitis associated with bronchial asthma At first sight these figures may seem encouraging, but unfortunately in 20% of patients with bronchitis and asthma the inhalations increased wheezing so much that the treatment had to be discontinued It appears that penicillin administered intramuscularly to these patients gave less benefit than inhalations One reason for this was that with inhalations the concentrations of the antibiotic in the sputum ranged from 50 to 2000 units per ml—a range high enough to swamp many organisms not normally regarded as sensitive to penicillin BARACH et al remark that this applied to many apparently penicillin-resistant staphylococci It may also have applied to *Hæmophilus influenzæ*—a gram-negative organism which MULDER et al [15] believe to be the most significant pathogen in all types of respiratory infection

The studies by BARACH et al of the effects of the broad-spectrum antibiotics on chronic bronchitis and bronchiectasis shed little new light on the rôle of different organisms in these diseases As with penicillin inhalations the clinical responses were encouraging "Marked or moderate improvement, as judged by cough, expectoration and clinical well-being," was observed in 26 out of 31 cases of bronchiectasis and in 37 out of 45 cases of chronic bronchitis But the changes in the bacterial flora of the sputum in cases improved by this therapy do not seem to have followed any consistent pattern BARACH et al apparently attach great importance to *Staphylococcus aureus* This was present in the sputum of 11 patients after therapy, yet the condition of 9 of these had been improved considerably Similarly each of 7 patients in whose sputum Friedlander's bacillus was found after therapy had been greatly improved by treatment With regard to the pneumococcus, however, there was closer correlation between clinical improvement and eradication of the organism pneumococci were present in the sputum of only 2 patients after therapy, in neither of these had definite improvement been observed, but the eradication of pneumococci from the sputum of 15 other patients was in each case associated with improvement The pneumococcus has been found to be distributed intermittently in the sputum [13], and thus organism may have been present, but not detected, in the sputum of some of BARACH's cases where clinical improvement could not be correlated clearly with changes in the bacterial flora This is important, since the antibiotic of choice in such cases would always be penicillin, intramuscular injection of which would be adequate and free from the side-effects that may accompany the use of the broad-spectrum antibiotics The need for avoiding unnecessary use of the broad-spectrum antibiotics is once again evident from the fact that in the 76 cases of respiratory infection treated with these by BARACH et al there were no fewer than 7 deaths, all of which were ascribed to the development of infection by organisms highly resistant to all antibiotics

Mealtimes

EATING, besides satisfying a physiological need, reflects a psychological state, as in the overeating of the emotionally deprived and the anorexia nervosa of the despairing It has also a religious symbolism, while communal meals and ceremonial feasts make for sociability The body likes a rhythm of recurring mealtimes but is less particular about the time The traditional Englishman starts his day with a good breakfast of porridge and bacon and eggs, and later has a light lunch The Frenchman living in a similar climate goes to work after a cup of coffee and a roll, but lunches substantially Kaffirs prefer to wait for their big meal till evening, when the heavy labour is finished [1] Babies fed whenever they cry for food usually establish their own timetable of feeds every 3-4 hours [2] Hunger probably reflects internal metabolic rhythms,[3] about which little is known [4], and, like other biological rhythms such as sleep, it can be modified by training There are said to be separate hunger and starvation centres in the hypothalamus, at least in white rats and cats [5] destroy one centre and the animal overeats to extreme obesity, destroy the other and henceforth it refuses all food

Under more or less natural conditions the healthy man need not bother about all this his stomach will tell him when to eat Modern industrial life, however, is far from natural, and the relation between working performance and frequency of meals is of interest to factory managers, and also to athletes, schools, and the Services If the worker's blood-sugar level begins to drop towards the end of a shift, perhaps an interim snack would stay this decrease and maintain his output [7] Unfortunately, HUTCHINSON,[6] from his review of published work, mainly American, concludes that with the possible exception of breakfast the ingestion of food is not followed by an increase in industrial productivity or improvement in athletic performance indeed, a large meal may impair both, since it causes drowsiness and lack of coordination Yet we know that long periods between meals may give rise to restlessness, irritability, and diminished concentration, and HUTCHINSON goes so far as to suggest that efficiency may be greatest with small but frequent meals, numbering as many as six a day In research of this kind it is very difficult to disentangle the physiological effects of meals from the psychological value of the accompanying rest pauses, particularly when these break the monotony of repetitive work (BERGIN [7] advises meals every two

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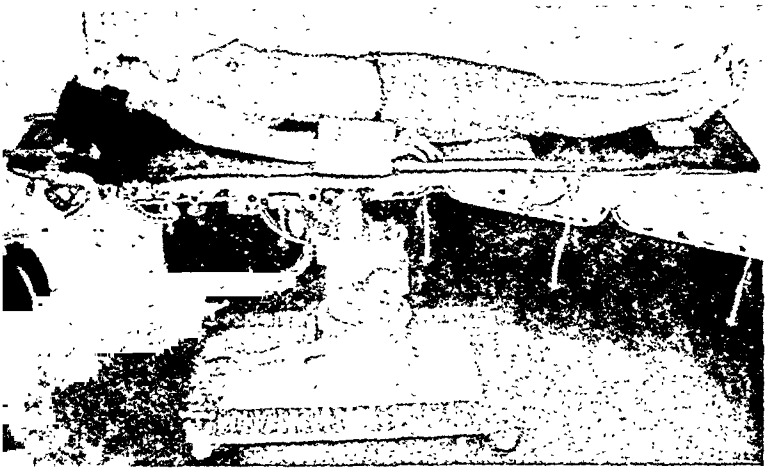

Fig. 2—Patient in position at start of operation, showing gap of 6 in. between shoulder rests and shoulders.

of the head and neck are increased. Two types of pelvic rests have been designed to take the pressure on the iliac crests (Ward 1950, Hans 1952), but both tend to get in the surgeon's way, and in fat patients bunch up the skin of the anterior abdominal wall. Suspension from the knees is sometimes practised by bending the lower part of the table, often in conjunction with shoulder-rests, but this causes stasis in the calf veins and almost certainly increases the risk of thrombosis with subsequent pulmonary embolism.

All the methods so far considered use pressure or traction on very limited areas of the body, and many years ago it seemed to me that it should be possible to "spread the load" over a much greater surface. Skin friction of the back is the most obvious choice, and indeed always plays some part in maintaining a patient in position. A 'Sorbo' mattress is usually laid upon the metal top of the operating-table, both for its cushioning properties and to limit the loss of body heat by conduction of the metal. When the table is tilted, slip first occurs between the rubber mattress and the table top. This can be avoided by sewing two canvas straps and buckles to the underside of the end of the mattress, and securing them to the bar which forms a hinge of the leg pieces of the table. An angle of about 20° can be obtained before the patient starts slipping down the mattress. The next step is to increase the frictional area between the patient's skin and the mattress, and this can be done by sewing on to the mattress sheets of the corrugated rubber which is supplied for cutting up into surgical drains. With this device (fig. 1) a tilt of 40° can usually be obtained before slip takes place, and this is sufficient for most gynæcological operations.

PRACTICAL DETAILS

If straps are used to secure the mattress to the table they should be crossed over diagonally to prevent slip over the corners of the table. Messrs. Allen & Hanburys are now making up this mattress with flat hooks which simply fit on to the foot of the table, and this eliminates the need for straps.

The patient's bare skin must rest directly on the mattress. This should be kept dry, but moisture does not affect the angle of slip as much as might have been expected.

Shoulder-rests should always be fitted as a precaution, and should be 6 in. from the patient's shoulders in the horizontal position (fig. 2). When the table is tipped, the initial slip *due to stretching* of the skin is about 3 in., and the shoulder-rests should then be 3 in. clear of the shoulders (fig. 3).

If possible, the height of the table should be adjusted before tilting, because jerky movements may start slip in a steep Trendelenburg position.

When the table has been tilted, the position of the oblong sorbo ankle-pad should be checked. This should not be under the heels but under the tendines achillis to prevent any pressure on the calf veins.

The patient's arms are usually secured at the sides with malleable metal strips covered with rubber which are pushed under the mattress and round the wrists (figs. 2 and 3).

If desired, one or both arms can be outstretched on a single or double arm splint, which is no more likely to cause brachial plexus palsy than if this position is adopted in the flat supine posture. It is then easy to read the blood-pressure in the right arm and to set up an intravenous drip in the left.

RESULTS

The ribbed mattress has now been in use for a large number of gynæcological operations, and so far no case of soreness of the back has been noted, although the horizontal ridges may be visible on the skin for some hours after operation. No antiseptic of any kind should be used on the mattress, scrubbing with soap and water being the method of cleaning.

I wish to thank Mr. N. E. Winstone, late senior resident anæsthetist to St. Bartholomew's Hospital, for his energy and patience in sewing the original prototype of the mattress; and Mr. N. K. Harrison, of the photographic department of St. Bartholomew's Hospital, for the illustrations.

ADDENDUM

Since the above was written, it has been found possible to eliminate the shoulder-rests completely. This has been accomplished by using three transverse bolsters under the patient. These are ⌓-shaped in section and are made of sorbo rubber, their upper surfaces being smooth and their bases corrugated. The smallest bolster is used as a tendo achillis pad as before described; the middle and largest one is placed under the patient's lumbar curve; while the upper pad fits behind the

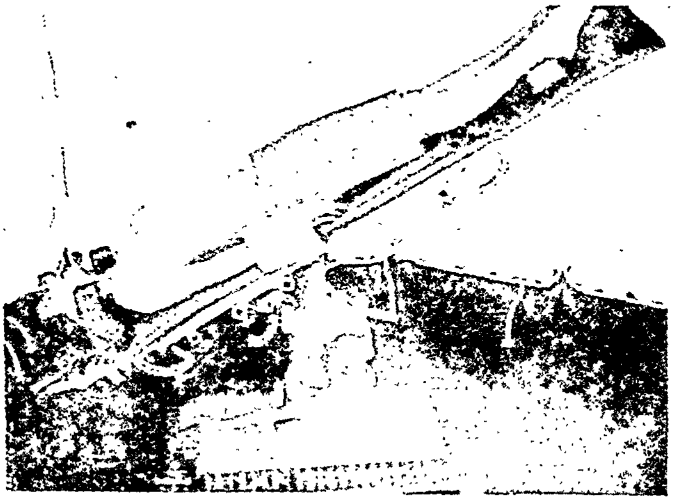

Fig. 3—Patient in Trendelenburg position, showing how initial slip has shortened gap between shoulder-rests and shoulders to 3 in. Note also method of securing wrists and position of ankle-pad keeping weight off the calf muscles.

published their final recommendations, prefaced by a short explanatory article [6]

The inquiries showed that opinions varied as to whether reading charts should be standardised in some form that could be readily reproduced, or whether they should merely consist of a series of standard graduated printer's types The types do not provide a regular gradation in the size of the detail, as is the case with Snellen charts, because the detail—e g , the gaps—is usually enlarged relative to the over-all size of the letters as the type gets smaller—a device which increases the legibility of the smaller types The recommendations of the council are designed to satisfy both schools of thought They suggest, for the first, facsimiles of Snellen distance charts photographically reduced to $^1/_{17}$ of the original size, to be read at 35 cm (14 in) To meet the second opinion, they recommend suitable passages of text printed in *Times* Roman type-face with "standard" spacing These should be in 5, 6, 8, 10, 12, 14, 18, 24, 36, and 48 point sizes (this type is 9 point) In addition a few isolated words made up of lower case small letters without ascenders or descenders—e g , arrow, cocoa, ransom—should be printed in each size These should remove the possibility of getting unduly high scores by guessing words from their context and from clues given by distinctively shaped letters The print should be on dead-white matt-surface cartridge paper or board, which may be varnished to increase durability The test may also include reproductions or actual examples of tasks important to individual patients, such as music, shorthand, or blue print work Suitable notations to be used for recording the results are also suggested

The council were clearly right in attempting to provide both a really scientific test, which should give comparable results in the hands of any competent tester, as well as one likely to ensure that the special needs of the individual patient are covered The suggested photographic reductions of Snellen charts are, from the scientific point of view, much superior to the miscellaneous types at present in use, particularly if the distance at which they are to be read is kept constant as recommended But no method of fixing the reading distance is suggested This could easily be done by mounting the test card on a holder at a specified distance from a facepiece—a method in common use in the classroom If, however, a test like this, which may well seem irrelevant to the patient, is to be commended for its scientific value, it seems a pity to use the Snellen letters at all All letters are not equally legible, and recent work has shown that this is because legibility is dependent not only on the size of detail, as Snellen thought, but also on such things as the relation of height to width and the thickness of the lines The relative importance of these factors varies with the shape of the letter A test should therefore consist of different positions of a symmetrical pattern or letter, and for this purpose the Landolt C is probably as good as any, particularly since much work has already been done with it Admittedly, the scoring of results with the C is rather more troublesome than with Snellen letters, but the gain in repeatability should outweigh this difficulty

As the council point out, it is important to use a test chart at a fixed distance, in spite of possible difficulties with patients whose reading distance is not that recommended It is, therefore, surprising that they have made no recommendation about, or indeed any mention of, the illumination to be used Unless the test is made with an illumination of about 20 foot candles or more (this applies not only to the chart but to its surroundings), the visual acuity recorded will be considerably affected by the amount of light used The importance of standard (and adequate) illumination for distant vision tests is now generally recognised , and standard lighting is no less important in testing near vision

One small point arises out of the recommendation that type should be printed on a dead white matt surface In this way maximum contrast and absence of specular reflection are ensured But, realising that the charts will quickly get dirty and lose their contrast, the council go on to suggest that the charts may, if necessary, be varnished to increase durability Varnishing produces the specular reflection that is avoided by using a matt surface, and at once makes the direction of lighting a matter of importance Probably all test charts should be varnished

But these criticisms are slight, and the greater part of the recommendations are excellent, although there may be differences of opinion as to whether *Times* Roman type-face is likely to be the most satisfactory Moreover, the recommendations aim at standardising reading types, not reading tests All the same, a really standard test, based on the best available data, is needed There are, for instance, many compensation cases where the question of a possible deterioration of vision arises and where no satisfactory answer can be given unless comparable tests have been made, often many years apart Further, nearly every young man in the country (to say nothing of children at school) has his sight tested when he starts his National Service These records could be, and indeed are, used for statistical analyses The results would be more convincing if the tests were not suspect on the point of standardisation It seems unlikely that industrial concerns or the Armed Services will revise their methods of sight-testing unless the ophthalmologists point the way

ADRENALECTOMY AND CARCINOMA OF THE PROSTATE

THE inhibition of growth of prostatic tumours which follows the suppression of the action of the testes, whether by orchidectomy, hormones, or irradiation, is unfortunately only temporary Renewed prostatic growth, presaged by rising levels of serum acid phosphatase, is accompanied, according to Huggins, by a growing tide of androgens, which even continuous œstrogen therapy is unable to stem It is not unreasonable to interpret the reappearance of androgenic metabolites as a compensatory increase in the activity of the adrenal cortex, and to assume that the androgens are responsible in some way for renewed prostatic growth, but it seems a bold step to use these deductions as a basis for the treatment of prostatic cancer by bilateral adrenalectomy and orchidectomy It is interesting, however, to hear of the results obtained by the Harvard school [1] in attempting to control the adrenal cortex as a supplementary source of androgens by means of the inhibitory effect of cortisone upon its growth and secretion In each of 9 patients with prostatic carcinoma receiving 23–37 mg of cortisone per day, a fall in the daily excretion of urinary 17-ketosteroids suggested considerable adrenocortical inhibition, yet the clinical improvement claimed was modest An improved sense of well being and some relief of pain, in the absence of any objective signs of tumour regression, failed to reflect the considerable reduction in androgen background By contrast, an impressive fall in serum acid phosphatase from 333 to 5 8 Gutman units in ten days, accompanied by loss of pain from bony metastases, was observed in a patient receiving 100 mg of cortisone per day, but no details of 17-ketosteroid output are given It is an unfortunate feature of this treatment that high doses of cortisone can themselves be responsible for an increase of urinary 17 ketosteroids

The 7 patients selected for bilateral adrenalectomy were manifestly poor material, showing, in spite of orchidectomy and continuous œstrogen therapy, a renewal of primary growth and well established secondaries Yet in spite of these initial disadvantages, the hazards of operation and of cortisone substitution therapy seem to have been overcome 5 patients, who had previously needed sedatives, were free from pain after adrenalec-

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[6] Law, F W *Ibid*, 1952, 36, 689

[1] Harrison J H Thorn, G N , Jenkins D *New Engl J Med* 1953, 248, 86

TABLE I—URINARY FINDINGS IN 5 CASES OF CONGESTIVE FAILURE DUE TO EMPHYSEMA AND EXACERBATION OF CHRONIC BRONCHITIS

Case no.	Age (yr.)	Duration of failure on admission to hospital	Blood-pressure on admission (mm. Hg)	Electrocardiogram	Urinary findings: First examination: Colour	Sp. gr.	Reaction	Albumin	Other abnormalities	Subsequent examinations: Colour	Sp. gr.	Reaction	Albumin	Other abnormalities	Microscopy of centrifuged deposit	Blood-urea (mg. per 100 ml.)	Remarks
1	69	3 mos.	160/100	..	..	1·010	Acid	—	—	Straw usually	1·010–1·025	Acid	—	—	..	..	Died 3 weeks after admission. Preterminal blood-urea of 120 mg. per 100 ml.
2	66	3 weeks	70/46	R.A.D. pulmonary P waves in leads II and III	Straw	1·022	Alkaline	—	Slight reduction of Benedict's solution	Straw usually	1·012–1·020	Acid or Alkaline	—	Slight reduction of Benedict's solution on two occasions	No abnormality	34	Recovered. B.P. rose to 120/70
3	64	4 weeks	134/70	Large S waves, pulmonary P waves in leads II, III, CR_1 and CR_4	..	..	Acid	—	—	Straw or amber	1·010–1·020	Acid	—	—	No abnormality	37	Died 3 weeks after admission. Preterminal blood-urea of 152 mg. per 100 ml.
4	58	3 mos.	90/70	..	..	1·010	Acid	—	—	..	..	..	..	..	..	..	Died 37 hours after admission
5	61	3 weeks	140/90	R.A.D., pulmonary P waves in leads II, III, CR_1 and CR_7	..	1·018	..	+	— (Specimen obtained while patient was in circulatory collapse)	Straw usually	1·010–1·022	Acid or Alkaline	—	—	No abnormality	35	Recovered

TABLE II—URINARY FINDINGS IN 2 CASES OF CONGESTIVE FAILURE DUE TO EMPHYSEMA WITH BRONCHIECTASIS AND PULMONARY FIBROSIS

Case no.	Age (yr.)	Duration of failure on admission to hospital	Blood-pressure on admission (mm. Hg)	Electrocardiogram	Urinary findings: First examination: Colour	Sp. gr.	Reaction	Albumin	Other abnormalities	Subsequent examinations: Colour	Sp. gr.	Reaction	Albumin	Other abnormalities	Microscopy of centrifuged deposit	Blood-urea (mg. per 100 ml.)	Remarks
6	56	Several weeks	115/70	R.A.D., pulmonary P waves in leads II, III, and CR_1	Amber	1·030	Acid	+	—	Amber	1·018–1·030	Acid	—	Occasional slight reduction of Benedict's solution	Red cells and leucocytes	49	Œdema and hepatomegaly disappeared with treatment; urine became normal; blood-urea level fell to 25 mg. per 100 ml., heart remained large, B.P. 110/75
7	19	Several weeks	160/110	Right bundle-branch block	..	1·020	Acid	—	—	..	..	..	+ or —	—	No abnormality	21	Œdema and hepatomegaly disappeared with treatment; heart remained large

All patients were males. R.A.D., right axis-deviation; +, present; —, absent. Chest radiograms in case 6 showed persistent shadowing in left lower lobe; a bronchogram had previously revealed bronchiectasis in this lobe. In case 7 radiography showed shadowing in left upper and middle zones, with mediastinal shift to the left, and shadowing in the region of the right middle lobe; a bronchogram of the right lung had previously shown bronchiectasis in the right middle lobe.

Perhaps severe oliguria, a raised blood-urea level, albuminuria, and abnormalities of the urinary deposit are not features of congestive heart-failure due to chronic pulmonary disease when there is a high cardiac output and reversible pulmonary hypertension.

I wish to thank Dr. J. Robertson, M.R.C.P., for permission to report on patients admitted under his care; and Dr. D. P. Belgrave and Dr A Griffiths, house-physicians at St. Clement's Hospital, and Sister V. Morse and her nurses for their cooperation.

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with pyridoxine is confirmed in a controlled trial Meanwhile Waldman and Pelner cannot explain the adjuvant effect

PULMONARY HYDATID DISEASE

PULMONARY hydatid disease is unusual in this country, but it does crop up from time to time among those who live in close contact with dogs Infection with *Tænia echinococcus* is commonest in country districts but it is also found in towns where stray dogs can gain access to the offal of infected sheep in slaughterhouses When an ovum excreted by a dog enters a human stomach, the small embryo develops and finds its way in the portal blood-stream to the liver A few embryos may get through the liver and will not then be held up until they reach the lungs Wherever it lodges the embryo may give rise to a hydatid cyst

In the lung, the cyst usually grows silently, and the majority are found unexpectedly on X-ray examination of the chest Sometimes, however, the enlarging cyst causes cough, hæmoptysis, and pain, and it may rupture, producing sudden expectoration of a large amount of sputum containing blood, hydatid fluid, and fragments of membrane After a cyst has ruptured the foreign protein of the fluid may cause severe anaphylactic shock, which is occasionally fatal There are several possible consequences of rupture the entire cyst and all its membranes may be coughed up, leading to spontaneous cure, but more often the rupture is partial, and after the loss of some fluid the cyst seals itself and the parasite continues to grow A partial rupture may open up the potential space between the outer laminated membrane of the cyst and the surrounding adventitia of compressed lung If this happens air may leak in from the surrounding lung and the cyst develops a small crescentic cap of air, which gives it a characteristic radiological appearance, the so called "perivesicular pneumocyst" Sometimes after rupture the parasite dies, if it is not expectorated it remains as a foreign body in the lung, and sooner or later infection gives rise to a hydatid abscess Hydatid fluid is always potentially dangerous because of the risk of anaphylactic reactions and of dissemination There is a distinct chance of fresh daughter cysts developing if hydatid fluid enters the pleural cavity, but surprisingly the spilling of fluid within the lung itself does not lead to fresh lesions, so that multiple cysts in the lungs show that more than one embryo has reached the lung from the liver The Casoni intradermal test may help in diagnosis, and, though reliable fluid for the test has been hard to get, the use of standardised reagents both for the intradermal and the complement fixation tests has lately given very good results[1]

The treatment is surgical, for there is no drug which will kill the parasite in the tissues, and, even if there was, it would still leave a dangerous foreign body in the lung Hitherto, all the operations designed to deal with hydatid cysts in the lung have involved a risk of contaminating the pleura with hydatid fluid and they have often been followed by severe postoperative complications Lobectomy or pneumonectomy certainly enable the cyst to be removed entire, but they mean the sacrifice of healthy lung tissue, and this operation is now reserved for infected cysts To get round these difficulties, Barrett and Thomas,[2] whose experience of 71 cases in fourteen years must be unique in this country, have devised an ingenious operation whereby the whole cyst can be removed without lung tissue The operation takes advantage of the potential space between the adventitia and the cyst proper After dissecting down to the laminated membrane, the cyst, protected by a sort of rubber sponge bag, is allowed gradually to herniate out of the lung with each breath until finally it is free "The moment when a hydatid rolls out of the lung intact is one of the most satisfying in surgery" Since this operation was devised, it has been performed successfully on 17 occasions It is suitable for smaller cysts, provided that they are uncomplicated, but not for the large ones, which are better removed through the plane of cleavage which separates the adventitia of old cysts from surrounding lung After a cyst has been removed the empty space within the lung may persist for many months, but Barrett and Thomas say that this seldom gives rise to any trouble Complicated and infected cysts must still be dealt with by lobectomy, pneumonectomy, or even pleuropneumonectomy

AN INTERNATIONAL MEDICAL CHARTER?

THE movement towards closer study and more rapid development of international medical law is of such recent origin that many doctors and lawyers in this country are still unaware of its purpose and practical importance We therefore welcome the publication of a series of lectures[1] delivered last year by Prof Paul de la Pradelle to fifth year medical students of the University of Aix en-Provence and to student members of the French Overseas Army Medical Corps, for they should bring before a wider audience a survey of the beginnings, aims, and methods of this movement M de la Pradelle, professor of international law at Aix, is closely associated with the group of lawyers and doctors in France and Belgium who have recognised the need for clear definition and international protection of the status of the medical profession in war and peace, and who are trying to persuade their colleagues all over the world of the urgency of this task International medical law has already been given a place in the medical syllabus at the Universities of Marseilles and Bordeaux in accordance with the wish of the Académie de Médecine

The humanitarian work of the doctor has always been a subject for truly international cooperation The international medical law movement seeks definite legal recognition of the special status of the medical profession at the international, as well as the national, level, and it wants international guarantees and safeguards which will protect and, as far as possible, facilitate medical work in times of international tension no less than in war itself To this end, the movement hopes eventually to obtain acceptance by all governments of what, for want of a better term, is provisionally called an "international medical charter," which will define, regulate, and above all protect the rights of medical men vis à vis their own and foreign States in peace as well as war

Before it can find such general recognition, international medical law has a long way to go, but already several important bodies, such as the World Health Organisation, the World Medical Association, and the Mixed Medico Legal Commission of Monaco, have made a beginning, albeit embryonic, of an international organisation for medicine Moreover, there is already a hard core of positive international law, affecting the status of doctors in war, in the Hague and Geneva Conventions, discussed in one of Professor de la Pradelle's lectures Though the Geneva conventions were generally respected during the late war, and have proved of great benefit as far as they go, many people consider that they do not give nearly enough protection to civilian doctors who find themselves either in captivity as temporary members of the army medical services or under an occupation régime Moreover, it is now clear that there are two very different points of view there are those who insist on a belligerent's right to detain enemy medical personnel and to treat them as prisoners of war in order to prevent them from aiding, once again, in the recuperation of a satisfactory response. In others it appeared possible to stabilise the mother's condition. The longest course lasted thirty-eight days. In terms of fœtal survival, however, the results were poor: 6 live infants from 10 mothers receiving oral hexamethonium, and 5 from 14 treated intramuscularly. Analyses of cord blood and amniotic fluid showed that hexamethonium quickly crossed the human placenta. 2 infants who died about the seventh day showed gross intestinal dilatation, and another, who survived, was late in passing meconium; this might mean that the drug was inducing a paralysis of the child's gut. Another infant, who died of bronchopneumonia, might have aspirated liquor containing the drug. Further investigation might reveal other reactions in the fœtus.

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[1] Bensted H J, Atkinson, J D *Lancet*, Feb 7 1953 p 265

[2] Barrett, N R Thomas, D M E *Brit J Surg* 1952 40, 222

[1] de la Pradelle, P Le Droit Médical International Paris, 1952

Salmonella Infections in Man and Animals

THE society's section of epidemiology and preventive medicine met on Feb. 20, under the chairmanship of Prof. ROBERT CRUICKSHANK, president of the section, to discuss the epidemiology of salmonella infections in man and animals, with special reference to *Salmonella dublin*.

Dr. JOAN TAYLOR, discussing infection in man, said that salmonella infections were very common, the number reported having increased in recent years. This increase was only partly due to improved methods of collecting reports. Excluding the enteric organisms, *S. typhi-murium* was the commonest, accounting for almost 75% of the 5094 cases in 1949–51. Endogenous types—those recognised in this country before 1939—caused about 92% of cases. The endogenous type of *S. dublin* was responsible for comparatively few cases —about 1–2%. Irrespective of the type of infecting organism, each year the total number of patients in epidemics exceeded the number of sporadic cases. An analysis of patients' clinical histories in relation to type of infecting organism showed that with *S. typhi-murium*, *S. enteritidis*, *S. newport*, and *S. thompson* the largest group of patients were ill for 4–7 days, whereas, with *S. dublin* the largest group were ill for over 17 days. In addition, the fatality-rate was higher for *S. dublin* than for the other organisms mentioned.

Mr. REGINALD LOVELL, D.SC., discussing disease in animals, said there were three main groups of salmonella infections: those almost exclusive to man, those exclusive to animals, and those which attacked both man and animals. *S. dublin* was associated with cattle, and *S. thompson* with poultry; yet before the late war the only infections in poultry were *S. pullorum* and *S. gallinarum*. By contrast, in the U.S.A. poultry were then regarded as the main reservoir of infection. There was a high frequency of *S. dublin* infection in Wales, but not in other parts of the country. Dr. Lovell believed that the pattern of host-organism infections, and also the range of susceptibility to a given type, might change. Many diseases (for example, distemper and swine fever) that were now known to be caused by viruses had been attributed to salmonellæ. In South Africa calves with both parasitic and *S. dublin* infections were more likely to die than if they had either infection alone. The effect of dual infections must always be borne in mind. In a *S. dublin* outbreak in a dairy herd in Wiltshire useful information was gained from the agglutinin titres of the cows' serum. The titre at which infection could be presumed to be present varied with the age of the animal.

Dr. A. M. MCCALL described his experiences in Somerset. Since 1947 there had been 14 outbreaks of *S. dublin* infection—3 human, 10 bovine, and 1 among foxhounds. Of two human outbreaks in 1947 the first was at Bishopsworth, where 30 people were known, and 200 believed, to have been infected; and the second at Wadford where 29 cases were reported. A third outbreak occurred in 1953 at Chard, where there were 600 known cases. This outbreak was notified by a headmaster; later the same morning it was found that twelve schools were involved. All general practitioners were notified. From an examination of school lists and a knowledge of the absentees it was evident that the outbreak was milk-borne. Tuberculin-tested milk was supplied from a single farm; the morning and evening milkings were pooled and transported to the dairy, where it was bottled and refrigerated. Of the daily production of 150 gallons, 90 were supplied to schools. A surprising finding was that among children taking milk the infection-rate was higher in a secondary than in an infants' school. The incubation period was 20–30 hours. The main symptoms were nausea, vomiting, fairly severe abdominal pain, severe frontal headache, and pronounced pallor. The temperatures varied from 99° to 105°F. There was very little diarrhœa, and most patients had recovered in 4 days. There were no deaths. The infection of the milk was traced to a sick cow with *S. dublin* infection of the udder. Subsequently three other cows were found to be infected; all were slaughtered. The origin of the cows' infection was not discovered. As a result of the outbreak more than 3000 school days were lost. Only 2 adults reported ill.

In the subsequent discussion Dr. B. FREEDMAN described the case of a girl, aged 13, admitted to hospital with acute nephritis and rigors. *S. dublin* was isolated from the urine. It was debatable whether *S. dublin* caused the nephritis, from which the patient died. It was pointed out that Dr. Taylor's figures suggested that *S. dublin* was invasive, whereas Dr. McCall's evidence suggested a relatively trivial illness. The PRESIDENT suggested that this difference might be due to differences in age.

Reviews of Books

Anatomy of the Autonomic Nervous System

G. A. G. MITCHELL, O.B.E., CH.M. Aberd., professor of anatomy and director of the anatomical laboratories, University of Manchester. Edinburgh: E. & S. Livingstone. 1953. Pp. 356. 55*s*.

A BEAUTIFULLY produced and illustrated book, this deals mainly with the anatomy of the autonomic nervous system in man. As Professor Mitchell emphasises, some people make sweeping generalisations based on comparative anatomical studies without due allowance for differences in various species, and he takes special care not to commit this error. There is a very full account of the peripheral autonomic system and there are admirable descriptions of the hypothalamus and its connections and of the connections of the frontal lobes. This is not a book to read straight through, but it is a work of inestimable value for reference—the best modern account of the complexities of the autonomic nervous system.

Office Psychiatry

LOUIS G. MOENCH, M.D., assistant clinical professor of medicine and of psychiatry, University of Utah School of Medicine. Chicago: Year Book Publishers. London: Interscience Publishers. 1952. Pp. 310. 45*s*.

MUCH of the day-to-day psychiatry in this country is done by the general practitioner, who will be glad of any textbook that will help him in an exacting and often thankless task. Dr. Moench reminds his readers that whereas organic disease is socially acceptable mental disease is not; and he discusses in everyday language the commoner neuroses and psychoses and outlines a reasonable psychiatric approach to them. The first step in successful psychiatry, he says, is for the doctor to be willing to suffer neurotic patients gladly. Rapport cannot be established between the patient and a doctor who is gruff, aloof, superior, cold, or bored; "he must be broadminded and like people." Among the many aspects of this vast subject, tackled in an agreeable conversational style, are the development and growth of personality, adolescence, suicide, toxic psychoses,

Special Articles

SOME CONDITIONS TREATED IN SCHOOL ORTHOPÆDIC CLINICS

K F HULBERT
M B Lond , F R C S , D A
CONSULTANT ORTHOPÆDIC SURGEON TO THE DARTFORD GROUP OF HOSPITALS, TO THE BECKENHAM, BROMLEY, AND WELLING SCHOOL CLINICS, AND TO SYDENHAM CHILDREN'S HOSPITAL

THE school orthopædic clinic has come to be regarded by many as a waste of time and effort This is largely because of the monotonous nature of the cases and the poor results of treatment

The school clinic allows little time for any positive clinical research , but it does provide a good opportunity for studying those statements on the treatment of minor orthopædic deformities, which have been handed on from teacher to pupil for so long without being questioned or tested For instance, for deformities of the feet, a stock remedy is prescribed, the futility of which is there for all to see

The following observations on some of the problems confronting the school orthopædic surgeon are therefore presented in the hope of stimulating some interest in this rather stagnant clinical backwater

Valgus Ankles

This is an unfortunate term because the ankle-joint is the only joint of the foot not involved in the deformity It is a good term, however, because everyone happens to know what it means—an inward falling of the longitudinal arch of the foot, like the handle of a bucket —and its use is preferable to the older term " flat foot " The longitudinal arch is very rarely flattened , on the contrary, there is often a cavus deformity present

Valgus ankles can be divided into two main groups —those associated with organic deformity, and those not The former, or organic group, is the minor group, but the recognition of organic deformity is important in the understanding of the condition The deformities usually encountered are pes cavus, tight tendo Achillis, and unstable inner segments

PES CAVUS

This deformity appears to be more common than is generally realised About a quarter of the cases referred to my clinics for " flat feet " were found to have various degrees of pes cavus The high longitudinal arch is less stable and more difficult to maintain in its erect position than the normal arch, and it falls over sideways, giving the appearance of flattening when viewed in perspective from the medial aspect Mild degrees of pes cavus are best seen from the lateral side, from which aspect the lateral longitudinal arch is seen to have an upward bend at the level of the tarsometatarsal joint The condition may or may not be associated with a tight tendo Achillis The cavus foot with a tight tendo Achillis is a nasty foot, because it seems to destroy shoes with alarming rapidity The lesion in the shoe is variable in some cases the sole wears out beneath the metatarsal heads, while in others the heels are trodden down at the back, and the uppers are broken down behind the heel The most puzzling lesion of all is the shoe trodden down on the outer side, producing in advance a valgus wedging The lesion is serious in that only the expensive high-quality shoe can stand up to the trauma, unless we concede a point and allow crêpe-rubber soles, which seem to have an elastic defence to aggression

I have treated this condition for some time now with metatarsal insoles I was frankly sceptical to begin with, but have been agreeably surprised with the results There are two kinds of metatarsal insole, the comfortable and the corrective The comfortable type, like the middle aged spread for which it is prescribed, is broad and soft The corrective type, like the youth for which it is fitted, is slim and tough—to be precise, it is 1/4 in. high by 1/2 in broad and is straight The insole is deliberately made uncomfortable to produce a withdrawal reflex , and, if it is worn constantly, many mild cases are improved and symptomatic relief is obtained in others

TIGHT TENDO ACHILLIS

This has been claimed as a major cause of valgus ankles, but in my experience this is not so, and this group has been found to be only a small proportion of the whole

The patients were all treated by exercises to relax the tendo Achillis, and it was found that, whereas most of them responded to treatment, quite a number were totally resistant The cases that responded showed quite clearly that curing the tight tendo Achillis does not cure or influence in any way the valgus ankles The cases that were resistant were mostly discharged with no functional disability, but some of these children persisted in treading out the back of the upper of the shoe round the heel Some of these cases were treated by stretching under anæsthesia, followed by immobilisation in plaster I was saved from doing a tendon elongation by seeing a boy on whom this had been done his calf was wasted, he had a calcaneus deformity of the heel, and, whereas before he could run and jump, now he could do neither

UNSTABLE INNER SEGMENT

Various names are attached to this deformity— inverted forefoot, supinated forefoot, metatarsus primus elevatus—and it is a true deformity of the foot When the foot is viewed from in front, with the heel held in the hand in correct alignment with the leg, the forefoot should be parallel with the floor The most intractable variety of valgus ankle is that in which the forefoot is inverted when viewed from the front as described, the inversion being anything up to 60° The reverse deformity may occur in pes cavus—a kind of metatarsus primus depressans (an ethnographical monstrosity that I trust will be stillborn) Care must be taken when examining the infant's foot, because an infant can raise and depress its inner segment at will

The treatment of unstable inner segment is one of great difficulty, and is apt to cause disappointment and often depression It is said that we tend to judge ourselves by our intentions and others by their achievements, and in nothing is this more true than in the treatment of this deformity

The aim of treatment is one of derotation of the forefoot, and the usual way is to start with simple procedures (inside) Firstly, then, valgus wedges to the heels only should be tried , wedging of the sole also defeats its object by inverting the forefoot Valgus wedging of the heels, and varus wedging of the soles, while appearing sound in theory, usually fails because the rigid shoe of today does not conform to the altered alignment of the sole, and because the deformity does not respond to the glib formula " wedges and exercises " Where the child, in response to wedging, treads inwards on the upper, a valgus stiffening must be added The usual complaint, however, is not of the feet but of the shoes The parent presents a pair of shoes trodden down on the inside (when the treatment is valgus wedging to the heels) or with the upper broken down on the inside (when the treatment, besides wedging, is the addition of valgus stiffening), or a pair of shoes trodden down on the outer side It is this last mentioned deformity of the shoe that is most interesting and baffling The first reaction (" You have a very clever child who anticipates treatment by wedging his shoes

THE LANCET

LONDON: SATURDAY, MARCH 14, 1953

Determination of Blood Volume

Measurement of the plasma volume by means of dyes,[1 2] or of the total red blood-cell volume by labelling with radioactive phosphorus,[3] causes the patient very little discomfort, is quickly completed, and is reasonably accurate; yet neither of these methods has been brought into general clinical use. Berlin et al.[4] now claim that "the determination of the blood volume turns out to be of great importance in the handling of major medical and surgical problems," but we doubt whether this need be added to the load of "routine investigations" borne by the long-suffering patient. On the other hand patients are benefiting every day from such estimations in research—as may perhaps best be illustrated by reference to the management of hæmatemesis. Nowadays in deciding for or against transfusion it is assumed that the hæmoglobin level and red blood-cell count soon after hæmatemesis are *misleadingly high*, giving little indication of the amount of blood lost. This assumption is made without subjecting the patient to determination of the plasma volume; but it is based on many blood-volume determinations in patients with hæmatemesis by the late Izod Bennett and his colleagues.[5] Similarly, the demonstration by Berlin et al.[6] themselves that large amounts of blood are lost during thoracic operations is not a reason for extending their research procedure to *all* such cases, though it is a good ground for liberal transfusion—a measure which they take by giving routinely a litre of blood.

Measuring total red-cell volume with radioactive phosphorus, Berlin et al. have shown that in cancer, uræmia, pulmonary tuberculosis, and hepatic cirrhosis there is a true reduction in red-cell *mass* and not merely a reduction in the red-cell count due to hydræmic plethora. Unfortunately, extension of this method to measure total blood volume, by dividing the red-cell volume by the hæmatocrit percentage and multiplying by 100, involves an additional source of error in the hæmatocrit percentage. It is almost certainly wrong to suppose that the venous hæmatocrit represents the proportion of red-cell volume to total blood volume throughout the circulation; Barnes et al.[7] found that the red-cell volume, calculated from hæmatocrit and plasma volume, was 13% greater than the red-cell volume measured directly by the Ashby technique; and from a further analysis[8] they concluded that the chief cause of this discrepancy was unequal distribution of plasma and red cells through the circulating blood. Mixing of the blood is not likely to be any better in patients with congestive cardiac failure, and the figures given by Berlin et al. for total blood volume and for plasma volume, *obtained* by difference, must be accepted with some reserve. They claim that patients in congestive failure secondary to "arteriosclerotic or hypertensive cardiovascular disease" have a blood volume which is "low, normal, or at most slightly elevated." In rheumatic heart-disease with congestive failure, however, the "blood volume was almost uniformly elevated." Some of the patients with a normal blood volume did have an increased plasma volume; and these workers express surprise that some patients with normal blood volume had "engorged vessels and tissues full of blood." Other studies on the blood volume in congestive heart-failure, by means of the labelled red-cell and hæmatocrit method, are similarly conflicting[9 10]; and until closer agreement is reached physicians will be tempted to accept the witness of their unaided senses that these patients are plethoric. One possible further method, which has already been applied in congenital cyanotic heart-disease,[11] is to measure red-cell volume and plasma volume simultaneously by a dye method. This evades the use of the hæmatocrit percentage, but is open to the criticism[12] that in congestive heart-failure dye may leave the vessels with abnormal facility, so giving an exaggerated estimate of the plasma volume. Comparison of "direct" determinations of the plasma volume with "indirect" determinations involving the hæmatocrit might help to decide whether loss of dye in congestive heart-failure is in fact excessive.

Our sympathy goes out to investigators of congestive heart-failure, which cannot be induced in animals, has a *guilty* liaison with that mysterious organ the kidney, and complicates the interpretation of the methods used for its study.

Antibiotics in Chronic Respiratory Infections

Clinicians are alive to the dangers of administering antibiotics indiscriminately. In such diseases as chronic bronchitis and bronchiectasis, however, it is often difficult to be sure which organisms are pathogens and which are harmless saprophytes; and this uncertainty is increased by the risk that orthodox methods of culture may fail to reveal the true bacterial flora of the sputum.[13] In these chronic diseases, therefore, antibiotics cannot be administered as rationally as in, for example, acute pneumococcal pneumonia or streptococcal sore throat: the chemotherapy of chronic bronchitis and bronchiectasis is to some extent "blind."

Barach et al.[14] have investigated in some detail the response of these two conditions to penicillin, given mainly by inhalation, and to "broad-spectrum" antibiotics—chloramphenicol, aureomycin, and terramycin. They name the indications for penicillin therapy in cases of chronic productive cough as "the demonstration of pus cells in the sputum as well as

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A case of genu varum should therefore be reviewed at the age of 3

Envoi

The school orthopædic clinic has become the ugly duckling of the orthopædic world I hope that the present observations will have shown that it is not devoid of interest or humour, and that it is still a profitable sphere for human endeavour and enterprise For those who feel that their talents are being wasted and aspirations unrealised in this kind of work, it is well to remember that even Napoleon came to feel himself "as the prisoner of necessity and the plaything of a relentless destiny"

THE WORLD'S FOOD-SUPPLY

On Jan 28 the food group (nutrition panel) of the Society of Chemical Industry held the second meeting of their series on Food and the Future The meeting was devoted to present methods of attack on the problem

Mr G A C Herklots, ph d , secretary for Colonial Agriculture Research, spoke of semi-starvation from personal experience, having been interned by the Japanese for 43 months During this time he cultivated yeast on old flour and soya-bean residue, and thus cured the early stages of pellagra and checked the spread of central blindness among the inmates of the camp

Before the late war Chinese refugees from the Sino Japanese war poured into Hong-Kong and swelled the population to 1,800,000 Many were in poor health, and deaths from beriberi reached 1000 per month with a rising, though smaller, mortality from pellagra The diet was grossly inadequate and food production was low

One contributory cause to the low production of food was the plight of the fishermen They normally marketed their catch through a middleman with little profit to themselves In hard times they borrowed money from the middleman and finally lost their independence As a result the fishermen were never able to better their position or to experiment with new gear or methods In accordance with plans drawn up during the late war, the fish is now sold by public auction, which results in prompt payment to the fishermen of the full value of their catch Thus fishing-boats from many coastal villages of China bring their catch to Hong-Kong , fishermen are able to modernise and re equip their boats and gear , and the quantity of fish for the inhabitants of the area has increased enormously A similar scheme for marketing vegetables has trebled the 1947 output and local production now accounts for 75% of the consumption

The result of these improvements is that the $2^1/_2$ million population of Hong-Kong, including 1 million refugees, shows little evidence of malnutrition or deficiency disease

Prof J Yudkin described the methods that are being adopted in Israel to feed its expanding population

The swamps round Lake Huleh are being drained, so that fertile soil has been reclaimed and malaria virtually abolished Artificial ponds are being created in which carp are grown which supply about 5000 tons of fish per annum—half the total consumption At the same time large deposits of peat are being discovered, which are useful both as fuel and as soil improver The Huleh project will provide nearly 15,000 acres of new cultivable land and save enough water to irrigate a further 50,000 acres

The hilly areas are fertile but strewn with huge rocks, which are mostly removed by hand In these areas heavy rains cause erosion which is being controlled by contouring and afforestation The water problem is also being dealt with by the construction of reservoirs and dams

The northern Negev is scheduled to play a large part in food production The Lowdermilk scheme for irrigating the Negev called for diversion of the river Jordan and a canal from the Mediterranean to the Dead Sea, which would also provide a considerable source of hydro electric power The full scheme is held up by external conditions, but smaller projects are in hand

As a result of these activities food production has increased rapidly in the last four years Vegetable production has doubled, and new crops, such as sugar beet, are being produced At the same time the local production of fish has increased from 16 to 30% of the consumption , the number of cattle has increased from 35,000 to 65,000, while milk and egg production have doubled The average consumption of milk, however, is still low and has been greatly supplemented with dried skim-milk

Professor Yudkin described the bread as excellent, being not only palatable but of 85% extraction and fortified with dried yeast and vitamins He emphasised the importance of mechanisation in agriculture in Israel—the number of tractors has risen in four years from 360 to over 4000—and of the use of waste products, such as orange peel and olive waste, in animal feeding Limitations are imposed by shortage of power and deficiencies in transport Israel is being transformed by the aid of severe rationing—the sacrifice of present living conditions for the future

In the discussion, Sir Harold Tempany referred to the production of foodstuffs for export by peasant communities—for example, the production of groundnuts in Nigeria Western countries are too apt to regard these areas as convenient sources of supply which can be relied on indefinitely India exemplifies the fallacy of such a belief , here the export of groundnuts, formerly the largest in the world, has almost ceased because of increased home consumption With regard to expansion of yields and acreage, only an over all authority could operate schemes for improvements of the sort accomplished in the Sudan Gezira by the government working in collaboration with the Sudan Plantations Syndicate

Mr F Wokes, ph d , pointed out that in Israel the small ration of meat does not seem to have lowered the vitality of the people According to Dr Herklots's experiences with Prof B S Platt's team in Nyasaland, variety of food is an important factor , and he mentioned the recent finding that a diet of bananas, soya, and maize supplemented with vitamin B_{12} cured kwashiorkor

Dr J F de Wijn contrasted the rapid progress in Hong-Kong with the much slower progress on similar problems in Indonesia One of the fundamental difficulties is protein supply , and as more vegetable protein than animal protein can be produced on a given acreage, much progress would be made if requirements of animal protein could be reduced At the Dutch Institute of Preventive Medicine 60 subjects who had eaten no animal protein for periods varying from six months to over two years were examined clinically and biochemically Although dietary calories, calcium, protein, and vitamin B_2 were lower than normal, this was not reflected in biochemical changes A slight reduction of serum phosphate and increase of serum-phosphatase indicated possible vitamin-D deficiency Macrocytic anæmia appeared in those who had taken this diet longer , and 9 subjects had symptoms, including angular stomatitis atrophy of the tongue, paradentosis, pyorrhœa, and recession of the gums Such symptoms also arise in the normal population, and their significance is uncertain

Mr A L Bacharach contrasted the two papers with those at the first meeting,[1] when speakers seemed to have few hopes for each of the accepted methods of increasing food production Dr Herklots and Professor Yudkin had shown that such methods could make an industry flourish and a desert bloom

Mr N W Pirie, f r s , remarked that the problem in food production was not so much to get the research hours for air passengers, almost solely to break the monotony of long journeys.) Nor is it easy to distinguish short-term effects from those resulting more slowly from a gradually changing biological rhythm. **Magnus Pyke**[8] points out that the hours of shift work in themselves affect a worker's daily meal pattern, since even if he eats on the job he also likes to eat at home. Night shifts change meal patterns in an extreme way, and the nature of the work also plays a part. Really heavy work at the coal face demands additional calories; and when and how these are to be provided depends on individual conditions—whether the man crouches at his work, his shift times, the distance of the canteen from the coal face, the eating customs of his people, and so on.

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[1] See Lancet, 1952 ii 1269

Invalids, on the other hand, and especially those in hospital, live under more nearly standard conditions; and new work in the U.S.A. suggests that we still have much to learn about restoring the convalescent invalid's appetite to normal. Experimentally it has been found that rats can be trained to eat three times their normal diet if any food left uneaten is removed at once; and **Keeton**[9] has successfully applied this form of appetite training to patients. They are started on a single large meal a day; this is given in the morning, and anything uneaten is removed. If they feel hungry later in the day they must still wait till 8 A.M. before receiving more food. When they are eating all their food they are started on a second meal every day at 4 P.M., and they are finally promoted to having a third at 10 P.M. In this way **Keeton** has persuaded patients to double or even quadruple their daily calorie intake. It will be interesting to see whether this method can be generally applied, and whether the food intake of the obese can likewise be painlessly lowered by offering small quantities of food all the time until the patient hates the sight of it.

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[8] Pyke, M. Industrial Nutrition. London. 1950.

[9] Keeton, R. W. *J. Amer. med. Ass.* 1953, 151, 253.

Annotations

CHILDREN IN HOSPITAL

To be civilised seems, at times, to consist in learning to do consciously what natural man does instinctively. No savage needs to be told that separation from the mother damages young children, because his young children spend their entire time with their mothers as a matter of course. We, on the other hand, introduce the young child into a highly complex society, and in attempting to fit him for it find a hundred good and convenient reasons for parting him for longer or shorter periods from his natural collaborator; and we have only lately come to see that it does him no good. Evidence has been accumulating for some years now that children in hospital suffer psychologically unless they are visited often by their parents; but an astonishingly large proportion of hospitals have chosen to ignore such findings. A Ministry of Health inquiry, made last year (p. 539) showed that only 300 out of 1300 hospitals taking children were allowing daily visiting; and 150 prohibited the visiting of children altogether. The Ministry's request that all hospitals should allow daily visiting of children is thus not only wise but necessary. Hospitals which have already adopted the plan have not found it impossible or even specially difficult to administer; and they agree that it has been beneficial. Nurses are often credited with resisting the principle of daily visiting on the grounds that it upsets the children: and it is true that the moment of departure of the mothers is usually a time for tears. But nurses are reasonable people, willing to learn. A few set lectures putting the known facts before them would change their outlook, and help them to accept the tears as part of a normal emotional reaction. Once they are convinced that a thing is good for their patients they support it: that is their great virtue.

TUBERCLE BACILLUS UNDER ATTACK

Streptomycin and isoniazid appear to have different effects on the growth of tubercle bacilli. Electron microscopy has shown that normally the bacilli grow to up to seven times their original length in twenty-four hours, and there appear two dense polar bodies which are said to resemble the mitochondria of the cells of higher organisms in appearance and cytochemical reactions.[1] After three days the uniform bipolar filaments have broken down into individual rods. Brieger and his colleagues[2] have found that in cultures containing streptomycin the bacilli grow more slowly; the filaments are much broader and show less definite internal structure, although the polar bodies still present often increase in size and become distorted. The mycelial tendencies in some strains are exaggerated by streptomycin, and the polar bodies become irregularly arranged. Isoniazid produces very different results. Low concentrations have very little effect, but with 20 µg. or more per ml. the rods of the inoculum do not elongate and indeed appear to shrivel and become less transparent. Later the culture seems partly to recover and filaments are produced. Isoniazid has therefore an immediate inhibitory action, whereas that of streptomycin is delayed.

Possibly these complementary actions on the bacilli might be one of the reasons for the good clinical results when the drugs are used together.[3] Brieger and his colleagues carried out their investigations on an attenuated avian strain in Tween 80 medium, which itself affects tubercle bacilli. Growth in certain concentrations of Tween 80 causes virulent bacilli to behave like non-virulent organisms and enhances the action of many inhibitory substances. Bloch and Noll[4] suggest that Tween 80 causes "cord factor" to be secreted into the surrounding medium; the bacilli become less virulent in mice and give the positive methylene-blue test typical of avirulent tubercle bacilli and saprophytic mycobacteria. Similar changes occurred when the bacilli were cultured in one of the thiosemicarbazones; but, although the bacilli became less virulent, cord factor was not detected in the medium, and Bloch and Noll suggest that the thiosemicarbazone had inhibited its synthesis.

READING TYPES

For a long time the reading types used by ophthalmologists to test near vision have been wandering further and further from the standards first suggested by Jaegar and supposedly used ever since. The main reason for this seems to be that the original founts from which the types were produced are now obsolete, so that, although the Jaeger notation is still attached to many reading charts, this no longer has any real meaning, for different firms print the charts in different types and often, therefore, in different sizes. In 1951 Law[5] described the position with admirable clarity, made some recommendations of his own for improving matters, and, on behalf of the council of the Faculty of Ophthalmologists, asked for suggestions and comments. The council received suggestions from a number of sources, and they have now

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[1] Winterscheid, L. C., Mudd, S. *Amer. Rev. Tuberc.* 1953, 67, 59.

[2] Brieger, E. M., Cosslett, V. E., Glauert, A. M. *Nature, Lond.* 1953, 171, 211.

[3] Medical Research Council. *Brit. med. J.* March 7, 1953, p. 521.

[4] Bloch, H., Noll, H. *J. exp. Med.* 1953, 97, 1.

[5] Law, F. W. *Brit. J. Ophthal.* 1951, 35, 765.

Parliament

Economy in the Hospital Services

IN the House of Lords on March 4, Lord AMULREE called attention to the difficulties imposed upon the work of hospital committees by the implied rigidity of recent instructions from the Ministry of Health After working in a hospital or upon a committee one felt that the Ministry of Health was showing a desire to control more and more the day-to-day running of the hospitals, and particularly the staff appointments, both medical and lay He welcomed any attempt to eliminate waste, but that did not necessarily mean a rigid and firm central control

For instance, the wording of a circular letter sent out on Sept 30 last year suggested that it should be permissible for a board to increase the approved medical establishment in any grade or specialty only with the Minister's consent There had since been some substantial modifications in that point of view, and it was now possible for boards of governors to appoint their staffs under a certain budget, and recently they had been allowed, he thought, to appoint an extra consultant over and above that budget But a great amount of trouble and confusion was brought about between September, when the first circular came out, and the final modification, which had been issued only the other day It looked as if there was not much in the way of consultation between the bodies involved On Dec 5 another circular, entitled *Economy in Man-power*, had been sent to regional hospital boards and management committees asking for returns of medical and administrative staffs within 14 days That was the second return which had been demanded since 1951 Later survey teams visited the hospitals and made inquiries and recommendations It was hard to see why outside people, not knowing much about the running of a particular hospital, should interfere in details concerning the staff If hospital boards were not allowed to do their work without so much control, the time would come when the Minister would not be able to get people of sufficient responsibility to accept seats on these boards

Lord SALTOUN complained of the rigidity of the regulations relating to payment for drugs and appliances He had, for instance, been shocked to learn that a chemist who supplied on a doctor's prescription 72 penicillin dressings, two inches square, had been refused payment by the local executive council on the ground that this size of dressing was not included in the Drug Tariff Yet similar dressings, four inches square, were in the tariff, the cost being 36*s* compared with 10*s* 6*d* for the smaller size In Scotland this difficulty could not have arisen, because there the sizes and details of appliances were not specified This was not a solitary case, there were many other instances of this kind

The EARL OF ONSLOW, replying for the Government, said that the Drug Tariff to which the chemists worked was 99% fool-proof, but he admitted that there were one or two small things which were not included because they were so rarely used He assured Lord Saltoun that the matter was already in hand, and that in a few weeks a scheme would be devised with a small enough mesh in the net to catch up all anomalies which resulted from the structure of the Drug Tariff The size of dressing mentioned was so rarely used in general practice that it was thought the inclusion of this pack might lead to waste The original scheme had been reviewed from time to time, but it was felt that if England had the same system as Scotland it would be a great deal more expensive

Turning to the circular on staffing, Lord Onslow said that the object of the original National Health Service Act was to gather up resources and distribute them so that each hospital achieved a reasonable standard Once that sort of thing was done public money was more closely involved and a watch had to be kept on its use The first of the two documents referred to by Lord Amulree was a letter written to teaching hospitals Its intention was this medical review teams had studied the medical staffing of the teaching hospitals and had made suggestions to the Minister, and the teaching hospitals were asked for their views on those suggestions No order was conveyed to the hospitals to alter their day-to-day arrangements, if they thought they could benefit by the suggestions, well and good A great advantage of the nationalised hospitals would surely go by the board if the experience and suggestions of various hospitals and medical authorities were not pooled from time to time and brought to the notice of others, so that all could get the best That was the point of the first document

The other document mentioned by Lord Amulree was a circular, but it again, Lord Onslow insisted, was not an order The main intention was to keep a check on proposals for increases of staff, particularly on the administrative and clerical side The review on which this document was based started in 1950 One aim was to produce an eventual reduction of something like 5% on the administrative and clerical side, a target set by the present Minister These targets were not orders but merely suggestions designed to keep costs down There was no wish to interfere on the medical side or with the general efficiency of the hospitals or institutions concerned The comparable figures, administrative and clerical, for 1948 and 1951 were 21,933 and 29,021 The increase was not as great as it might appear, since in 1948 a certain amount of the administrative and clerical work of the hospital service was still being carried out by local authorities on an agency basis, whereas now these people were whole-time servants of the hospital organisation The number of maintenance, transport, and similar staff in 1948 was 22,803 and in 1951 22,125 The figures for professional and technical staff (other than medical, dental, and nursing staff) were 11,825 for 1948, 16,631 for 1951 Where this sort of provision was expanding for the good of the community Lord Onslow did not think that anyone would grumble at increased figures, nor did he think that anyone would say that staffs had swollen too much since the National Health Service had been started

Lord LUKE affirmed that those who had responsibility for hospital finances were *doing their best to economise* But their task was rendered more difficult because many unavoidable expenses were outside their control Hospitals were not static units, and there would have to be a great deal more progress in all our hospitals if they were to tackle successfully the ever-increasing work of giving everybody immediate and proper attention He hoped that the Ministry would always remember that each hospital unit was different from the others It was impossible to frame legislation or directives that would fit everybody or every unit But could not a general policy be laid down on hospital administration in its wider sense, and each unit be allowed to place its own interpretation on that policy? Lord BURDEN held that with rising prices and increased wages it was impossible for the hospital services to maintain the standards of two years ago without increased Exchequer grants On the Government's present policy lower standards of service were inevitable

Lord MILNE thought that nine-tenths of our troubles were due to lack of money and the birth pains of a new system Those in authority must either declare openly for lower standards in some quarters or adopt some means of supplementing income, however unpopular It would be hypocrisy to suggest impracticable remedies, but he would put forward the following modest suggestions institution of a costing system, block grants for hospital management committees, a survey of the whole system with a view to economy by the elimination of redundancies and waste through alternative or improved methods, and, since administration was so expensive, a realistic survey of the activities of the regional boards to prevent overlapping between them and the hospital management committees, and to restrict, if possible, their task to policy and planning

Lord SIMONDS, the Lord Chancellor, winding up the debate, said that it was the duty of the Minister to see that so far as possible there were fair shares for all For that reason he would find it difficult to accept the suggestion that each regional board or hospital authority should be allowed to pay staff whatever it thought fit Clearly that would mean that one hospital by offering higher rewards would draw from another badly needed staff For hospital services alone the health service was now demanding annually some £300 million, and it was therefore essential that supervision should be strict tomy; they felt better and stronger, and they were able to get about more easily without discomfort. In 3 cases the pelvic mass decreased in size, and micturition was easier. 1 patient showed X-ray evidence of the healing of deposits in bone. With the exception of 1 patient who went rapidly downhill, they have all maintained progress for several months since operation. Laboratory findings, however, were less satisfactory. There was no consistent fall in the serum acid-phosphatase or in 17-ketosteroid output after adrenalectomy. The full data may perhaps show such changes, but on the evidence of the published laboratory figures control of serum-phosphatase levels by the administration of corticosteroids seems more effective than that achieved by the irreversible process of bilateral adrenalectomy. Moreover, the determination of total 17-ketosteroids is inadequate in work of this kind. For example, 11-hydroxy-etiocholanolone has been found as an abnormal compound in the urine of 9 out of 10 patients with cancer of the prostate,[2] and a differential analysis (for which practical methods are already available) could usefully be included in current work on the effect of Kendall's compounds E, B, and F on adrenocortical inhibition.

HÆMOGLOBIN METABOLISM

In the last six or seven years the scientists have added greatly to knowledge of hæmoglobin metabolism, largely through the use of isotopes; but the fuller picture that we now have is still clouded here and there by uncertainties.

Hæmoglobin, as every student knows, consists of a protein (globin) linked to a porphyrin (hæm) containing iron. An adult man destroys and remakes about 8 g. of it a day, carefully employing most of the same iron and protein (or anyway its constituent amino-acids), but throwing away all the porphyrin—about 300 mg.—and synthesising a fresh lot. He can afford to be thus wasteful because the bone-marrow requires for the synthesis only glycine and succinic acid (a simple four-carbon organic acid), which arise directly or indirectly in normal carbohydrate metabolism in most body cells. For globin manufacture the marrow has first call on any protein eaten: hæmoglobin is the first protein to be regenerated after severe bleeding and the last to decrease in long-continued starvation. The only dietary shortage which may hold up hæmoglobin synthesis, therefore, is lack of iron. Hypochromic anæmia is so common because iron has no free entry to the body by simple diffusion, and because the free element, being toxic, circulates only in chemical combination. Thus even though the food eaten may be iron-rich the special absorbing mechanism may fail to take advantage of this, and the iron may pass out in the fæces. Fæcal iron is almost wholly unabsorbed iron, for very little is excreted through the colon. The cells of the duodenal, and probably the ileal, mucosa contain a protein—apoferritin—which is iron-avid and takes up iron from the food. It is then slowly passed on to a plasma-protein, siderophilin—a β-globulin which binds it and circulates it. Normally the siderophilin carries about 0·1 mg. Fe per 100 ml. serum, but it can transport three times this quantity: its level may drop during infections.

A healthy man weighing 70 kg. contains about 4·2 g. iron. Just over 3 g. of this is in hæmoglobin in the circulating red cells; 0·7 g. is in storage (chiefly in the liver); and about 0·005 g. is bound to siderophilin in the plasma.[3] Some of the remaining iron is present in other iron-porphyrin-protein compounds. Myoglobin, the intracellular hæmoglobin of red muscle, accounts for some of it; in man the total is about one-twentieth of the total blood hæmoglobin (in the horse it may be as much as a third). Catalase, the enzyme of liver and red cells which splits hydrogen peroxide, also contains hæm, but has another protein in place of globin. *Cytochrome-c*, an intracellular respiratory enzyme, is an iron-porphyrin related to hæm and linked to yet another protein. Breakdown of these pigments may account for some bile pigment, quite apart from hæmoglobin destruction. The cytochrome system is almost universal in living organisms, so ability to make porphyrins is also almost universal. Thus hæmoglobin is found not only in vertebrates but sporadically throughout the living world—in earthworm blood; in the waterflea, daphnia, when it inhabits stagnant ponds; and in the nodules on the roots of peas, beans, and other leguminosæ where its synthesis is a joint effort by the plant and its symbiotic bacteria. All these hæmoglobins are red, contain the same hæm, and can combine reversibly with oxygen; but their globins are not identical.

It is now clear that there are at least three varieties of human hæmoglobin. These are the ordinary adult form, the fœtal form usually present in the newborn up to about three months of age, and a form present in the red cells of people who have inherited the sickle-cell trait. This third type remains dissolved in the red cell when it is oxygenated, but precipitates out and distorts the cell when it loses its oxygen. There is evidence that fœtal hæmoglobin may be found in children and adults during some attacks of hæmolytic anæmia—for instance in Mediterranean (Cooley's) and sickle-cell anæmias. As Itano[4] points out, more than one kind of hæmoglobin may be present in the same individual.

FAILURE OF MERCURIAL DIURETICS

Mercurial diuretics increase the excretion of water in patients with œdema; but after a time patients with chronic œdema from heart-failure may fail to respond. This refractory state may be associated with various abnormalities of electrolyte balance, which are sometimes evinced by weakness, drowsiness, headache, and nausea.[5]

These diuretics increase the urinary excretion of sodium, potassium, and chloride.[6] Some patients become depleted of sodium: they show a characteristic picture with sunken cheeks and prominent eyes; the peripheral circulation is poor and the collections of œdema fluid remain. Potassium may also become deficient.[7] Other patients may develop an alkalosis because the loss of chloride is greater than the loss of sodium and potassium. Even, however, when these abnormalities are corrected the refractory state may remain[7]; indeed sodium depletion may result from giving mercurials in the refractory state. Thus in many cases there is no explanation for the failure to respond to these compounds.

The response can often be enhanced by giving ammonium chloride, 6 g. daily for two or three days before the mercurial; and possibly the effect of cationic exchange resins in improving the diuresis from mercurial substances may be due to the acidosis that accompanies administration of resin—though this explanation is open to doubt.[8] Theophylline has an adjuvant effect. Waldman and Pelner[9] have empirically given pyridoxine, 100 mg. added to a 2-ml. dose of mercurial, to 10 "mercurial-fast" patients. They claim a good diuretic effect from this combination in every case. One patient ultimately failed to respond to the new combination but then responded to other treatments which had previously become ineffective. It will be interesting to see whether this claim for the combination of mercurial compounds mental health officer was called in there was a justifiable reluctance to certify such cases More accommodation was needed for those whose mental deterioration made them unsuited for ordinary residential accommodation but who were not certifiable

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[2] Reifenstein, E. C., Homburger, F., Dobriner, K. Abstracts 4th Int. Cancer Research Congr. 1950; vol. vi, p. 1050.

[3] Drabkin, D. L. *Physiol. Rev.* 1951, 31, 362. Laurell, C. B. *Pharmacol. Rev.* 1952, 4, 371.

[4] Itano, H. A. *Science*, 1953, 117, 89.

[5] Blumgart, H. L. *Circulation*, 1953, 6, 127.

[6] Thesser, G., Dunning, M. F., Epstein, F. H., Berger, E. Y. *Ibid.* 1952, 5, 85.

[7] Elkinton, J. R., Squires, R. D., Bluemle, L. W. jun. *Ibid*, p. 68.

[8] Elkinton, J. R., Squires, R. D., Klingensmith, W. C. jun. *Ibid.* p. 747.

[9] Waldman, S., Pelner, L. *Amer. J. med. Sci.* 1953, 225, 39.

Mr Somerville Hastings doubted whether the problem of the aged and chronic sick would be solved until there was in every locality a single authority for all health and welfare functions, so that the care of old people, whether well or ill, might be a continuous process Short of that the more liaison there was between existing authorities the better He took this view for two reasons first, because the line of demarcation between health and sickness in old people was a constantly changing and irregular one, secondly because old people removed very badly when they were ill Many taken to hospital were dead within a fortnight of removal Therefore the aged sick should be treated at home as far as possible In many areas there were preventive geriatric outpatient departments to which old people were encouraged to come for physiotherapy and other treatment One hospital which he knew, where a case was not urgent, sent a geriatric specialist to consult with the doctor to see if the old person could be looked after at home Local authorities, too, were doing a great deal to bring the hospital to the patient, but the trouble was that everything locally was arranged to encourage the patient to be sent to hospital instead of being nursed at home He would like to see in each of the regions an all-purpose planning authority whose hospitals could be treated as a unit and used to best advantage, with a second tier for administrative purposes of a much smaller area containing perhaps not more than 250,000 people, so that individual care could be given to those concerned

Dr Edith Summerskill said that the care of the aged offered a challenge to the welfare State which she hoped the Minister of Health would take up She welcomed the development of geriatrics as a specialised branch of medicine because it focused the attention of the public, and of those engaged in the administration of the social services, on this problem It was unfortunate that many hospitals, including the teaching hospitals, were reluctant to allocate a fair proportion of beds to the aged sick She contended that the medical student without training in the care and treatment of this type of patient was not adequately equipped to enter medical practice Every hospital authority should recognise that the chronic diseases of the aged, which went untreated in the past, today yielded to treatment

The proper classification of elderly patients was of first importance In some London hospitals old people were being kept in beds which cost the State £15 a week each, whereas the cost of a long-stay annexe was perhaps £3 10*s* It was in the interests of the patients themselves to be catered for in different institutions according to their needs and capabilities When the sorting out had been completed it would be found that only 3% of the 5 million who were today over sixty-five were in institutions Therefore the problem was clearly a domiciliary one a comprehensive geriatric service, including a well-staffed district nursing service was essential in every locality

Miss Patricia Hornsby-Smith, parliamentary secretary to the Ministry of Health, was sure that the urgency and magnitude of this problem was recognised by the local authorities, the regional hospital boards, and the hospital management committees The Ministry were doing their utmost to bring in to their fullest extent all the voluntary social services interested in the care and welfare of the old Their gravest limitations were mounting expenditure, the difficulties of the capital investment programme, and the shortage of nurses She agreed that this problem by its magnitude and the speed with which it was growing, could make or break the over-all programme and the idea behind the welfare State Whereas there were 2,750 000 old people of pensionable age in 1911, there would be 9,500,000 in 1977 Put in another way, instead of 1 in 15 of the population being of pensionable age there would be 3 in 15 Not only had we to meet an increased birth-rate during the earlier part of the century, but we had also thanks to medical science, to face the problem of longevity Today the expectation of life of a man of 65 was another $12\frac{3}{4}$ years, and of a woman of 60 $18\frac{3}{4}$ years According to the latest estimates of the Government actuary the cost of retirement pensions would be £420 million in 1958, £580 million in 1968 and £700 million in 1978 There were 82 000 more people over 65 at mid-1952 than there were at mid-1951 The hospital management committees and local authorities, she added, were doing their best in face of a problem which was growing faster than their facilities to meet it

She would bring to the Minister's attention the suggestion that there should be another review of how we could improve the link between the health and welfare services Their desire and aim was to get the right person in the right bed, and the Minister had been most anxious to encourage the geriatric service and the local authority services so that as far as possible people should be treated at home But in the last resort beds must be found for them in the hospitals There were 70 specialist geriatric units in hospitals, and during the last year a further 10 geriatricians had been appointed by regional hospital boards In 1951—the last year for which figures were available—the number of beds in use for chronic sick patients rose by 1700 or just over 3% and the number of patients treated rose from 83,852 to 92,390 Some arrangements had been made by the regional hospital boards whereby patients might be treated at hospitals outside the service, and 1770 patients were so treated in 1951 For 1952 she had figures for only five out of the fourteen regions, but they showed another increase of $1\frac{1}{2}\%$ in the patients treated and of 1% in the beds in use The hospital authorities had been asked by the Minister to work to the present programme for outpatients and domiciliary services, and there were some plans to provide long-stay annexes

Residential accommodation was now provided by local authorities for 62,000, a rise from 47,900 in 1949 Since the war over 500 new small homes had been built, accommodating 14,000 patients, and homes for another 4200 were being built or adapted Plans had been prepared for a further 2200 In 500 voluntary homes there were 16,000 people, of whom between 6000 and 7000 were partially maintained by the local authority The number of home helps had risen from 11,000 in 1948 to 25 000 at the end of 1951, and this service was largely given in households containing old people More staff was required for the home nursing service The objectives of Mr Janner's motion were common to both sides of the House, and the Minister had asked her to accept it The problem was vast and could not be solved by the State alone But jointly by the State, the community, the voluntary organisations, and not the least the family, the conditions of the aged sick could be improved

Replying to Mr Janner who once more raised the question of the so-called mental cases, Miss Hornsby-Smith said that the annexes she had mentioned were intended for senile people who were not suitable for a general hospital chronic sick ward, but who were certainly not certifiable It was the policy of the Ministry to encourage as much as possible—and to permit as far as they were able—the building of annexes which would receive patients who were senile and might otherwise be improperly certified

QUESTION TIME

Chemical Composition of Flours

In a supplementary question Mr H Hand asked the parliamentary secretary to the Ministry of Food whether he recalled advising the public against white flour and saying that it was as dangerous to allow chemists to take out certain elements and to add others by artificial means as it would be to allow a milkman to skim the milk or the butcher to paint his meat with chemicals to make it look better —Dr Charles Hill replied I recall that many times in comparing pre war white flour with higher extraction flour during and since the war, I emphasised that the higher extraction flour was much healthier What is now proposed is that there should be at the subsidised price a high extraction flour, and also, if the public choose to buy it, a 70% extraction flour to which have been added three important nutrients to bring its nutritional condition up to that of the high extraction flour

Mr Arthur Woodburn Will the Minister arrange for an appreciation by the Medical Research Council of the effects enemy "effectives"; and there are those who consider it a serious retrograde step to prevent trained medical men from carrying on their calling where it is most needed. Certainly the distinction now made between enemy and neutral members of the same medical services, who may be captured at the same moment doing the same job, suggests that heed is paid only to the nationality, and not to the work, of the prisoner.

We are still very far from achieving neutrality for medical personnel in war—perhaps the only solution worthy of civilised nations. But even in peace vital questions arise which may be insoluble except on an international level, but which have hardly been tackled at all so far. For example, what of the independence of the doctor who is torn between the interests of his patients and his loyalty to an increasingly powerful bureaucratic State? The trials of German and Japanese doctors for their terrible experiments on human beings established, after the late war, some rudiments of an international criminal law on the subject of microbe research; but the preparatory phases of atomic, bacteriological, and chemical warfare open to doctors all over the world many distasteful prospects which involve the gravest moral and indeed legal issues. Among those which have lately come to the fore, and are discussed in Professor de la Pradelle's lectures, are the questions of which line of conduct should be adopted by a doctor who, in the course of research into defences against bacteriological warfare, discovers a new aggressive weapon, and how far the defence of superior orders can be pleaded by a member of an army medical service engaging in prohibited research.

These are some of the open issues which await eventual solution by a properly developed and acknowledged body of international medical law. In his last lecture Professor de la Pradelle discusses whether the task of preparing for this far-reaching work and of marshalling public opinion can be carried out with the best prospect of real progress by national or international professional bodies, such as the World Medical Association, by international agencies, such as W.H.O., or by a special supranational council, comprising both doctors and lawyers. He leans to the view that W.H.O., though primarily concerned with epidemiology and public health on the widest scale, may have the best chance of eventual success because, as an institution attached to the United Nations, it is sponsored by the very governments on whom acceptance of the necessary international conventions will depend. But this is perhaps looking too far ahead. In the meantime something will have been achieved if the movement towards international medical law succeeds in stimulating discussion and thorough examination of the practical possibilities of gaining wider protection for the status of doctors. The difficulties are great, but once the urgency of some kind of action, however gradual and tentative, is recognised, the first and perhaps the most awkward step will have been taken.

TUBERCULOSIS AND SOCIAL CONDITIONS IN LONDON

Benjamin[1] has lately examined in detail the relation of tuberculosis mortality and notification rates to various indices of social and economic conditions in the London boroughs. He points out that in this type of study a fundamental difficulty is that "these indices represent broad averages and the conditions described are by no means uniform over an individual borough." Benjamin finds that between 1931 and 1948 the mortality and morbidity rates declined in each borough; but the inner industrial boroughs had rates above the general average, and they tended to lag behind in the general improvement. In the other boroughs the changes were complex, and were as likely to be related to movements of population, and to changes in the distribution of industry during and after the war, as to anything else. Calculating from the figures for 1931, Benjamin found statistically significant associations between mortality and all the indices of social and economic factors, but no significant association between mortality and attendances at dispensaries or expenditure on clinic services. He also calculated partial correlation coefficients between tuberculosis mortality and the various economic indices. This part of the study showed a very high correlation between the various indices of social and economic circumstances; so it seems that little is to be gained from investigating more than one such index.

STAPHYLOCOCCAL SCARLET FEVER

ALTHOUGH it is certainly uncommon for staphylococcal infection to simulate scarlet fever, there is a wealth of evidence that it occasionally does so. Most clinicians with a long experience of scarlet fever have seen a few examples. In one London infectious-disease hospital there are records of 3 cases, all with abscesses and a generalised bright, somewhat coarse, scarlatiniform rash, but no significant throat infection. 2 of these patients died. *Staphylococcus aureus* was cultured from the abscesses. As early as 1927, Stevens[1] reported 3 cases in which the hæmolytic *Staph. aureus* was the only pathogen isolated. Simpson[2] has lately described 3 more cases; 1 followed an intramuscular injection of streptomycin, the site of which had become infected; the 2nd resulted from a septic sore on the knee, and the 3rd from a large boil. All 3 infections were due to a coagulase-positive *Staph. aureus*, and in none of these cases was *Streptococcus pyogenes* isolated. A soluble toxin was prepared from each of the three strains of staphylococcus isolated. This toxin produced in the convalescent patients, and in a known positive and a known negative Dick reactor, virtually the same reactions as a standard Dick toxin. These results strongly suggest that the antigenic structure of both toxins was similar, and that the erythrogenic toxin produced by the staphylococcus was responsible for the negative Dick reaction in the 3 convalescents.

Others have obtained supporting bacteriological data. Reme[3] tested 15 strains of hæmolytic *Staph. aureus* and found that 12 of them produced an erythrogenic toxin. Satake[4] cultured from the throat of a scarlet-fever patient a *Staph. aureus* whose toxin produced in Dick-positive volunteers a systemic reaction with generalised punctate erythema, characteristic tongue changes, and subsequent desquamation. von Bormann[5] studied 28 cultures of hæmolytic *Staph. aureus*, a few from cases of scarlet fever, but the majority with no known relation to the disease. Of these cultures 17 produced an erythrogenic toxin which could be specifically neutralised by scarlet-fever antitoxin prepared with *Strep. pyogenes*.

There can be little doubt that staphylococci can produce a soluble erythrogenic toxin antigenically similar to that of the hæmolytic streptococcus, and that they can, by this means, reproduce in man the scarlatinal syndrome. That they very rarely do so may merely mean that the quantity of the toxin is usually insufficient to produce this effect. Clinicians should, however, be prepared to recognise the occasional case of staphylococcal scarlet fever, for adequate treatment will usually depend upon early recognition.

Dr. W. J. HORNE, consulting surgeon to the Metropolitan Ear, Nose, and Throat Hospital, London, and a former president of the section of laryngology of the Royal Society of Medicine, died on March 7 at the age of 87.

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1. Benjamin, B. *Brit. J. Tuberc.* 1953, 47, 4.

1. Stevens, F. A. *J. Amer. med. Ass.* 1927, 88, 1957.
2. Simpson, J. *Med. Offr*, 1953, 89, 85.
3. Reme, G. *Z. ImmunForsch.* 1930, 69, 25.
4. Satake, T. *J. orient. Med.* 1927, 6, 17.
5. von Bormann, F. *Klin. Wschr.* 1938, 17, 120.

In England Now

A Running Commentary by Peripatetic Correspondents

TWENTY senior students of St Thomas's Hospital recently returned from Holland where they had been assisting in flood relief in the gravely stricken Province of Zeeland The idea was born on the top of a bus taking two of the students to a 9 o'clock lecture on the morning when the news of the disaster became fully known Within twelve hours the team was formed and ready to fly direct to the flood area, equipped with collapsible boats and outboard engines, thigh-boots, life-jackets, and everything else needed for such a project—much of it an outright gift to the expedition Unfortunately a last-minute hitch over the problem of logistics in Holland delayed departure for forty-eight hours The party then flew to Amsterdam and travelled by road to Dordrecht in the flood area and by sea to Zierikzee, the centre of the flood area in Zeeland The craft were prepared for action in a howling blizzard on the decks of the river transport sailing down the East Schelde estuary, and on arrival at Zierikzee the party was mobilised for action

The delay in arrival meant that the task of rescuing the marooned islanders from trees, churches windmills, and house-tops had virtually been completed, here Royal Navy and U S Air Corps helicopters performed feats of prodigy in atrocious flying conditions Many marooned people however, died of exposure in the bitter weather, and many were drowned through houses collapsing The main task of the party was to bring in all the bodies which could be located in the island of Schouwen-Duiveland for identification and mass burial in Zierikzee There was no other organisation capable or willing to undertake this task, for which the party was well equipped Conditions remained very bad for the first week with snow, sleet, and a bitter north-easterly gale which occasioned fairly rough water in the sea-filled polders All the inhabitants of the island, except essential workers were compulsorily evacuated at the end of the week because of shortage of food and water and fear of epidemics from the presence of innumerable carcasses of cattle, sheep, pigs, and domestic animals The party had brought its own food and was therefore more or less self-contained It was quartered in a school gymnasium, the headquarters of the regional Red Cross, and slept on mattresses closely laid on the floor In this room slept over 150 men of various nationalities Dutch soldiers, workers on the dykes, Flemish sailors, German technicians, British Servicemen, and many others came and went in this dormitory

Fears of further devastation from the much-dreaded spring tides proved groundless since the wind dropped completely and strangely for the two days of the peak tides, and although the rise of the waters was anxiously watched no sea-defences were newly breached The hospital party returned via Amsterdam where, through the generosity of the Netherlands Red Cross, all the members were hospitably entertained for the night The luxury of the first calculated bath for two weeks was unbelievable, and the burning of flea-infested clothing a ritual not without vicarious pleasure

* * *

I prefer not to know how tables of random numbers for clinical trials are compiled I like to think of eminent statisticians hunched over roulette wheels, while their colleagues stick pins into calendars and draw housey-housey counters from a large bag But what of random names? When Messrs Distill and Retort, the pharmaceutical chemists, discover that 2 5-dichloro-1-aminodamitol is good for, say, ichthyosis, they may market it as D & R 376, and risk having it prescribed for general debility Or they may call it '*Noscalc*,' and find that boilermen and modern composers use it To call it 'DAD' might make slogan-writing simpler but could lead to difficulties In fact advertisements suggest that usually a new name with no associations is invented Thanks to 'Syllabwords,' a card game received at Christmas, I am now in a position to supply $\frac{52!}{(52-2)!}$ random names containing two syllables $\frac{52!}{(52-3)!}$ with three syllables, and $\frac{52!}{(52-4)!}$ with four syllables Prices are moderate firms supplying blotting-paper which is shiny on one side will be charged extra

* * *

Psycho-analysis has made such huge strides in the past fifty years that it is difficult to predict future trends However, those who are best informed believe that within the analytical field the present tendency towards specialisation will develop The following letter from a pædiatric analyst of the future to her practitioner analyst colleague shows the sort of thing we may expect

"DEAR DOCTOR,

I wish to recommend to you James Binks who has been my patient for the last 11 years He has now reached the age of 12 and should, therefore, come under the care of a practitioner analyst He originally came to me because of a complaint that he slept during the day and stayed awake at night On analysis, evidence of deep seated insecurity and anger was found associated with repression and feeling of guilt There are also very obvious childhood repressions (see pages 238–263 of the enclosed case history), and it is interesting to note that James has lied about his age, presumably in an attempt to remain a pædiatric analytical patient I would suggest that he should be seen by a guiltologist and possibly a repressionologist in addition to the routine analyst

Yours sincerely,

PETITA YUNG

PS James now remains awake during the day and sleeps at night"

* * *

The foreign book I wanted was out of print—or so the London agents told me, after a long delay Since it was a well-known standard work, I didn't believe them, and wrote to the publishers abroad A prompt reply said that the book was reprinted five years ago and that a copy was on its way to me The only problem now was how to pay for it Before the war, it was easy enough I used an ordinary cheque, crossing out the £ sign and writing rupees or yen Now, the bank told me, I must first of all fill in Form X, in duplicate As this would be a long job, I was advised to make an appointment with the foreign exchange man, who would guide me through it While we were at it, an assistant drafted a letter of instruction to himself, telling him to do what he always does in such cases All was at last signed, sealed, and delivered, and taken into the manager's office for approval My adviser reappeared without the expected smile and asked me if I had kept the materials the book was packed in I certainly hadn't I had carefully scissored out the foreign stamps for one of my regular customers, and the remains had been cremated A declaration was then slowly dictated to me It was to the effect that the wrapper could not be sent because it had been destroyed "Shall I say *inadvertently* destroyed?" I asked My friend cheered up at once "Yes, that's just the sort of word they like There'll be no difficulty now The dossier goes to the Bank of England and you'll hear no more about it We shall debit your account with the sterling equivalent, plus a small charge for service" And well earned this time, I thought, as our conference ended

* * *

THE OBESE PATIENT TO HER DOCTOR

I am the great ungainly lump,
  The one unassailable she
Others must diet because they are plump,
  That doesn't apply to me

I don't eat meat and I don't eat veg
  I peck like a tiny bird
I am not a glutton as you allege,
  Your suggestions are quite absurd

My family worry because I don't eat,
  They say you must feed a big frame
And, though I would like to be less round the seat,
  I don't think it's food all the same

So give me a chit for those dear little tabs,
  You'll find me all ready and willing
And I'll keep my comforts and you keep your fads,
  I'll slim without tears for a shilling

on the inside ") does not last long. The conventional —$^{1}/_{8}$ in. valgus wedge heels only, and valgus stiffening—obviously finds no place here: nor does varus wedging or floating out the heel, because this only encourages the child to tread out the upper on the lateral side of the heel, and destroys the shoe. The problem is largely an economic one forced on us by the high initial cost of shoes and of repairs, and the complaint is not "Look at his feet; they are flat" but, "Look at his shoes; I cannot afford to keep pace with him."

There is no single answer to this problem, and there is definitely no certain answer. Sometimes crêpe-rubber soles will stand the strain when leather will not, and crêpe-rubber is cheaper to maintain and always lasts longer. My initial prejudice against crêpe-rubber has had to give way to its economic advantages.

Valgus insoles I have found of little use, metatarsal bars soon wear down on the outer side, and metal protectors will not remain in place long. Others have tried derotating springs for the forefoot, either inside or outside the shoe. In one case I tried a Whitman's brace after all else had failed, to the ultimate delight of patient and parents, who found that it gave a normal tread.

Forcible derotation may be done either with a Thomas's wrench (one round the forefoot, twisting in eversion, and one on the heel, twisting the opposite direction into inversion) or with a plaster applied in two stages. To apply a two-stage plaster the leg and heel are plastered with the foot strongly inverted, the plaster stopping short at the mid-tarsal joint. The plaster is allowed to set with the heel fixed in inversion, and the forefoot is then twisted into eversion and the plaster completed. The child walks in the plaster for six weeks, and then goes into a shoe with valgus wedges to the heel and stiffening. The correction thus obtained is maintained to some extent, but relapses do occur.

To say that the results of treatment for this condition are not too good is an understatement.

POSTURAL TYPE

When no organic deformity can be found, valgus ankles are labelled "postural." This is by far the largest group of cases, but it is gradually being whittled down by the discovery of more obscure anatomical variations in the structure of the foot. This process is likely to go on in the future.

It is said that postural valgus ankles are associated with other postural defects. This is quite likely to be true: but, in view of the frequency of the condition and the wide variance in normal structure and function, it is one of those generalisations which leave one no wiser or better informed.

Valgus ankles are probably normal when a child begins to walk, but it is not true to say that the deformity disappears. In most cases it probably does, but in others it certainly persists in spite of treatment. This tendency towards spontaneous cure makes all dogmatic statements about treatment sound rather unreal. The standard treatment is "wedges and exercises," and everyone who has dealt with these cases can produce plenty of patients who have not derived the slightest benefit after years of treatment. To treat these children at all is probably a waste of time and effort, for when left untreated they never seem to suffer functional disability of any kind. The prescription of $^{1}/_{8}$ in. valgus wedges to the heels satisfies the parents, and, though it probably does no good, at any rate produces a little peace and quiet in the clinic.

The way of life we follow, in which we never walk on anything other than a flat hard surface in shoes, does not develop the intrinsic muscles of the feet. Running about in bare feet on a shingle beach is probably the best treatment of all, but it is a painful remedy. I have toyed with the idea of the Spitzi insole, but decided that, though it may have a place in the adamantine core of the mountainous regions of Central Europe, it would not be tolerated in England's green and pleasant land.

The problem of valgus ankles is still an unsolved problem. The treatment of the postural type is a waste of time. The functional disability is negligible.

Knock-knees

Nowadays knock-knee or bow-leg is seldom due to rickets, yet many cases are still being treated with cod-liver oil and ultraviolet rays.

The "normal child" is not a well-defined being but varies widely; and $1^{1}/_{2}$ in. of knock-knee (measured with the child seated and with the knees fully extended and just touching) is not abnormal in the first few years of life.

Knock-knee tends to correct itself spontaneously, and most cases seen at the age of 2 years will have cured themselves by the age of 5, whatever treatment is prescribed. To say, however, that all cases cure themselves is not true, and for this reason they should not be dismissed as a nuisance, because sometimes the condition definitely progresses. It has been claimed that all cases of knock-knee are associated with valgus ankles, but I could not confirm this in my clinics, and I found that the incidence of valgus ankles was no higher than in any other group of children. The treatment of knock-knee is however the same as that of valgus ankles—i.e., $^{1}/_{8}$ in. valgus wedges to the heels, with or without valgus stiffening. That this treatment usually works cannot be denied, but it is surely ingenuous to believe that $^{1}/_{8}$ in. valgus wedging of the heels can modify growth on one side or other of the lower femoral epiphysis. Wedging, however, appears to correct the deformity and satisfies the parents.

Where wedges fail, knock-knee splints, such as Eric Lloyd's type, can be tried; but it is not easy to persuade children to wear them continuously. When the splints are used properly and worn conscientiously success is usually achieved; but only too often the species *Homo sapiens juvenilis* runs true to form and non-violent or even violent non-coöperation is exhibited.

When a case is resistant to treatment, such diseases as cœliac or renal rickets should be excluded.

It is stated that knock-knee is never seen in a good athlete, as opposed to bow-legs, which are associated with good muscular development and hence athletic prowess. I have not yet found a patient with knock-knee who was a good runner; but I understand that mild knock-knee is one of the points looked for by the glamour scouts of the entertainment world, because it produces the gluteal roll that so delights the groundlings.

Genu Varum

Many infants are sent to the orthopædic clinic because they are "bandy." This condition is not due to rickets, in spite of persistent beliefs to the contrary; nor is early standing a causal factor. These infants all show good muscular development, as a result of which they may stand early, and for the same reason they often become good athletes in later life. Genu varum is a self-curing deformity in nearly all cases, and as a result it is a very satisfactory condition to treat. Cod-liver oil, ultraviolet rays, massage, and splinting all have their advocates; but none of these are necessary, because in nearly all cases the condition is corrected without treatment by the age of 2 years. If, however, the children are seen again when 3 years old, quite a number will then be found to have developed genu valgum. This is easily understood by a consideration of the deformity. The outward curvature of the tibia is accompanied by an inward torsion, the correction of which by osteoclasis or natural means will leave a genu valgum.

arteriotomy wound can be made There is little doubt that it reduces the chance of further occlusion by thrombosis, especially in the smaller arteries, and also the risks attending further embolism

3 The patient, who has severe mitral stenosis, has been advised to have valvotomy and left auriculectomy performed The one patient on whom I carried out left auriculectomy only, because of multiple emboli, is now well and active, with no further emboli, 3 years afterwards

I should like to endorse Mr Stevenson's recommendation of intra-aortic injections of papaverine in cases of acute occlusion in the arteries of the lower limbs The injection is easily made and the benefits are real I should hesitate, though, to carry out aortic puncture in a heparinised patient

Crumpsall Hospital
Manchester
H A HAXTON

OBJECTIVE TESTS FOR CORONARY INSUFFICIENCY

SIR,—I read with a great deal of interest your editorial of Jan 17 on this subject The exercise-tolerance and anoxæmia tests are well known and of proven value Yet they bear certain dangers and disadvantages, untoward effects have been reported with both

I should like to call your attention to another test for coronary insufficiency[1] The injection of ergometrine maleate intravenously produces the same electrocardiographic changes in the patient with angina pectoris as do the exercise and anoxæmia tests—i e, ST depression and T-wave inversion with or without typical chest pain In over 250 tests, there have been no untoward reactions, and in a recent study[2] the ergometrine test has been shown to be a more sensitive indicator of myocardial ischæmia than either of the other two tests

New York
ISIDORE STEIN

SELLY OAK HOSPITAL INQUIRY

SIR,—In your note last week (p 498) you mention my name and remark that " one dissatisfied critic has spoken of the report as mere ' white washing ' " As the press have identified me with the latter, may I state the reasons why I so labelled the inquiry ?

As a member of the management committee of the group of hospitals of which Selly Oak is one, I attended by invitation the first inquiry set up by the chairman (Alderman Bradbeer)

Evidence at that inquiry was given by nurses and doctors of the hospital the medical assessors were also servants of the hospital, and neither Prof J M Webster nor the coroner who had made the criticism was invited to be present The evidence fitted into a perfect frame not one searching question was asked, and, though it was apparent to me that the allegations were true and afforded an excellent reason to ask for more trained nurses, the chairman, who had invited many representatives of the press to be present but ruled that only certain people should ask questions, when the news men had left the room said that the subcommittee was satisfied that Dr Webster's statements were incorrect As soon as this statement was made I asked for permission to speak, and, being refused, protested and immediately left the meeting Within a few hours I delivered my resignation from the committee to the chairman of the regional board

The findings of the committee were reported to the management committee, of which Alderman Bradbeer is chairman, and were confirmed They were then reported to the regional board of which Alderman Bradbeer is deputy chairman Consequently upon this, and the correspondence in the press, a question was raised in the House of Commons and the Minister of Health asked for a further inquiry This was set up by the regional board, which appointed three of its members to form the body of the inquiry, the chairman and two assessors

The complaints in the press had concerned the nature of the first inquiry, but the new inquiry rigidly adhered to the allegations of the one case The chairman of the new inquiry refused to allow Dr Webster to see the evidence given at the first inquiry the regional board had refused to let either Dr Webster or myself see that evidence Dr Webster was also refused permission to call as witnesses patients of the hospital who were prepared to speak of bad nursing and a lady member of the Women's Voluntary Service who was prepared to testify to the bad service of bedpans to patients and the bribery required to obtain them

The evidence given by the " assistant nurses " indicated to me that they could not distinguish between incontinence and leakage from a bowel obstructed by impacted fæces for which nothing had been done No enema had been given The house surgeon who had discovered a large mass in the abdomen did not make a digital examination and did not report his findings to his chief, and the orthopædic surgeon treated the patient by telephone messages and did not know of the lump until death, but stated in evidence that it would have been dangerous to attempt to move it The consulting physician did not make a digital examination of the rectum and stated that an enema would have killed the patient All the doctors and consultants for the hospital said that the fracture was spontaneous and gave support to the concerted statements of the nurses that the femur had broken spontaneously without any known trauma It was also stated that the pain and shock due to the fracture were so great that a digital examination could not be made or an enema given

Dr Webster said that at necropsy he had tested the strength of the bone by trying to break it and failed he had sawn it and found it very hard He called me as his solitary witness I first asked permission to demonstrate to the court what a spontaneous fracture was the chairman immediately objected, and only the request to him by Professor Tunbridge caused him to allow me to give that evidence I then compared the radiographic evidence I produced with that of the patient and stated emphatically that the fracture in the patient was not a spontaneous fracture but was due to a blow The doctors for the hospital had said that the patient could not have the abdomen radiographed because the ward was not adapted for this I stated that radiography could be done in any room without causing the patient the slightest additional pain, and that it would have revealed that the mass was impacted fæces I further attempted to show that the physician of the hospital had done wrong in putting in evidence a radiograph of a woman in the early 30s as an indication of a normal bone against that of the patient nearly 60 years of age, but I was told by the chairman to leave proprieties alone

The patient had been taken to the X-ray department for examination of the fracture but no X-ray examination of the abdomen had been made, though it would have caused no additional pain or discomfort I stated that the enema was a life saving and not a death dealing treatment for a patient with impacted fæces Dr Teare said that he had made 32,000 post mortem examinations in fifteen years (average 6 per day with no holiday or Sunday leave) and that in some he had found death due to obstruction of fæces

I have examined the sister's record of the patient's bowel movements and consider them unreliable, and Dr Webster has since the inquiry seen the *Coroner's Officer's* inquiry note in which he records that the sister said that the nurses had bumped the patient in the bath—a positive proof that his judgment and mine was correct that it was not a spontaneous fracture

Examination of the report of the inquiry reveals that only evidence against Dr Webster is given significance It states that the members of the inquiry *prefer* the done as to persuade those in control to apply the results.

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[1] Stein, I *Amer Heart J* 1949, 37 36
[2] Stein I Weinstein J, Weiss J J, Slater S R *N Y St J Med* 1952 52 1409

Mr. A. E. BENDER, PH.D., referred to the pessimists *v.* optimists approach to the problem: Castro said that curing 300 million sufferers from malaria would provide that many pairs of hands for food production, whereas Vogt said that curing the sufferers would mean 300 million more mouths to feed. He suggested that progress in Israel was largely due to the early application of scientific findings, fostered by close association between the government and the research centres, and willingness to make use of new methods.

DISTRIBUTION OF MEDICAL MAN-POWER

THE fourth report of the Medical Practices Committee for England and Wales deals with the 18 months up to Dec. 31, 1952. For the first time the committee has published as an appendix to the report an analytical survey illustrating the movement of medical man-power throughout the country since July, 1948. The uncertainty of the post-war years contributed much to the flow of doctors on and off the medical lists during the first months of the National Health Service; and this influence is still apparent today. But it was clear that the introduction of the Working Party's plan for allocating the Danckwerts award would have rapid effects on the distribution of medical man-power, and the committee knew that the survey would have to be completed before these effects had developed if it was to give a proper indication of the results of the National Health Service Act and its amendments as originally planned.

Between July, 1948, and July, 1952, the number of principals on medical lists in England and Wales increased from 16,864 to 17,383. The average number of patients per principal was 2461 in 1948 and 2430 in 1952. The main change, however, has been the levelling-up of average lists in different parts of the country. In 1948 variations were wide: for example, in one part of Wales the average list per principal was 1120, and in another over 8000; but in 1952 the corresponding figures for the same areas were 1320 and 2832. In general, where average lists have been high they are coming down—in other words, additional principals are working where their services are most needed. Turning to the low-list areas, the committee finds that there has been a considerable decrease in the number of principals in practice; in 1948 the total in these areas was about one-third greater than it was in 1952. The report continues:

> "It appears doubtful . . whether the number of doctors practising in these areas will or should be much further reduced. A number of these practitioners have held during their more active years busy practices in other areas and have preferred to take smaller practices later in life rather than carry on work that had become too heavy for them or to retire completely. It is right that they should still be permitted to do this. Since 1948 some Executive Councils and Local Medical Committees have, not unnaturally, been reluctant to allow this position to continue and have dispersed practices which such doctors might have taken. Now that there is no longer a question in this type of vacancy of the practitioner being entitled to claim a fixed annual payment at the expense of the other doctors practising locally, it is probable that the attitude of the local bodies will be more tolerant towards the doctor seeking a semi-retired vacancy in their area."

Following the Danckwerts award and the Working Party's report, the committee's proposals for classifying the country into three main categories instead of four were accepted by the Ministry of Health and by the General Medical Services Committee. The new classification was published last October, and the latest amendments are issued as an appendix to the fourth report. Any area with an average list of patients of between 1500 and 2500 for each effective unit of medical man-power is classified as "doubtful" or "intermediate." With an average above the upper limit the area would be "designated" and below the lower limit it would be "restricted." Of the position in "designated" areas, the committee says:

> "It appears probable . . . that, while there will be a number of new practices started in 'designated' areas, particularly in those where building projects begun or planned involve an influx of population, the majority of additional new principals will enter general practice as partners to established practitioners. Already there is evidence to support this view as the rate of admission of new partners to the list since July has increased considerably and appears likely to continue to do so during the next few months. The stimulus of the Danckwerts Award and the Working Party's plan should lead to an improved service where it is most needed. Our experience so far suggests that it will do so speedily."

CARE OF MOTHERS AND BABIES

THE Ministry of Health has called on hospital authorities, local health authorities, and general practitioners to coöperate in order to ensure continuity in the care of mothers and babies (R.H.B.[53]19). The following steps are suggested: (1) the hospital authority should inform the family doctor and the medical officer of health of all impending discharges of maternity patients; (2) mother and child should be visited by the appropriate officer of the local health authority as soon as possible after discharge; (3) the hospital staff should supply the family doctor and, where appropriate, the M.O.H., with information regarding any matters that seem to need special attention; and (4) the hospital authority should consult with the family doctor or the M.O.H., whichever is appropriate, where there is any doubt, having regard to the home circumstances, about the advisability of discharge. Hospital authorities are asked to ensure that in maternity cases the patient is retained in hospital until she is ready to resume home life (here the home circumstances should be taken into account); and she should not be discharged, except in very special circumstances, before the tenth day.

VISITS TO CHILDREN IN HOSPITAL

THE Ministry of Health has urged all hospital authorities to allow daily visiting of children by their parents, with adequate safeguards against the introduction and spread of infection (R.H.B.[53]18).

In 1949 hospital authorities were asked to arrange for parents or guardians to visit children in hospital, under adequate safeguards, with reasonable frequency and, if necessary, by appointment.

An inquiry by the Ministry last year showed that of the 1300 hospitals which admit children only 300 were at that time allowing daily visiting. The majority of the remainder allowed visiting more than once a week, but there were still about 150 (only half of which were fever hospitals) which prohibited visiting of children altogether.

> "Recent communications to medical journals have suggested that the danger of visiting has been over-emphasised in the past and that there are important advantages to the child in maintaining contact with its home. At the Minister's request the subject has therefore been re-examined by the Central Health Services Council and it is in accordance with their advice that the Minister now urges all hospital authorities to allow daily visiting of children by their parents, with adequate safeguards against the introduction or spread of infection. The Minister is advised that the advantages to the child in maintaining real contact with its parents outweigh any of the objections which have been advanced against daily visiting and he hopes, therefore, that all hospital authorities will accept and put into practice the advice given by the Central Health Services Council."

with the utmost possible thoroughness, for the vague "rheumatic" symptoms for which the *tonsils* are being removed may be caused by a disc lesion.

No laryngologist could fail to agree with Sir Charles that "symptoms [of cervical spondylosis] existing before operation should certainly be an *indication for caution*", but it would be unfortunate if the hyperextended position were to be abandoned without further careful thought.

Last year, with the assistance of Dr. H. L. Thornton, we examined the tracheo-bronchial tree bronchoscopically in *100 consecutive children after removal of the tonsils* by dissection and adenoids by curettage.

In a first group of 50 cases the operation was performed in the hyperextended position with a "*thyroid*" pillow placed under the shoulders and the *free portion of the* Boyle-Davis gag supported manually by the anæsthetist. On completion of the operation a bronchoscope was passed before the pillow was removed. In none of these cases was *any blood found* in the tracheo-bronchial tree.

In a second group of 25 cases the operation was per*formed in the same position* and by an identical technique, but the bronchoscope was passed after the pillow had been removed. Macroscopic blood was found in 7 (28%) cases. The blood was on the anterior tracheal wall in 2 cases, and in the posterior commissure of the larynx in 4 cases; in the 7th case it was present in considerable quantity throughout the trachea and in the right main bronchus. Hæmorrhage had been controlled, and any residual blood removed from the mouth and pharynx by suction, in every case before bronchoscopy was performed. We believe that the blood was introduced through the open and anæsthetised glottis from the "nasopharyngeal sump" as the head was brought into the anatomical (or even flexed) position when the pillow was *removed*. *We recommend, therefore, that* the patient should be placed in the correct postoperative position before the pillow is removed; and we have found that, with little practice, the pillow can be removed and the patient easily effected in a single movement.

The third group of 25 cases is even more important *to the present problem,* for it relates to head-position *during* the operation. *In this group the Boyle Davis gag* was supported throughout the operation by a Mayo table, *not* manually as in the other two. Bronchoscopy was performed (as in the first group) before the pillow was removed. With this method of support, satisfactory hyperextension was rarely attained; it was consequently difficult to maintain a good airway, and macroscopic blood was found in the tracheo-bronchial tree in no fewer than 5 (20%) cases. The blood was on the anterior tracheal wall in 1 case and in the posterior commissure of the larynx in 2 cases; it was present in considerable quantity in the trachea and main bronchus in the other 2 cases—in 1 case in the left main bronchus, in the other in the right.

The blood in the tracheo bronchial tree was aspirated by bronchoscopic suction in those cases (in the second and third groups) where it was present, and there were no respiratory complications.

He*ad-position during* tonsillectomy has become very important medicolegally, in view of the case (no. 5) cited by Sir Charles Symonds.[1]

The laryngologist is faced with two possible courses, neither of them without risk. In the first place, he can perform tonsillectomy in the *hyper*extended position and run the extremely small, but equally serious, risk of paralysis from protrusion of an intervertebral disc. Such a possibility can be minimised by the exclusion, through investigation, of an existing disc lesion; but a disc lesion may be present without symptoms and accidents can also occur with a normal disc. The second course is to perform the operation in a position of less extension and to run the risk of allowing blood to be aspirated into the tracheo-bronchial tree. This hazard though numerically much greater, is obviously less serious than the first, as the blood is effectively removed by coughing when the depth—or, more correctly, the shallowness—of anæsthesia is properly controlled. (*The depth of anæsthesia in our cases was considerably greater than it would normally be on completion of the operation, to allow the passage of the bronchoscope.*) Furthermore, most of the respiratory complications that may follow *aspiration* can be readily detected and efficiently treated.

We feel that a satisfactory position could probably be *attained by placing the* "thyroid" pillow under the shoulders *and maintaining,* but not in any way exaggerating, the extension so afforded by gentle support *of the Boyle-Davis gag. This manœuvre* would aim primarily at maintaining an efficient airway; any further tilt required to prevent *aspiration of blood could then* be made by lowering the head of the table.

It would be of great interest to learn the views of others on the attitude to be adopted in this, the commonest of all operations.

J. CHALMERS BALLANTYNE
Senior E.N.T. registrar

St Mary's Hospital,
London, W. 2

J. MACDERMOTT
Late resident anæsthetist

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[1] See also *Lancet*, 1952, ii. 1077.

PRACTICAL PENICILLIN

SIR,—I should like to comment on some of Mr. Cohen's remarks (Feb. 28). He states that no mention was made *of bacteriology* in his paper because general practitioners in Liverpool have neither time nor facilities to subject *pus to examination.*

I should like to point out that there is a very fine service offered by the City Laboratories at 126, Mount Pleasant, where a report on the nature of the organism *is forthcoming in 24 hours and its sensitivity* to penicillin, streptomycin, chloramphenicol, &c., is given in 48 hours.

In this practice in a working-class area similar to Dr. Sytner's, we have availed ourselves of this service and frequently found penicillin-resistant organisms which have responded to other antibiotics as shown in *their sensitivity tests.*

I feel that giving a tremendous dose of 'Distaquaine' is rather unscientific when one has such good facilities at hand.

Liverpool

B. DOVER.

HALLUX VALGUS

SIR,—In discussing the causes of hallux valgus (Feb. 14) you made no mention of the civilised habit of turning the toes outwards.

The natural way to walk is with the long axis of the foot fore and aft, so that knee, ankle, and toe joints are all working in the same plane. Barefooted races normally walk like this, and any normal young child *if left to its own devices,* will do so too; but we products of civilisation are taught in our nurseries to turn our toes outwards, thus imparting a pronating movement to the foot with each pace and forcing the big toe into a valgus position. (This pronating action is also a prime cause of flat foot.)

It is true that hallux valgus occasionally occurs in *barefooted people; but, in my experience,* it is found only among those who turn their toes outwards. Unprotected big toes are liable to injury, and the foot is *then* externally rotated to avoid pressure on the painful *toe*; in some cases this becomes a habit, with the *inevitable* result—hallux valgus and a rigid flat-foot.

Unsuitable shoes will certainly contribute to the production of hallux valgus and other foot *troubles* but I believe *that external rotation of the foot* while walking is a *primary* cause of the prevalence of hallux valgus among civilised races.

Royal Naval Sick Quarters,
Shotley, Ipswich

E. B. POLLARD

He claimed that the circular on the need for economy in man-power in the hospital services had struck a not unfair balance between supervision of finance and flexibility of administration.

A Question of Priority

In the House of Commons on March 3 Mr. ALBERT ROBERTS drew attention to the unsatisfactory living accommodation provided for the nurses of the General Hospital, Wakefield. He agreed that this was a matter which was delegated to the regional board, but he felt the Ministry could not escape responsibility. The hospital committee since 1948 had been asking the regional board to do something in the matter. But there was a good deal of remote control, and some of these things had been brushed aside without consideration of the human element.

Mr. Roberts quoted a report from the nurses' council stating that

> 43 nurses had to share one wash-basin and one lavatory. There was one bathroom with two hand-basins and one separate lavatory to serve 13 people. The sister-tutor and a medical officer shared a bathroom with the domestic staff. There was a hand-basin in the medical officer's room. The nurses' homes were dark and cheerless. There were no facilities for study. Only breakfast was provided in the detached hostels, and nurses had to go to the hospital, which was a mile away, for meals during their off-duty times.

When approached, the regional board had sent a curt official reply to the effect that owing to financial stringency they did not class this matter as a high priority and saw no hope in the near future of granting the necessary capital.

Colonel MALCOLM STODDART-SCOTT said those who knew this hospital realised that it would not be possible to staff it with nurses unless better accommodation was provided for them. The message that must go out from the House of Commons to the regional board was that they should put first things first.

> "When we see," he continued, "that regional hospital board housing themselves in a great luxury hotel in Harrogate, only two-thirds of which they can use for their own purposes for the hospital service they administer, and the nursing school they run, and when we see them spending £1000 a year on gardeners' wages, and spending money on hothouses so that they can have plants in their offices and provide the hospital with flowers, we remember that these were not the purposes for which this House voted the money to that board."

It was not for the Minister of Health, he agreed, to alter a decision of the regional hospital board, but the Minister should see that the vast sum of money voted to that board was spent on the things which were necessary for carrying on the National Health Service in the West Riding of Yorkshire.

Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry, said it was admitted by the regional board and accepted by the Minister that this accommodation at Wakefield was unsatisfactory. The house committee would prefer to have a new nurses' home built at the hospital; pending that they would like to improve the sanitary accommodation and amenities of the present hostels. The board had decided that a new home was out of the question at present. Prices at the moment were in the range of £[illegible] per place. The policy of non-residence for nurses, other than students, was also being adopted more widely. After reviewing all the priorities, the board, unfortunately, had decided that they could not fit into their capital programme for the year beginning April 1 the comparatively small expenditure necessary to improve the sanitary arrangements for nurses in the three homes. Improvements in the toilet and bath facilities would mean a curtailment of the present sleeping accommodation, and there was at present room for only 52 nurses while [illegible] was needed.

She agreed that better accommodation for nurses was needed, but she pointed out that if the Minister overrode the regional board on priorities the position would become intolerable. Once the money was allocated to the board the priorities were decided by them. It was fair to say that the Leeds board had to meet a substantial programme of capital expenditure for both patients and staff in the area and had before them a number of projects of considerable urgency, mostly for the benefit of patients. The board's capital allocation for the next financial year was £380,000, but because of a large number of building projects and other schemes still in progress and carried on to the following year they had only £115,000 to be devoted to new works.

Most of the money spent at Harrogate, she added, was maintenance money and did not come into the capital allocation. The small amount of capital work which had been done at Harrogate had been on the nurses' home and the preliminary training-school. She agreed that the accommodation at Wakefield was unsatisfactory, but for the Minister to override the decision of the local board would be to set a precedent indeed. She could only recommend members to use all their influence to see that higher priority was given to accommodation for nurses in their own areas.

Care of the Aged

In the House of Commons on March 6 Mr. BARNETT JANNER moved:

> That this House expresses its concern at the shortage of hospital beds for the chronic and aged sick, and the lack of accommodation for those who need care and attention rather than medical treatment; urges the Government and hospital authorities to hasten the establishment of a comprehensive geriatric service to cover the whole country, in view of the increasing proportion of old people to the total population; calls upon local authorities and voluntary bodies to use to the full their powers to safeguard the welfare of the aged; and urges the Government to take all possible steps towards a solution of this grievous human problem.

Today, he continued, there were more than 5,250,000 people over 65, nearly 11% of the population, and for every old person there were only about 6 of full working age. In twenty-five years the number of aged persons would probably be 8,250,000 men and women over the age of 65, or 16% of the population. Despite praiseworthy sacrifices on the part of relatives and many voluntary bodies, sufficient action was not being taken to look after the aged and chronic sick. There were old people who, because they were not sick enough for hospital and yet needed more care and attention than could be given to them in their own or in local-authority homes, were not receiving adequate care. There were aged people in local-authority homes who ought to be in hospital, but who could not be admitted because of the shortage of beds. There were others in their own homes who should be in local-authority homes to prevent them becoming hospital cases. On the other hand, there were aged persons occupying hospital beds who could be sufficiently restored to health to enter hostels or residential homes if such places existed.

In 1950 the Ministry of Health issued a circular to regional hospital boards and boards of governors of teaching hospitals asking them to set up annexes or special homes for old people who were well on the way to being cured and did not need the detailed care which normally sick persons must have. Too little, he thought, had been done to implement that circular. The amount which the Government allowed hospital authorities to spend on maintenance and repair was small in comparison with what needed to be done. In each group of hospitals there should be a complete geriatric unit which should work in conjunction with the domiciliary services. Closer liaison was required between local authorities and hospitals. It should be the duty of one person to inquire into the requirements of old people on waiting-lists and to allot beds in hospitals or other accommodation. If adequate domiciliary services were available the demand for hospital beds could be decreased and better use made of the existing beds.

The accommodation of old people suffering from mental deterioration was, he [illegible], a most [illegible] problem. Despite assurances given to the House in past debates, it was common knowledge among those dealing with old people that many were being certified and admitted to mental hospitals because there were few other places to which they could go. Voluntary organisations and local authorities would not provide special homes for these people because they knew that the National Health Service was unable to take them off their hands when they reached an advanced stage, and also that if the mature trained personnel and of money"[4] but probably also through "the failure of some workers to employ similar objective methods for the evaluation of the mode of treatment under consideration, even though superficially they have appeared to do so"[5] There are, for example, still investigators studying the adrenal responsiveness on groups including "30 male patients, aged 30 to 63 years, who have been hospitalized because of schizophrenia for 2 to 19 (average 11) years" These investigators[6] were repeating some earlier experiments[7] in 34 chronic cases "20–40 years old and with an average duration of hospitalization of 2 5 years" Another report describes eighteen male patients with dementia præcox who "ranged in age from 20 to 45 years, with the mean age being 31 years"[8]

Surely schizophrenia, being a regressive process, should not be investigated in terms of average values Analogously, in the case of human growth and maturation, another but differentiating process, it would be futile to determine hormone values in a group of males aged 2 to 19 (average 11) years Obviously before investigating groups of individuals at a certain stage of the process under study, one must first observe the development of the process in individuals

ROLAND FISCHER

Division of Psychiatric Research,
Psychiatric Services Branch,
Saskatchewan Department of Public Health,
Regina General Hospital, Canada

PROVINCIAL MEDICAL JOURNALISM

SIR,—It was with melancholy pleasure that I read Dr Brockbank's graceful obituary of the *Bristol Medico Chirurgical Journal a Journal of the Medical Sciences for the West of England and South Wales*—to give what was always its full title For such, alas, his tribute is A journal may change hands or policy, but when it changes its name it becomes merely a memory Nay, less than that—who today even remembers the *Morning Post*, the *Bristol Times and Mirror*, the *Medical Circular*, the *Transactions of the Provincial Medical Association*, or (to return to the subject) the *Transactions of the Bristol Medico-Chirurgical Society*? *Fuerunt!* Vain now our efforts to keep the journal afloat throughout the war, vain the Sisyphian struggle for subsequent solvency

Dr Brockbank's suggestions for the local journal ignore the dilemma he himself has stated—rapid rise in costs contrasted with meagre prospects of increased income The editor, always conscious that to set the type for one page consumes four annual subscriptions, must severely limit original articles, and jettison reports of discussions, correspondence, humour

> "Economic pressure led to the abandonment of 'Notes on Preparations for the Sick' in 1921 and of 'Progress of the Medical Sciences' in 1924 [In 1951] no sooner did the increase in subscriptions and in advertisement income promise some relief than a further advance in expenses of production snatched it away We have eliminated Reviews, Lists of Books Received, Obituary Notices and most of the examination results, and can hardly go further in this direction Without constant care it would be quite easy to squander a whole year's income on a single quarterly issue"[9]

Compelled, after serving the journal for 29 years to resign the chair, and all unconscious of this eluctable doom, at least I handed on my charge punctual and solvent *Absumet heres*

Clifton, Bristol

E WATSON-WILLIAMS

DIRTY ANÆSTHETIC MACHINES

Messrs Howards & Sons Ltd, of Ilford, Essex, wr
"One of the manufacturers of anæsthetic ether rece
received a complaint from a hospital that the ether suppl
was below standard and that the patients would not take
On investigation it was discovered that the fault lay in t
bottle of the anæsthetic machine itself, which had not b
properly cleaned We are writing on behalf of the makers o
anæsthetic ether to draw attention to the danger of us
such machines without old ether having first been removed.

Public Health

Influenza

THE subsidence of the influenza epidemic, alread
apparent for some time to general practitioners in man
areas, is now reflected in a substantial decrease in th
number of deaths from influenza in the last week o
February In the 160 great towns of England and Wal
there were 311 deaths in the week ended Feb 28, com
pared with 521, 530, and 416 in the three preceding week
Deaths in the London and south eastern region decreas
to 90, as against 201 in the week ended Feb 21, an
there were also fewer deaths in the northern half of th
country, where there had been a slight increase in th
preceding week But the number of claims for sickne
benefit received by the Ministry of National Insuranc
is still considerably higher than at the correspondin
time last year

Infectious Diseases in England and Wales

Disease	Week ended Feb			
	7	14	21	28*
Diphtheria	16	24	16	[illegible]
Dysentery	286	320	241	[illegible]
Encephalitis				
Infective	4	—	4	3
Postinfectious	—	4	4	6
Food poisoning	76	40	104	101
Measles excluding rubella	31 194	32,359	32,024	30 591
Meningococcal infection	15	53	63	41
Ophthalmia neonatorum	42	28	44	[illegible]
Paratyphoid fever	15	6	4	9
Pneumonia primary or influenzal	2338	2131	2144	[illegible]
Poliomyelitis				
Paralytic	20	15	25	12
Non paralytic	6	2	2	1
Puerperal pyrexia	260	294	258	[illegible]
Scarlet fever	1515	1515	1550	1455
Smallpox	—	—	—	—
Typhoid fever	2	4	8	4
Whooping cough	2571	2238	2197	[illegible]

* Not including late returns

Medicine and the Law

Negligence Negatived

HEADLINES in the daily press are accustoming th
public to findings of negligence against hospital manag
ments and medical practitioners and to the consequenti
award of damages which are often substantial Th
result of the case of Slater *v* Liverpool and Distric
Eastern Hospital Management Committee and Pugmir
is the more satisfactory to the successful defendant
inasmuch as the plaintiff's claim was put forward a
one in which the facts spoke for themselves

A three month old baby, it was said, was admitte
to hospital on Nov 11, 1947, suffering from gastro
enteritis, she was a perfectly formed, normal child
A fortnight later, as the baby could not take her food,
it was decided to give an intramedullary drip into th
left tibia The fluid was dripping continuously into th
leg for 32 hours, during which time (it was alleged) a
condition was set up which ultimately led to the los
of a foot The left foot became gangrenous and o
Dec 15 it dropped off Here, it could be said, was a
baby which entered a hospital with two feet and cam

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[4] Kubie, L S *Science*, 1952, 116, 239
[5] Hope J M, Elmadjian F, Malamud, W *J clin exp Psychopath* 1951, 12 267
[6] Hiatt, H H Rothwell W S, Horwitt, M K *Proc Soc exp Biol*, N Y 1952, 79, 707
[7] Pincus G, Hoagland, H *Amer J Psychiat* 1950, 641 651
[8] Young, M K jun Berry, H K Beerstecher, E jun Berry, J S *Univ Tex Publ* 1951 no 5109, Biochemical Studies no 4, p 189
[9] *Bristol med chir J* 1951, 68 121

the arts and sciences of peace Indeed much of Marc Daniels's work, as J C points out, was done quietly behind the scenes

"Often the only acknowledgment was a small footnote to say that he had compiled a report Yet few people have contributed so much to the attack on tuberculosis, both by the work he did himself and by his influence on other people Not only did he help to clarify much heterogeneous epidemiological data but his practical sense enabled him to give advice which, in more than one country, materially contributed to the control of the disease Only a remarkable personality could have coordinated with so little friction the long series of Medical Research Council trials of chemotherapy in tuberculosis The secret of this success was probably his complete honesty of purpose, his intellectual integrity, and the obvious fact that he was quite uninterested in any personal credit The striking advances in knowledge made by these trials would by themselves be a fitting memorial

"But he was not only valued by his friends for his clarity of mind and his professional knowledge His interests ranged over music, art, politics, philosophy, and much else If to be civilised is to be able to discuss any idea without prejudice, he was the most civilised of men He had a talent for friendship He once said that his life was made up of the friends he had known Certainly anyone who had known him was the better for it He faced his illness with astonishing courage, and up to a few days before his death he was giving valuable advice on the conduct of investigations His main care was still that the work should be well done"

Dr Daniels had two children by his first marriage to Anne Burgess In 1949 he married Kay Graw

RALPH NORMAN

M D Lond

Dr Norman, who died on Feb 21, at his home in Thorpe Bay, Essex, at the age of 77, had been in practice in Southend-on-Sea for over 40 years

From Epsom College he went to the London Hospital, where he qualified in 1899 After holding house-appointments at the London, he became deputy medical superintendent of St Andrew's Hospital, Northampton In 1903 he took his M B and in 1904 he proceeded to the M D He went to Southend-on-Sea in 1907 and he rapidly established a reputation for sound clinical judgment and versatility He was assistant physician to the former Southend-on-Sea Victoria Hospital and later assistant physician to the new Southend-on-Sea General Hospital For some years he was consultant physician to the poor-law hospital at Rochford, where the staff were grateful for his opinion and help, especially in difficult midwifery During the first world war he served as physician to the Queen Mary's Hospital, Southend-on-Sea

He was also associated with the work of the local authority as medical officer at the infant centres and antenatal clinics from the earliest days of this work, and even after his retirement from active practice he remained faithful to his infant clinic until his last illness During the late war he served on the local medical war committee, and he was also a member of the local obstetric committee

In his young days Dr Norman was a fine tennis-player, and he helped to found the Southend-on-Sea Doctors' Cricket Club At the bridge table he was brilliant and formidable

His colleagues recognised his gifts and judgment, and in the days when specialists were not as readily available as they are today, writes J S L, Dr Norman was often called into consultation

"A very modest man who avoided controversy and never criticised others, yet he had strong convictions He seemed to know instinctively and without self questioning what was the right course of conduct, to this he held unfalteringly He never wasted time and could be brusque with those who tried to waste it for him Completely honest, always forthright, generous, helpful, and courageous, he was greatly liked by those to whom he gave his friendship Not the least engaging of his qualities was his quiet pervasive sense of humour and genuine love of fun He loved small children and was very successful with them"

He is survived by his wife, a daughter, and a son, who succeeded him in his practice

Notes and News

THE CIBA FOUNDATION

THE hospitable work of the Ciba Foundation, now in its fourth year, was extended in 1952 to include a scheme of Anglo French exchange bursaries, arranged in conjunction with the Institut National d'Hygiène Last year five British and six French doctors were awarded bursaries which enabled them to spend two to four months abroad gaining clinical experience or carrying out medical research The foundation's latest report also tells of further conferences held at 41, Portland Place, London, W 1 Research workers from many countries are invited to these informal meetings, which are proving one of the most popular and helpful features of the foundation's programme Last year the three colloquia on endocrinology dealt with the Bioassay of Anterior Pituitary and Adrenocortical Hormones, Hormonal Factors in Carbohydrate Metabolism, and the Synthesis and Metabolism of Adrenocortical Steroids At the three general symposia the subjects were the Spinal Cord, Mammalian Germ Cells, and the Chemical Structure of Proteins The proceedings of some of the foundations conferences have been published in London by Messrs J & A Churchill and in New York by the Blakiston Company

CENTRAL MIDWIVES BOARD FOR SCOTLAND

THE members of the reconstituted Central Midwives Board for Scotland are

Miss J H Beckett, matron Elsie Inglis Maternity Hospital Edinburgh, Miss Phyllis Bennett, superintendent, Queen's Institute of District Nursing, Edinburgh, J Bruce Dewar F R C O G, consultant obstetrician, Dumfries, Member of Western Regional Hospital Board, Miss J P Ferlie, matron, Simpson Memorial Maternity Pavilion, Royal Infirmary Edinburgh, Rev J A Fisher convener of Stewartry of Kirkcudbright, Mrs J Wolridge Gordon, member of North Eastern Regional Hospital Board and of board of management, Aberdeen Maternity Hospital, Dr Katherine Harrower, general practitioner, Glasgow David McKay Hart F R C O G gynæcologist, Glasgow, W F T Haultain, F R C O G, consultant obstetrician and
gynæcolog A Lennie, F R C O G, regius pro
fessor of of Glasgow, Bailie Mrs Mary
McAliste ealth committee of Glasgow Cor
poration, Miss E Renwick, matron
Glasgow, Miss J M Stefl, domici
poration, Miss Jean Stenhouse, sist
Ayrshire Central Hospital, Irvine,
non medical supervisor of midwives
officer for Angus County Dr Nora
medical officer, Glasgow Corporation

The new board, like the old, consists of 16 members, but 7 instead of 4 of these members are now practising midwives Of these, 3 are appointed by the Secretary of State and the remaining 4 elected by midwives practising in Scotland This is the first time that midwives have elected members to their governing body The other 9 members are representative of medical bodies, local authorities, the universities, and the hospital services

GUY'S HOSPITAL DENTAL SCHOOL

THE annual clinical meeting of Guy's Hospital Dental School was held on March 7 According to the well established teaching methods of this hospital, emphasis is always laid on the close relation of dentistry to general medicine—a relation which sometimes tends to be forgotten in the routine of dental practice

The morning operating session was mainly devoted to operations on the mandible, which were performed by Mr Patrick Clarkson, Mr S H Wass, and Mr N L Eckhoff This session ended with a lecture by Prof R V Bradlaw on lesions of the oral mucosa Mr R D Gain demonstrated new techniques for constructing cleft palate obturators A system of classification for cleft palates has now been evolved, and, thanks to the present perfection of acrylic resins and to the ever increasing knowledge of how best to use them, many patients with apparently inoperable palatal clefts can now be given a truly functional occlusion, greater facility in speech, and much improved appearance In the department of dental medicine, Mr M V Stack showed the results of further research on the organic constituents of enamel He has proved that "chalky" enamel has almost twice the organic content of normal enamel, and it seems likely that further work on enamel proteins may help to elucidate at least some of the problems of dental caries

The results of a pilot survey, started two years ago, on the efficacy of topical applications of sodium fluoride in preventing decay have now been evaluated Unfortunately, they have

Society of Chemical Industry

Mr H S Holden, D SC, will read a paper on Microbiology and Crime to the microbiology group of this society, at 11, Chandos Street, London, W 1, on Thursday, March 19, at 6 15 P M.

Emergency Bed Service —In the week ended last Monday applications for general acute cases numbered 1433 The proportion admitted was 88 %

The British Pharmacopœia, 1953, which was reviewed in our issue last week (p 477), was published for the General Medical Council by the Pharmaceutical Press, 17, Bloomsbury Square, London, W C 1, and costs 50*s*

Dr Bryce R Nisbet medical officer of health for Kilmarnock, has been awarded a W H O travelling fellowship and he leaves this month for a two month visit to the U S.A and Canada, where he will study public health administration

Dr J C Sawle Thomas has resigned his appointment as civil principal specialist in psychiatry to the Royal Air Force

Messrs Vitamins Ltd have available a number of tickets for doctors who wish to view the Oxford *v* Cambridge Boat Race from the Bemax premises Application should be made to dept B R 1, Vitamins Ltd, Upper Mall, London, W 6

Appointments

Boyd, Mary, M B, PH D Edin M R C P, D OBST, D C H asst M O, Surrey County Council

Burke, Alice, M B Manc, D P H senior M O, nursing service division, health department, Manchester

Cooper, Christine M A, M B Camb, M R C P D C H consultant pædiatrician, Northumberland council children's committee

Lees, William, M B Manc, D OBST asst M O.H and asst school M O, Bolton

Leitch, I D M B Glasg, D P H M O H and principal school M O South Shields

Murtagh, G P, M B Belf D A consultant anæsthetist, thoracic surgery unit Castle Hill Sanatorium, Cottingham

Park, Anna M B Belf, D P H asst M O, Surrey County Council

Pond, D A, M D Camb, M R C P D P M visiting consultant, electro encephalographic department, Guy's Hospital, London

Woods, John, M B N U I asst anæsthetist, Bingley Keighley Skipton and Settle group Leeds Regional Hospital Board

Appointed Factory Doctors

Brooks Alexander M B Aberd Brynmawr, Brecknockshire

Jones, H W F, M B Camb M R C P Tamworth Staffordshire

Tilsley, G E M R C S Sheffield East Yorkshire

Newcastle Regional Hospital Board

Bell, H E, M B N U I, D A consultant anæsthetist, regional thoracic surgical service

Davies T D, M B Lond asst physician, regional blood transfusion service

Duggan Keen, G E, M R C S, D P M medical superintendent and consultant psychiatrist, Winterton Hospital, Sedgefield

Grimson, T A. M D Lond, M R C P consultant physician, Durham H M C

Heller, A D M.D Zagreb M.D, D P M Prague asst psychiatrist, Prudhoe and Monkton Mental Deficiency Hospital

Henry Gerald M B N U I asst chest physician S E Durham tuberculosis area

North-east Metropolitan Regional Hospital Board

Arnott, D C M B Lond D C H D PHYS MED part time physician, Queen Elizabeth Hospital for Children, London

Citron Lewis, M B Lond F R C S D L O part time E N T surgeon (consultant), Chase Farm and other hospitals in the Enfield group

Milne Elizabeth, M B Aberd, D A part-time anæsthetist (consultant) St Margaret s Hospital Epping

Savage, C S M A Camb, F R C S part-time E N T surgeon (consultant), Southend on Sea group of hospitals

Stephen Elizabeth M B St And, D A part time anæsthetist, Broomfield Hospital

Woolf, D L, M R C S, D PHYS MED part time physician (consultant), Connaught Forest and Woodford Jubilee Hospitals

South-east Metropolitan Regional Hospital Board

Goldsmith Eric, M D Koenigsberg, L R C S E D A consultant anæsthetist Seamen s group of hospitals

Hall Smith S P M D Edin, M R C P consultant dermatologist, Hastings group of hospitals

James C D T, M R C S D A consultant anæsthetist Camberwell group of hospitals

James G A, M D Lond, D C H asst pathologist Hastings group of hospitals

Knowles C H R M D Lond asst pathologist Greenwich and Deptford group of hospitals

Lee R E D M Oxfd D A consultant anæsthetist, Medway and Gravesend group of hospitals

Merry, A J M B Lond D A consultant anæsthetist, Woolwich and Lewisham group of hospitals

Moore, W E D, M A M B Camb asst chest physician Bermondsey and Southwark group of hospitals

Sutton S J M D Lond D P H asst chest physician Hastings group of hospitals

Ticehurst R N M A M CHIR Camb F R C S consultant general surgeon Hastings group of hospitals

Williams I G M B Lond M R C P consultant pathologist, Woolwich group of hospitals

Diary of the Week

MARCH 15 TO 21

Monday, 16th

Medical Society of London, 11, Chandos Street, W 1
8 30 P M Dr E R Cullinan Disorders of the Liver and Bile Passages (Last of three Lettsomian lectures)

Royal Eye Hospital St George s Circus, Southwark, S E 1
5 15 P M Dr T H Whittington Science and Art of Refraction

Tuesday, 17th

Royal Society of Medicine, 1, Wimpole Street, W 1
5 30 P M *Section of Experimental Medicine* Prof R V Christie Dyspnœa (Presidential address)
8 P M *Section of Pathology* Dr J Pepys Effect of Local Adrenaline and Histamine on Tuberculin Reactions Sir Francis Teale Tissue Reactivity and Bacterial Invasiveness *Prof* R J V Pulvertaft, Mr W H W Jayne Culture of Human Lymph-glands on Agar Dr D Robertson Smith Effect of Therapeutic Agents on Leukæmic Cells in Vitro

Institute of Dermatology, St John's Hospital, Lisle Street W C 2
5 30 P M Dr F R Bettley Antibiotics

West End Hospital for Nervous Diseases, 40, Marylebone Lane, W 1
5 30 P M Mr Ian R McCaul Investigation of Cerebral Tumour

South West London Medical Society
8 30 P.M (Bolingbroke Hospital, S W 11) Mr Douglas MacLeod Causes of Pelvic Pain in Women

Wednesday, 18th

Royal Society of Medicine
5 P M *Section of Comparative Medicine* Sir Howard Florey, F R S Prof W T J Morgan, F R S, Dr A E Pierce, Dr H Smith Biological Aspects of Mucin
8 15 P M *Section of General Practice* Dr R M McGregor Accident and Sickness proneness in Family Practice

Royal Institute of Public Health and Hygiene, 28, Portland Place, W 1
3 30 P M Dr J A Scott Contribution of the Health Centre to the Public Health

Faculty of Anæsthetists, Royal College of Surgeons, Lincoln's *Inn Fields W C 2*
5 P M Prof E A Pask James Brown (Joseph Clover lecture)

Institute of Dermatology
5 30 P M Dr H Haber Keratoses and Keratodermias

Institute of Urology, St Paul s Hospital, Endell Street, W C 2
5 P M Mr A W Badenoch Hæmaturia

Midland Medical Society, 154, Great Charles Street, Birmingham
8 15 P M Prof J M Webster Medical and Legal Aspects of Criminal Abortion

Thursday, 19th

British Institute of Radiology 32, Welbeck Street, W 1
8 P M Prof Olle Olsson (Lund) Roentgendiagnostic Problems Connected with Bright s Disease

Harveian Society of London
8 15 P M (Royal College of Surgeons) Mr Geoffrey Keynes William Harvey—and his Books (Harveian lecture)

Royal Eye Hospital
5 30 P M Miss M Savory Eye Surgery in the Elderly and Infirm

Manchester Medical Society
4 30 P.M (University of Manchester) Dr Maurice Campbell Surgical Treatment of Mitral Stenosis

North Western Tuberculosis Society
4 30 P M (Royal Infirmary, Manchester) Mr J F Dark, Mr P Jewsbury Results of Lung Resection in Pulmonary Tuberculosis

Friday, 20th

Royal Society of Medicine
4 30 P.M *Section of Epidemiology and Preventive Medicine* Dr W P D Logan, Mr William Gissane Epidemiology of Accidents
8 15 P M *Section of Radiology* Dr George Simon, Dr G H du Boulay Value of Radiological Control in Treatment of Duodenal Ulceration

Faculty of Radiologists
2 P.M (Royal College of Surgeons) *Diagnosis Section* Dr Andrew G Morrow (Philadelphia) Percutaneous Portal Venography and its Surgical Application Dr I B D
Middlemass Deformity of the Œso
Carcinoma Dr N K Blaxland
in Spine Dr L L Ralph Intern

Institute of Dermatology
5 30 P M Dr R M B MacKenna *Local Treatment*

Osler Club of London
7 45 P M (11 Chandos Street, W 1) Dr W R Bett History, Folk lore, and Anthropology of Enuresis

Births, Marriages, and Deaths

BIRTHS

Brandreth —On March 2 at Laundon Maternity Home Sleaford to Janet (*née* Cattell), wife of Dr Keith Brandreth—a son (*David Richard*)

Warin —On Feb 22, at the Maternity Hospital, Bristol to Anne, wife of Dr R P Warin—a daughter

DEATHS

Hutchinson —On March 4 at Laverstock Nursing Home Kingswood Road, Tunbridge Wells, Samuel Hutchinson, M R C S, D.A, aged 70 evidence of the doctors and consultants for the hospital. It ignores my emphatic statement that I disbelieved the evidence of the nurses, but it includes the untruthful suggestion made that I implied that a light tapping of the bone with a pencil could have fractured the bone.

It is these facts which lead me to consider that the new inquiry was but a more elaborate and expensive white-washing party, the acceptance of which necessitates the rejection of the evidence of at least one member of the profession whose integrity and truthfulness has never before been challenged.

Birmingham. J. F. BRAILSFORD.

SOME RELIGIOUS ILLUSIONS IN ART, LITERATURE, AND EXPERIENCE

SIR,—In your kindly appreciation last week of my book you plead for "honest doubt"—a phrase surviving, like a cœlacanth, from among the fossils of *In Memoriam* (1850), or perhaps from still older strata. One would like to know what doubts are not honest.

The Athenæum, London, S.W.1. E. L. KENNAWAY.

FOG AND FALLACY

SIR,—Your annotation and the replies of Dr. John Fry and others to my letter (Feb. 14) prompt me to make further comment. My original letter seems to have been entirely misconstrued insomuch as the question of quality of service, or worth and quality of any general practitioner, was neither mentioned nor implied; and I consider it invidious that both you and Dr. Fry should attempt to make such comparisons of individual practitioners in the columns of your journal. The entire point of my letter was to inquire into the great disparities, in demands for service by the public in various areas, which obviously exists from the figures quoted in your journal. The fact that the public demands made on Dr. Fry are so considerably less than those made on myself is neither a criticism of him nor a eulogy of myself.

In your annotation you state: "Dr. Cort, on the other hand, *prefers* to give his Northern patients more than twice as many items of service as are nationally usual." I do not *prefer* to do this, but the demands of the public give me no option. My normal day's work involves working from 9 A.M. to 11 P.M. at least 6 and sometimes 7 days a week. I do not do this as a matter of personal choice; but as the work is there, perforce it must be done, and I might add that a good proportion of it is not trivial pathology. To keep to the national average, as detailed in Dr. Fry's rejoinder, would necessitate seeing only 50% of the patients who attend my surgeries and only making one visit to each new call regardless of the actual condition of the patient. For example, on Saturday, Feb. 28, attendances at surgeries totalled 75 and visits made totalled 32, which is about an average day's work. The same day I read in your columns that Dr. A. Fry, with a similar list to my own, has an average of only 836 visits and 5633 attendances per annum. To me these figures are more incredible than those of Dr. John Fry, since they represent less than 3 visits and 18 attendances per day. By comparison I find that I am compelled to undertake approximately 800 visits per annum to complete the antenatal, delivery, and postnatal care of the 45–50 midwifery cases I complete each year. The 40 cases of myocardial infarction during the past twelve months have also necessitated visits equivalent to 50% of Dr. A. Fry's perambulations.

With a similar experience of over twenty years in general practice I can only conclude that to avoid the obvious addition to my cases of myocardial infarction I must apply for transfer to a more somnolent area of the National Health Service.

Whitburn, co. Durham. FRANK CORT.

TRAUMA AND CERVICAL SPONDYLOSIS IN COMPRESSION OF THE CERVICAL CORD

SIR,—In his article last week, Sir Charles Symonds raises the important question about damage sustained during operations, with the inference that manipulation under anæsthesia is dangerous. The article will have achieved its purpose if much greater care is exercised in handling patients under anæsthesia and the risk realised that material mechanical injury can follow faulty positioning during operations and mishandling before and after operations. On the other hand, it would be a pity if the impression got around that all manipulation of the cervical spine in cervical spondylosis is dangerous.

The truth is that specific controlled and accurate manipulation of the affected joints in the cervical spine is invaluable as a treatment for cervical spondylosis. I would admit that where there are advanced changes in the cervical spine little can be achieved by manipulation, but many earlier cases will fail to yield to any form of treatment until manipulation of the affected joints has released the fixation or the restricted movements in those joints.

The important point is that the manipulation should be accurate and only carried out by one who has acquired the art of specific manipulation. This art is rarely achieved without much training. Such training is virtually unobtainable outside the reputable schools of osteopathy. It is only in such establishments, where manipulation is the keystone of treatment, that sufficient attention is paid to the details of technique. It is in this detailed technique and its accurate application that the osteopath scores.

It is my practice at hospital to apply intermittent sustained traction, using a halter, with the patient lying supine, in cervical-disc lesions with root-pressure signs. Many cases yield to this traction alone, but those which do not respond invariably do so after the neck has been manipulated. It is never necessary to use hyperextension of the neck to release the lower cervical joints, and it is rarely necessary to give an anæsthetic.

The incidence of cord compression from disc protrusion must be very small indeed compared with nerve-root compression from disc protrusion. It would indeed be a pity if manipulation carefully applied were to fall into disrepute because manipulation, carelessly applied, had on rare occasions caused injury.

London, W.1. ALAN STODDARD.

POSITION FOR TONSILLECTOMY

SIR,—We were extremely interested in Sir Charles Symonds's article last week on the interrelation of Trauma and Cervical Spondylosis in Compression of the Cervical Cord, particularly as one of us (J. C. B.) was also a witness (common, not expert) in one of the cases (no. 5) cited by him.

He records 2 cases of quadriplegia following tonsillectomy, with proof in 1 case of compression of the cervical cord by a prolapsed intervertebral disc. Such a disc may be injured by flexion or hyperextension of the cervical spine, especially with the muscles relaxed under anæsthesia and in the hyperextended position used in such a procedure as tonsillectomy. "This may happen," says Sir Charles, "when the disc is normal, but is more likely to occur . . . when there is cervical spondylosis with disc degeneration."

"Rheumatic" pains, in their great diversity, are occasionally attributed to the presence of a septic focus, and tonsillectomy is sometimes recommended for the alleviation of such pains. The normal movements essential to the performance of tonsillectomy can apparently cause protrusion of a cervical intervertebral disc. Therefore it is obviously of the greatest importance that the laryngologist should investigate all such cases bellyache for forty-eight hours afterwards Many agents, thermal and chemical, can irritate and eventually damage the gastric mucous membrane The traveller who gulps a mug of hot coffee because the guard has blown his whistle suffers for it The man who swallows an aspirin tablet whole may have a brisk hæmatemesis Many of the things we eat or drink may cause lesions of the stomach of which we are unaware, because nobody looks inside our stomachs till a real chronic ulcer calls for investigation On those parts of our body that we can inspect ourselves, our hands and limbs, our tongues, our throats, we are constantly seeing lesions due to heat or cold, trauma, irritants, infection, exanthemata, allergy, or drugs They come, they heal, and they are gone It is not merely possible, but highly probable, that similar lesions appear from time to time on the inner surface of the stomach, destroying the natural protection of that layer Being exposed to a highly digestive fluid they do not heal and they do not go , they become chronic ulcers On this view the acid is not the cause of origin of peptic ulcers, but the cause of persistence

If the ulcers arise in a destruction of the protective surface layer of the gastric mucosa, exposing the deeper layers to peptic digestion, why are they found as a rule only in certain situations, on the middle third of the lesser curve of the stomach, and in the first inch of the duodenum ? The explanation lies, I believe, in the relative fixity of these parts The lesser curve of the stomach is a sling from which the rest is hung, around which the rest expands and contracts to accommodate itself to its contents After a full meal the fundus blows out and the greater curve descends, but the lesser curve remains very much where it was when the stomach was empty The first inch of the duodenum, too, is relatively still compared with the remainder It holds the barium long enough to show us the duodenal cap, whereas the second and third parts hurry it along The mucous membrane in these two relatively immobile parts is smooth and moderately fixed with little submucous tissue, the mucous membrane elsewhere is corrugated, lying in complex folds when the stomach and the duodenum are empty, and stretching out when they are full, and is loose on the muscle coats so that it can yield to their movements when they contract A lesion on the fixed parts remains open long enough for the digestive juices to attack the deeper layers and make a chronic ulcer , a lesion elsewhere falls together before the damage is done

Causes of Increase

The second observation is that peptic ulceration, as a problem of major importance, is new In 1890 gastric ulcer was allotted a few paragraphs in the standard textbooks of medicine and duodenal ulcer was not mentioned In the first decade of the present century gastric ulcer received increasing attention, and duodenal ulcer, largely owing to the pioneer work of Moynihan, was recognised for the first time as a disease deserving attention Since then both have risen steadily in numbers During the first world war 709 men were discharged from the Army for ulceration of the stomach between Aug 4, 1914, and the end of 1915 During the recent war 23,574 men were discharged for peptic ulcer between September 1939, and the end of 1941 Today it is estimated that 10% of the adult population of Britain suffer from peptic ulceration

Can we find in the history of this half century any factor responsible for this increase in the number of ulcers ? It is not poverty malnutrition, or protein shortage Never has Britain been more prosperous, never has wealth been so evenly distributed, never before has the science of nutrition been so well understood or applied so impartially for the benefit of the people What is new is the increasing struggle for existence, between the nations, and between the individuals in the nation There have been two wars, neither of which has resulted in a peace that brings any sense of lasting security Government by the people has been succeeded by government by professors The Welfare State has enveloped us, a State in which the greater part of our wages goes to make a world fit for Civil Servants to tell us what we may do in it In this world the inefficient cannot be made efficient, but they can be and are spared the humiliation of seeing others more efficient doing better work or more of it, or paid higher wages The ambitious man is labelled a spiv If he is bourgeois enough to seek advancement for himself or a better chance for his children, he finds himself struggling in the clutches of the octopus whose tentacles drag him down when he reaches for a higher rung in the ladder He takes his struggles home and re enacts them in his dreams His life is keyed for combat, and his basal ganglia, his autonomic system, and his ductless glands go on working at combat level when they should be at rest A whole group of stress diseases, which have the common factor that they occur in the young, the intelligent, the ambitious, and the anxious, and that they are characterised by over action in extent or in duration of the autonomic and endocrine systems, has become prevalent There can be no agreement about the classification or the ætiology, but hypertension, thyrotoxicosis, ulcerative colitis, Crohn's disease, thrombo-angiitis obliterans, and rheumatoid arthritis seem to belong to this group Chief among the stress diseases seen in Britain is duodenal ulcer In keeping with its membership of this group, we find the evidence of excessive and purposeless overaction of the autonomic and hormonic systems in the production in the stomach of acid between meals and during sleep, and the secretion of acid at a higher concentration than the upper limit regarded as normal

Different Causes and Different Diseases

Three factors can therefore be accepted as related to the ætiology of ulcer (1) local injury to the gastric mucosa by swallowed irritants, (2) secretion of acid at an abnormally high level, and (3) secretion of acid when it is not wanted for the digestion of food But it is surely as futile to seek " the cause " of peptic ulceration as it is to seek " the cause " of aeroplane accidents In each case the causes are many and diverse , in each case a single factor coming in later—acid in the case of the stomach and gravity in the case of the aeroplane—converts what might otherwise have been a remediable fault into a permanent calamity

It is just as wrong to regard peptic ulceration as one disease To do so has practical advantages in the teaching of students, but unless we encourage the postgraduate to split up this omnibus category into its constituent parts, to seek the ætiology of each and to find the treatment appropriate to each, we shall not get much further than we did with pneumonia when pneumonia was just " pneumonia "

There are at least four duodenal ulcers Duodenal ulcer A is the ulcer of textbooks, occurring mostly in young ambitious over conscientious males, characterised by bouts of pain coming on two hours after meals and relieved by further food, progressing slowly to worse and worse pain and eventually to stenosis Duodenal ulcer B is the ulcer that perforates It gives no history of ulcer pain, indeed no history at all beyond a vague feeling of unwellness for three or four days before the perforation It is an acute punched out lesion surrounded by œdema but no scar tissue, and it bears no resemblance except in its site to ulcer A Duodenal ulcer C is the posterior ulcer of prosperous old gentlemen that penetrates the head of the pancreas and is first discovered when it erodes a large vessel and causes catastrophic and often fatal hæmorrhage It has given rise to backache, to pain that has been attributed to kidneys or to

S.H.M.O. GROUP

SIR,—The S.H.M.O.s of the Leicester area have formed a group for the following purposes:

1. To ensure that full justice be done in the interests of its members.
2. To represent S.H.M.O.s on various committees.
3. To assist, wherever possible, the smooth running and efficiency of the Health Service.

In view of the extreme dissatisfaction expressed by S.H.M.O.s in many letters from various regions, it is hoped that groups will be started in other areas, and eventually an organisation formed to cover the whole country.

This committee will willingly help in any way—either individuals, or with the formation of other groups. Correspondence will, therefore, be welcomed from anyone interested.

G. WARING ROBINSON
Chairman,
S.H.M.O. Group,
Leicester area.

53, Stoneygate Road,
Leicester.

COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS

SIR,—What are patients with cavitated disease? Will pneumothorax treatment produce decavitationisation? Or do the authors mean patients with cavities?

Public Health Department,
Smethwick.

HUGH PAUL.

THE MECHANISM OF SALICYLATE SHOCK

SIR,—Salicylate given in large single doses had at least two different actions in our experiments on normal, hypophysectomised, adrenalectomised, demedullated, or deeply anæsthetised rats.

A part of its effect is exerted through a pituitary-adrenocortical mechanism, involving adrenocorticotropic hormone (A.C.T.H.) and in which suprahypophyseal centres may play a part. The adrenal ascorbic-acid depletion and the eosinophil response are examples of this sort of action. The simultaneous increase in metabolism seems to be responsible for the failure to demonstrate increased amounts of substances with cortisone-like activity in the urine of salicylate-treated humans.[1, 2]

A second group of actions, probably more important in human pharmacology, includes the "antihyaluronidase" and "anti-histamine" effects. Large single doses of A.C.T.H. did not simulate these salicylate effects in normal animals.[1] Adrenaline, however, in pharmacological doses produced all the neuro-endocrine effects of salicylate.[3]

Barbiturate experiments demonstrated that the anti-hyaluronidase and anti-histamine effects of salicylate could be produced without the usual signs of activation of the adrenocorticotropic mechanisms, and vice versa. Excision of the adrenal medulla inhibited salicylate and adrenaline protection in these permeability tests, whilst adrenocorticotropic stimulation remained unimpaired.

These facts seem to rule out the otherwise acceptable possibility that the cortisone-hydrocortisone system also functions in these permeability experiments, changed only by the participation of the adrenal medulla. Partial protection, however, could still be achieved with A.C.T.H. and salicylate or adrenaline in normal animals, and by cortisone and salicylate or adrenaline in adrenalectomised animals by injecting these drugs in otherwise insufficient amounts.

Apart, therefore, from the adrenocorticotrophin-cortisone mechanism, which is activated hypothalamically and indirectly also peripherically, salicylate and adrenaline seem to mobilise a different mechanism, affecting permeability and acting in the presence of the pituitary gland and both the adrenal cortex and medulla, or their active materials. It is, however, advisable to refrain from the premature interpretation that the active end-material originates from these structures. Common moderate stressful stimuli do not appreciably mobilise this latter mechanism, which operates under different conditions of shock.

Finally, we were able to give protection in our rat-limb permeability test[3] with anterior pituitary extract not containing appreciable amounts of A.C.T.H. Some chorionic gonadotrophin preparations were also active, but the gonadotrophin itself was not the active material. Further work now in progress is showing the specificity of these effects.

E. KELEMEN
B. TANOS
R. SOLTÉSZ
L. HAJDU.

Belklinika, Szeged,
Hungary.

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1. Kelemen, E., Majoros, M., Tanos, B. *Lancet*, 1950, ii, 457; Kelemen, E., Majoros, M., Iványi, J., Kovács, K. *Experientia*, 1950, 6, 435.
2. Kelemen, E., Majoros, M., Soltész, R., Tanos, B. *Dtsch. med. Wschr.* 1952, 77, 1317.
3. Kelemen, E. *Acta med. hung.* 1952, 3, 369.

WATER INTOXICATION

SIR,—As you say in your leader of Feb. 28, "water intoxication" sounds a strange name for this waterlogged condition of tissue cells in man. But Rowntree and his colleagues seem to have had lower forms of life in mind when they coined it; and the idea of plain water poisoning a mullet is no more paradoxical than large amounts of sea-water being "toxic" to shipwrecked mariners.

Your remark, "Voluntary intake of fluid is not likely ever to cause water intoxication," no doubt applies only to excessive drinking. Have you considered colon washouts in colostomy patients (or others) among the possible causes? Tap-water is the fluid most commonly used—rectal surgeons, indeed, no longer recommend saline—and the quantities tend to increase as the bowel tone weakens. In two cases known to me the "1–2 pints" originally prescribed had become 8–12 pints in ten years, though the amount retained may have kept fairly constant. One of these patients, after giving himself daily washouts for five years, developed muscle twitching and then epileptiform fits of grand-mal type. The fits occurred at long and irregular intervals (i.e., four to twelve months), always in the weekend, and almost always after some mild exercise involving stooping—mowing the lawn, shovelling coke, mending the family's bicycles, and (once) sampling the aroma of a low flowering shrub. Is it possible that the weekend washouts were more thorough, because he had more time to give them; and that stooping raised the pressure in any retained fluid sufficiently to cause the rapid absorption into the blood-stream that may precipitate water-intoxication?

Will the experts tell us whether saline has any advantages over tap-water for colon washouts, and whether small enemata under high pressure are more or less dangerous than large gentle washouts?

Tonbridge, Kent.

E. CLAYTON-JONES.

RESEARCH INTO SCHIZOPHRENIA

SIR,—The schizophrenic escape from reality is the result of a purposive adaptation to relatively excessive demands on a genetically predisposed person.

Some of the biochemical changes—mainly those concerned with metabolic unresponsiveness, and physiological disturbances of the central nervous system resulting in different levels of consciousness—have been described.[1–3] "The literature of schizophrenia is possibly more extensive than that of any other disease"[3]; but much remains to be learnt. "Research in psychiatry is starving to death," however, not only through lack "of ideas, of

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1. Hoskins, R. G. The Biology of Schizophrenia. New York, 1946.
2. Shattock, F. M. *J. ment. Sci.* 1950, 96, 32.
3. Fischer, R., Georgi, F., Weber, R., Piaget, R. M. *Schweiz. med. Wschr.* 1950, 80, 129.

of a peptic ulcer in one place and of cancer in another He cannot state the relationship of one lesion to the other When the history of these ulcer-cancers is investigated we find that it is unusually short, the age of onset has been above that of the ordinary peptic ulcer, and the response to treatment has been unsatisfactory, in fact they have been slow ulcerating cancers from the start The points that suggest an ulcer may be malignant are a first onset at the age of 45 or over, a situation in the prepyloric inch or on the anterior surface or the greater curve, a diameter of an inch or more, and the presence of anorexia or achlorhydria In the assessment of a possibly malignant ulcer lies the only real value of the fractional test-meal

Duodenal ulcers are a very different matter They are commoner than gastric ulcers and are becoming commoner every year They are the price we pay for civilisation, the sign that the bearings have run in an overstressed engine They are the stigmata of devotion to duty, the badge of the trusted and burdened executive. They are the local manifestation of a state of mind and body that surgery cannot cure, and operation is aimed, not at the cause, but at the complications

DUODENAL ULCER

The first part of the duodenum is not a reservoir or a mill, but the beginning of a passage It does not alter its position or its diameter appreciably, and it can carry on its functions, whatever they may be, reasonably well even though it is scarred, provided the ulcer is not active and the circumstances and the state of mind that first caused it have been overcome It often happens indeed that a man who has suffered for years from his duodenal ulcer ceases to be bothered by it when he reaches the age of fifty and acquires that state of mind that he calls philosophy and his wife calls laziness It is in duodenal ulcer that the indications for surgery must be considered most carefully

Three indications are absolute—perforation, stenosis, and hæmorrhage of two pints or more in a man over the age of 50 In the last two categories there are often indications that surgery, though it may not be needed immediately, will soon be advisable, and when this point has been reached the wise surgeon and the wise patient will decide on action while conditions are favourable and risks can be assessed When the patient starts to feel full after every meal, when he vomits occasionally, when he can hear a pint of beer splashing an hour after he has swallowed it, when in an X-ray examination some deformity and some delay can be shown even when the ulcer is clinically quiet, stenosis of a degree that brings malnutrition is not far off Again when a man of under 50 has hæmatemesis of moderate degree two or three times in a space of five years, the large hæmorrhage that may end fatally cannot be far off In both cases the time has come for surgery

The difficult decision is when operation is justified for that very vague indication "failure of medical treatment" The first question we must anwer is, has medical treatment failed the patient or has the patient failed his treatment? If he has not the moral fibre to obey instructions, to adjust his way of life, to curtail indulgences, and to modify his diet, operation may be necessary, but it will not make him a fit man He will go to swell that small group suffering from the "post-gastrectomy syndrome" in which the fault lies with the patient rather than the surgeon If, however, medical treatment conscientiously followed has failed to give relief, when should we advise operation? The answer was given many years ago by that very wise surgeon, Rowley Bristow, when he was asked "When would you operate for osteoarthritis of the hip?" He answered "When the patient comes to me cap in hand and begs me to do it,"—in other words, when it is abundantly clear, not merely to the surgeon but to the patient, that the future holds nothing but increasing misery beside which the risks, temporary discomforts, and possible failure of operation seem relatively unimportant

I have two working guides, the rule of 10 and the rule of 40 When the patient has lost either 10% of working time or 10% of weight in the previous twelve months, the time has come for surgery And when, having reached the age of 40, a man finds that he is constantly getting pain in spite of careful attention to diet and the taking of alkalis, and is unable to deal with anything but invalid fare, once again he should realise that his ulcer has "had it" and that it is time he should say goodbye to it and to the steamed fish and rows of bottles We can promise him that by next Christmas he will be dealing with two helpings of turkey and asking for a third

The Operation

I may seem to imply that the surgical treatment of ulcer is entirely satisfactory, I do not, but I do intend to imply that it should be That it is not is one of the tragedies of today In some hands and in some centres it is very much the reverse If we have trouble with a motor-car we do not hand it for repairs to the first lad we see hanging about in greasy dungarees If we go to sea we like to be assured that the captain has had more than a brief experience in navigation If we wish our portraits painted, we should not go to the local chemist because he has been to an art school and painted a very nice sign for the Green Dragon In surgery we are very careful that the cerebral tumours, the fractures of the neck of the femur, the mitral stenoses, and the carcinomas of the bladder are handled only by men who have served a long apprenticeship in the technique of these particular operations But gastric surgery, more important than any of them because, perfectly performed, it should be able to restore a temporarily disabled citizen to perfect health, is handed over to Tom, Dick, and Harry Every candidate for even a humble surgical appointment tells of the number of gastric operations he has done as evidence of his skill Every newly appointed surgeon invents some modification of standard procedure, and the younger and the more self taught he is, the further does he practise from any contacts or supervision, the more bizarre is it likely to be

When I speak of gastric surgery in connection with ulcer, I mean gastrectomy, for that is the only operation that will stand the test of critical scrutiny of late results Gastrojejunostomy is a delightful technical exercise, it will overcome stenosis, it will relieve pain for a time, and in some patients, such as Sir Robert Hutchison, it will remain satisfactory for forty years, but it does nothing to overcome the factors that produced the original ulcer, but simply transfers their operation to a new site Short-circuiting operations have far too many failures to allow their retention as permissible, except in the very old and feeble Vasoligation is one of the most ill-considered and disastrous human experiments of our time Vagotomy is being quietly dropped, even in the country of its origin, and by the man who first advocated it

Rudyard Kipling once wrote, "There are nine and sixty ways of constructing tribal lays, and every single one of them is right" We might say that there are nine and sixty ways of doing gastrectomy, and sixty of them are wrong and seven of them are not as good as they might be What should we ask of gastrectomy for ulcer? At any rate that the mortality should be negligible, well under 1%, and that it should have a cure rate of at least 90% The remainder are not symptom-free, but if the indications for operation that I suggested have been followed, they are so much better that they find the symptoms of which they still complain a small price to pay for relief from their former suffering ut with only one. Evidence was offered that the cost f supplying and repairing an artificial limb till the hild reached the age of 65 would be nearly £1000. One uestion was whether the decision *not to* amputate was right. The defendants contended that it was more important to build up the child's health, that amputation would have shortened the eventual length of the limb, that the gangrene would not be painful, and that, as the foot was already dead, no poison would be carried from it to the rest of the body. It was contended further that the patient's clinical condition made the drip treatment necessary.

Mr. Justice Gorman directed the jury to concentrate upon the facts given in evidence and to discard emotion. After an hour's deliberation they found in favour of the defendants. The legal costs were stated to be £7500. The claim was brought forward under the Legal Aid and Advice Act. The judge made no order as to costs. Counsel for the plaintiff had suggested that the jury might take the view that the defendant doctor was "a little out of his depth." They evidently did not.

Obituary

MARC DANIELS

M.D. Paris, B.Sc. Manc., M.R.C.P., D.P.H.

THOUGH Marc Daniels came late to medicine and died while he was still in his forties, he had won an international reputation as an epidemiologist. His application of statistical technique to the complex problems thrown up by tuberculosis was masterly. The success of the impressive M.R.C. clinical trials of the new drugs for tuberculosis was largely due to his gift for translating paper plans into practice.

He was born in Cairo in 1907, but in 1912 he returned with his parents to Manchester where his father had a textile business. He was educated at Manchester Grammar School and spent a year in Paris where he took a course in the basic sciences. He graduated B.SC. from Manchester College of Technology and then joined his father's firm. But after two years he was convinced that he did not wish to spend his life in commerce, and in 1929 he returned to Paris to study medicine. In 1936 when he took his M.D. Paris he was awarded a bronze medal. After spending some months at a post in a French sanatorium he decided to return to this country. As his Paris degree did not admit him to the English register, he took the Scottish triple qualification in 1937.

After holding a house-appointment at Hereford General Hospital, he came to London to take a D.P.H. course at the London School of Hygiene and Tropical Medicine. He also served as an assistant medical officer at the North Western Fever Hospital. At this time he was attracted to work in the public-health service, and in 1940 he was appointed an assistant medical officer of health and tuberculosis officer in Lincolnshire, where some of the rural conditions shocked his social conscience. He was rescued from work that he was finding increasingly frustrating by his election in 1942 as scholar to the Prophit Survey of the Royal College of Physicians on the incidence of tuberculosis among young adults. Here for the first time his special capabilities in medical research showed themselves. The outbreak of war had disturbed the plans for the survey, and Daniels's first task, V. H. S., who later joined him in this work, recalls "was to reorganise its scope to meet war-time conditions, abandoning some sections in which further work had become impossible, but expanding others to obtain the greatest possible amount of information. He then turned to the analysis of results, and it was here that his clear precise methods were of the greatest possible value. His interim report in 1943 on the results in nurses paved the way for the final report, the complete plan of which he designed before a word of text was written. Writing papers in collaboration is a difficult task; assisting him with the compilation of the Prophit report was the pleasantest and most instructive experience of my professional life."

The final report of the survey, published in 1948, established the importance of exposure to contact as a cause of the disease, and it was one of the factors which later led to the recognition of tuberculosis among nurses and hospital workers as an industrial disease.

Before the Prophit report was complete Daniels was already working part-time with UNRRA in London, and as soon as the draft was ready he went overseas, as one of the organisation's tuberculosis consultants, to work in Italy, Poland, Czechoslovakia, Austria, and Germany. The wide experience he gained during these next twelve months he later described in his Milroy lectures to the Royal College of Physicians (1949) when he spoke on Tuberculosis in Post-war Europe. Part of his success in this work was due to his command of languages, for he was at least as much at home in French as English (he once asked whether a particular grammatical construction often used in French was good idiomatic English); and he could read German and had some knowledge of Italian.

In 1946 the Medical Research Council set up a committee under the chairmanship of Sir Geoffrey Marshall to report on the new drug streptomycin which had that year been introduced into this country. The clinical trials of the drug were entrusted to the group of workers which later became the M.R.C. tuberculosis research unit; and the director, Dr. P. M. D'Arcy Hart, invited Daniels to return to London to take charge of the project. Here he was the right man in the right job at the right time. For during the next few years one new promising antituberculosis drug has followed the other, and Daniels's trials of streptomycin widened to include comparable investigations into the efficacy of *p*-aminosalicylic acid in pulmonary tuberculosis, and into tuberculous meningitis, and still more recently into the efficacy of isoniazid. The last report with which he was associated appeared in the *British Medical Journal* last week. Since 1950 he had also been engaged in trials of B.C.G. and vole bacillus vaccines in groups of school-leavers.

But during these years of research Daniels was not allowed to remain quietly at home, for his work had made his name known in many countries. In 1947 he was a member of the fact-finding mission sent to Germany by the Foreign Office to investigate the prevalence of tuberculosis in the British Zone. In 1948 he visited New York as a member of the W.H.O. streptomycin subcommittee. In 1951 he inspected for the U.N. High Commissioner for Refugees and for W.H.O. displaced persons' camps in Trieste. The same year he was also in Dublin to take part in a colloquium on the chemotherapy of tuberculosis held by the Medical Research Council of Ireland. Last year, he lectured in Oslo, Bergen, and Paris, and only last month, when already gravely ill, he sent a stimulating letter to a debate in our columns on tuberculin sensitivity. He died on March 3 in Westminster Hospital.

Daniels was tall and handsome, always dressed with colourful taste; but it was difficult to guess his character except that he was certainly artistic. In committee he often looked detached, even bored, but when something stirred him, or he spoke, he was transformed. He was able to convey to others the enthusiasm which lay behind all his own work, and his satisfaction in the *success of any team-work* in which he shared was his greatest reward. He held that a man's work and his philosophy can be effectively merged, and his stern sense of duty in research was backed by a strong social conscience. He was a member of the Association of Scientific Workers and of the Socialist Medical Association, and he gave active help to trade unions and other bodies in their tuberculosis problems. He was also a member of the Medical Association for Prevention of War, and in his unobtrusive way he *did much by example* and persuasion to focus the attention of his fellows on

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heated the toe temperature began to rise after a latent period of 20-30 min, and reached a maximum above 30°C within 30-40 min (fig 1) except in a patient aged 66 in whom occlusive vascular disease of the right leg prevented the toe temperature from rising above 28°C (fig 2). In all cases the mouth temperature remained normal and in 2 it rose to 99°F. Profuse sweating of the whole body, including the feet, was noted in all the cases. The findings were within the range for normal people established by Brattgard et al (1951).

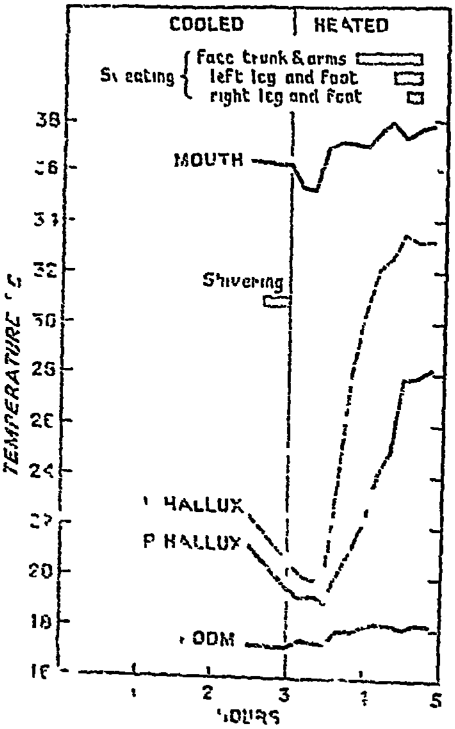

Fig 2—Vasomotor response in non-diabetic aged 66: normal in left hallux, impaired in right hallux, indicating occlusive vascular disease.

Diabetic Patients without Neuropathy

In the 6 newly discovered diabetic patients without a history of nerve involvement and without clinical evidence of peripheral nerve disease reflex vasoconstriction, vasodilatation, and sweating took place normally.

Diabetic Patients with Peripheral Neuropathy

In all 20 patients with diabetic neuropathy conclusive evidence of impairment of the function of the vasomotor and sudomotor nerves was obtained. Three types of response were shown.

(1) In 9 patients peripheral vasodilatation with the toe temperature above 30°C was present at the beginning of the experiments and persisted throughout the three hours' observation. Vasoconstriction did not come on in the toes in response to cooling of the body, in spite of shivering and of vasoconstriction in the thumb. Normally, vasoconstrictor tone is greater in the toes than in the fingers (Pickering and Hess 1933, Doupe et al 1937). The patients behaved like patients who have undergone sympathectomy (Scott and Morton 1931, Wilkins and Kolb 1941, Lewis 1946), and this suggests damage to the sympathetic vasoconstrictor fibres, presumably the result of the diabetic neuropathy. This type of response is illustrated in fig 3.

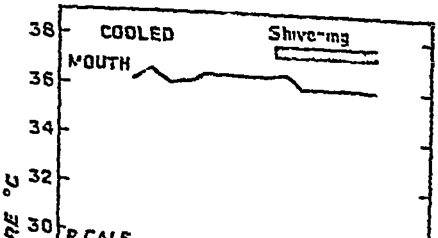

Fig 3—Vasomotor response in patient, aged 36, with diabetic neuropathy: absence of reflex vasoconstriction in toes.

(2) In 10 patients the feet and toes were always cold and vasoconstriction appeared to be present already at the start of the experiments. Time was allowed for the temperature of the thumb to fall, to gain evidence that vasoconstriction was occurring in the arm. The trunk of each patient was then heated. Reflex va
ably took place in the thumb the s
rapidly rose to 35°C or more The mout
above normal and usually reached 100°F b
investigation In no instance did the toe t
fact, in many cases it continued to fall
been heated for about 30 min., most patient
sweating usually starting on the trunk In
was noticed in the legs, but the feet remaine
Heating of the body was continued for 80-
time it was certain that reflex vasodilata
to occur Moreover by that time most p
of discomfort, and some even of distress

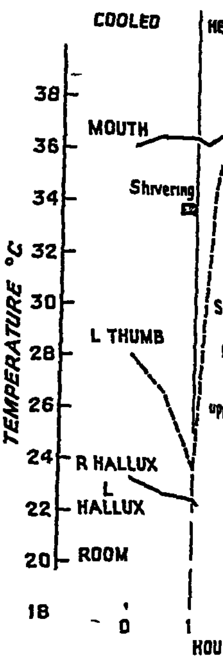

Fig 4—Vasomotor response
with diabetic neuropathy
vasodilatation, intraven
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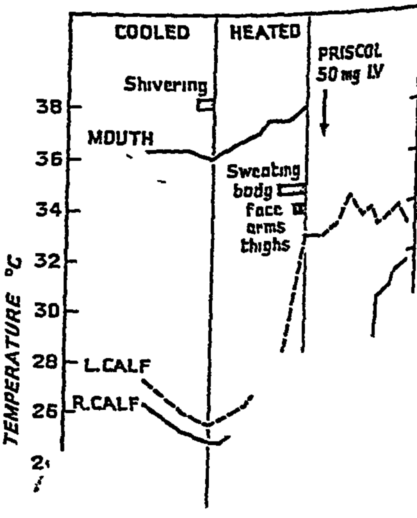
indicating absence of



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proved disappointing; in the sample of 106 children who have been under observation, there has been no significant reduction in the incidence of caries as measured by the M.D.F. (missing-decayed-filled) rate. It remains to be seen whether fluoridation of water-supplies will give better results. Another investigation, carried out, like the last, by the department of preventive dentistry, was concerned with chlorophyll. By the use of the osmoscope—an instrument in which air carrying some particular odour is diluted with pure air until the odour is no longer perceptible—it has been shown that chlorophyll, at least in vitro, does have some effect. It can, for instance, abolish the smell of onions and of carbon disulphide (although this substance retains its lacrimatory power) and considerably reduce that of paraldehyde.

Probably the most important dental advance during the past year has been the steady improvement in the autopolymerising acrylic resins for conservative treatment. Mr. G. F. Thompson demonstrated the use of these materials, which seem to offer almost limitless scope for restorations in anterior teeth.

AUSTRALASIAN ANNALS OF MEDICINE

In the fifteen years since its foundation the Royal Australasian College of Physicians has done much to foster high standards in postgraduate medical education and in research. Last year it initiated its own journal,[1] with Dr. A. W. Holmes à Court as chairman of the editorial committee and Dr. Mervyn Archdall as editor. The first two issues contain original articles covering a wide range of observations and investigations; one, by Sir MacFarlane Burnet, F.R.S., on the Pattern of Disease in Childhood, was reviewed in these columns last week. The college has done well to establish this gathering-place for some of the best work in Australia and New Zealand. The production of the journal, which is printed on art paper, matches the excellence of its contents.

University of Oxford

On Feb. 28 the degree of D.M. was conferred on D. S. Lewes.

Scottish Conjoint Board

On March 7 the following, having passed the final examination, were admitted licentiates of the Royal Colleges of Physicians and of Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow:

I. D. Archibald, B. R. Bayne, I. C. Beard, Sudhir Chandra Bose, Stanley Burton, Lydia F. G. Cowen, J. A. W. Dressler, Catherine B. Gregor, L. A. Harris, Mohamed Lebbe Mohamed Izzadeen, C. R. Lee, W. T. M. MacNeish, Dara Naservanjee Randeria, R. H. Rosen, Mahfouz Ragheb Soliman, Sheila C. Spark, D. C. Stevenson, Margaret J. Taylor, J. R. Ward, G. J. Whiston.

Royal College of Physicians of Ireland

On March 6 Dr. Andrew H. Davidson, F.R.C.P.I., F.R.C.O.G., was elected King's professor of midwifery in the School of Physic, Ireland.

King's College Hospital Medical School

Dr. D. G. Rushton has been appointed lecturer in morbid anatomy at the school, and Dr. D. Robertson Smith lecturer in clinical pathology at the school and honorary assistant clinical pathologist at the hospital.

Chadwick Public Lecture

Mr. H. R. Oakley, M.SC., will deliver a lecture at the Chadwick department of civil and municipal engineering, University College, Gower Street, London, W.C.1, on Tuesday, March 24, at 5.30 P.M. His subject will be *Public Health Engineering—Research and Training.*

Dextran for U.S. Army

Major-General George E. Armstrong, surgeon-general of the U.S. Army, has announced that Army doctors have been authorised to use dextran whenever they believe it may be suitably employed in place of plasma. General Armstrong added that the Army's requirements for whole blood, at present used in the ratio of three to one with plasma, would be undiminished by the substitution of dextran or serum-albumin for plasma. A small trial of dextran by the U.S. Army has been followed by extensive tests in Korea, the results of which are expected to be published in April.

Pensions for Incurables

The National Hospital, Queen Square, has a pension fund for needy sufferers from incurable nervous diseases. The board of management will shortly hold an election to fill vacant pensions (£20 per annum each). Forms of application and further particulars may be had from Mr. H. Ewart Mitchell, the secretary of the hospital, Queen Square, London, W.C.1.

Lebanon Hospital for Mental and Nervous Disorders

The fifty-fourth annual meeting of this hospital will be held on Friday, March 27, at 4.45 P.M., at 26, Portland Place, London, W.1, under the chairmanship of Mr. Fadlo Hourani, honorary consul for Lebanon in Manchester. The speakers will include Dr. Angus MacNiven, physician-superintendent of Glasgow Royal Mental Hospital. The London office of the hospital is at Drayton House, Gordon Street, London, W.C.1.

Congress on Fertility and Sterility

The first world Congress on Fertility and Sterility, which is sponsored by the International Fertility Association and the American Society for the Study of Sterility, is to be held in New York from May 25 to 31. Further particulars may be had from the office of the congress, 1160, Fifth Avenue, New York, 29, N.Y., U.S.A.

World Federation of Mental Health

The sixth annual meeting of the federation will take place in Vienna from Aug. 16 to 22. The theme of the meeting is to be Social Provisions for Mental Health. In 1954 the annual meeting will be held in Toronto, at the same time as the fifth International Congress on Mental Health, from Aug. 14 to 21, and the theme will be Mental Health in Public Affairs. Further information may be had from the secretary of the National Association for Mental Health, 39, Queen Anne Street, London, W.1.

Association of Whole-Time Salaried Specialists

At the annual general meeting on Feb. 20, it was decided to change the name of this association to the Whole-Time Consultants Association. The following officers were elected for 1953: president, Dr. E. N. Allott; hon. treasurer, Dr. J. Duncan White; hon. secretary, Dr. C. Allan Birch.

It was reported that, as a result of representations made by the association, Committee B of the Medical Whitley Council had decided to set up a subcommittee to reconsider problems affecting whole-time consultants. This subcommittee would consist of the whole of both the Management and Staff sides of Committee B together with three representatives of the association.

Medical Society of London

At this society's 173rd anniversary dinner on March 5, each of the four speakers commanded rare brevity and wit. Sir Harold Nicolson praised Dr. John Lettsom, the society's founder, and friend of Samuel Johnson. Lettsom, alone of all the doctors he knew of, was terrified about his own health. Among writers, however, such fear was common. Probably no writer could be great without a vivid imagination; and if he had this he would be concerned with his health. Sir Harold, owning that he had no taste for the collective clinical eye that was fixed on him, urged doctors to treat literary hypochondriacs with great consideration. He was proposing The Society; and in reply Dr. Cuthbert Dukes, the president, declared that this was in robust health. Dr. F. M. R. Walshe, F.R.S., responded for The Visitors to a toast proposed by Dr. S. Cochrane Shanks.

Mount Vernon Centre for Plastic Surgery and Jaw Injuries

The plastic and jaw unit of this group is moving on March 16 from Hill End Hospital, St. Albans. The unit will now be known as the Mount Vernon Centre for Plastic Surgery and Jaw Injuries, and its new address will be Mount Vernon Hospital, Northwood, Middlesex (Northwood 1234, ext. 51). In its new premises the unit will have a well-equipped teaching department, an excellent dental department, and in due course a special burns unit, as well as the general wards. There are also some facilities for private patients.

To ease the changeover it will still be possible to obtain a consultative dental opinion at Hill End Hospital, and a surgical opinion at the Luton and Dunstable Hospital. But if possible patients should be referred direct to Northwood.

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[1] Australasian Annals of Medicine, published twice yearly in May and November. Annual subscription 30s., payable to the Royal Australasian College of Physicians, 145, Macquarie street, Sydney.

heated the toe-temperature began to rise after a latent period of 20–30 min, and reached a maximum above 32°C within 20–40 min (fig 1), except in a patient, aged 66, in whom occlusive vascular disease of the right leg prevented the toe-temperature from rising above 28°C (fig 2) In 3 cases the mouth-temperature remained normal, and in 2 it rose to 99°F Profuse sweating of the whole body, including the feet, was noted in all the cases The findings were within the range for normal people established by Brattgard et al (1951)

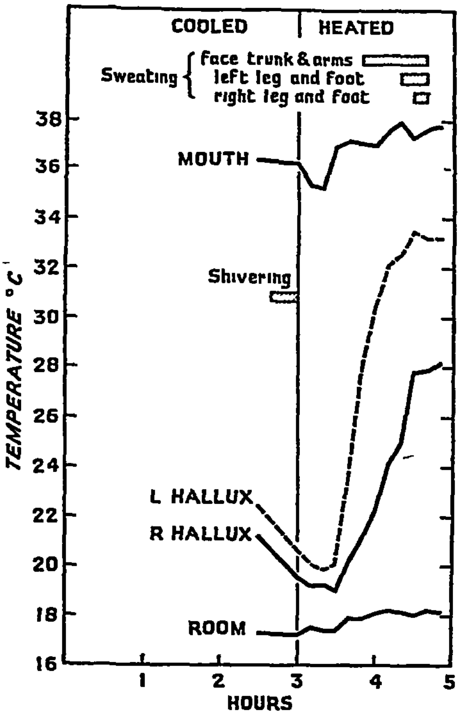

Fig 2—Vasomotor response in non-diabetic aged 66 normal in left hallux, impaired in right hallux, indicating occlusive vascular disease

Diabetic Patients without Neuropathy

In the 5 newly discovered diabetic patients without a history of nerve involvement and without clinical evidence of peripheral nerve disease, reflex vasoconstriction, vasodilatation, and sweating took place normally

Diabetic Patients with Peripheral Neuropathy

In all 20 patients with diabetic neuropathy conclusive evidence of impairment of the function of the vasomotor and sudomotor nerves was obtained Three types of response were shown

(1) In 9 patients peripheral vasodilatation with the toe temperature above 30°C was present at the beginning of the experiments and persisted throughout the three hours' observation Vasoconstriction did not come on in the toes in response to cooling of the body, in spite of shivering and of vasoconstriction in the thumb Normally, vasoconstrictor tone is greater in the toes than in the fingers (Pickering and Hess 1933, Doupe et al 1937) The patients behaved like patients who have undergone sympathectomy (Scott and Morton 1931, Wilkins and Kolb 1941, Lewis 1946), and this suggests damage to the sympathetic vasoconstrictor fibres, presumably the result of the diabetic neuropathy This type of response is illustrated in fig 3

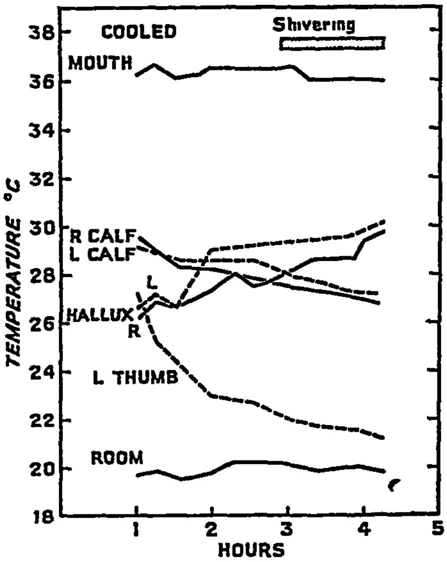

Fig 3—Vasomotor response in patient, aged 36, with diabetic neuropathy absence of reflex vasoconstriction in toes

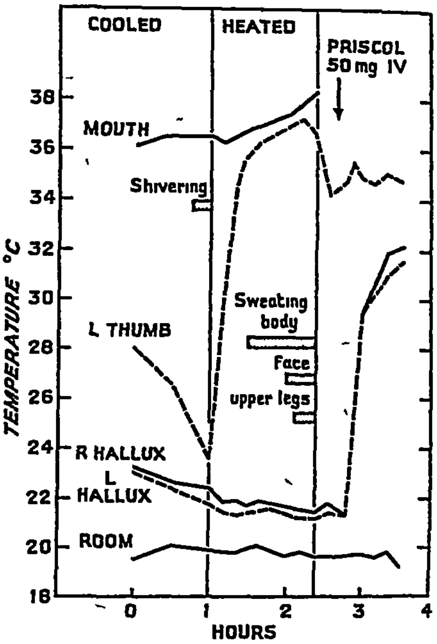

Fig 4—Vasomotor response in patient, aged 84 with diabetic neuropathy absence of reflex vasodilatation intravenous priscol 50 mg caused maximal peripheral vasodilatation, indicating absence of occlusive vascular disease

(2) In 10 patients the feet and toes were always cold and vasoconstriction appeared to be present already at the start of the experiments Time was allowed for the temperature of the thumb to fall, to gain evidence that vasoconstriction was occurring in the arm The trunk of each patient was then heated Reflex vasodilatation invariably took place in the thumb, the skin-temperature of which rapidly rose to 35°C or more The mouth temperature rose to above normal and usually reached 100°F before the end of the investigation In no instance did the toe temperature rise, in fact, in many cases it continued to fall After the trunk had been heated for about 30 min, most patients began to perspire, sweating usually starting on the trunk In some cases sweating was noticed in the legs, but the feet remained dry in every case Heating of the body was continued for 80–90 min, by which time it was certain that reflex vasodilatation was not going to occur Moreover by that time most patients complained of discomfort, and some even of distress

Complete absence of vasodilatation might have been due to occlusive vascular disease, although the pedal pulses were present in most cases Therefore the patients showing this type of response were given intravenous priscol 50 mg, and further temperature changes were recorded In all the cases there was a prompt response, and within 20–30 min the toe temperature began to rise, reaching a level above 30°C in all but two patients, in whom occlusive vascular disease

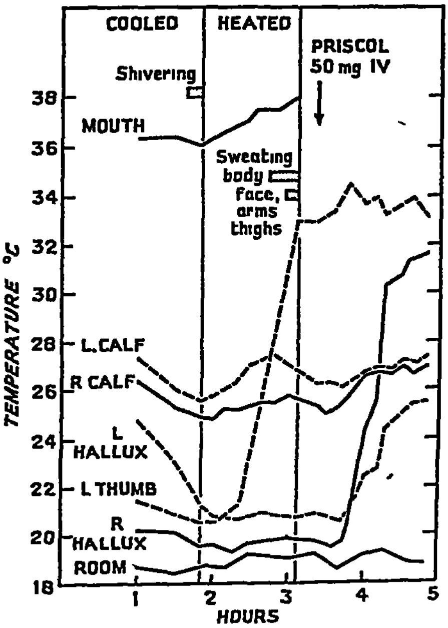

Fig 5—Vasomotor response in patient aged 60 with diabetic neuropathy and occlusive vascular disease in left leg absence of reflex vasodilatation, intravenous priscol 50 mg caused maximal vasodilatation in right hallux but response in left hallux was impaired

THE PROBLEM OF PEPTIC ULCERATION*

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Any discussion on the ætiology of peptic ulceration involves setting the views of one expert against those of another and quoting apparently conclusive experiments only to show that the conclusions have been proved fallacious by other experiments equally conclusive. Nervous, bacterial, toxic, and traumatic influences have all been blamed. Peculiarities in the arrangement of the arteries in the so-called ulcer-bearing areas, and arterial spasm of central or reflex origin have been held to account. The literature is enormous and, on the whole, self-cancelling.

I am particularly concerned not with the wickedness but with the folly of experiments on animals as a means of giving an answer to this particular question. The gastric digestion of each animal is peculiar to itself to its habits and its dietary. That of a dog, a pack-hunting carnivore, is based on the need of a very tired and hungry animal to digest an enormous meal of raw and freshly killed meat, bolted without chewing. The dog's chief need is for vagal secretion to provide a digestive bath into which this meal shall drop. Man's gastric digestion is that of a creature who seldom knows real hunger, and who soon loses that wild enthusiasm that gets the vagus working soon after the meal has started. Man's chief need therefore, is for a hormonal secretion to carry on the job of gastric digestion while his mind turns to other matters. To apply the results of experiments on dogs to the ætiology and treatment of peptic ulceration in man is as scientific as to base a course of postnatal lectures to mothers on a study of the maternal habits of the female kangaroo.

The Dangerous Fluid

It is only natural that there should be a constant tendency among investigators to blame hydrochloric acid for peptic ulceration. Peptic ulcers are normally found only in those parts of the alimentary tract that are exposed to the action of unneutralised acid. They seldom occur when acid is congenitally absent or lost through disease; and they may be found in any region which is brought into contact with acid owing to the presence of ectopic gastric mucosa (as in Meckel's diverticulum or the upper reaches of the œsophagus), owing to sphincteric deficiency (as in the lower œsophagus in the presence of incompetence of the cardia), or owing to surgical anastomosis (as in gastrojejunostomy, cholecystogastrostomy, œsophagogastrostomy, or gastric fistula). On the other hand, hydrochloric acid is part of the natural mechanism of protein digestion, and Nature seldom makes mistakes—never stupid ones. Hydrochloric acid is part of the vertebrate heritage. It first appeared in the stomachs of fishes, to enable them to dissolve the shells of the marine creatures they swallowed. It is present in the stomachs of all animals and of all healthy men, and animals and healthy men do not get ulcers.

It may help us if we put our question the other way round—why do we not all get ulcers? The natural resistance to disease is an aspect of pathology that we are apt to forget. Lister looked on sepsis as an attack by evil germs on helpless mankind; it was not till the first world war that we learned that the resistance of healthy tissues is a more powerful antiseptic than any chemical. Tubercle bacilli and the virus of poliomyelitis are all around us. They descend, like God's rain, on the just and on the unjust. Why are some taken and the others left? The œsophagus enters the abdomen through a hiatus in the diaphragm large enough to let through a swallowed toothplate or a small orange, or, at laparotomy, to admit three of a surgeon's fingers. Why does only one person in ten develop a hiatus hernia?

Why then do so few of us get ulcers? We have in our stomachs this devastatingly destructive fluid; why does it not attack the walls of the cavity in which it is contained? There are two reasons at any rate:

(1) The surface of the gastric mucosa consists of a layer of columnar cells between which are many mucus-secreting cells, and mucous cells surround the mouths of the gastric glands. The secreting glands lie deep to this surface layer and open on it by small pores. A layer of mucus then separates the gastric contents from actual contact with the stomach wall.

(2) Hydrochloric acid is normally secreted only in response to a meal. The acid is buffered by the food during digestion, and at the end of digestion it is neutralised by the alkaline secretion of the glands lining the pyloric antrum. Any unneutralised acid that escapes into the duodenum is neutralised by the secretion of Brunner's glands, which are similar in appearance and function.

It seems likely therefore that hydrochloric acid will be able to attack the stomach wall and produce an ulcer only when there is a breach of the protecting surface epithelium, or when it is secreted in amounts in excess of that required to digest the food, or at times when there is no food to digest.

Instead of trying to learn about peptic ulcers by attempting to produce them in animals that never get them unless subjected to trauma or insults fantastically in excess of anything that can happen to man, we can learn a good deal more by the experiments that man carries out on himself. What races and what men get ulcers, and why do they get them? I will deal with two observations only.

Injury of the Mucosa

There is in India an "ulcer belt" extending along the south eastern seaboard from the southern tip about two-thirds of the way to Calcutta and about a hundred miles inland, an area that corresponds roughly to the State of Madras. In this belt peptic ulceration is about ten times as common as in the rest of India, and the ulcers that come to hospital, chiefly duodenal ones, are large chronic indurated lesions beside which the ulcers that we see in Britain would seem trivial. The staple diet of the peasants is rice in the north and tapioca in the south, with occasional small portions of fish added. This diet provides 2770 calories but only 48 grammes of protein per head. On these figures it has been suggested that malnutrition, particularly protein shortage, is the cause of the ulcers. But malnutrition and protein shortage are as prevalent in many other districts of India where peptic ulceration is extremely rare. The same factors are found in Egypt, but the fellaheen seldom get ulcers. In Africa protein shortage has been one of the reasons for cannibalism. It has been aggravated by the virtual abolition of this pastime. But the Negro never suffers from peptic ulceration until he goes to America and lives in comparative plenty. Protein shortage must therefore be dismissed as responsible for the ulcers in the Indian ulcer belt, and the most probable cause is red pepper, which is used liberally to enliven the insipid carbohydrate diet. That this may be the cause is further suggested by the fact that the average acid level in this district is significantly higher than in Calcutta or in Great Britain.

That strong condiments irritate the stomach is no news to those who seldom take them. The polite visitor to Madras who swallows a large helping of "real Indian curry" to please his generous host suffers the agonies of

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* Based on a lecture to the Leeds Medical Society on Dec. 12, 1952.

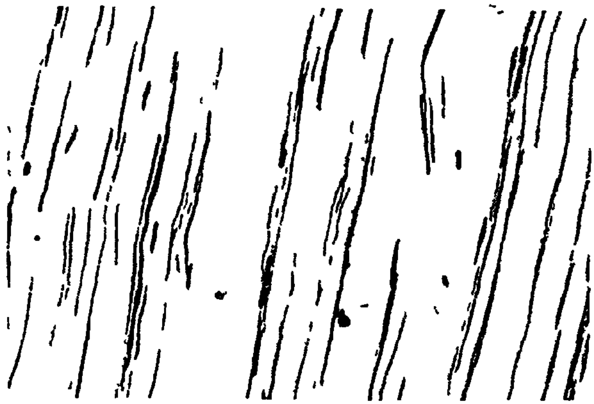

Fig 8—Biopsy specimen of sural nerve in diabetic neuropathy, showing reduction in number of axis-cylinders (Holmes) (× 320) cf fig 9

In the present investigation biopsy specimens of the affected nerves were obtained from 10 cases of diabetic neuropathy The age and sex distribution, duration of diabetes and of the diabetic nerve complication, the clinical evidence of occlusive vascular disease, and the pathological findings are set out in table II

The preparations were stained with osmic acid, hæmalum, and eosin, and by the methods of Van Gieson, Holmes, and Bielschowsky

The sections of nerves from cases of diabetic neuropathy showed conspicuous degenerative changes in all the specimens There was considerable reduction in axis-cylinders (figs 8 and 9) and in myelin sheaths (figs 10 and 11) as reported previously, without, however, any evidence either of endoneural or perineural fibrosis or of cellular infiltration The degree of degeneration met with in the different cases varied and seemed to correspond to the clinical severity of the neuropathy Actual counts, however, have not yet been made In the most severe cases the degenerative change was diffuse, but in the milder cases it was more patchy and appeared to involve isolated bundles of fibres surrounded by more normal-looking ones Close scrutiny of the silver-stained sections suggested that there was a greater reduction in the number of non-myelinated nerve-fibres, compared with the myelinated ones (figs 12 and 13) That the closely packed clumps of "naked" axis-cylinders adjacent to, and in between, the large myelinated fibres were in fact non-myelinated autonomic nerve-fibres was suggested by Nevin (1930) This question is still under investigation

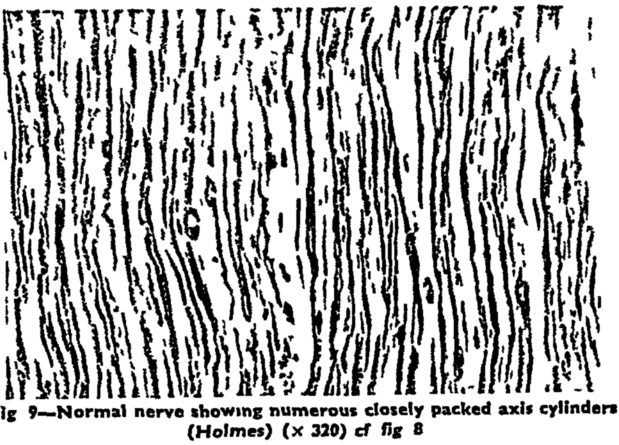

Fig 9—Normal nerve showing numerous closely packed axis cylinders (Holmes) (× 320) cf fig 8

Diabetic neuropathy thus appears to be a degenerative condition of nerves in which the non myelinated small-calibre fibres degenerate more extensively than the larger myelinated ones Further, the primary lesion seems to be a degeneration of axis cylinders, with a reduction in the myelin sheaths as a secondary phenomenon

DISCUSSION

Involvement of the nervous system in diabetes appears to be much more common than the published reports suggest Severe diabetic neuropathy with muscle weakness and extensive loss of sensory perception, such as used to be called tabes diabetica, may not be a common finding in smaller diabetic clinics, but every physician treating diabetic patients must be familiar with the common complaints of pains and paræsthesiæ, particularly in the legs and often associated with calf tenderness and vasomotor disturbances Although neuritic symptoms in the absence of physical signs have been regarded as separate from diabetic neuropathy with its more permanent findings of peripheral nerve involvement (Rundles 1945), there is little doubt that both have a common ætiology

The earliest phase in the development of diabetic neuropathy seems to be characterised by a diffuse and ill localised pain, vasomotor disturbances, thermal paræsthesiæ, changes in tendon reflexes, and often an alteration in pain sensibility in the feet without much impairment of perception of touch or pressure If the disease progresses, shooting pains develop, vibration sense is lost, and, lastly, sense of touch and position as well as motor power becomes involved (Martin 1953)

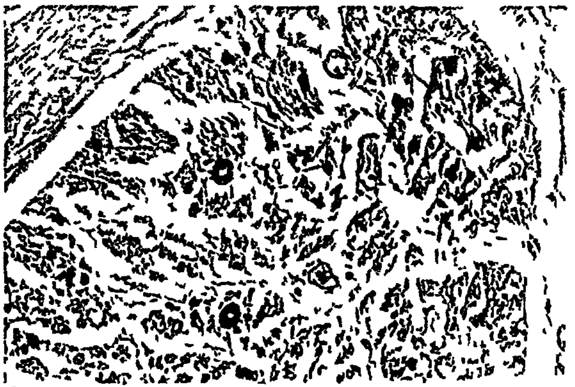

Fig 10—Biopsy specimen of sural nerve in diabetic neuropathy, showing reduction in number of myelin sheaths (osmic) (×230) cf fig 11

The modalities of pain and temperature sensation as well as the vasomotor responses are conveyed by non myelinated or thinly myelinated nerve fibres (Gasser and Erlanger 1929, Ranson 1931, Ranson et al 1935, Clark et al 1935, Lewis and Pochin 1937, Woollard et al 1940), which tend to be affected by noxious influences long before the myelinated sensory and motor fibres It is now generally accepted that this susceptibility is due to the difference in the size of the nerve fibre (Gasser and Erlanger 1929)

The finding that autonomic fibres seem to be involved early in the development of diabetic neuropathy, and

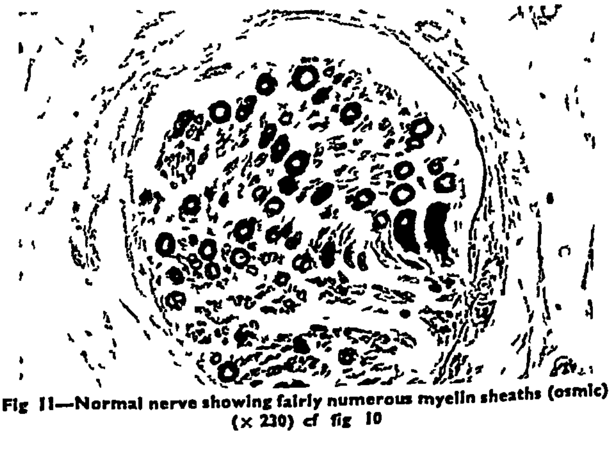

Fig 11—Normal nerve showing fairly numerous myelin sheaths (osmic) (× 230) cf fig 10

lumbago, to belching and distension after meals, but not to typical ulcer pain. The Madras duodenal ulcer is a fourth type, for it has no single point of resemblance to the three ulcers of Britain beyond its anatomical site.

Gastric ulcers probably represent an equal diversity of types, but the opportunity to classify them is seldom permitted to the surgeon. The gastric patient and his physician are linked by an oath of mutual allegiance, "till death do us part."

Diagnosis

The diagnosis of peptic ulcer is usually a straightforward matter; but many cases are atypical, and even the best radiologists may describe ulcers where there are none and miss them when they are there—a fact which radiologists, particularly the best ones, are ready to admit. It is the atypical case for which we should be prepared; for to discover the true cause of a symptom-complex that has puzzled others, and to put it right, is to go to bed with the warm glow of self-awarded approbation. We should suspect peptic ulceration in all cases of unexplained loss of weight, and in all cases where the symptoms, whatever they may be, have a tendency to come at the same time every day, a tendency to wake the patient in the small hours of the morning, and a tendency to be associated with periods of stress, and to be relieved at weekends or on holidays.

It is above all necessary to remember that when a peptic ulcer becomes adherent to and invades another organ, the pain to which it gives rise is that of the organ it penetrates and is not necessarily associated with meals. When the ulcer involves the parietes, the pain is somatic rather than visceral in nature.

A gentleman of 62 fell from his yacht in 1948 and injured his right shoulder. Ever since he had suffered intense pain in his back and right scapula. He had been under the care of eminent physicians and rheumatologists. He had been treated by physiotherapy. He had visited foreign spas. He had been investigated by a cardiologist. Like the woman in the New Testament with the issue of blood, he "had suffered many things of many physicians but was nothing better, but rather grew worse." He had become a pethidine addict. Then one day he fainted in his bath, and passed a copious motion consisting almost entirely of blood. Operation disclosed a large duodenal ulcer, adherent to liver, common bile-duct, and pancreas, and surrounded by a measles of black silk knots left there by a disciple of Halsted who had removed his gall-bladder in New York in 1941. It was necessary to perform gastrectomy in two stages, but all went well. He has not had an ache or a tablet of pethidine since.

For five years a lady of 47 had suffered pain in the back entirely unrelated to meals. Her spine had been radiographed four or five times. She had undergone a complete renal investigation, but a barium meal had never seemed necessary. She had been under the care of several orthopædic surgeons and had been manipulated and put in a plaster jacket. Finally she had been labelled a neurotic. Eventually clues denied to her former advisers made their appearance, for she started to lose weight and to vomit At operation a large gastric ulcer was found, involving the liver and the pancreas and explaining all her troubles. Gastrectomy was remarkably easy, as it nearly always is when the ulcer is in the stomach rather than in the duodenum. Today, instead of a tearful hypochondriac living under the shadow of the psychiatric Gestapo, she is a cheerful happy normal woman.

Medical Treatment

When we come to discuss the treatment of peptic ulceration, we must first remember that we are dealing with a non-malignant condition—one that is disabling rather than dangerous. Ulcer patients have pain and indigestion and come to us for relief; but they would rather keep these symptoms than lose their lives, and they would rather keep their normal digestive apparatus if it can be repaired than accept some man-designed substitute, however well it may appear to work. Medical treatment therefore comes first, and medical treatment can heal an ulcer that is recognised early and treated vigorously. The longer an ulcer has been present, the more often it has recurred, the more likely is it that normal structures will have been replaced by scar tissue covered with a single layer of epithelial cells, and the more certain is it that the ulcer will break down again as soon as normal habits are resumed.

It is difficult to assess the value of medical treatment in peptic ulceration; for physicians are by nature optimists, and few of them have risked taking the fine glow off their enthusiasm by a long-term follow-up of their results. Seven years ago, for the purpose of a lecture in Australia, I asked one of my former house-surgeons, who now holds the chair of surgery in a northern university, to let me know the results of the medical and non-surgical treatment of peptic ulcers in the large teaching hospital where he was then working. These figures I have published in full elsewhere. I can summarise them very roughly by saying that of the patients treated medically 1% died in hospital and 99% were discharged as cured: five years later, however, 10% of those discharged patients were dead, 55% were classified as unsatisfactory, and only 34% as satisfactory. There is a definite tendency at the present time to resort to surgery at a very much earlier date—a tendency which can very easily be allowed to go too far.

Indications for Surgery

Surgical treatment is indicated when medical treatment is useless, when it has failed, when it is certain to fail, or when, after long trial, it can offer no more than a life of continued invalidism. These indications assume different values in gastric and duodenal ulcers.

GASTRIC ULCER

Gastric ulcers are a good deal less common than duodenal ones, and their cause remains shrouded in mystery. They do not seem to affect any particular district, occupation, or physical or psychological type. They are not clearly associated with stress. They are not accompanied by hyperchlorhydria, by continual secretion. or by gastric hurry. On the whole they tend to affect the placid and the unambitious rather than the strivers. Gastric ulcers seldom perforate. They seldom undergo stenosis sufficient to obstruct the passage of food. On the other hand they soon pass into a state of chronicity from which only temporary relief is obtainable by medical means. The stomach must be free to expand to accommodate a meal, to transmit vigorous waves of contraction that break up the food, and to adjust its position in relation to other viscera according to whether its owner is lying or standing, replete or hungry. These movements and these adjustments are interfered with by a scar that interrupts the muscular continuity and by adhesions that lead to fixation.

A gastric ulcer, once it has penetrated neighbouring structures, once it has produced a breach of continuity involving all coats that exceeds the diameter of a sixpence, will never heal more than temporarily. It is a safe rule that a gastric ulcer should be submitted to surgery if it is not soundly healed after a year of medical treatment conscientiously followed, or very much sooner if there is any doubt about its innocence.

I have said repeatedly that a gastric ulcer never becomes malignant—using the word "never" in the sense of the captain of the *Pinafore*: "What! never? Well, hardly ever." In an experience of gastric surgery that now extends over several decades and several hundreds of cases, I this year encountered the first patient in whom I was convinced that this change had taken place. I have been told in the past by pathologists that an ulcer I have removed was an ulcer-cancer; but all the pathologist can say is that the ulcer has the typical appearances

SPECIFICITY OF INCOMPLETE "COLD" ANTIBODY IN HUMAN SERUM

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B Sc Queensland

MARIE CUTBUSH
B Sc Melb

P L MOLLISON
M D Camb, M R C P

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Dacie (1950) showed that normal human red cells, left in their own serum at 2°–5°C for two hours and then washed in warm saline solution, often gave a positive direct anti-globulin test He stated that the incomplete "cold" antibodies responsible for this reaction could be found in most, if not all, sera from apparently healthy persons

Crawford and Mollison (1951) reported that when the red cells of different normal people were exposed to a given sample of normal serum at 0°C, washed at room-temperature, and mixed with anti globulin serum, there were considerable differences in the strength of agglutination In further investigation of this phenomenon the red cells of different people were tested against their own serum and against the serum of each of the others The results showed immediately that group-O cells were more strongly sensitised than group-A_1 cells, and that the reactions of group-A_2 cells were intermediate This suggested the possibility that the antibody concerned might be anti-H (using the terminology of Morgan and Watkins 1948)

The present observations show that the incomplete "cold" antibody present in all normal human sera does in fact give the reactions expected of anti H

METHODS

H substance—Saliva from "secretors" was used as a source of H substance, saliva from "non-secretors" was used as a control The presence or absence of H substance in saliva was determined by testing the power of the saliva to inhibit the agglutination of group-O cells by a 1/30 dilution of rabbit anti-H serum Saliva containing H substance but not Le^a or Le^b substance was obtained from four people A 1% solution of purified H substance (supplied by Prof W T J Morgan) was used to confirm the specificity of the inhibition produced by saliva

Eel serum (anti-H)—The serum of an eel, *anguilla anguilla*, was used (Jonsson 1944) At a dilution of 1/50 this serum very strongly agglutinated group-O cells but gave weak or negative reactions with cells of groups A_1 or A_1B

Rabbit anti-H serum—Serum prepared by injecting purified H substance into a rabbit was used

Anti globulin serum—Several different anti-human globulin sera, prepared in rabbits, were used After absorption with ten-times-washed red cells of different ABO groups, serial dilutions of each serum were tested against red cells sensitised with different antibodies With "cold sensitised" red cells the greatest agglutination was always obtained with undiluted anti globulin sera, although cells sensitised with Rh antibody were most strongly agglutinated by dilutions of anti globulin sera ranging from 1/16 to 1/64

Cold sensitisation—This term may conveniently be used for the phenomenon described by Dacie (1950) One volume of a 50% suspension of red cells was mixed with 7–10 volumes of serum and left for an hour at 0°C Fresh serum was used for all tests since, as shown by Dacie, complement (or a factor with similar properties) is necessary for cold sensitisation After sensitisation the cells were washed three times in warm saline solution and finally resuspended in saline solution to give a 20% suspension of red cells A drop of the suspension was then mixed on an opal glass tile with a drop of anti-human globulin serum The tile was rocked gently over a source of light, and the mixture was examined for agglutination Results were read finally at five minutes

Inhibition of incomplete "cold" antibody—Serial doubling dilutions of saliva or of a 1/10,000 solution of H substance in saline solution were added to equal volumes of fresh serum and left for half an hour at 20°C 1/10 volume of a 50% suspension of group-O cells was next added and left at 0°C for an hour The cells were next washed and tested with an anti-globulin serum

RESULTS

Effect of ABO Group on Degree of Cold Sensitisation

When the red cells of people of different ABO groups were tested with their own serum in the cold by the method described, considerable differences in the degree of sensitisation were observed

To determine whether this was due rather to differences in the amount of antibody or to differences in the amount of antigen the sera of people of different blood groups were tested against their own red cells and the red cells of all the other people To prevent anti-A and anti B from interfering with the reactions, sera from people of group A, group B, and group O were first absorbed with A_1B cells at 27°C Representative results of such an experiment are shown in table I

TABLE I—EFFECT OF ABO GROUP ON COLD SENSITISATION, CELLS OF FIVE PEOPLE TESTED AGAINST SERA FROM THE SAME FIVE PEOPLE

Serum	Cells				
	A_1B	A_1	B	A_2	O
Group A_1B	−	W	+	++	++++
,, A_1*	−	W	+	++	++++
,, B*	−	W	+	++	+++
,, A_2*	−	W	+	+	+++
,, O*	−	W	+	+	+++

* Anti A and anti B removed with A_1B cells at 27°C

The results show that the failure of A_1B cells to be sensitised by their own serum is not due to lack of incomplete "cold" antibody, for the serum of A_1B people appears, in fact, to contain the most antibody, judged by its reaction with group-O cells The main factor determining the differences in the reactions is evidently variation in antigen content between the red cells of one group and another, the groups arranging themselves in the following order $O > A_2 > B > A_1 > A_1B$

Test in Parallel with Eel Serum

These results suggested that the reactions might be due to anti-H To test this hypothesis red cells from forty donors selected to give about equal numbers of groups AB, A, B, and O were tested, firstly at 0°C with serum from an A_1B person (cold sensitisation), and secondly with an eel serum (agglutination at 20°C)

TABLE II—RED CELLS OF ELEVEN GROUP A DONORS TESTED WITH A_1B SERUM (COLD SENSITISATION) AND WITH EEL SERUM (ANTI H) REACTIONS OF SAME CELLS WITH α_1 SERUM ARE ALSO SHOWN

Donor	Reaction with anti globulin serum after sensitisation by A_1B serum at 0°C	Reaction with eel serum 1/50	Reaction with α_1 serum
1	+	+	+
2	(+)	(+)	+
3	−	Trace	+
4	+	++	−
5	−	Trace	+
6	+	+	−
7	++	++	−
8	(+)	(+)	+
9	(+)	(+)	+
10	++	++	−
11	(+)	+	+

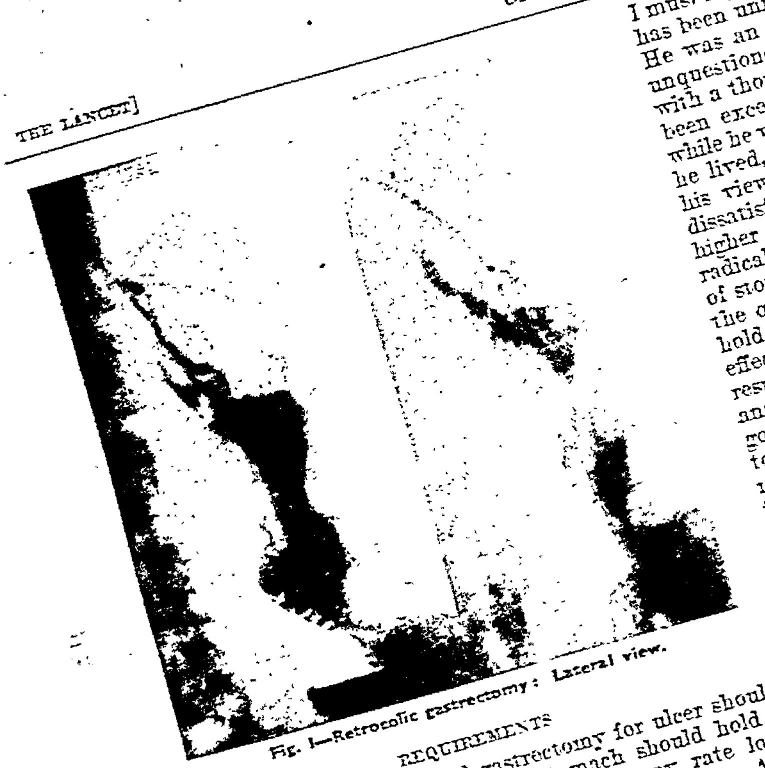

Fig. 1—Retrocolic gastrectomy: Lateral view.

REQUIREMENTS

In my view, a successful gastrectomy for ulcer should satisfy two criteria. First the stomach should hold a reasonable-sized meal and retain it at any rate long enough for some gastric digestion to take place. And secondly it should still secrete some hydrochloric acid without which it cannot function as a stomach, but in a concentration low enough to be safe and only at such times as it contains food. To attain this ideal there are at any rate five technical requirements:

1. The whole pyloric mucous membrane must be removed, to abolish hormonal secretion of acid.

2. The body of the stomach containing the most thickly studded gastric glands must also be resected.

3. The perigastric tissues on the lesser curve must be divided at the level of the cardia to free the stomach from the tethering of the left gastric artery and to divide a high proportion of the vagal fibres which are aggregated here.

4. The size of the stoma must be no larger than the diameter of the small intestine into which it empties.

5. The passage of food after leaving the stomach must be in an onward direction only.

There are other considerations: the anastomosis must be supple, and any use of unabsorbable sutures, any method of suturing that uses more than two layers, and any wide infolding of the edges, make a bad stoma; and the re-formed stomach must be free to move in its surroundings as it fills and empties, contracts and relaxes, as do all functioning hollow organs—the oesophagus, the ascending colon, the rectum, and the ureters. Both the Billroth-I operation, when it is done for gastric ulcer and the reduced stomach is anastomosed to an unscarred and unshortened duodenum, and the Billroth-II operation with a long Lake-Finsterer valve, an opening no more than $1\frac{1}{2}$ in. in diameter, an afferent loop brought above the mesocolon, and an efferent loop passing through it, satisfy all these requirements.

CAUSES OF FAILURE

Why then are not all gastrectomies successful? Here I am on very unsafe ground: for the methods I condemn are practised by many surgeons to their satisfaction, and my pet devices are looked on with horror by others. t the risk of giving offence, however, I must mention hat I regard as three fundamental errors.

First, because to my mind it is the most important mistake of all, is removing too much stomach; and here I must say with great regret that I think Visic has been unfortunate. Visick was a man we all admi He was an excellent operator, a man of enterprise and unquestioned integrity, and he followed up his cases with a thoroughness and an impartiality that have never been exceeded. The tragedy is that death caught him while he was rushing headlong along the wrong path. Had he lived, I have no doubt that he would have changed his views, for his policy was one of despair. He was dissatisfied with his results and he divided the stomach higher; he was still dissatisfied and he became more radical, till in the end he was leaving only a small cuff of stomach that was little more than a sleeve connecting the oesophagus to the jejunum. Such a stomach cannot hold food, nor can it conduct gastric digestion. Its effect is to impose permanent jejunal feeding. Visick's results were reported fully by him and they have been analysed recently by Pulvertaft,[1] and they are not as good as we have the right to expect today. I am obliged to discuss this matter because it appears to me that most of the reports on postgastrectomy syndromes come from centres where the influence of Visick has led surgeons to perform a gastrectomy that is too radical for anything but cancer.

The level of gastric division cannot be laid down by rule. Some surgeons say they go as far as the lower pole of the spleen, but the statement has no meaning since the spleen and the stomach have no firm relationship: the greater curve alters its shape and contour as the branches from the splenic vessels are divided, and if the division is continued the oesophagus is finally reached without the spleen having been displaced from its bed. I suggest that the left gastric artery should be divided at its origin, but that the lesser curve itself should not be cut too high or the competence of the cardiac sphincter will be destroyed. The vessels of the greater curve should be divided till we come to the end of the left epiploic branches, but we should not decide how much to remove till we have lifted up the left costal margin and looked at the prepared stomach where it lies, and have chosen a plane of section that will leave a cavity able to contain about a pint.

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[1] Pulvertaft, C. N. *Lancet*, 1952, i, 225.

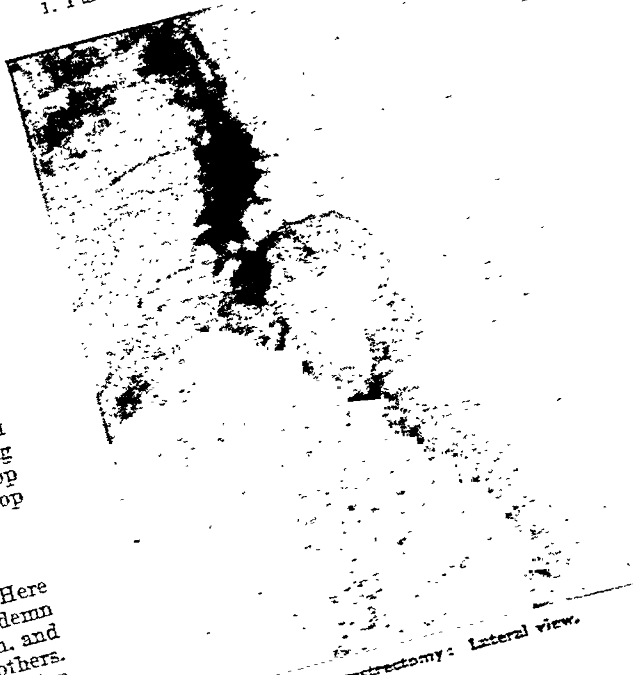

Fig. 2—Antecolic gastrectomy: Lateral view.

ISOLATION OF PITUITARY ANTIDIURETIC PEPTIDE AND SIMILAR URINARY PEPTIDE BY PAPER CHROMATOGRAPHY

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From the Department of Child Health, University of Glasgow, and the Royal Hospital for Sick Children

IN 1948 Dent, using two-dimensional paper chromatography, detected an unusual peptide in the urine of patients with nephrosis This finding has been confirmed on numerous occasions during the last five years at the Royal Hospital for Sick Children where we have consistently found the "nephrotic peptide" in the urine of patients with nephrosis, although the quantity has varied considerably We have also obtained a similar peptide from the urine of patients with œdema due to other causes (such as acute hæmorrhagic nephritis, anaphylactoid purpura, polyarteritis nodosa, and pre-eclamptic toxæmia) and of patients who have sustained acute trauma (such as a burn, a scald, or a fracture) or have undergone a surgical operation

Barlow (1952) found excessive antidiuretic activity in the blood of patients with nephrosis, and this finding suggested to us that the diuresis which occured during the administration of adrenocorticotropic hormone (A C T H) to a number of nephrotic patients in our hospital might be due to a lessening in the production of pituitary antidiuretic hormone Further, it seemed possible that the urinary peptide might be related in some way to antidiuretic activity We therefore decided to examine some commercial extracts of the posterior-pituitary gland to ascertain whether a similar peptide was present in them, and, if so, whether it possessed antidiuretic activity Eight such preparations in everyday use as antidiuretic and oxytocic agents were subjected to two-dimensional filter-paper chromatography by the technique described by Consden et al (1944), firstly to analyse the amino-acid and peptide structure of the extract, and secondly to separate the components for individual investigation

METHODS

The extracts were run on no 1 Whitman's filter paper with phenol ammonia and butanol acetic acid as solvents and developed with 'Ninhydrin' The various amino acids could then be identified by their position on the filter paper The nephrosis peptide has a high Rf in phenol and a very low Rf in butanol acetic acid

To separate the different fractions of the commercial extracts for individual testing the following method was devised The contents of an ampoule of the extract were pipetted as a line of spots 3 in from the edge of the sheet of filter paper This was then run in phenol ammonia for about forty hours, by which time the preparation had moved about 15 in from the line of application of the material This 15 in length of paper was next cut into six or seven strips at right angles to the line of flow of the phenol The strips were eluted separately by capillary flow of distilled water, and each eluate then contained the amino acids or peptides according to their Rf in phenol (fig 1) The snuff preparation was dissolved in 2 ml of water and centrifuged, and the supernatant fluid was applied to the paper in the same way as before

To make sure that a hydrolysable peptide was present alone in the end strip, the following technique was adopted The contents of an ampoule were applied as a line of spots as before, but after being developed in phenol ammonia the paper was reversed and run back in butanol acetic acid By this means traces of amino acids such as arginine and lysine which would otherwise have been in the end strip, were run back and any acetylated amino acids which might have been present were removed The peptide (which does not run in butanol) remained in the end strip The strips were then eluted and divided into two portions—one for analysis on paper to show that the peptide was present, and the other for hydrolysis in 6*N* hydrochloric acid for thirty six hours and further analysis by chromatography

Peptide from urine for analysis and assay was prepared in essentially the same way The urine was deproteinised by bringing it to boiling-point, adjusting to pH 5 5, and filtering when cool The filtrate was treated with sodium tungstate and sulphuric acid, which precipitate the peptide The precipitate was centrifuged, washed in water, recentrifuged, and dissolved in ammonia The concentrate was pipetted on to the paper in a line of spots as described above, and eluates were prepared for assay By this means the residue of 20–30 ml of urine could be applied to one sheet of paper A control paper containing the tungstate and sulphuric acid was run, and a corresponding strip was eluted and tested as a control

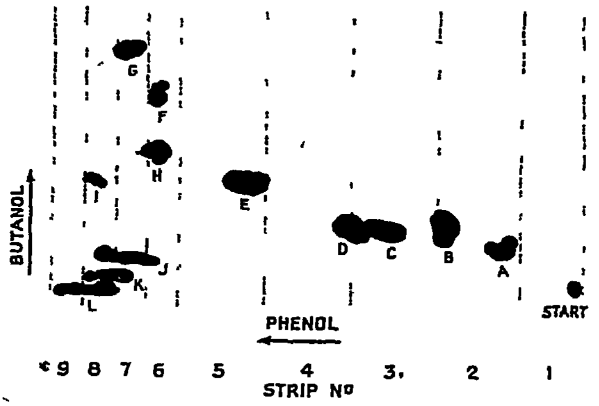

Fig 1—Chromatogram of posterior-pituitary extract A K, amino acids, L, peptide

POSTERIOR-PITUITARY EXTRACTS

A substance similar in position and behaviour to the nephrotic peptide was obtained on chromatographic analysis of each of the eight commercial preparations For the following reasons we believe that this unknown substance is a peptide

(1) *The substance is not a protein, being soluble in phenol* ammonia

(2) The substance can be dialysed through a 'Cellophane' membrane and retain its form and activity

(3) The substance when hydrolysed yields at least twelve amino acids These are arginine, leucine, isoleucine, valine, aspartic acid, glutamic acid, cystine, lysine, glycine, alanine, and traces of threonine and serine

The presence of such peptide in these extracts having been established, it became necessary to determine the antidiuretic activity of the substance The end strips of the chromatograph paper were prepared as described, and the peptide eluted by distilled water and reduced in volume to 1 ml The antidiuretic activity of this eluate was assayed in rats by the method of Burn (1931) The time of half diuresis—i e, the time between the gavaging of 5 ml of water per 100 g of rat and the excretion of 50% of this fluid as urine—was accepted as the critical measurement The results obtained on testing eight

ANTIDIURETIC ACTIVITY OF PEPTIDE EXTRACTED FROM COMMERCIAL POSTERIOR PITUITARY PREPARATIONS BY CHROMATOGRAPHY TESTED IN RATS BY ESTIMATING TIME OF 50% DIURESIS

(After Burn 1931)

Preparation	Peptide in strip	Time of 50% diuresis (hr)				Antidiuretic activity
		1	2	Control	Control	
A	Yes	8 –	8 –	1½	1¾	+
B	Yes	8 –	8 –	1½	1½	–
C	Yes	4½	6	1¼	1½	–
D	Yes	6½	3¼	1½	1¼	+
E	Yes	3 +	5 +	1¾	1	+
F	Yes	7 +	3¼	1½	1¼	+
G	Yes	4	7 +	1¾	1½	+
Snuff	Yes	3	6 +	1½	1¾	+

prevented a rise above 26° and 27°C. The response of this oup of patients is shown in fig. 4. The response of 1 of the patients with peripheral vascular disease is shown in fig. 5. (3) The 1 remaining patient gave the response shown in fig. 6. On cooling, the right big toe behaved abnormally, though its temperature eventually fell below that of the thumb. Reflex vasodilatation on heating took place normally. The tests of autonomic function were made when his neuropathy was recovering except for residual loss of his knee-jerks and ankle-jerks, and it is believed that the test indicated normal function of the vasodilator nerves with partial recovery of the vasoconstrictor fibres.

Diabetic Patients with Neuritic Manifestations but no Neurological Signs

A patient, aged 33, with twenty-three years' diabetes, a diabetic retinopathy, occasional ankle œdema in the past, and impotence, complained of neuritic pains in his legs, worse at night. On examination no abnormal neurological signs were found. Tests of sympathetic function showed persistent vasodilatation and lack of vasoconstriction on cooling (fig. 7). The same response was obtained in another patient with symptoms only. A similar result was recorded in a patient with diabetic nocturnal diarrhœa, fæcal incontinence, and impotence. Another patient with diarrhœa showed a normal response in his legs.

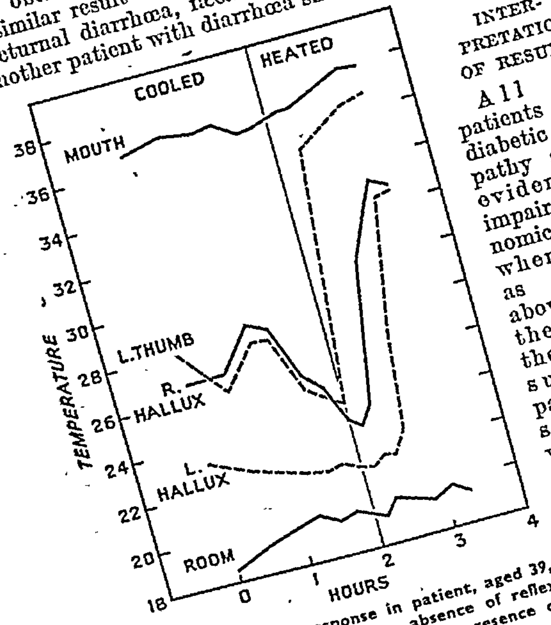

Fig. 6—Vasomotor response in patient, aged 39, with diabetic neuropathy: absence of reflex vasoconstriction in right hallux; presence of reflex vasodilatation in both toes.

INTERPRETATION OF RESULTS

All the patients with diabetic neuropathy showed evidence of impaired autonomic function when tested as described above. In half the patients the response suggested paralysis of the sympathetic vasoconstrictor and sudomotor fibres, as seen after sympathectomy. In the other half the legs remained persistently cold and did not respond to heating of the body, as observed after complete denervation (Lewis and Pickering 1936). Lewis (1946) ascribed this to degeneration of the nerves of the posterior root system, in addition to degeneration of the sympathetic vasoconstrictor fibres. That this was not the case in the patients with diabetic neuropathy was shown by their response to the intradermal injection of 0·1% histamine into the skin of the feet. Neither in the patients in whom the legs were cold and did not respond to heating of the body nor in the patients with persistent peripheral vasodilatation was the flare of the triple response present (Lewis 1927). This indicates that the posterior root system was involved in both types of cases, as was to be expected in view of the loss of pain perception in both groups, and was not the explanation for the different vasomotor changes observed.

The findings therefore suggest not only the presence of damage to autonomic vasomotor fibres in all the cases of diabetic neuropathy examined but also the separate existence of vasqdilator and vasoconstrictor fibres. The existence of vasodilator fibres had been demonstrated previously by Lewis and Pickering (1931) and Fatheree and Allen (1938), but Uprus et al. (1935) questioned the conclusions of other workers.

TABLE II—PARTICULARS OF PATIENTS FROM WHOM BIOPSY SPECIMENS WERE OBTAINED

Case no.	Sex	Age (yr.)	Duration of diabetes (yr.)	Duration of neuropathy	Clinical evidence of arteriosclerosis	Nerve examined	Degeneration of	
							Myelin	Axis cylinder
1	M	47	14	2 yr.	0	Sural	+ + +	+ + +
2	M	41	22	5 yr.	0	Sural	+ + + +	+ + + +
3	F	64	2	1 mo.	0	Anterior tibial	+ + +	+ + + +
4	M	56	Unknown	9 mos.	0	Sural	+ +	+ + +
5	M	66	9	7 yr.	+	Posterior tibial (amput.)	+ +	+ + +
6	F	32	8	3 mos.	0	Sural	+ +	+ +
7	F	59	Unknown	4 yr.	+	Sural	+ + + +	..
8	M	27	2	6 mos.	0	Sural	+ + +	+ + +
9	M	36	9	4 yr.	0	Sural	+ + + +	..
10	M	37	12	4 yr.	0	Sural	+ + +	+ + + +

+ Some degeneration. + + Moderate degeneration. + + + Severe degeneration. + + + + Very severe degeneration.

Evidence has also been obtained of autonomic dysfunction in patients with neuritic pains in the legs without signs and in 1 of 2 cases with diabetic nocturnal diarrhœa, but no symptoms or signs in the legs.

PATHOLOGY

Further evidence of involvement of autonomic nerve fibres in diabetes was obtained from the histological examination of biopsy specimens.

Very few studies have been made on nervous tissue in diabetic neuropathy:

Woltman and Wilder (1929) collected the published reports on the pathology of diabetic neuropathy and reported 10 cases of their own. Their material showed extensive degeneration of peripheral nerves in 8 cases and less severe degeneration in 2. Jordan et al. (1935) emphasised the susceptibility of the myelin sheaths to degeneration in diabetic neuropathy. Foster and Bassett (1947) found, in 1 case after amputation, a striking reduction in the number of myelin sheaths and axis-cylinders, an increase in Schwann cells, and advanced endoneural and perineural fibrosis. Muri (1949) reported demyelinisation of peripheral nerves but found no evidence of fibrosis.

Thus the reports on the pathology of nerves in diabetic neuropathy are very scanty. Joslin et al. (1947), thought this was due to the fact that this complication of diabetes is reversible and not fatal, and they did not consider biopsies of nerves feasible, because of the danger of paralysis.

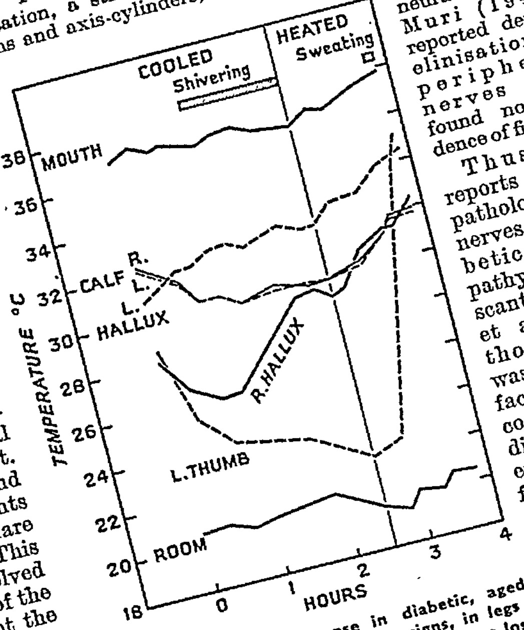

Fig. 7—Vasomotor response in diabetic, aged 33, with neuritic pains, but no signs, in legs: absence of reflex vasoconstriction indicates loss of function of vasoconstrictor fibres.

by the presence of an excess of such urinary peptides. The excretion of increased quantities of this urinary peptide following trauma or surgical operation suggests the possibility that an excessive output of pituitary hormone may occur at this time. It may be that excessive protein katabolism or other factors contribute, and we suggest that such substances in urine be termed a "peptide group" until more information is available.

These peptides raise many interesting problems, and their presence should be sought wherever excessive antidiuretic activity, shock, or œdema is present. Since it is possible that their presence in disease is due to an excessive excretion of a physiological end-product, it is important that quantitative methods of estimating the daily output in urine and the plasma levels be devised. Perhaps the investigation of disease caused by an excess of other pituitary hormones may be helped by applying the methods described here.

SUMMARY

By paper chromatography a peptide containing at least twelve amino-acids has been extracted from eight different commercial posterior-pituitary preparations. This peptide has strong antidiuretic activity and is the only part of these extracts possessing this property. It probably contains the antidiuretic factor.

The "nephrotic peptide" is present in the urine of œdematous patients with such diseases as nephrosis, acute hæmorrhagic nephritis, and pre-eclamptic toxæmia. On chromatography, electrophoresis, and hydrolysis followed by chromatography, it behaves exactly like the posterior pituitary peptide, but on injection into rats it seldom inhibits diuresis and often causes convulsions.

"Nephrotic peptide" was found in the urine of two normal people after antidiuresis had been induced by nicotine, and on injection into rats it caused convulsions.

The relationship of the peptides is discussed, and it is suggested that, until more is known about them, the urinary peptides should be termed a "peptide group".

It is a privilege to acknowledge our indebtedness to Prof. Stanley Graham for his encouragement and assistance in this work, and to thank him and Dr. J. H. Hutchison for permitting us to use material from patients under their care.

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TREATMENT OF DELIRIUM, PSYCHOSIS, AND COMA DUE TO DRUGS

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THE standard treatment of coma due to barbiturates or analgesics and alkaloids of the morphine group is by gastric lavage, measures to combat shock, artificial respiration, repeated injections of analeptics such as nikethamide, picrotoxin, and caffeine, and a glucose-saline drip when the patient is dehydrated or unable to swallow. Locket and Angus (1952) recently advocated a conservative approach to the treatment of barbiturate coma, mentioning unsatisfactory experience with analeptics. Sodium succinate has also been recommended as a means of providing an oxidisable substrate during the inhibition of glucose metabolism in the brain in barbiturate coma (Pinschmidt et al. 1945, Glaister 1950), but the method has not been widely accepted.

It is well known that the metabolism of glucose is disturbed and reduced by the administration of anæsthetics, and both anæsthetics and barbiturates (including those that are more hypnotic than anæsthetic in the usual concentrations) exert their action through solution in the brain lipids. The delirium, coma, and psychosis caused by drugs may well be manifestations of disordered brain metabolism—predominantly of glucose metabolism. The chemical reactions involved in glucose metabolism in the brain are at each stage subject, presumably, to the laws of mass action, and the exogenous substances that are important in brain metabolism are oxygen, glucose, ascorbic acid, aneurine hydrochloride, pyridoxine, and nicotinic acid. The treatment described in this paper therefore consists in the intravenous administration of large quantities of components of the vitamin-B complex, of ascorbic acid, and of glucose. It has been used in states of delirium and coma due to drugs of the barbiturate group, the near-alkaloids, such as methadone and pethidine, and alkaloids such as 'Omnopon' and heroin, and also in postoperative psychosis, acute alcoholic psychosis, and delirium tremens. It was in the treatment of the alcoholic group that the technique was first evolved, to be later modified and extended. Deliria and confusional states associated with infections have also responded to this method.

Method of Treatment

Direct moderately rapid injection into a vein, or a rapid drip is used. A typical prescription (to be given by *drip*) is:

Glucose 10 g. (10% solution)	100 ml.
Aneurine hydrochloride	1000 mg.
Nicotinamide	200 mg.
Pyridoxine	200 mg.
Ascorbic acid	1500 mg.
Distilled water or normal saline solution to	250–300 ml.

The total quantity is delivered in forty to seventy minutes. If a drip is not used, the same quantities of the vitamins are given intravenously in 30–50 ml. of 10% glucose solution. Concentrations of glucose up to 33% have sometimes been administered when there was no question of dehydration, but on the whole these concentrations are better avoided because of the risk of venous thrombosis. After the initial dose (which may be repeated if the patient does not respond satisfactorily), it is usual to give two more injections, each containing half the above amounts, at four-hourly to eight-hourly intervals, as indicated by signs of recurring sopor, alteration of behaviour, or clouding of consciousness.

Analeptics, such as nikethamide and picrotoxin, and cerebral stimulants, such as the amphetamines, are usually unnecessary; but when analeptics are used (usually in comatose patients) relatively small amounts seem to suffice—e.g., picrotoxin 2–6 ml. (6–18 mg.), nikethamide 4–6 ml. (250 mg. per ml.), and amphetamine 15 mg. They should be given intravenously after the glucose-vitamin solution. These drugs should be avoided in cases of delirium. It is inadvisable to give any one of the vitamins alone in very large doses because disturbances of autonomic function have been observed in such circumstances.

Conditions Treated

Several different types of case have been found to respond favourably:

(1) Effects of overdoses of barbiturates.
(2) Collapse under continuous narcosis.
(3) Postoperative psychosis.
(4) Drug-induced delirium.
(5) Acute alcoholic psychosis and delirium tremens.

The first two groups are examples of coma or near coma.

The *postoperative psychoses* do not seem to be due to excessive sedation. They are often paranoid in type, but may be depressive or toxi-confusional. The hallucinations and delusions tend to be florid and unsystematised, and illusions add to the prevented a rise above 26° and 27°C. The response of this group of patients is shown in fig. 4. The response of 1 of the 2 patients with peripheral vascular disease is shown in fig. 5.

(3) The 1 remaining patient gave the response shown in fig. 6. On cooling, the right big toe behaved abnormally, though its temperature eventually fell below that of the thumb. Reflex vasodilatation on heating took place normally. The tests of autonomic function were made when his neuropathy was recovering except for residual loss of his knee-jerks and ankle-jerks, and it is believed that the test indicated normal function of the vasodilator nerves with partial recovery of the vasoconstrictor fibres.

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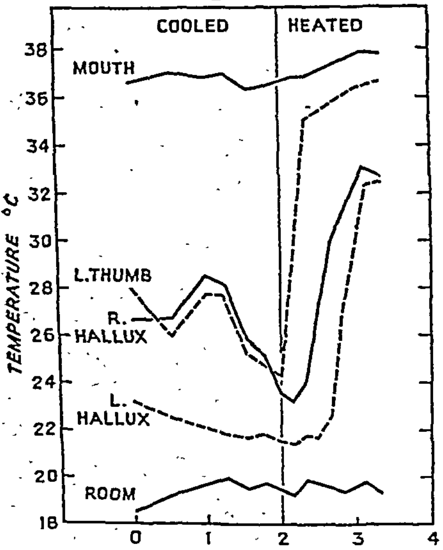

Fig. 6—Vasomotor response in patient, aged 39, with diabetic neuropathy: absence of reflex vasoconstriction in right hallux; presence of reflex vasodilatation in both toes.

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4	M	56	Unknown	9 mos.	0	Sural	+ +	+ + +
5	M	66	9	7 yr.	+	Posterior tibial (amput.)	+ +	+ + +
6	F	32	8	3 mos.	0	Sural	+ +	+ +
7	F	59	Unknown	4 yr.	+	Sural	+ + + +	..
8	M	27	2	6 mos.	0	Sural	+ + +	+ + +
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Further evidence of involvement of autonomic nerve fibres in diabetes was obtained from the histological examination of biopsy specimens.

Very few studies have been made on nervous tissue in diabetic neuropathy:

Woltman and Wilder (1929) collected the published reports on the pathology of diabetic neuropathy and reported 10 cases of their own. Their material showed extensive degeneration of peripheral nerves in 8 cases and less severe degeneration in 2. Jordan et al. (1935) emphasised the susceptibility of the myelin sheaths to degeneration in diabetic neuropathy. Foster and Bassett (1947) found, in 1 case after amputation, a striking reduction in the number of myelin sheaths and axis-cylinders, an increase in Schwann cells, and advanced endoneural and perineural fibrosis. Muri (1949) reported demyelinisation of peripheral nerves but found no evidence of fibrosis.

Thus the reports on the pathology of nerves in diabetic neuropathy are very scanty. Joslin et al. (1947), thought this was due to the fact that this complication of diabetes is reversible and not fatal, and they did not consider biopsies of nerves feasible, because of the danger of paralysis.

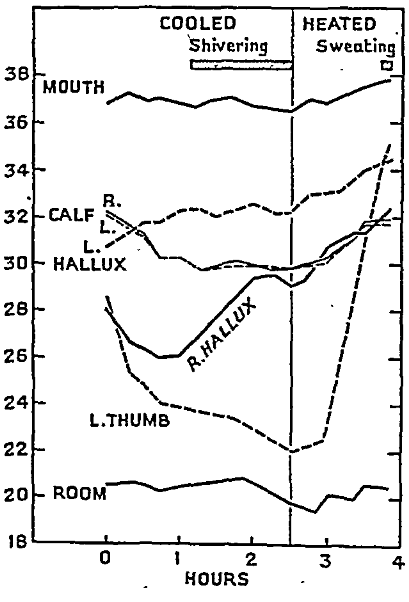

Fig. 7—Vasomotor response in diabetic, aged 33, with neuritic pains, but no signs, in legs: absence of reflex vasoconstriction indicates loss of function of vasoconstrictor fibres.

condition quite clearly did not warrant the doses used This suggests (as in case 3) that the psychotic process can be reversed by intensive vitamin therapy, even in the presence of adverse factors

Case 6.—A youth of 17 sustained a blow on the right knee while working in a mine, and in the subsequent six months he noticed increasing pain and swelling He was admitted to hospital for investigation Three days later he was informed of the intention to perform biopsy, and it was noticed that he became anxious, needing phenobarbitone (gr $^{1}/_{4}$) three times a day and pethidine (100 mg) twice a day for the intervening two days

Biopsy was performed, and later revealed an osteogenic sarcoma The anæsthetic given was thiopentone, nitrous oxide, oxygen, and trichlorethylene, with omnopon (gr $^{1}/_{3}$) and scopolamine (gr $^{1}/_{150}$) preoperatively He had papaveretum (gr $^{1}/_{3}$) after the operation Induction was difficult and he needed unusually large amounts of anæsthetic

When he recovered from the anæsthetic, he was restless, tried repeatedly to get out of bed, complained of pain, shouted, threw objects about the ward, occasionally sang, and showed extreme apprehension at the suggestion of an injection Sedatives and analgesics were given, rather less intensively than in case 5, though in much larger doses than are normally required after such minor operations His mental condition became steadily worse

When I first saw him, he was in a mild delirium, but it was possible to gain and hold his attention for a couple of minutes at a time He was restless, retching, anxious, and visually hallucinated by jeering faces whose expression altered as he watched He was convinced that the nurses were against him, and he was impulsively violent towards them He threatened to kill the surgeon who performed the operation, and he had made several not very determined attempts at suicide in the previous twenty-four hours It seemed that this boy's pain had assumed a rôle similar to that of the tactile illusions and hallucinations encountered in toxic deliria (particularly those due to heroin and cocaine) His conduct was quite uncontrolled and his insight very defective

The vitamin glucose mixture by intravenous drip was advised Owing to his refusal to have an injection, administration was delayed for twelve hours, but the vitamins were eventually given in 25% glucose solution by direct intravenous injection By the time the injection was completed he was rational, calm, and cooperative Six hours later, as there were signs of a return of mental clouding, half-doses of vitamins were given by injection, but on this occasion he was completely cooperative Further injections of half-doses were given on three occasions at twelve hourly intervals

No relapse into delirium occurred, although for the next few days he continued to be undisciplined in behaviour if in pain or thwarted, or when the effects of a sedative were wearing off During these times he repeatedly relived the accident to his knee, as he had continually done during his delirium Evidence suggested that his emotional and family background were very unsatisfactory, and that he was in fact an immature unstable individual of low average intelligence

Case 7—A man, aged 46, had a foot amputated for gangrene, and thereafter he needed sedation because of anxiety A week later hæmatemesis occurred on three successive days At laparotomy the gastric arteries were ligated, for portal hypertension was discovered instead of the peptic ulcer indicated by the history After operation hæmatemesis continued and large amounts of blood were given Heavy sedation, similar to that given in cases 5 and 6, was required At the end of a further week he had become confused, distended, and distressed , and when he was not torpid following sedation, he was difficult to manage in the ward, and continually begged for injections to relieve the pain An intravenous drip of the vitamin glucose mixture was given over a period of seventy minutes, and within two hours he became calm and rational He remained so, with the aid of reduced doses of the mixture, for three days when a further hæmatemesis proved fatal

Discussion

In health the amounts of these vitamins involved in brain metabolism, in terms of mg per 100 g of brain tissue, must be very minute, and the question arises whether the enormous doses used and the high blood-concentrations achieved are in fact necessary—quite apart from their mode of action They probably are important, and one of the main aims of this article is to enable more experience to be gained with the technique and to establish, if possible, a correlation between the concentration of drug in the body and the dosage of vitamins and glucose required Presumably, barbiturates and analgesics exert their action on the cycles of the various intracellular oxidation systems, and this suggests that there is no need to give glucose Indeed in the initial stages it was not used The clinical impression, however, is that glucose is of no disadvantage and often of advantage In case 1, four observers thought that there was a definite change in the body muscle tone as the glucose was injected, even though the patient was known to have a normal blood sugar level The advantage of glucose is further indicated by case 2 This girl had just undergone modified insulin therapy, and had gained nearly a stone in weight Her glycogen reserves were thus high, and she responded rapidly to the administration of the vitamins, without glucose, and did not relapse into torpor, even though no further vitamins or glucose were given Moreover, this patient had an abnormal electro encephalogram and a history of severe encephalitis due to pertussis at the age of 4 On two occasions in the past year the response of the E E G to glucose was recorded , when glucose was given intravenously the record became normal for two and a half minutes, whereas when glucose was given by mouth no change was observed

It is interesting that in case 1 the patient went into deep coma after 21 grains of amylobarbitone That this relatively small dose should have produced so deep a coma may perhaps be connected with the signs and symptoms of vitamin-B deficiency which she had had on and off for many years She also suffered from severe insomnia, and, before taking the amylobarbitone, she had not slept for a week following an emotional upset

In case 3, an apparently mixed barbiturate hypoglycæmic coma occurred on the tenth day of narcosis, and it seems likely that the effect of insulin, in lowering the already low blood sugar level, reinforced the effect of the barbiturate which had previously produced narcosis but not coma It may be therefore that the glucose metabolism and the cycles of the secondary intracellular oxidation-reduction systems are interdependent Case 4 recovered within twenty-four hours with intravenous administration of vitamins and a very similar case responded over a period of three days to intramuscular injections of 200 mg of aneurine hydrochloride twice daily with the other vitamins by mouth Similarly, case 5 responded over a period of three days in which 300 mg of aneurine hydrochloride was given four times a day Case 6 was also treated with analgesics and sedatives, though for a shorter period and less intensively than case 5, and responded within a few minutes to intravenous injection of the vitamin mixture Case 7 responded less rapidly, in very similar circumstances, to a rather slower administration of the mixture (by intravenous drip as opposed to direct injection)

The unusually high blood levels achieved in these cases may have been important in producing improvement , but, on the other hand, a 60 year-old man, with a falling hypertension and a rising blood-urea (over 150 mg per 100 ml), was given pethidine 400 mg daily to relieve the pain of a pulmonary infarction, and a confusional mental state developed which did not respond at all to the vitamin mixture given intravenously over a period of several hours in a litre of 5% dextrose and normal saline

The cases described in this paper show the range of conditions in which the technique seems valuable I have not had an opportunity to use it in cases of poisoning with massive doses of barbiturates, and clearly a response may be much more difficult to obtain in coma due to, say, 50 grains of phenobarbitone There is some evidence, however, of the benefit to be expected in such cases,

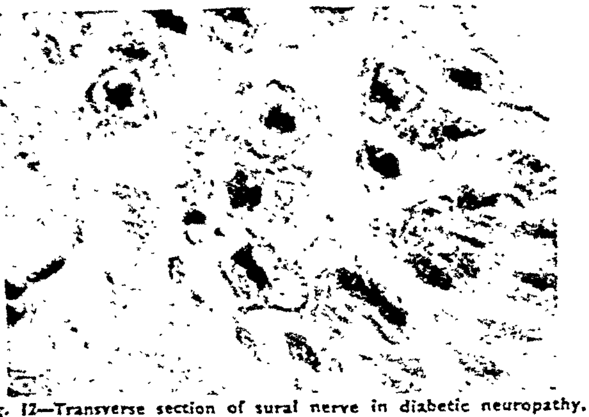

Fig. 12—Transverse section of sural nerve in diabetic neuropathy, showing striking absence of non-myelinated nerve-fibres (Holmes) (× 1000) cf. fig. 13.

were affected in all the cases of diabetic neuropathy investigated, suggests that non-myelinated nerve-fibres may be the first to suffer damage from the pathological process responsible for the nervous complication of diabetes. This would explain such diverse manifestations in diabetes as impotence, bladder paralysis, and diabetic nocturnal diarrhœa, often in the absence of neurological symptoms or signs elsewhere (Martin 1953).

The studies with priscol have shown a good functional response of the blood-vessels in the great majority of patients with diabetic neuropathy. Diabetics with intermittent claudication and evidence of occlusive peripheral vascular disease invariably showed a poor response to reflex heating and priscol, although there was no indication of involvement of the nervous system in these patients. This is rather against the contention that ischæmia plays an important part in the ætiology of diabetic neuropathy. Further support for this belief is given by the fact that non-myelinated nerve-fibres, which seem to be involved early in diabetic neuropathy, are known to be more resistant to impairment of blood-supply than are the larger myelinated fibres (Gasser and Erlanger 1929, Lewis and Pochin 1938, Grundfest 1940).

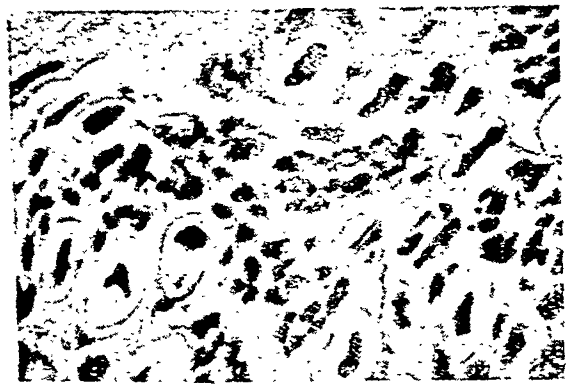

Fig. 13—Transverse section of normal nerve, showing closely packed clumps of non-myelinated nerve-fibres in between large myelinated ones (Holmes) (× 1000) cf. fig. 12.

The evidence presented supports the belief that the non-myelinated nerve-fibres subserving the autonomic vasomotor and visceral responses as well as the perception of pain and extremes of temperature are involved early in diabetic neuropathy and may be damaged in diabetes with no other evidence of a nerve disorder on routine clinical examination. The frequent loss of the tendon-reflexes in diabetics without other neuritic symptoms or signs is explained on the same basis, because the afferent pathways subserving the tendon-jerks appear also to be non-myelinated fibres. This is suggested by the finding that caudal analgesia by a method affecting only the smallest fibres produces loss of reflexes and pain without loss of other types of sensation or motor power (Martin 1953).

Whereas, in the past, neuritic symptoms without signs in diabetics were not regarded as indicating nerve disease, it now appears on the evidence presented that Jordan's (1936) "hyperglycæmic neuritis" and Treusch's (1945) "diabetes with pain" are early manifestations of diabetic neuropathy due to involvement of the non-myelinated pain fibres.

The concept of a degenerative lesion of small-calibre non-myelinated nerve-fibres subserving pain perception and the vasomotor and visceral responses as well as the tendon-reflexes, occurring in diabetes without necessarily being either followed or associated with involvement of larger fibres required for the clinical recognition of diabetic neuropathy, would explain many of the abnormalities at times met with in diabetics. The recognition of such a lesion is of great importance as a sign of nerve injury readily amenable to treatment.

I wish to thank Dr. R. D. Lawrence for his great kindness, advice, and encouragement; Dr. W. G. Oakley for much help and criticism; Dr. L. G Kilch for his help with the histological sections; Mr. G. Harwood for technical assistance; and Mr. W. Smith and Mr. A. J. Poole for the photographs; my thanks are also due to the patients for their tolerance and ready coöperation; and to the nurses of King's College Hospital for their assistance.

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the surface of the plate was completely covered with culture the excess fluid was pipetted off and the plates dried in the 48°C incubator for thirty minutes. A paper strip soaked in the solution of the substance to be tested was then laid across the surface of the agar plate. The plate was then incubated at 37°C and results recorded, usually after twenty-four or forty eight hours, but sometimes also after longer periods. The paper strips used as reservoirs for this technique were made from Ford's white blotting-paper ('Grade 428 Mill') 0·5 to 1·0 cm in width and of the required length, and they were sterilised in the hot-air oven at 160°C for one hour.

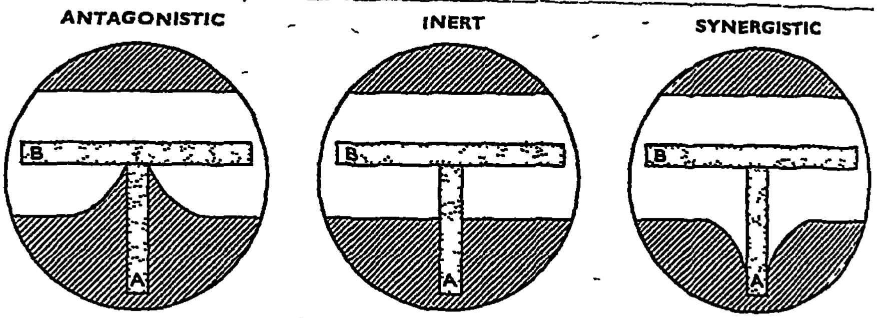
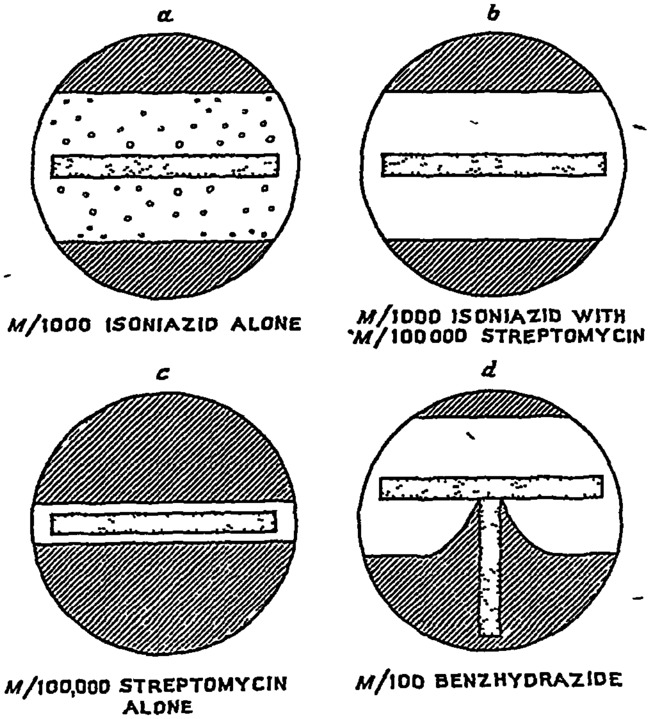


Fig. 2—Diffusion patterns shown by three types of substance in relation to isoniazid.

EXPERIMENTAL RESULTS

Testing Activity against Mycobacteria

A number of chemical compounds related to isoniazid were tested for activity against *Myco. smegmatis* by means of the screening plate. It was found that a 1000 µg. per ml. (*M*/137) solution of isoniazid gave a zone of inhibition on either side of the paper strip of between 2 and 3 cm. At first all the compounds were tested in a concentration of 1000 µg. per ml., but later they were retested together with isoniazid in a concentration of *M*/100 or *M*/1000. Whenever a compound was tested, an isoniazid solution of the same molecular concentration was put up as a control. When a compound was found to produce a zone of inhibition with the sensitive strain of *Myco. smegmatis*, it was then tested on the plate against the isoniazid-resistant strain and in the test-tube against the isoniazid-sensitive and isoniazid-resistant strains of H37RV. Fig. 1*a* shows the appearance of the screening plate with a strip containing *M*/1000 isoniazid, and inoculated with the sensitive strain of *Myco. smegmatis*.



M/1000 ISONIAZID ALONE

M/1000 ISONIAZID WITH *M*/100 000 STREPTOMYCIN

M/100,000 STREPTOMYCIN ALONE

M/100 BENZHYDRAZIDE

Fig. 1—Action of isoniazid and streptomycin alone and in combination on *Myco. smegmatis* on screening plate (*a–c*). In *d*, *M*/100 benzhydrazide and *M*/100 isoniazid are shown on strips at right angles, the isoniazid being horizontal. (Diagrammatic.)

Resistance

Resistant colonies.—It was found, when a screening plate with isoniazid in the strip was sealed to delay evaporation and was reincubated at 37°C for a further two or three days, that isolated colonies appeared within the zone of inhibition (fig. 1*a*). These colonies were shown to consist of cells which were more resistant to isoniazid than the parent culture.

Prevention of resistance.—The plate can be used to demonstrate the effect of combination of two or more compounds in preventing or delaying the appearance of resistant colonies. Fig. 1 shows that inside the zone of inhibition given by *M*/1000 isoniazid alone, large numbers of resistant colonies developed, that a strip containing *M*/100,000 streptomycin alone gave a negligible zone of inhibition, but that a strip containing both drugs in these concentrations gave a large zone of inhibition containing no resistant colonies.

Antagonism and Synergism

Perhaps the most striking and useful way in which the screening plate can be employed is in demonstrating antagonism or synergism between different compounds. In this method strips of blotting-paper soaked in the substances to be tested are placed at right angles. If a substance A is tested against an inhibitory substance B—for example, isoniazid—then interaction between the substances can be shown in three possible patterns on the plate, shown diagrammatically in fig. 2. (For convenience substance A is shown as having no inhibitory effect by itself in the concentration used.)

If substance A is inert in relation to isoniazid (B) then the zone of inhibition will be unaffected. If substance A is antagonistic to B then the zone of inhibition will be indented at the point at which the strip containing A crosses it. If substance A is "synergistic" to B, then where the strip containing A crosses the inhibitory zone, the edge of the zone will project in the region of the strip.

Antagonism could occur as the result of either direct chemical combination or "biological" competition for a specific enzyme. As an example of chemical combination, this pattern can be produced on the plate by placing *N*/10 HCl and *N*/10 NaOH on paper strips at right angles. An example which we think represents biological competition is the antagonistic effect of benzhydrazide on isoniazid. Fig. 1*d* shows the characteristic pattern of antagonism produced when these two drugs in *M*/100 concentration were placed on strips at right angles. So far we have been unable to find a clear-cut example of synergism between any of the substances tested.

Stimulation of Growth

We have used the method to investigate stimulation as well as inhibition of growth. Stimulation is most easily detected in a minimal medium, as in the auxanographic technique first attributed to Beyerinck (1889) and developed recently by Pontecorvo (1949).

DISCUSSION

The screening plate allows several points to be observed at the same time, and it is possible on one plate to

TABLE III—INHIBITION BY SALIVA OF "SECRETOR" AND BY PURIFIED H SUBSTANCE OF COLD SENSITISATION OF GROUP-O CELLS

—	* Dilution of saliva or of solution of purified H substance						Control: 1 vol. saline solution 1 vol. A_1B serum
	1/1	1/2	1/4	1/8	1/16	1/32	
Saliva of secretor	−	−	(+)	(+)	+	++	++
1/10,000 solution of H substance	−	(+)	+	+	++	++	+−
Saliva of non-secretor ..	++	++	++	++	++	++	++

* 1 volume of each of these dilutions was added to 1 volume of an A_1B serum.

When the reactions obtained with any one blood sample were compared, the results of the two tests agreed very closely. For example, cells that were most strongly sensitised in the cold by the A_1B serum were most strongly agglutinated by the eel serum. The reactions given by the cells of eleven group-A people are shown in table II; it will be noted that the strongest reactions were given by cells of subgroup A_2.

Inhibition of Incomplete "Cold" Antibody

The sensitisation of red cells by incomplete "cold" antibody could be prevented by first adding to the serum either saliva from a secretor of H substance, or a 1/10,000 solution of purified H substance (see table III).

The saliva of seventeen persons (eight group O, five group A, one group B, and three group AB) was tested for its ability to inhibit cold sensitisation of group-O cells. The saliva of the twelve secretors of H substance inhibited cold sensitisation; the saliva of the five non-secretors failed to do so.

TABLE IV—NEUTRALISATION OF INCOMPLETE "COLD" ANTIBODY IN SERA OF DIFFERENT GROUPS BY VARIOUS DILUTIONS OF SALIVA FROM A "SECRETOR"

(All tests with group-O cells)

Serum	* Dilution of saliva					Control: 1 vol. saline solution 1 vol. serum
	1/1	1/2	1/4	1/8	1/16	
Group A_1B ..	−	(+)	−	−+	+++	+++
" A_1 ..	−	(+)	+	++	+++	++−
" A_2 ..	−	−	−	−	++	+−
" O ..	−	−	(−)	++	+−	+−
" O ..	−	−	−	(−)	−	+−

* 1 volume of each serum was added to 1 volume of each dilution of saliva.

Four of the twelve "secretors" were specially selected because it was known that their saliva lacked Le^a and Le^b substance; thus any inhibition produced by their saliva could not be attributed to these Lewis antigens.

The cells of three of the "secretors" (one group A, two group A_1B) were known to be low in H substance, judged by tests with eel serum. Their saliva gave only partial inhibition of cold sensitisation and of agglutination by rabbit anti-H.

The saliva of two secretors of H substance was added to thirty different sera to discover whether there were some sera in which the incomplete "cold" antibody was not inhibited by the saliva of secretors of H substance; in all the cases the ability of the serum to sensitise group-O cells at 0°C was completely inhibited by undiluted saliva, and completely, or partially, inhibited by saliva diluted 1/4.

The technique of inhibiting cold sensitisation by the addition of varying amounts of saliva was used to demonstrate differences in the amount of antibody in different sera. This method was chosen since the alternative method of using serial dilutions of serum raised the difficult problem of supplying complement without supplying "cold" antibody. Table IV shows that the sensitisation of group-O cells by serum from a group-O person could be completely inhibited by a 1/4 dilution of saliva, whereas the serum from a group-A_1B person required undiluted saliva to inhibit completely the sensitisation of the same group-O cells.

Absorption of Incomplete "Cold" Antibody by Cells of Different Groups

Serum from an A_1B person was absorbed at 0°C with an equal volume of the subject's own washed red cells; these cells were known to react very weakly with anti-H. No appreciable amount of incomplete "cold" antibody was removed, judged by the reaction with group-O cells before and after absorption. However, when group-O cells were used for the absorption, the ability to sensitise group-O cells (or group-A_1 and group-A_2 cells) was completely abolished (see table V).

Similarly, when serum from a group-O person was absorbed with A_1B cells, there was no detectable weakening of the power of the serum to sensitise group-O cells, but after absorption with group-O cells the ability to sensitise group-O cells was lost.

TABLE V—RESULTS OF TESTING A_1B SERUM FOR ABILITY TO SENSITISE CELLS OF DIFFERENT GROUPS, AFTER ABSORPTION AT 0°C WITH GROUP-O AND GROUP-A_1B CELLS

A_1B serum	Test cells			
	A_1B	A_1	A_2	O
Before absorption	−	+	−+	+++
After absorption with O cells	−	−	−	−
After absorption with A_1B cells	−	+	−+	+−

DISCUSSION

Hitherto it has been generally assumed that the incomplete "cold" antibody present in normal human serum is a non-specific antibody—i.e., an antibody reacting on cells irrespective of their blood-group. The present observations show that the strength of the reactions of this antibody depends on the H content of cells. For example, if the donor belongs to group A_1B, his serum reacts more strongly with group-O cells than with his own cells.

The incomplete "cold" antibody appears to fulfil all the criteria for anti-H, the chief one being the ease with which it is inhibited by saliva from secretors of H substance.

In the light of these findings the specificity of other so-called non-specific antibodies requires re-examination. It has been generally assumed that the cold agglutinin found in almost all normal sera is a non-specific antibody, reacting as strongly with the donor's own cells as with any other cells. However, it is known that cold agglutinins with blood-group specificity (such as anti-P) occur in the sera of normal people; and it has been shown, too, that cold agglutinins of increased thermal amplitude —acting as auto-agglutinins—may also have blood-group specificity. For example, both Stratton (1943) and Dockeray and Sachs (1941) have described cases in which the patient's serum contained an agglutinin acting preferentially on group-O cells.

Investigations are now being made to determine how many of the apparently non-specific agglutinins have, in fact, blood-group specificity.

SUMMARY

The incomplete "cold" antibody present in all normal human sera has the specificity anti-H.

We are indebted to Prof. W. T. J. Morgan and Dr Winifred Watkins for gifts of anti-H rabbit serum and of purified H substance; and to Dr. J. D. James, of the North London Blood Transfusion Centre, for supplying a number of blood samples.

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TOTAL URINARY EXCRETION OF WATER, ELECTROLYTE, AND UREA FROM 10 30 A M TO 10 30 P M ON SUCCESSIVE DAYS, SHOWING OVER-ALL EFFECT OF BUTAZOLIDINE (CASES 1–3 ON DAY II)

(Difference between Day I and Day II indicates retention expressed also as percentage of first day's excretion)

Case no	Day	Urine					Blood			
		Volume (ml)	Sodium (g)	Potassium (g)	Chloride (g)	Urea (g)	Sodium (mg per 100 ml)	Potassium (mg per 100 ml)	Chloride (mg NaCl per 100 ml)	Urea (mg per 100 ml)
1	I II But	1114 297	3 895 1 217	1 956 1 525	5 720 2 165	10 170 9 504	333 329	20 6 18 5	562 562	30 31
	I−II	817(+73%)	2 678(+69%)	0 431(+22%)	3 555(+62%)	0 666(+6 5%)				
2	I II But	1639 914	3 853 1 485	2 043 1 516	7 160 3 540	10 770 10 490	322 322	20 4 18 5	596 596	33 25
	I−II	725(+44%)	2 368(+62%)	0 527(+26%)	3 620(+51%)	0 280(+2 6%)				
3	I II But	1091 331	3 143 0 883	1 977 1 706	5 550 2 025	11 245 10 480	325 329	18 4 17 0	608 602	28 27
	I−II	760(+70%)	2 260(+72%)	0 271(+14%)	3 525(+64%)	0 765(+6 8%)				
4 (Control)	I II	864 1067	2 825 3 322	2 332 1 897	4 940 5 480	11 050 11 880	329 334	17 1 19 5	562 596	31 27
	I−II	−203(−24%)	−0 497(−18%)	+0 435(+19%)	−0 540(−11%)	−0 830(−7 5%)				

and the reduction was still evident at twenty-four hours With the decrease in volume there was, of course, a decrease in excretion of total electrolyte , but, whereas the concentration of potassium increased about threefold (as did that of urea), the concentration of sodium in case 1 remained the same and in cases 2 and 3 decreased to half what it was previously The smallest amount of sodium excreted in cases 1–3 was from six to eight hours after injection These changes were most striking in case 3 (figs 1 and 2) One may calculate that the effect of butazolidine in the period from six to eight hours after injection, if maintained by continued dosage, would limit the urinary excretion of sodium to about 3 5 g of sodium chloride in twenty four hours

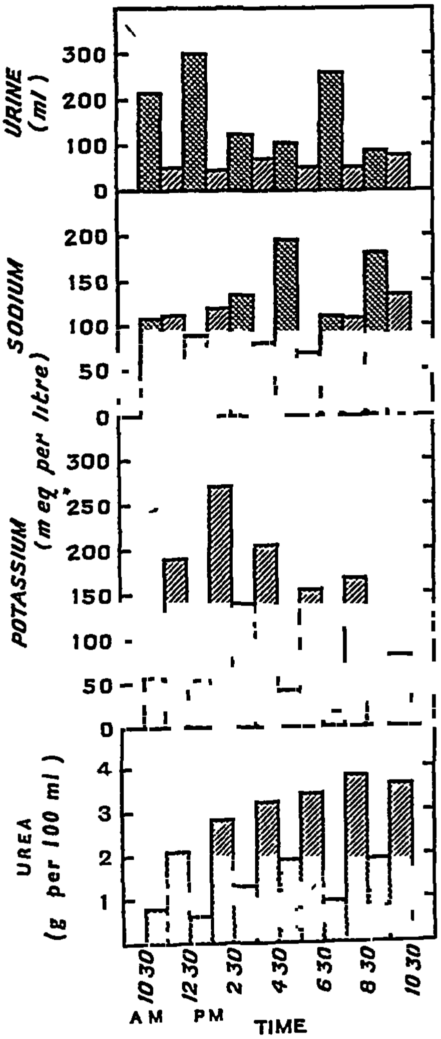

Fig 1—Two-hourly volume of urine, and concentration of sodium potassium and urea excreted by case 3 in twelve hours on day I (cross-hatched) with no butazolidine and on day II (hatched) after butazolidine 1 g at 10 30 a m

DISCUSSION

It is quite clear that the retention of water, sodium, and chloride is not merely an occasional toxic effect of butazolidine but the constant result in all cases studied It appears to be a selective effect on the excretion of electrolyte and water, without impairment of general renal function On this view the occurrence of œdema during therapy does not indicate intolerance of butazolidine but should prove amenable to control by restriction of sodium intake, coupled perhaps with mercurial diuretics

The effect appears to be due to increased reabsorption of sodium, bringing in its train retention of water and chloride, since the decrease in the volume of the urine is accompanied by a fall in the urine sodium concentration. If it had been a true "antidiuretic" effect, one would have expected a parallel rise in the urine sodium and urine potassium concentrations

The data presented do not distinguish between a direct or a mediated effect on the factors concerned (Berliner 1950) The resemblance to the action of the salt-conserving suprarenal hormones, and that of liquorice (Molhuysen et al 1950), is obvious

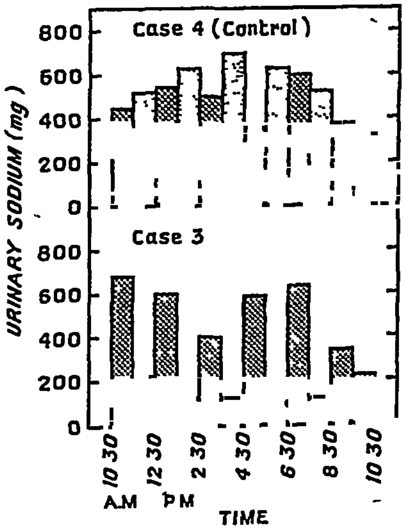

Fig 2—Two-hourly amounts of urinary sodium excreted by case 3 in twelve hours on day I (cross hatched) with no butazolidine and on day II (hatched) after butazolidine 1 g at 10.30 a m , compared with amounts of urinary sodium excreted by case 4 (control) in twelve hours on day I (cross hatched) and on day II (stippled) with no butazolidine

SUMMARY

The action of butazolidine on the retention of sodium has been studied

Selective retention of sodium took place in all persons studied and therefore should be expected when butazolidine is given

The resemblance to the action of the salt conserving suprarenal hormones is noted

We wish to thank the four volunteers for their cooperation, the endowment fund subcommittee and the board of governors of the Royal Free Hospital for facili

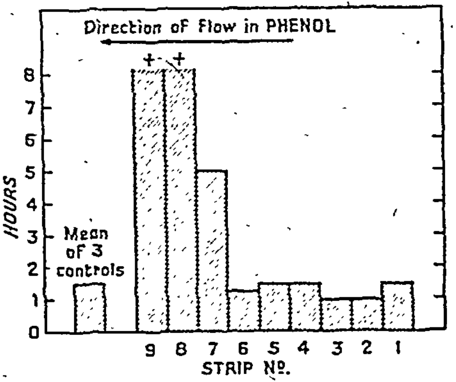

Fig. 2—Time of half-diuresis in rats injected with eluate from serial strips of chromatogram. Strips 8 and 9 exerted so great an antidiuretic effect that half-diuresis had not been completed after eight hours.

different extracts are shown in the accompanying table. In every case the strip of paper which contained the peptide had antidiuretic activity, and this was strong considering the minute amount of the substance present. On two occasions the chromatograph paper was cut into strips from one end to the other, and each strip in turn was tested for antidiuretic activity. In neither case was antidiuretic activity present in a strip which did not contain the peptide (figs. 1 and 2).

It therefore seems that this peptide contains the antidiuretic fraction of these preparations from the posterior lobe of the pituitary gland. No antidiuretic activity was detected in any other component of the extracts, and if the peptide was hydrolysed the antidiuretic activity was lost. The presence of at least twelve amino-acids, some in greater concentration than others, makes it likely that the molecular weight of the substance lies between 1200 and 2000. The finding of Turner et al. (1951) that the very pure vasopressin which they analysed contained only eight amino-acids suggests either that our peptide is a less advanced stage in the breakdown of the macro-molecule, or that some other substance, such as the oxytocic factor, has run identically on all these tests. A high concentration of similar peptide has been found in human pituitary gland, and small traces have been found in other organs.

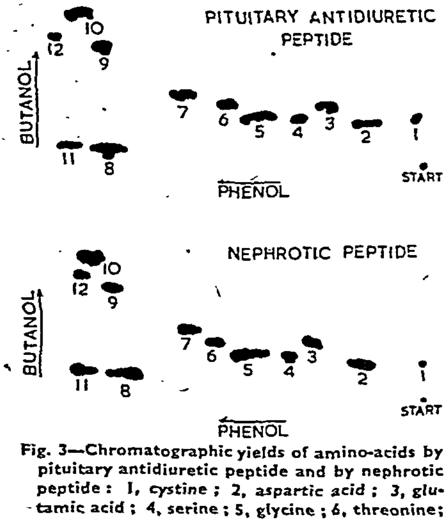

Fig. 3—Chromatographic yields of amino-acids by pituitary antidiuretic peptide and by nephrotic peptide: 1, cystine; 2, aspartic acid; 3, glutamic acid; 4, serine; 5, glycine; 6, threonine; 7, alanine; 8, lysine; 9, valine; 10, leucine; 11, arginine; 12, isoleucine.

URINE

"Nephrotic peptide" obtained from the urine of patients with acute hæmorrhagic nephritis, nephrosis, and pre-eclamptic toxæmia was then subjected to a similar investigation. Certain problems arose before successful chromatographic results were obtained, owing to the necessity of removing contaminants, such as albumin. On chromatography, the nephrotic peptide behaved exactly like the posterior-pituitary peptide, and hydrolysis showed that it contained the same twelve amino-acids in apparently similar proportions. The similarity of the pattern formed by the amino-acids of the two peptides is shown in fig. 3. When the nephrotic peptide and the posterior-pituitary peptide are subjected to electrophoresis they both move towards the negative pole, whereas A.C.T.H. does not.

Nephrotic peptide from seven patients was then injected subcutaneously into rats. This was done on twenty-two occasions, and in only three instances did a well-marked antidiuretic response result. It has been stated by Pickford (1952) that the method used was crude, testing only to 20 mU of antidiuretic activity, whereas the method of Jeffers et al. (1942) will detect 0·02 mU of antidiuretic activity. Though further observations with a more sensitive method are essential, it is clear that this urinary peptide has much less antidiuretic activity than the pituitary peptide. It is of great interest that on eight of the twenty-two occasions on which nephrotic peptide was injected subcutaneously into rats convulsions ensued shortly thereafter. These convulsions occurred within five minutes of the injection, lasted up to two hours, and appeared to leave no permanent damage (although large doses of postoperative urinary peptide killed some of the animals). This convulsant effect is much greater if the peptide is given intraperitoneally.

The following test was made on two volunteers who were non-smokers. Each of them drank a litre of warm water and, when brisk diuresis had started, smoked a cigarette, inhaling deeply and producing a well-marked antidiuretic response. No peptide was detected directly by chromatography of the urine passed by either person before smoking, and no antidiuretic or convulsant effect was demonstrated in rats. The urine passed after the "smoking antidiuresis" in subject G. A. possessed antidiuretic activity; and, although the nephrotic peptide was not visible when 0·5 ml. of urine was run, the presence of this peptide was clearly shown by the amino-acid yield on hydrolysis of the eluted end strip of a double-run chromatogram. In subject C. G. the "nephrotic peptide" was easily seen, antidiuretic activity was present, and the end strip of a sulphuric acid-tungstate precipitate of this urine caused convulsions in rats. It appears that the inhaled nicotine released an excess of antidiuretic hormone from the posterior lobe of the pituitary gland, leading to antidiuresis and the appearance of the urinary peptide. The fact that this urinary peptide from a normal person caused convulsions in rats strongly suggests that it is not an unaltered pituitary peptide.

DISCUSSION

The following possible explanation of the results so far obtained is tentatively advanced. Several of the hormones of the pituitary gland—e.g., A.C.T.H., oxytocin, and vasopressin—are peptides with a similar though not identical amino-acid content. Small quantities of similar peptide can be found in the urine of normal people, and the quantity present may be increased by inducing antidiuretic activity with nicotine. In a group of diseases characterised by oliguria and œdema (nephrosis, acute hæmorrhagic nephritis, and pre-eclamptic toxæmia) a considerable quantity of similar peptide is found in the urine. These urinary peptides closely resemble the peptide present in the posterior lobe of the pituitary, behaving similarly on chromatography, hydrolysis, and electrophoresis. They differ in having much less antidiuretic activity in rats and in the frequency with which they cause convulsions in this animal. It seems likely to us that at least some part of the urinary peptide is the altered form in which the antidiuretic peptide of the posterior lobe of the pituitary gland is excreted. The existence of similar peptides derived from the pituitary gland or other sources, failure of the liver to dispose of peptides, or failure of the kidney unit to maintain the peptides in the plasma may complicate the findings in disease. Byrom (1938) has shown that œstrin will increase tenfold the sensitivity of the rat's kidney to damage by vasopressin. It seems possible to us that an abnormal balance of hormones, together with an excess of pituitary antidiuretic peptide, may be concerned in some way with the production and course of the diseases characterised

Sept 23, she was in the kitchen when a 1 lb bag of ordinary flour was dropped and burst, and within a few hours she had severe irritation and rash affecting her face so that her eyelids were nearly closed The condition had almost cleared in three days It is to be noted that her hands were *not* affected On Sept 29 there was again a short exacerbation of her symptoms four hours after eating the chocolate from the outside of a shop-made chocolate cake

At 9 P M on Oct 12, when her skin was normal, she ate four sweets, later proved to contain agenised flour, and four hours afterwards she awoke with general irritation of the arms, hands, shoulders, and face By morning her eruption was present, and it lasted for five days

From this time onwards she lived on a flour free diet except for three loaves weekly made from C U T flour, and on one occasion she had a 7 lb bag of C U T flour for cooking purposes She was also sent the following list of foods which may contain agene-treated wheat flour

Tinned soups
Soup powders and cubes
Tinned meats
Gravy thickeners
Lemon curd } Inferior
Cocoa and chocolates } makes
Mustard mixtures
Sausages
Meat pastes
Pepper mixtures
Fish pastes
Sauces tomato, &c
Piccalilli
Ice cream
Wafers and waffles
Chocolate fillings
Certain sweets
Some blancmanges and custard powders
Semolina

There was no further skin disturbance

On Saturday, Jan 24, 1953, she was again given agenised bread This contained 6 g of nitrogen trichloride per sack of 280 lb and in addition potassium bromate 6 parts per million and benzoyl peroxide 20 p p m Having consumed one loaf of this bread, she was examined on Jan 26 (forty-eight hours later), when the findings were

1 The hands were warmer than unaffected skin

2 There was no hyperhidrosis

3 The contour of the fingers was modified by œdema and gave the fingers a "sausage shape" Œdema was evident in the palms and at metacarpophalangeal joints

4 Symmetrically placed at the fingers and palms were vesicles of varying size and depth—not aggregated, selecting mainly the centre palms and anterior surfaces of the wrists

5 The whole of the face, even under the locks of hair on the forehead, was warmer than unaffected skin There was dermal œdema which was changing its contour together with a pink flush The periorbital region was more evident than the rest of the face there were no vesicles The face felt "warm" and "tight" pruritus was moderate

She continued to take the agene-treated bread (total three loaves) and was again examined on Feb 2, when the full extent of the clinical picture was evident

1 The *hands* showed well defined vesicles of varying size mainly subepidermal (especially at the apposed surfaces of the fingers and palms) accompanied by eczematisation

2 The *forearms* were involved symmetrically in a warm erythemato squamous eruption—especially at the anterior aspect of wrists and adjacent forearm These appearances seemed to result from persistent rubbing

3 The exposed *face* and *neck* and *upper chest* showed marked œdema, mild desquamation, erythema, and heat, accompanied by pruritus and "a tight feeling" The skin had a thickened feeling when held between the thumb and finger and a lush semiresistant impression when pressed The face was immobile and lacking in expression

4 Gentle stroking of the skin provoked marked *dermographia*

5 The *mental disturbance*, which was a constant accompaniment of the skin eruptions, was insidious in its onset, and was described by the patient as a morose depression "I did not feel like mixing with people or holding conversation with them," she wrote, "all I wanted to do was to get away from everybody and be left alone But I have found that since I have been free from the rash, *I have felt in much better spirits* generally, and have felt the urge to get out and about more" Her husband, an intelligent observer, has repeatedly emphasised the improvement in his wife's mental state and outlook during the periods when she was only using C U T flour and bread made from it During the attacks she constantly had insomnia, associated with her irritability Whilst taking flour treated with agene, she felt disinclined to eat She states that her appetite "completely disappeared" and only her husband's prompting made her eat

TWO FLOUR IMPROVERS

An alternative to nitrogen trichloride for the chemical treatment of flour is chlorine dioxide We therefore decided to ascertain the effect on our patient of flour treated with chlorine dioxide

During February, 1953, she kept on a diet free from treated flour, being supplied with a weekly consignment of three loaves of C U T bread and a bag of 7 lb C U T flour Her skin was normal

On March 2 she was sent three loaves of bread made from flour treated with chlorine dioxide The treatment was the same as in the commercial process The gas actually introduced into the flour consists of 80% chlorine dioxide and 20% free chlorine, and the true amount of chlorine dioxide in the flour is about 25 p p m, the other 6 p p m being chlorine

The patient had no idea that these loaves were different from those she had been having made from C U T flour Within three hours of eating this bread, however, she had pruritus of the hands and forearms, and within twenty four hours there was pruritus of face and neck, which felt "dry and tight," together with anorexia and insidious mental depression Examined after forty eight hours, she presented essentially the same clinical picture as that following ingestion of agene-treated flour—but with the following differences

1 Although the same sites were selected, it was noticed that following chlorine dioxide treated flour all the sites were involved within forty eight hours and simultaneously The vesicles were all of the same size and mainly subepidermal The initial attack was acute and early, whereas following agene treated bread the initial attack was less acute and not all the sites were involved simultaneously, for example, the eruption took several days to spread from the hands to the wrists and up the arms

2 The attack following chlorine dioxide treated flour waned after about three days, but it must be remembered that anorexia was more profound and the patient was not able to take, over a given time, as much of the chlorine dioxide treated bread as of the agene treated bread

3 Constitutionally she seemed more affected she looked ill, and was pale, drawn, and apathetic

4 *Depression appeared earlier and was deeper*

The clinical manifestations associated with chlorine dioxide-treated flour were first observed by us after she had taken 11 slices of the bread within forty-eight hours, but waned when the consumption fell to 4 slices within twenty-four hours The patient then made a determined effort (despite her anorexia) and took 9 slices within twenty four hours This was followed by an acute exacerbation Thus within four days we produced two distinct attacks following the ingestion of chlorine dioxide-treated flour

The bread made from the chemically untreated flour (C U T) has been specially prepared for these experiments by the aeration process, and great care has been taken in all stages to avoid contamination Baker's flour would have been quite useless for these experiments, because it contains a proportion of imported flour, the percentage of which is varied from time to time by the Ministry of Food, and we could not be sure that this imported flour had not been subjected to chemical treatment

CONCLUSION

A case is described in which the patient shows an allergic response to wheat flour treated with nitrogen trichloride (agene) or chlorine dioxide The question arises Is this a rare case of allergy, or merely the first recognition of a common disorder?

We wish to record our appreciation to the patient for having been willing to submit herself to these tests, which have caused her a great deal of discomfort

psychotic picture. Generally, the condition starts within forty-eight hours of the operation. The patient is emotionally disturbed and restless, though he can often be influenced by a firm quiet approach. The course of the illness is short, and recovery usually takes place in ten days to three weeks.

In *drug-induced delirium* the predominant features are restlessness, noisiness, resistance, and unpredictability of mood and behaviour. The patient experiences visual illusions and hallucinations, usually of a hostile or threatening nature, and often complains unduly of minor pain in the abdomen or elsewhere. He shouts, throws things about, and exhibits general psychomotor pressure and anxiety. Such patients may or may not have had an operation, but they have usually had some painful condition, and they are often of an anxious or tense disposition, although not characteristically neurotic. Combinations of various analgesics and sedatives have generally been given in larger doses than are usual in similar conditions, sometimes for weeks on end. If an operation is performed, there is not uncommonly a sudden exacerbation of the delirium: otherwise the patient's condition gradually deteriorates as medication continues. Occasionally these patients die; or they may be admitted into mental hospitals diagnosed as toxic confusion. There may be short-lived "absences," similar to petit mal, and episodes of complete disorientation in a clear mental setting, in which the patient may believe he is at home and wrongly identify those around him.

The results in *acute alcoholic psychosis, delirium tremens,* and *toxi-infective delirium* will be dealt with in greater detail in another paper.

Case-reports

The following cases illustrate the favourable response in various conditions, and also different stages in the evolution of the method.

BARBITURATE COMA

Case 1.—A married woman, aged 47, took 21 grains of amylobarbitone sodium and became comatose within ten minutes. There was much to suggest that she had taken other sedatives, in all probability morphine. When seen four hours later, she was pale and collapsed; the pulse was thready and the blood-pressure low—80/45 mm. Hg. Respiration was slow and shallow. Tendon reflexes were absent.

Picrotoxin (6 mg.) and methylamphetamine (30 mg.) had been given with transient slight improvement in the general condition. She was given successively by injection 1200 mg. aneurine hydrochloride, 1500 mg. ascorbic acid, and 3 g. glucose in 20% solution. After the aneurine the respiratory rhythm became smoother; after the ascorbic acid it became deeper, and there was considerable flushing of the face. When the glucose was given the muscle tone improved, although the rate of injection made it impossible to connect the different effects with a definite substance. 5 mg. of methylamphetamine was also given.

Within twenty minutes of the start of the vitamin injections, the patient sat up, saying with some anxiety: "Forgive me for what I have done." Intravenous and intramuscular injections of vitamins were continued for two days; and, although the patient was sleepless for thirty hours and showed a good deal of distress, there was no relapse into coma.

NEAR-COMA DUE TO PHENOBARBITONE

Case 2.—A thin young unmarried woman, aged 26, was treated with modified insulin in an attempt to improve her general physical condition. She received up to 80 units without becoming comatose in spite of a fasting blood-sugar level of 60 mg. per 100 ml. The day after her discharge from hospital she took 8 grains of soluble phenobarbitone (a week's supply of the drug which had been given for what was probably petit mal, complicating the definite hysteria from which she suffered).

When seen by her doctor two and a half hours later, she was very drowsy and hardly able to speak. 4 ml. (1 g.) of nikethamide was given intramuscularly and she was admitted to hospital. Four hours after taking the phenobarbitone, and while she was still torpid and barely responsive, she was given by intravenous injection a mixture of 1000 mg. aneurine hydrochloride and 1500 mg. ascorbic acid. Glucose was not given. Within fifteen minutes of the injection she was able to talk and take an interest in her whereabouts, and she was much more active, physically and mentally.

COLLAPSE UNDER CONTINUOUS NARCOSIS

Case 3.—A married woman, aged 40, was undergoing continuous narcosis for a depressively coloured hysteria (the diagnosis was later revised to climacteric depression in a hysterical psychopath). The narcosis had reached the tenth day, the patient obtaining eighteen to twenty hours' full sleep daily on hyoscine hydrobromide (gr. $^{1}/_{150}$), amylobarbitone sodium (gr. 18), phenobarbitone (gr. 3), and paraldehyde (6 fl. drachms) in the twenty-four hours. In addition aneurine hydrochloride (100 mg.) and insulin (6 units) were given by intramuscular and hypodermic injection twice daily, as well as generous doses of the rest of the B group and ascorbic acid by mouth. The pulse-rate varied from 80 to 100, the blood-pressure (normally low) between 110/80 and 95/60, the respirations between 16 and 24, and the temperature between 97·6° and 98·6°F. It was known that her fasting blood-sugar level was relatively low; hence the cautious use of insulin.

On the tenth day, it was noticed that she could not be roused for a meal. In the next two hours, her pulse-rate rose to 136, the blood-pressure fell to 70/45, the respirations rose to 32; and the temperature rose to 99°F. The face and palms were sweating.

This is the typical picture of collapse in continuous narcosis, and the standard practice is to omit barbiturates and to give nikethamide. Recovery of consciousness may be expected in three to eight hours or more. The patient was given the mixture of glucose and vitamins (excluding pyridoxine). and she regained consciousness in forty-five minutes from the start of the intravenous injection. In this case, an acute barbiturate (and possibly hypoglycæmic) coma occurred while vitamins were being given, and it was reversed by more intensive treatment with vitamins and glucose intravenously.

POSTOPERATIVE PSYCHOSIS

Case 4.—A widow, aged 44, with four children, developed a paranoid psychosis, with depressive features, two days after an operation for stress incontinence. The anæsthetic consisted of thiopentone, trichlorethylene, nitrous oxide, and oxygen; and omnopon (gr. $^{1}/_{3}$) and scopolamine (gr. $^{1}/_{150}$) were given preoperatively. After operation she had omnopon (gr. $^{1}/_{3}$) and pethidine (100 mg.) followed by sedation with paraldehyde and quinalbarbitone. When seen four days later, she was acutely psychotic, exhibiting nihilistic delusions and ideas of reference and persecution. She was restless and dashed from her bed from time to time.

She was given the vitamin mixture but without glucose. The dose was divided into four parts, given at six-hourly intervals. Clinical improvement was apparent after the first injection. She was suspicious and needed persuasion to accept the second injection, for she was sure it was poison. The psychosis had disappeared by the time she had had the full dose.

DELIRIUM OR TOXI-CONFUSIONAL STATES

Case 5.—A very ill man, aged 44, was admitted to hospital suffering from virus pneumonia. He needed large doses of analgesics and sedatives, for he had severe pain in the chest and he was anxious, restless, garrulous, and at times confused. He mistook, on occasion, the identity and intent of those around him and exhibited marked impairment of memory for events of a few hours earlier, and almost complete lack of recall for the duration of his stay in hospital. He often became abstracted, silent, inaccessible to stimuli, and near-comatose for a minute or so at a time.

In the three weeks before vitamin treatment began he had had large doses of phenobarbitone, pethidine, methadone, amylobarbitone, and quinalbarbitone. On one day, for example, he had pethidine (400 mg. by mouth and 200 mg. intramuscularly), methadone (20 mg.), paraldehyde (2 fl. drachms per rectum), and amylobarbitone (gr. 18).

He was so restless that several nurses were needed to control him. Aneurine hydrochloride (300 mg. intramuscularly six-hourly) was prescribed for three days, because there were no veins suitable for injection, and the other vitamins were given freely by mouth. Barbiturates and other sedatives were withheld by day and given generously at night. In the twenty-four hours following the first injection of aneurine, he was quieter and could be left alone for periods. Thereafter his need of sedatives and analgesics rapidly diminished.

In three days the disordered mental state, which had been increasing in intensity until the vitamins were given, had cleared up completely.

In this case the total amount of analgesics given daily was unaltered until, during the second day of vitamin therapy, his

We welcome this new edition and confidently recommend it to young surgeons A single index and list of contents for the whole book, which appears at the end of the last part, suggests that the publishers are planning to issue the book in one, or at the most two, volumes and not in the five separate parts in which it has appeared

An Introduction to Universal Serologic Reaction in Health and Disease

REUBEN L KAHN, D SC, University of Michigan Medical School and Hospital, Ann Arbor, Michigan Cambridge, Mass Harvard University Press London Oxford University Press 1951 Pp 155 22*s* 6*d*

"False positive" results in the serological diagnosis of syphilis are a commonplace to clinical pathologists, and this fact, presumably, has stimulated the application of a modified Kahn reaction, the "universal serologic test," to a large number of normal and pathological sera

The test, carried out in saline solutions of different concentrations, involves 270 readings on each serum and the results are plotted graphically using semilogarithmic coordinates Nearly 1000 graphs of this kind are reproduced in the book Although a typically normal serum is clearly differentiated from a typical syphilitic, the range of variation is so great that it is easy to see how "false positives" and "false negatives" occur Graphs show the results obtained with normal human and animal sera and with the sera of patients with syphilis, yaws, leprosy, and malaria There seems to be no future for so time consuming and non specific a test in the clinical laboratory, and in fact no claim is made for such routine use Little progress seems likely to come from frequent repetition of the test under empirical conditions our need is rather for chemical and physicochemical studies of the serum protein fractions responsible for precipitating the lipid "antigen" After inspecting the charts pathologists may well be surprised that the correlation between clinical diagnosis and serological tests is as high as it is, and clinicians may cease to wonder when contradictory reports are sometimes obtained from different laboratories

The book has been elegantly produced under the auspices of the Commonwealth Fund

The Practice of Life Assurance

A Textbook for Actuarial Students N E COE, F I A, M E OGBORN, F I A London Cambridge University Press 1952 Pp 440 32*s*

DESIGNED as a text for actuarial students, this book can have only a limited appeal to doctors—even those engaged in insurance work For these last, however, it may serve as an outline of the problem of the actuary in determining company policy in relation to the underwriting of special risks due to physical disability The chapter dealing with this is aimed at a lay audience but is useful in its insistence that although "life assurance is based upon averages," physiological measurements ranging between fairly wide limits are quite compatible with health, and that the successful "loading" of a premium needs both the clinician's prognostic skill and the actuary's mathematical knowledge

Ophthalmic Pathology

An Atlas And Textbook JONAS S FRIEDENWALD and others Philadelphia and London W B Saunders 1952 Pp 489 90*s*

FOR thirty years the American Armed Forces Institute of Pathology has collected, sifted, and filed its pathological material, and this volume is the outcome of that work It replaces earlier atlases produced by this institute by De Coursey and Ash in 1938, 1939, and 1942 and is based on Friedenwald s well-known but now unobtainable *Pathology of the Eye* Friedenwald himself heads the list of collaborators in the present volume, and with such distinguished parentage and authorship the work is naturally outstanding It begins with normal physiology and histology, the changes in growth and ageing, and the nature and mechanism of inflammation Each chapter ends with a series of photographs and photomicrographs illustrating the text Intended as a teaching aid rather than a reference book, the book can be said, as the authors claim, "to give the most widely accepted concepts of pathology as they are now understood and taught in the leading medical colleges" Its lucid writing and fine pictures will make it welcome throughout the world as a basis for medical teaching

Medicine

Essentials for Practitioners and Students 6th ed G E BEAUMONT, D M, F R C P, physician, Middlesex Hospital London London J & A Churchill 1953 Pp 831 37*s* 6*d*

THE sixth edition of Beaumont appears in time to celebrate the 21st birthday of the book It has been popular with students during its adolescence, and now that it is of age it is no less likely to remain a favourite Admittedly the reader ought to know a great deal about medicine before he graduates to reading the condensed and truncated descriptions of dise
given in books such as this which
of medicine in one volume But all the essentials *are* here, and Dr Beaumont must again be congratulated on compressing into less than 1000 pages so vast a store of information

He has managed to keep pace with recent advances without any corresponding increase in size and a formidable list of new articles has not enlarged the total reading matter Most of the diagrams are clear and useful, and the book does not lose by omitting the many X ray photographs which so often encumber medical textbooks without adding noticeably to their value It is interesting to find many references to such new therapeutic agents as terramycin, but no comment on the importance of gluten in cœliac disease, or the more liberal ideas on the dietetic treatment of peptic ulcer which would certainly allow a patient to eat a lightly boiled egg before the fifth week of his treatment

Shock and Circulatory Homeostasis

Transactions of First Conference October, 1951, New York Editor HAROLD D GREEN, M D New York Josiah Macy, Jr, Foundation 1952 Pp 245 $3 50

THIS book records the discussions at the first of a new series of conferences on shock, arranged by the Josiah Macy Foundation, in which 23 experts took part Five topics were chosen for discussion—human vaso active and other metabolic derangements in shock (B W Zweifach), nervous system in shock (J W Remington), acute and chronic hypotension after hæmorrhage in man (E P Sharpey-Schafer), infectious element in shock (J Fine), and the therapeutic implications of current concepts in shock (F D Moore) To take part in a discussion among a small group of people all of whom have something of value to contribute is stimulating, but when the discussion is reproduced verbatim, as in this instance, it is not easy to read Much information useful to the specialist is embedded in this book

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Nutrition and Health (London Faber & Faber 1953 Pp 125 12*s* 6*d*)—Sir Robert McCarrison's Cantor lectures were delivered and first published in 1936, yet, as Dr H M Sinclair notes, the knowledge gained about nutrition since then everywhere supplements, and nowhere corrects, Sir Robert's thesis The lectures, packed with information collected and set in order by his original and penetrating mind, read as well as ever They are accompanied here by two earlier essays, on deficiency diseases Dr Sinclair's final chapter ably summarises the advances made in the science of nutrition since the lectures first appeared

Menstrual Disorders and Sterility (3rd ed London Cassell 1951 Pp 583 75*s*)—Despite its publication date, this American book has only recently been issued in England Dr Charles Mazer and Dr S Leon Israel, the authors, have rewritten it, they say, because the advances in the diagnosis and treatment of menstrual disorders, and of sterility, have been too many to incorporate in a merely revised text This valuable, and in some respects unique, work now carries among other new matter a clinical evaluation of the Papanicolaou vaginal smear, an explanation of the menstrual toxin theory, the new international classification of carcinoma of the cervix, and an account of the current view of the part played by the luteotropic hormone in the physiology of menstruation Dr William H Perloff contributes a chapter on the hormonal balance of the normal menstrual cycle, and Dr Charles W Charny writes of recent advances in the diagnosis and treatment of male sterility for a patient of Dr. K. M. Bell was comatose for several days after taking 150 grains of amylobarbitone, and she seemed to respond over twenty-four or thirty-six hours to injection of ascorbic acid, with ascorbic acid and aneurine hydrochloride given by Ryle's tube. Quite large doses of picrotoxin and methylamphetamine had had no effect. Gastric lavage in such cases commonly retrieves a considerable amount of the drug, and it is the amount absorbed, and unreachable in the small gut where it acts as a store for further absorption, which will determine the patient's condition. In such circumstances massive doses of the vitamin-dextrose mixture should probably be given, and repetition determined by the return of signs of sopor. Although transient anuria has been described in children after large doses of aneurine, it has not occurred in any patient treated by this technique.

It was a matter of some surprise that the delirium due to the mixture of drugs including pethidine and methadone responded so dramatically, for it was expected that these drugs would be more slowly excreted. Some response was expected, however, for large doses of aneurine hydrochloride have proved valuable in the treatment of the withdrawal syndrome in a few cases of heroin and pethidine addiction.

Summary

The part played by glucose, ascorbic acid, aneurine, pyridoxine, and nicotinic acid in brain metabolism suggested their administration in large doses in the treatment of drug-induced coma, delirium, and psychosis. Favourable results were achieved in barbiturate poisoning, in collapse under continuous narcosis, in postoperative psychosis, in delirium due to drugs, and in acute alcoholic psychosis.

I wish to record my thanks to Dr. Geoffrey Bourne, Mr. Rupert Corbett, Mr. Basil Hume, and Mr. Wilfrid Shaw for giving me the opportunity of treating patients under their care, and for their permission to use their clinical records. My thanks are also due to Dr. E. B. Strauss for much encouragement and advice.

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INVESTIGATION OF ANTITUBERCULOUS SUBSTANCES

AN AGAR DIFFUSION METHOD USING MYCOBACTERIUM SMEGMATIS

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The discovery by Fox (1951) that isonicotinic acid hydrazide (isoniazid) was effective against *Mycobacterium tuberculosis* in vitro has now been confirmed by clinical trial, but it is also clear that its initial effectiveness against the tubercle bacillus is not sustained, either in vitro or in vivo, and its later ineffectiveness is associated with the development of resistance to the drug (Robitzek et al. 1952, Medical Research Council 1952, Joiner et al. 1952). The most promising method available at present for delaying the development of resistance to isoniazid is the combination with it of streptomycin and other drugs (Aitoff 1951, Knox et al. 1952). It is also clearly desirable to test other substances related to isoniazid which may have an activity of the same order as isoniazid but to which resistance does not develop. Research is proceeding along these lines in this laboratory, but the investigation is complicated by the fact that *Myco. tuberculosis* grows very slowly in laboratory media, and the speed of research is limited by this. For this reason an agar-plate diffusion technique has been developed in this laboratory for screening the activity of substances against mycobacteria either alone or in combination with one another.

MATERIALS AND METHODS

Preparation of Solutions

The substances to be tested were made up in solution either in distilled water, or in propylene glycol if they were insoluble in water. Each solution was made up in molar concentration or in decimal dilutions of this, according to the solubility of each compound and the conditions of the experiment.

The solutions were sterilised either by autoclaving at 115°C for ten minutes or by filtration through a Seitz E.K. filter.

Media

For these investigations the liquid medium was that described by Dubos and Davis (1946) and was supplied by the Southern Group Laboratory, Lewisham. The basal medium containing 'Tween 80' was supplied in 100 ml. amounts and 5% bovine albumin in 10 ml. amounts. The bovine albumin from several bottles was pooled and resterilised by filtration through a Seitz E.K. filter. For use, 4 ml. of this was added to each 100 ml. of Dubos basal medium.

Preparation of Solid Medium for Screening Plate

Dubos agar plates were prepared in $4^1/_2$ in.-diameter petri dishes, using the Dubos basal medium solidified by the addition of 'Oxoid' (New Zealand) agar (1·5%). After the addition of the agar the medium was steamed for sixty minutes to dissolve the agar, then resterilised by autoclaving at 115°C for ten minutes, and allowed to cool to 48°C before plates were poured. No bovine albumin was added to the Dubos agar. At first, tryptic digest agar plates were used for this technique but it was found that the growth of *Myco. smegmatis* was more uniform on Dubos agar.

Cultures

A culture of the H37RV strain of *Myco. tuberculosis* var. *hominis* was grown at 37°C, usually for ten days, in screw-capped bottles containing 10 ml. amounts of the complete Dubos liquid medium (with albumin).

A culture of *Myco. smegmatis*, obtained from the National Collection of Type Cultures (no. 523), was maintained on nutrient agar slopes and before use subcultured into 20 ml. amounts of Dubos liquid medium contained in screw-capped bottles and incubated at 37°C for forty-eight hours. The cultures were grown in screw-capped containers because it was found that if very little air space was left above the culture during incubation the growth remained uniform in turbidity (Anderson 1952). An isoniazid-resistant strain of *Myco. smegmatis* was obtained by the technique of serial transfer from the highest concentration of isoniazid in which growth occurred into higher concentrations of the drug. By this technique it was possible to obtain a strain resistant to 400 µg. per ml. of isoniazid. This organism was subcultured every seven days into drug-free Dubos medium and the sensitivity of the culture was retested before further use.

Screening-plate Technique

A forty-eight-hour culture of *Myco. smegmatis* in Dubos liquid medium was inoculated on to the surface of a Dubos agar plate by means of a Pasteur pipette.

changes in cats, rabbits, and ferrets, while in monkeys it caused weakness and tremors , but rats, guineapigs, and hens were apparently unaffected The chemical agent responsible for these disorders has naturally been sought with vigour , and the hunt has been progressively narrowed, first to the protein component of wheat flour,[8] then to an unidentified crystalline substance,[11] and finally to a relatively simple derivative of methionine [12] The toxicity of this derivative to bacteria is negatived by the addition of methionine itself, which replaces the toxic substance [13]

Five years ago we urged that no precipitate action should be taken to replace agene and emphasised the need for research, especially on the alternative processes that might be adopted [14 15] We expressed our opinion, however, that observations over a short period on human beings—whose susceptibility might vary at least as widely as that of dogs—could not be held to prove that agene-treated flour is harmless [15] Today, though there has been some reassuring evidence,[16] we still do not know of any clinical investigation extending beyond a few months , and after five years there still seems to be no satisfactory answer to give to the plain man who asks why, if agenised bread is poisonous to growing dogs, he should be virtually obliged to give it to his growing child Perhaps if the profession and the public knew more about the discussions that have taken place between the Ministries, the milling industry, and the nutritionists, any serious anxieties would be set at rest , for undoubtedly some of those with fullest information are least impressed by the risks of agene and by the need for any immediate alteration in practice The authorities are certainly wise to be cautious about the possible exchange of the suspected improver for another that may be open to similar objections , and it will escape nobody's notice that—for what the evidence is worth—Sheldon and Yorke's patient is as hypersensitive to flour treated (according to the 1950 committee's recommendation) with chlorine dioxide as to flour treated with agene itself But the attentive reader will also observe that this patient was supplied with loaves, made from untreated flour, which she could not distinguish from ordinary bread , and he may reasonably inquire whether the mechanical aeration process by which these loaves were produced is not a practicable alternative to the use of any chemical improver Is it in fact still demonstrably true that bread acceptable to the public cannot be made without exposing the flour to chemicals ? The fact that these questions can be asked, and are being asked, shows how desirable it is that the Government, or the milling industry, or both, should now give the facts on which their action or lack of action is based We still do not want a precipitate decision, which might presently have to be reversed , but we do think that the time has come for a full and frank explanation in terms that everyone can understand Doctors, in particular, would like to be in a better position to form their own opinion on what may well prove to be an important medical issue

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[11] Bentley H R McDermott E E Pace J Whitehead, J K Moran T *Nature, Lond* 1949, 164 438

[12] Bentley, H R McDermott E E , Pace, J Whitehead, J K , Moran T *Ibid* 1950 165 150

[13] Heathcote J G *Lancet* 1949, ii, 1130

[14] *Ibid* 1947, ii 284

[15] *Ibid*, 1948 i, 27

[16] Elithorn A Johnson D M Crosskey, M A *Ibid*, 1949, i, 143

Ureteric Calculus

It is true that many, probably most, ureteric calculi are passed without the intervention of the surgeon, and perhaps without treatment of any kind But they may give serious difficulty in diagnosis and treatment, and may even lead occasionally to the destruction of a kidney or the loss of a life Some of these problems have been reviewed lately by Dix[1] in an account of 740 cases which had all come under his own care 276 of these patients had renal colic but the diagnosis of ureteric calculus was never proved, though he thinks it may be presumed He rejects the diagnosis " oxaluria " as an explanation of these attacks of colic, and he considers that minute crystals floating in the urine cannot cause colic, though they may cause mild dysuria (as any concentrated urine may do) Renal colic must have a macroscopic cause—even a concretion only half the size of a pin's head. This is a reasonable view, for not uncommonly a patient who has had renal colic, and who has been investigated with negative results, passes without further symptoms of any kind a small stone which he may only discover by chance On the other hand, we know that in tropical climates (many of Dix's patients were in the Middle East) it is very common for large numbers of oxalate crystals to be present in the urine without symptoms For example, the urine of more than 25% of a group of British troops in Calcutta had more than ten oxalate crystals per high-power field and several had over a hundred, but none of them had urinary symptoms

Undetected ureteric calculi are a challenge to the methods of urological diagnosis which have in so many ways reached a pitch of great refinement and accuracy If a shadow can be seen in the straight X-ray film it is almost always possible to prove whether or not it is that of a ureteric calculus, though a phlebolith very near the ureter may give difficulty Excretion urography may often settle the matter, but it gives no ready-made answer and may easily be misinterpreted Dix goes so far as to say " I believe that it has been responsible for more errors of diagnosis and unnecessary operations than any other method of urological examination " And, he continues, the ureteric catheter must remain our most potent diagnostic weapon Failure to pass the catheter beyond a certain point in the ureter is a most unreliable sign , for this can often happen when there is no organic obstruction in the ureter The catheter's best use is as a radiological marker If it is passed beyond the stone, as it usually can be, a plain film, or two films from different angles (which may be stereoscopic), will settle the diagnosis Not all urologists will share Dix's liking for two exposures on one film, for interpretation may be difficult when there are several doubtful shadows to be sorted out If the catheter can be passed up to, but not beyond, the suspected stone it must be held in this position while films are taken , and films taken after the injection of radio opaque fluid through the catheter may give further information A urological X-ray table is a great help in these examinations Dix believes that the diagnosis should not be considered proved unless these investigations give at least two positive findings On the other hand, a relatively large number of ureteric calculi detect inhibition, the presence of resistant colonies, the stimulation of bacterial growth by a compound, the occurrence of antagonism or synergism between two or more compounds, and the abolition of resistant colonies by their combination. The obvious criticism of this technique is that we have used *Myco. smegmatis* as the test organism for screening substances for activity against *Myco. tuberculosis*. So long as this is borne in mind, the advantages and uses of this technique outweigh this disadvantage. By the use of a few culture plates it is possible to gather information about the action and interaction of a large number of substances in the space of a few days' incubation. To do this with *Myco. tuberculosis* involves a large amount of media, apparatus, incubator space, and technical assistance, and requires experiments which may not give a result until several weeks have elapsed.

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[1] Dix V W *Ann R Coll Surg Engl* 1952 11, 137

This technique is of particular use in searching for antagonists. In fluid culture, with *Myco. tuberculosis* as test organism, the search for antagonism requires a complex "chess-board" experiment with a wide range of dilutions of each compound. The agar-plate diffusion method with two blotting-paper reservoirs produces a diffusion gradient of each compound with a range of overlapping concentrations, involving the minimum of technical time and labour. For screening a large number of compounds for inhibitory activity, it is possible to use small discs rather than long strips of blotting-paper in order to limit the consumption of culture media.

This paper describes only the information which can be obtained with this plate and the method of performing the screening tests. The degree of correlation between the results obtained by this plate with *Myco. smegmatis* and those using *Myco. tuberculosis* in fluid media has been very close in our hands, and an account of these results will be given in detail in subsequent papers.

SUMMARY

An agar-plate diffusion method using *Myco. smegmatis* as the test organism has been developed for investigating substances for antituberculous activity. The method consists of inoculating Dubos agar plates with a culture of *Myco. smegmatis* and placing on the inoculated medium blotting-paper strips soaked in the material to be tested.

This technique has been found of use (1) in screening rapidly a large number of compounds for inhibitory activity against mycobacteria, as judged by the size of inhibition zones; (2) in demonstrating antagonism or synergism between compounds; (3) in detecting the development of resistant colonies and their suppression by combination with other substances; and (4) in detecting substances which stimulate the growth of mycobacteria.

Substances which show activity in one or other of these ways can be selected for fuller investigation with *Myco. tuberculosis*.

The Dubos medium used in these experiments was supplied by Dr. E. H. Bailey, of the Southern Group Laboratory. We are grateful to Dr. R. J. W. Rees, of the scientific staff of the Medical Research Council, for the strain of H37RV used. Our thanks are also due to Mr. D. E. Seymour, of Herts Pharmaceuticals Ltd., for the supply of isoniazid and other compounds tested in this laboratory.

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EFFECT OF BUTAZOLIDINE ON THE EXCRETION OF WATER AND ELECTROLYTES

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BUTAZOLIDINE (3, 5-dioxo-1-2-diphenyl-4-n-butyl-pyrazolidine), introduced in the treatment of the rheumatic diseases by Currie (1952), may cause œdema (Wilhelmi 1949), which has been ascribed to retention of sodium chloride and water. Fabre and Mach (1951) had found this to happen with 'Irgapyrin' (amidopyrine and butazolidine). Search for evidence of adrenocortical stimulation has been inconclusive. The following experiments were designed to throw some light on this unusual property.

METHOD

Preliminary studies of the urinary excretion of sodium and potassium in patients after the intramuscular injection of butazolidine 1 g., indicated that the volume of the urine was promptly reduced, and that within four hours of injection there was a steep fall in the urine-sodium level, with the result that the ratio of clearance of sodium to that of potassium fell by about 70%.

Next, a healthy volunteer was given sodium chloride 5 g. on successive days and intramuscular butazolidine 1 g. on the second day, at the time of ingestion of the sodium chloride. It was found that about 2 g. of sodium chloride was retained between the second and eighth hours after administration.

Four healthy volunteers were then placed on a diet low in sodium and potassium, with adequate fluid, and constant sodium and potassium intake maintained by two-hourly ingestion of 250 ml. of water and a cachet containing 1 g. of sodium chloride and 0·2 g. of potassium chloride. This gave a total daily intake of 2 litres of water, and about 9 g. of sodium chloride, and 4 g. of potassium chloride. With one initial day for stabilisation these volunteers were studied for one day as a control period; then three (cases 1, 2, and 3) were given intramuscular butazolidine 1 g., case 4 serving as control, and study was continued for a further twenty-four hours. None suffered any ill effects.

Samples of urine were collected every two hours from 8.30 A.M. to 10.30 P.M. and the overnight urine from 10.30 P.M. to 8.30 A.M. was pooled. Samples of blood were taken at 4 P.M. each day. The amounts of sodium and potassium in the blood and urine were estimated with an 'Eel' flame-photometer. Standard methods were used for chloride and urea.

RESULTS

The accompanying table shows the total urinary excretion of water, sodium, potassium, chloride, and urea in the twelve-hour period from 10.30 A.M. to 10.30 P.M. on the two days, butazolidine 1 g. being given to cases 1, 2, and 3 at 10.30 A.M. on the second day.

The average retention by the three volunteers in the twelve hours after the butazolidine injection amounted to 766 ml. of water, 2·4 g. of sodium, 0·4 g. of potassium, and 3·56 g. of chloride. Although the volunteers were not in very good equilibrium, comparison of the excretion in the same two-hour periods on the two days reveals a common pattern in the butazolidine cases. The volume of urine decreased within two hours of the injection commonly associated with transections and compressions, the site was most commonly lumbosacral, with thoracolumbar lesions coming second The bowel reaction was regarded as abnormal if the abdomen was distended, tense, rigid to palpation, and without peristalsis, or if the patient was continuously vomiting, incontinent of fæces, or had diarrhœa The segmental nervous control of the rectum, like that of the bladder, lies in the 2nd, 3rd, and 4th sacral segments of the cord, but the function of the entire gastro-intestinal tract can (though it need not) be affected by any type of injury to any part of the cord or cauda equina The degree of spinal shock is probably more important, MUNRO thinks, than the part of the cord injured

During this phase of shock he allows patients no food or fluids (not even water) by mouth A rectal tube is inserted and left in place for one hour out of every two, and, if there is vomiting, Wangensteen suction is used He emphasises that the stomach must be kept clear of swallowed air, a particularly common complication in cases of cervical injury If the distended stomach is not promptly decompressed, movements of the diaphragm are hampered, and the patient may easily die Bladder distension is controlled by tidal drainage In cervical injuries the chest is strapped tightly while in inspiration, and oxygen is given by nasal catheter at the rate of 2 litres a minute MUNRO finds that these measures, together with traction immobilisation, are life saving, particularly with injuries in the cervical and upper thoracic cord Once peristalsis is audible, and there is no further tendency for the stomach to distend, fluids are given, followed by small two-hourly feeds of gruel The diet is then gradually augmented until the patient is taking a full mixed diet of 3000 calories, containing 150 g of protein During the phase of intestinal paralysis, MUNRO insists, no drugs should be given, no applications made to the abdomen, and no laparotomy attempted, and if the measures outlined are begun at once and rigorously enforced (especially the ban on water) distension, he says, will not develop

Until the bladder acquires reflex activity the bowels are controlled by enemas—he mentions "soapsuds, oil retention or milk and molasses"—and by manual extraction of fæcal impactions (In passing we would urge that nurses need to be instructed in the necessity for this last measure Patients have been known to undergo for days, even weeks, great unnecessary pain and discomfort from impacted fæces, which could—and should—have been quickly extracted by a gloved finger) Development of the bladder reflex is a sign that the segmental innervation of the bowel is again active, and—provided the patient is fit enough in other ways—bowel training can begin It should not be attempted while he is getting too many uncontrolled involuntary spasms, or while spinal shock, or such complications as a major infection, inanition, exhaustion, or hypoproteinæmia are present these, MUNRO holds, should be dealt with first by appropriate treatment

For bowel training to be successful the external anal sphincter must be active, indicating that the nerve supply of the large bowel, and internal anal sphincter is intact The bedpan should be given up as soon as the patient can move enough to be helped on to a commode or to the toilet Since the aim is to establish *a conditioned spinal bowel reflex*, external surroundings should be favourable—the toilet clean, the seat comfortable, the room warm, the time ample The patient is taught to give himself every morning at the same time a small enema, just adequate to ensure emptying of the bowel He does best, MUNRO finds, if seated on the toilet, not so well on the commode, and—as might be expected—least well on the bedpan (It is probably bad policy in any case to try to get the patient to establish a conditioned reflex in the company of an object so unsympathetic to body, mind, and spirit as the bedpan, only a masochist could be expected to get results) After a week the enema is omitted every third day, and a small—just adequate—dose of milk of magnesia is substituted It is given long enough in advance to ensure evacuation at the agreed time The remaining enemas are then gradually eliminated one by one, until the bowel is being stimulated only by milk of magnesia Liquid paraffin is also given from the start, to soften the fæcal mass The final step is to eliminate the milk of magnesia by regular periodic withdrawal, and when this has been done the conditioned bowel will respond to the temporal stimulus alone The patient, confident that he is not going to soi himself, can then set about moving, walking, and reablement with zest

Of the 310 patients studied by MUNRO, 106 died in hospital and 2 others later, and 5 more could not be reabled for mental or other reasons There were thus 197 patients suitable for training on the lines he suggests, and 123 of these recovered bowel control by themselves without added training Of the remaining 74, 14 would not cooperate, and in 12 the results are unknown The method succeeded in 42 cases, but failed in 3 for unknown reasons, despite keen cooperation from the patients, and in 3 for psychological reasons This means that of the 74 patients who could have profited, well over half (57%), and probably more, gained bowel control as a result of this type of training

Annotations

CIRCULATION OF ASCITIC FLUID

THE volume of any pathological accumulation of fluid represents the amount by which the inflow exceeds the outflow An increase of the one or a decrease of the other, or a combination of both, leads to a further fluid accumulation Owing to the remarkable absorptive capacity of the peritoneum, the formation of ascites implies either an enormous increase in filtration in the splanchnic area or considerable impairment of absorption In the latter case the ascitic fluid would be relatively stagnant, and in the former there would be a more rapid turnover The introduction of radioactive and other isotopes has greatly simplified the study of this circulation, both in animals and man

Whipple and his colleagues[1] have produced ascites experimentally in dogs by partial ligation of the inferior vena cava in the thorax By injecting plasma protein labelled with lysine containing C^{14}, and then following the rate of equilibration between the ascitic fluid and the circulating blood, they were able to show a surprisingly rapid turnover of the ascitic fluid proteins They assessed the rate of turnover as 5–7 days, although they admitted that 2–5 days might be more nearly correct A similar study,[2] in which tritium labelled water was used, has produced even more striking results Of 6 patients with ascites, 4 had cirrhosis and 2 had carcino

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[1] McKee F W Wilt W G jun Hyatt, R F Whipple G H *J exp Med* 1950 91 11

[2] Prentice T C, Siri W Joiner F E *Amer J Med* 1952 13, 668

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A SYNDROME ASSOCIATED WITH THE INGESTION OF CHEMICALLY "IMPROVED" FLOUR

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The object of this paper is to record a syndrome associated with ingestion of chemically treated flour. The syndrome comprises (1) eczema, (2) mental disturbance, and (3) anorexia. The chemicals used for treating the flour which produces the syndrome are nitrogen trichloride (agene) and chlorine dioxide.

The patient is an intelligent housewife, aged 50, who gives no personal or family history of allergic disorders. She has had a skin disorder since October, 1940, and was first seen by one of us (G. C. S.) in 1945, and by both of us together since 1947. She has been constantly under medical care since then.

The chronic eruption involved the face and neck and also the upper limbs symmetrically; it was subject to acute irregular exacerbation, and pruritus was troublesome during the acute phase. The essential lesions followed two patterns:

1. *Hands and Wrists.*—Plump well-defined vesicles of varying sizes and depth, associated with darker areas representing inspissated vesicles. In the subchronic stage eczematisation and fissuring were imposed upon this background. No increase in sweating was observed.
2. *Face and Neck.*—Lesions symmetrically placed. Epidermal and subepidermal œdema associated with erythema, heat, and mild desquamation. The periorbital regions were most severely involved, with immobile expression and loss of contour.

Because of the appearance of the hands, she was treated for *dysidrotic eczema*; but she did not respond, even temporarily, to superficial X-radiation or to belladonna internally. Because depression was a dominant feature of the recurring skin episodes, accompanied by sporadic flushing, she was then regarded as a case of neurodermatitis associated with the climacteric; but there was no response to X-radiation or to œstrogens and sedatives.

Despite active and varied treatment the condition smouldered until 1952, with occasional exacerbations. In January, 1949, the eruption was so severe that she was admitted to hospital and remained there for five weeks.

THE IMPLICATION OF FLOUR

During March, 1952, she noticed that when she came into contact with flour, it increased the severity of her existing lesions. It was evident, however, that external irritation by flour was not the cause of her condition, for there had been long periods in which she had no contact with it.

From the beginning of April she was given a flour-free diet, consisting of 'Ryvita,' meat, chicken, fruit, and vegetables. On this diet her skin continuously improved and by mid-June it was normal. During this time there were, however, two very brief relapses, with onset a few hours after taking food which contained flour. On one occasion she had eaten a ham sandwich consisting of two pieces of white bread, and on the other she had eaten a meal including gravy which had been thickened with flour. These were the only two occasions on which she had taken any food containing flour, and she recovered rapidly from both attacks.

In June we consulted Mr. X, an authority on the chemistry of milling, seeking his advice and help, which he has given most generously. He suspected that our patient suffered from a wheat-protein sensitivity, and accordingly on June 16, 1952, he sent her two loaves of bread made by a special aeration process from flour which was entirely untreated with chemicals. These loaves did not affect her skin. (In future this type of loaf will be referred to as C.U.T.—chemically untreated.)

During the week beginning June 22 he sent her two more loaves: the first was C.U.T., identical with the previous loaves, and the second was made at a commercial bakery by the same process, except that a small quantity of edible fat was used in the dough. The flour used in this second loaf contained a small addition of mono-glycerol stearate and 8 oz. of acid calcium phosphate per 280 lb. of flour, and the dough was made in mild steel pans, whereas the C.U.T. flour had been mixed in stainless steel containers and fermented in aluminium bowls. These loaves produced no symptoms in the patient.

On July 4 she was informed that two loaves were being sent to her in separate containers marked R. and S. One was made from C.U.T. flour and the other from ordinary commercial flour. Neither she nor we had the key to their identity—this was in the hands of Mr. X, who at no time had contact with the patient. She ate loaf R. (C.U.T. flour) on Wednesday, Thursday, and Friday, July 8–10, with no reactions, and loaf S., made from ordinary commercial agene-treated flour (7 grammes of agene per sack of 280 lb.) on Saturday, Sunday, and Monday. (During this time she did not handle any flour.) On Saturday evening she noticed pruritus and discomfort and irritation of her hands, and by Monday the full clinical cutaneous and mental picture had developed.

She maintained her flour-free diet, with the exception of three loaves of C.U.T. bread, which were sent to her weekly, and she completely recovered. During the last week of August she came into contact with a fine cloud of flour in her kitchen, produced by another person experimenting with a mechanical flour-mixer. Within five minutes she had irritation of the hands and face which lasted for about twenty-four hours.

She went on holiday until Sept. 9 and maintained her flour-free diet. On her return the skin was normal. At this time we explained to her that we thought her symptoms were due to the ingestion of chemically treated flour. She agreed to continue her flour-free diet except for bread or flour which was sent to her. She was told that at some time the bread would be made from chemically treated flour, but she has never been told what kind of bread she has received.

In the week beginning Sept. 9 she received two loaves of C.U.T. flour, and she ate these on the 10th, 11th, 12th, and 13th. On the evening of the 10th there was a slight aggravation of her skin lesion, which was attributed to taking vegetables to which a white sauce had been added. On the 14th she had two loaves of bread which, unknown to her, were made from agenised flour. This flour was precisely similar to that which she had been using without ill effect, except that nitrogen trichloride had been added to it. The lesions of her hands, arms, face, and neck again became manifest within twenty-four hours. After this the weekly consignments of three loaves of C.U.T. bread were continued, and her skin returned to normal.

It was decided to repeat the test, but that a considerable time should elapse before its repetition. Meanwhile, on but they would like more investigations of the validity of narco-analysis as a method of interrogation, and more discussion between the psychiatrists and the lawyers of the ethical problems involved

NEW ŒSTROGENS FOR OLD

THE œstrogens are used widely and sometimes indiscriminately By a biochemical freak, œstrogenic effects are produced not only by naturally occurring substances but also by some compounds, such as stilbœstrol, with very different formulæ, and the number of these synthetic forms steadily increases Among them the dimethylpentanoic acid derivatives of "allenolic acid" (6-hydroxy-2-naphthalenepropionic acid) have been found to possess considerable œstrogenic activity Judged by their effect on the vaginal smear in the female castrated rat, they are more potent than œstradiol when given by injection, and they seem to be effective, though less notably, when given by mouth When injected into the spleen of castrated cats they are not destroyed by the liver as are the natural œstrogens

Sturnick and Gargill[1] have used one of these allenolic acids—namely, the *methoxy derivative of the dimethylpentanoic acid series* ('Vallestril') in treating 32 women, of whom 28 had menopausal symptoms, 3 postmenopausal osteoporosis, and 1 (a young woman) pustular acne (A man with bony metastases from a prostatic carcinoma was also included in their series) They formed the opinion that vallestril was effective in many cases where other œstrogens had failed and singularly free from toxic effects and complications, especially uterine bleeding In 9 of the women vaginal smears were examined daily, but the evidence of benefit consisted mostly in relief of symptoms, principally hot flushes Unfortunately this method of clinical assay can never be regarded as very satisfactory, for the average patient is unlikely to keep an honest or accurate record of flushes day after day Most doctors know well how little of the medicine which they prescribe is swallowed by the patient after the first few doses, and the better the psychological integration of the patient the less likely is she to continue to remember or bother to take it The same applies to diary records of symptoms Other factors, such as the sympathetic interest of the doctor prescribing a new preparation and spontaneous remissions also undermine the accuracy of such observations as these, profound effects can even be produced by treatment which is impressive only for its pharmacological nonsense Moreover, the menopausal patient is at best an unstable observer whose response level is liable to alter as time goes on

Other methods of assaying potency include the suppression of lactation, but this is almost useless, because the experiment cannot be repeated in the same patient until after the next pregnancy, and this prevents comparisons Vaginal smear assays in the human are unsatisfactory because the changes take place too slowly to give a reliable guide, and in castrated animals the results do not parallel those in women, since œstrogen potency varies from species to species For such reasons as these, Bishop's method of clinical assay[2–4] seems the most reliable it consists in determining the minimum dosages of different œstrogens which cause œstrogen withdrawal bleeding in the same amenorrhœic women Results may occasionally be vitiated by spontaneous menstruation, but this can often be detected by a study of basal temperatures The primary effect of all œstrogens is on the endometrium, and it is here that the potency of a particular form is most accurately assessed The effects on pituitary and thyroid activity; on hot flushes, on vaginal acidity and cornification, and on lactation are less direct

So far it appears that the potency and toxicity of œstrogens go hand in hand, and are together related to dosage Hexœstrol, for example, is less toxic than stilbœstrol only in doses that are therapeutically less effective If an allenolic acid derivative were found to relieve secondary symptoms of œstrogen deficiency without producing the primary effect of endometrial bleeding it would certainly represent a real advance, and it may yet prove possible to segregate the pharmacological effects of these or some other œstrogens Meanwhile œstrogen therapy directed towards one symptom will continue to carry penalties in other directions, such as the suppression of ovulation, menstrual anomalies, postmenopausal bleeding, fluid retention, and nausea and vomiting

MODERN OUTLOOK ON EPILEPSY

"A convulsion is but a symptom," and "the mode of onset of the seizure is the most important matter in the *anatomical investigation of any case of epilepsy*" With these two quotations from Hughlings Jackson Daly opened his discussion of the pattern of the epileptic attack in a recent symposium at the Mayo Clinic[1], and he went on to advise, as did Hughlings Jackson, that both site of origin and ætiology of seizure must be considered Modern clinical practice seems gradually to be catching up with Hughlings Jackson's views of eighty years ago Although his dicta on the subject have always been revered, and quoted as a part of neurological *pietas*, they have been slow to diffuse into the general body of clinical medicine Now that we have new methods of medical and surgical treatment and the electro-encephalogram (E E G.) for more accurate diagnosis, interest in epilepsy has increased, and many of Jackson's observations and the hypotheses derived from them are being confirmed and strengthened, both in the clinic and in the laboratory

Episodic behaviour disorders in epileptic attacks have attracted renewed attention Such disorders may at first seem primarily psychiatric, but their episodic and strange nature, and possibly associated neurological abnormalities, including E E G changes, may help to suggest their true origin When, however, they arise in a setting of constitutional epilepsy, the diagnosis may be more difficult, they may largely merge into lack of self control and other oddities of personality which can hardly be regarded as specifically "epileptic" even when associated with some E E G abnormality The response of such cases to treatment may sometimes be of diagnostic value Drugs of the hydantoin group may control these abnormalities of conduct, and lately 'Mysoline,' a new British preparation, has been introduced[2] as a treatment for all forms of epilepsy, including this psychomotor group

With regard also to petit mal, new views are abroad In this disorder the bilateral "wave and-spike" pattern in the E E G at first suggested some generalised cerebral or cortical abnormality Now, however, this electrical pattern, and indeed some of the clinical features of the attacks, have been reproduced in animals by stimulating a limited area of the medial intralaminar region of the thalamus,[3] and petit mal may be regarded as the "local sign" of discharge from a specific subcortical area There was a tendency to regard the wave and spike E E G pattern as almost essential for the diagnosis of petit mal, but it is now usually agreed that "petit mal" should be a clinical term that may cover borderline cases

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[1] Sturnick, M I, Gargill, S L *New Engl J Med* 1952, 247 829

[2] Bishop, P M F Kennedy, G C, Wynn-Williams, G *Lancet*, 1948, ii 764

[3] Bishop P M F Richards N A, Neal Smith, D J, Perry, W L M *Ibid* 1950 i, 848

[4] Bishop P M F, Richards N A, Perry W L M *Ibid* 1951 i 818

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[1] *Proc Mayo Clin* 1953 28 25

[2] Handley R Stewart A S R *Lancet* 1952 i 742

[3] Jasper H H Droogleever Fortuyn J *Ass Res nerv ment Dis* 1947 26 272

Medical Societies

ROYAL SOCIETY OF MEDICINE

Survival and Rescue

AT a meeting of the United Services section on March 5, with Sir STANFORD CADE, the president, in the chair, three Royal Air Force medical officers discussed Survival and Rescue.

Wing-commander A. J. BARWOOD said that in the air the most serious emergency was a failure in pressurisation of the aircraft cabin through technical accident or enemy firing. R.A.F. policy was to maintain a cabin pressure equivalent to a height considerably exceeding the 8000-feet level of civil airliners, to save weight of equipment and to reduce the risk of explosive decompression if pressurisation suddenly failed at high altitude. A man breathing pure oxygen at 45,000 feet without cabin pressurisation would become unconscious from anoxia in a few seconds. He could, however, wear a pressure breathing waistcoat and a mask with a loaded expiratory valve, which would take him safely from 47,000 to 42,000 feet. When modern aircraft flew above this height some form of pressure suit was essential.

The pilot could be ejected from the aircraft at high altitude by operating a trigger mechanism which fired the ejection seat. With the most modern equipment everything else, including the opening of his parachute at a predetermined distance from the ground, followed automatically. Rapid cinematography of actual ejections showed that a visor was needed to protect the face if a blind-type seat-firing mechanism was not used. Once he was on land or sea his rapid location by rescuers was important, and a small radio beacon which could be worn on a life-jacket had been developed. It was about 5 in. long, roughly tubular in shape, with a short antenna which popped out vertically when it was switched on. An aircraft could home on this transmitter with great accuracy from a far greater distance than had previously been possible.

Squadron-leader D. G. V. WHITTINGHAM dealt with the possibilities of walking home and the food ration carried. An unpractised man might walk 25–30 miles a day, and his feet swell as a result by anything up to 10% of their initial volume. This swelling varied in onset in different men, and might not be reduced by rest at night; it was mainly in the fore part of the foot. Flying-boots had been redesigned to allow space for this swelling.

Survival rations were grouped in two packs, one giving a high carbohydrate diet (8 parts carbohydrate to 3 parts fat to 1 part protein), and the other more fat and protein to make the ratios 5 : $2^{1}/_{2}$: 1. The first was taken alone when the daily water intake was less than $2^{1}/_{2}$ pints, because a high fat diet could increase the likelihood of ketosis and increase the water-intake requirement. With a water-supply of more than $2^{1}/_{2}$ pints per day both packs were used.

Squadron-leader T. N. N. BRENNAN had recently carried out a test of jungle survival with seven volunteers in Sarawak. They were jettisoned in a swamp wearing jungle boots and khaki flying-overalls which were mosquito and sandfly proof, and jungle hats with malleable brims to which the upper end of mosquito nets over the face could be tied. They walked for a week through swamp-jungle, over a mountain, and then down river, living on their survival rations since jungle provides no worth-while extra food. They covered in all about 30 miles, but only $1^{1}/_{2}$ miles the first day and 2 miles the second. Talcum powder was invaluable for drying the feet.

Morale was lowest in the first few hours of the exercise and then slowly improved. It was essential not to hurry in this kind of travelling. They took 10–15 g. salt a day to replace sweat loss, and this was adequate although the official recommendation was 30 g. They also took daily proguanil, and there were no cases of malaria. One man acquired *Ankylostoma braziliense*, probably from a native dog. Leeches were not painful or harmful, though a few got through clothing from each trouser leg; when necessary, leeches which had attached themselves to the flesh were removed with a cigarette-end as a routine at each rest halt. Fortunately none entered the urethra. In northern Malaya and Burma leeches had been known to cause serious anuria; condoms should therefore be provided in jungle survival kits for men sleeping in leech-infested country. The kit should also contain an antiseptic jelly for use on abrasions, soap (no razor was necessary), and sulphaguanidine in place of a cathartic.

Reviews of Books

Man and Epidemics

C.-E. A. WINSLOW, professor emeritus of public health, Yale School of Medicine. Princeton, N. J.: University Press. London: Oxford University Press. 1952. Pp. 246. 25s

THIS is a first-rate book. Professor Winslow is the Grand Old Man of American public health, and he is writing for the educated general public "who would like to know by what roads the science of public health has reached its conclusions and what results it has achieved." But this is exactly what the medical student wants to know, too—now that he no longer has to memorise the detailed techniques of public health. The book gives most readably the basic facts about sanitation applied to epidemiology; and, unlike some textbooks, it does not attempt to club the reader into being interested. The plain story of public health, well told, is sufficiently interesting in itself; and there are chapters on epidemics spread by water, excreta, milk, food, and insects, as well as on public-health programmes, great epidemics of the past, and challenges of the future. The preface gives a hint of volumes to follow on other aspects of what Professor Winslow calls "constructive medicine." They should help us to recognise, whether we are inside or outside the profession, that "the real—though unrecognised—triumphs of public health are the things which do not happen."

Emergency Surgery

6th ed. HAMILTON BAILEY, F.R.C.S., F.A.C.S., emeritus surgeon, Royal Northern Hospital, London; assisted by NORMAN M. MATHESON, F.R.C.S., M.R.C.P., F.A.C.S., surgeon, Ashford Hospital, Middlesex. Bristol: John Wright & Sons. 1952. Part IV. Pp. 193. 1953. Part V. Pp. 180. 21s. each.

THESE last two parts complete the sixth edition of this popular book. They contain sections on the chest, head and neck, blood-vessels, tendons, nerves, and joints, amputations, the hand, burns, the eye, and ear, nose, and throat. It is unfortunate that Mr. Hamilton Bailey's illness prevented him from taking an active part in the preparation of these last parts, but Mr. Norman Matheson has well maintained his tradition for clear, concise, and practical presentation. Indeed the number and quality of the illustrations, which is an important part of this tradition, has been still further improved.

No reviewer would be likely to agree with everything in a book on the art of surgery, but we think that most surgeons would disagree with two points in the recommended treatment of acute osteomyelitis: the dose of penicillin should be bigger and surgical intervention earlier if delayed complications such as necrosis and sequestration are to be avoided. The article on burns, by an American, is too short. This is no doubt a good fault, but the rather sketchy outline lacks some of the definite detailed instructions for which an inexperienced surgeon will look. In American fashion, blood is preferred to plasma in this condition. The line between emergency and "cold" surgery is hard to draw but surely a brain abscess should not, and need not, be treated by a surgeon who has to rely on a manual of emergency surgery. But this is no criticism of the way in which this subject has been dealt with.

Special Articles

THE AGED IN THEIR OWN HOMES

H D Chalke
O B E , T D , M A Camb , M R C S , D P H

B Benjamin
B Sc Lond , F I A *

From the Public Health Department, London County Council

In 1950, in two Metropolitan boroughs, Lewisham and Camberwell a preliminary survey was made of households assisted by the domestic help service because of general illness This survey aimed at obtaining a general picture of the severity of the problem of home care of the aged and chronic sick An account of the findings (Chalke and Benjamin 1951) laid stress on the need to provide domestic assistance before the old people, living alone, became bedridden and helpless, and before infirmity, aggravated by lack of assistance, had become irreparable , it emphasised the importance of obtaining better cooperation between the many voluntary and statutory bodies concerned in this problem , it indicated that home care was not only cheaper than hospital care but was vital to the morale of the old person , and it drew attention to the needs of the aged which are not met by the domestic help service—the need for real help with laundry, and the need for companionship, especially at night

THE NEW SURVEY

To add detail to this preliminary account, a further survey was undertaken in the same area in the latter months of 1951 The homes studied contained at least one person over the age of 65 assisted by either the domestic help service, the home nursing service, or both services The households covered comprised the following groups

Assisted by	*No of households*
Domestic help service only	776
Domestic help service *and* home nursing	157
Home nursing only	149
	1082

These households are only a small fraction of the total of households in Lewisham and Camberwell containing persons over the age of 65 At the 1951 Census (1% Sample Tables, 1952) there were 3,410,500 households in the London and South-Eastern region, of which 835 300 or 24% were one- or two- or three-person households with a head of the household over the age of 60 If this proportion could be applied to the 130,300 households in Lewisham and Camberwell it would yield 31,000 households with older people living practically on their own Of these only a proportion would at one time be seeking assistance from the home nursing or domestic help service At the end of 1951, in Lewisham and Camberwell there were 1107 general cases (i e , not maternity) on the books of the domestic help service, and most of these households contained old people living alone or with a relative who was compelled to leave them during the day Over and above the home nursing cases contained within this group, it is estimated there were some 400 old people being attended by the district nurses at the end of 1951 Coming within the definition of the survey there were therefore some 1500 households of which the 1082 actually surveyed represents 72% This is a large sample it is a sample built up neither in any systematic nor in any purely random way, but consisting of all those households that could be recorded in the limited time available by the willing but hard-pressed staff of the two services, and, all things considered, reasonably representative of the problem under discussion—namely, the care of the aged infirm people living alone or almost alone

Within the 1082 households there were 1537 persons.† Most of them (81%) were aged 65 or over, but a few relatives, companions, or lodgers of younger ages were incorporated in some of the households (which were surveyed as a whole) The proportion over the age of 85 (10%) was strikingly high More than two thirds (70 8%) of the total persons were women These proportions agree fairly closely with the earlier survey (Chalke and Benjamin 1951) as was to have been expected

The disabilities existing among members of the households were recorded distinction being made between those ailments sufficiently severe to require treatment and those ailments which were not being treated Naturally, in such a segment of the population, most of the complaints, whether treated or not, related to degenerative conditions—heart or other circulatory disease, high blood-pressure, cerebral vascular lesions, and chronic bronchitis as a condition so often associated with degeneration There were cases of diabetes (especially among women), a few advanced cases of cancer, and a few elderly tuberculous There were larger numbers with rheumatism or with a whole complex best described by the term senility Only 20 in all were on the waiting list of a hospital , 52 had recently been discharged from hospital treatment Hospital treatment is only a very small part of the problem , for the rest it is the familiar picture of chronic sickness—the lesser illness but the major worry of restricted movement, pain, and discomfort—requiring some regular nursing but most of all constant companionship and encouragement

The degree of infirmity was measured Of the male patients 13%, and of female patients 21%, were bedridden These percentages are somewhat higher than in the earlier survey in the same area—8% and 13% A further 9% of men and 18% of women were confined to the house by restriction of movement The proportion able to go out from the house declined with advancing age, but even at ages over 75 more than half the men and nearly half the women were *not* confined to their homes Cases of incontinence were fortunately comparatively rare (only 1% of men and 3% of women), but even a small number constitute an important problem , there is the difficulty of the washing of soiled linen, for which there is as yet no real solution, and the personal distress It underlines the uncongenial character of chronic sick nursing of which the District Nursing Association carry the major burden so unobtrusively and so well

The total volume of nursing care has been analysed About one third of the cases required daily attention (e g , diabetics) , a little more than one third needed visiting weekly or less often (e g , heart cases), while the remainder were graded between these two extremes The distribution of visits is similar to that of the earlier survey and is typical of the day-to day work of the district nurse

The general practitioner was visiting weekly or more frequently in 16 8% of cases, monthly in 19 1%, less frequently in 32 3%, and not at all in 31 8%

With regard to chiropody we found that 11% of men and 18% of women were receiving foot treatment and a further 9% of men and 11% of women were in need of such treatment though not yet receiving it In other words, chiropody could be an important element in the preservation of normal life for about one quarter (401 out of 1537) of the older population Physiotherapy, perhaps unexpectedly, was *not* an important element , only a handful of patients received or required such a service

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* Since this survey was completed Mr Benjamin has joined the statistical staff of the General Register Office

† In publication the statistical tables have been excluded in order to make the report more readable but a stencilled set of the full tables may be had on request from Dr Chalke (29 Peckham Road London, S E 5)

THE LANCET

LONDON: SATURDAY, MARCH 21, 1953

Improved Flour

In our present issue Dr. G. C. Sheldon and Dr. Allan Yorke report the case of a woman who from time to time since 1940 has suffered from a skin disorder associated with anorexia and mental depression. Their investigations have shown that this patient's symptoms are directly related to the consumption of bread or flour of the kind now supplied to the public: she can be freed from these symptoms, and restored to health, simply by removing ordinary bread from her diet and substituting bread made from flour which has not been treated with the usual chemical improvers. Sheldon and Yorke pertinently inquire whether this is a rare case of allergy or the first recognition of a common disorder, and this is clearly a question that will have to be answered. From the facts of this one case it would be quite unjustifiable to conclude that flour treated with nitrogen trichloride or chlorine dioxide is unsuitable for human consumption; for the patient's condition suggested that she was allergic or hypersensitive to this particular substance, and it is of course a commonplace of medicine that, through individual idiosyncrasy, some people are sensitive to all manner of substances which are entirely harmless to almost everybody else. Probably most of the foods we eat have at some time or another produced an allergic response in somebody; but we do not stop using milk because some people are sensitive to it, and the fact that children with cœliac disease are harmed by the gluten of wheat has not led us to abandon the use of this staple food of the Western nations. On the other hand, the demonstration that current methods of processing flour so change its character that it becomes noxious to even one person is bound to reinforce the arguments of those who deprecate the increasing and often insidious sophistication of our food. Sheldon and Yorke's patient is not sensitive to wheat flour in its natural condition but only to wheat flour which has been treated with chemical improvers. And we already know that such treatment can convert flour into a product which is poisonous to certain animal species.

This knowledge dates from 1946 when Sir Edward Mellanby, F.R.S., reported from the National Institute for Medical Research that canine hysteria had been induced in dogs by including in their diet flour that had been improved and bleached with nitrogen trichloride (the agene process).[1] As this process had for some twenty years formed part of the preparation of most flour sold in this country (95·5% of National flour in 1948 [2]) this news created some concern, and an interdepartmental committee was set up to consider the possible risk to human beings. The committee, reporting in 1950, were unable to find any evidence that agenised flour is in any way toxic to man, and they said that experiments both in this country and in the United States had failed to produce any toxic symptoms, even when large amounts of treated flour were given. Nevertheless, in view of the deleterious effects of agene on some kinds of animals, the committee felt that its use should be discontinued.[3] They believed, however, that if bakers were to provide a loaf acceptable to the general public, some form of improver would still have to be employed, and they recommended the substitution of chlorine dioxide for nitrogen trichloride, on the ground that extensive tests had shown that flour treated with chlorine dioxide causes no toxic symptoms in animals or man. These recommendations were accepted by the Government, and later in 1950 Mr. Maurice Webb, then Minister of Food, said that it would take about two years to complete the change from agene to chlorine dioxide, at an estimated cost of 337,000 American dollars.[4] (The change had already been effected in the United States [5] and Canada.) Since then, however, repeated questions in the House of Commons have elicited equivocal replies indicating doubt about the improver of choice. This year, for example, Major Lloyd George, the present Minister, offered the following information:

> "These complex and important investigations into possible alternatives to agene as a flour-improver are requiring considerably more time than was originally thought necessary. They are being pursued with all possible speed, but it would be premature to take any action until they are completed. One or two possible alternatives have been presented, but it is obvious that very careful research must be undertaken before either can be accepted." [6]

What Sir Edward Mellanby [1] found was that growing dogs fed with bread made from agenised flour developed, in two to four weeks, canine hysteria (otherwise known as running fits or fright disease), a nervous condition first recognised in the 19th century but particularly common in this country and in the United States during the past quarter-century. The identity of Mellanby's syndrome with canine hysteria has been questioned,[7] but there can be no doubt that the animals became irritable, with increased motor activity, and later had major epileptic fits. This finding was confirmed and extended here [8] and in America,[9] [10] and it was found that dogs fed with flour containing large quantities of agene began after a day or two to have major fits with electro-encephalographic changes indistinguishable from those associated with fits in man. Agene-treated flour induced similar

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1. Mellanby, E. *Brit. med. J.* 1946, ii, 885.
2. See *Lancet*, 1949, ii, 1159.
3. *Ibid*, 1950, i, 227.
4. *Ibid*, ii, 70.
5. *Federal Register*, Nov. 27, 1948, p. 6969.
6. See *Lancet*, Feb. 21, 1953, p. 391.
7. Clark, M. H., Hodgman, S. F. J., Joshua, J. O., Parry, H., Uvarov, O. *Ibid*, 1948, i, 346.
8. Moran, T. *Ibid*, 1947, ii, 289.
9. Newell, G. W., Erickson, T. C., Gilson, W. E., Gershoff, S. N., Elvehjem, C. A. *J. Amer. med. Ass.* 1947, 135, 760.
10. Silver, M. L., Johnson, R. E., Kark, R. M., Klein, J. R., Monahan, E. P., Zevin, S. S. *Ibid*, p. 757.

in full, 14 3% made part payment, but in 81 2% of households the cost had to be borne by public funds Even so this was not as costly as institutional care On the average, the home helps worked 5 8 hours per household per week at an average net cost to public funds of 13*s* 7*d* Where a district nurse attended, the average cost per household to the health service was 12*s* 10*d* per week We may compare this with an average weekly cost per inpatient of £11 17*s* 2*d* in chronic sick hospitals in the South-East Metropolitan Region (Ministry of Health 1952)

Thanks are due to Dr J A Scott, county medical officer of health, for his encouragement, to Lord Amulree for helpful suggestions, to the Ranyard nursing staff and the home help organisers and visitors for the painstaking field work without which this survey could not have been carried out, and to Mr T A Barry for valuable assistance with the tabulations

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HEALTH IN ISRAEL

THE old idea that a country got the medical services it deserved has given way to the idea that at best it gets those it can afford There are even some who say that in Britain we now enjoy health services that we can scarcely afford, and yet perhaps we could ill afford to be without them

Special interest attaches to the medical services in Israel This State has existed independently since May, 1948, when it was born out of the militant partition of Palestine by a war which even now lacks the formal conclusion of a peace treaty

The population has doubled in the past four years[1] and is now $1^{1}/_{2}$ million, of whom 173,000 are non Jewish One remarkable fact emerging from a report edited by Prof Theodore Gruschka[2] is that the medical services have been able to cope with the problems presented by the continuous unselected mass immigration of thousands of disturbed and impoverished persons from North Africa, Yemen, Persia, Iraq, Turkey, and Central Europe, bringing with them tuberculosis, trachoma, schistosomiasis, tropical ulcer, malaria, leprosy, ringworm, treponematoses, poliomyelitis, diphtheria, dysentery, typhus, and infective hepatitis Only 25% of the population were born in Israel, 63% of the immigrants hail from Europe and 27% from Asia

STATISTICS

The Jewish population has a 1% male preponderance and an age-distribution comprising 14% under 5 years, 17% of 5–14 years, 48% of 15–44 years, 17% of 45–64 years, and 4% over 65 years Israel's geriatric problems are yet to come Three-quarters of the population live in the three large towns of Tel-Aviv, Haifa, and Jerusalem or in small urban settlements

The 1951 vital statistics for the Jewish population record a birth-rate of 32 7 and a death-rate of 6 4 per 1000 population Infant mortality was 39 2 per 1000 infants under 1 year alive during the year—i e, including immigrant infants Tuberculosis mortality was 0 17 per 1000 population

Some 3000 doctors and 850 dentists (mainly immigrants) are licensed by the ministry of health to practise in Israel There is, according to the report, a shortage of specialists in obstetrics, radiology, chest diseases, and public health In May, 1952, the first 63 medical graduates qualified from the medical school of the Hadassah—Hebrew University in Jerusalem

800 nurses are employed in public and private hospitals and 300 in the public-health services Expansion of hospital and public-health services is hindered by the serious shortage of nurses, which is offset to some extent by the employment of "practical nurses" with one year's training and of nursing auxiliaries with an even shorter training

"The food situation in Israel is precarious," says the report Bread is practically the sole foodstuff that is continuously unrationed Vegetables come off ration in summer, and citrus fruits—the country's main export—become more plentiful in winter Additional rations are provided to expectant mothers, young children, sick people, and heavy manual workers

Owing to the mass immigration there is a serious shortage of houses Sewerage, even in the large cities, is primitive, but there are plans for large regional sewerage schemes, in which the effluent is to be used for irrigating desert agricultural areas

COMMUNICABLE DISEASES

Widespread use of D D T has reduced to insignificance disease borne by sandfly Bacillary dysentery, enteric fever, diphtheria, and poliomyelitis are the day-to day epidemiological problems Epidemic poliomyelitis was unknown in Israel before 1949 Since then there have been severe epidemics each spring and summer, the worst was in 1950 when 1602 cases were notified, 30% of them in children under 1 year of age

Murine typhus is endemic and resists available rodent control measures There has been no louse borne typhus and no plague during the past five years Tick borne relapsing fever is endemic but uncommon Leptospirosis occurs, transmitted by cows and by voles Schistosomiasis is endemic in certain river areas Infective hepatitis is prevalent, and a subicteric form is found in children, this disease has affected immigrants particularly severely Smallpox is uncommon, vaccination is compulsory Trachoma was reintroduced to the country by immigrants, and it is estimated that there are 70,000 active cases Malaria transmitted by *Anopheles superpictus* and *Anopheles sergenti* has increased recently Throughout the mosquito breeding season control measures are in operation along watercourses and seepages

TUBERCULOSIS

Tuberculosis is widely prevalent among Yemenite immigrants Country wide tuberculin testing and B C G vaccination have been carried out during the past three years with help from the World Health Organisation

In the past three years mass radiography of 288,000 immigrants revealed an average prevalence of 5 active cases of pulmonary tuberculosis per 1000 It is estimated that there are 3500 cases needing hospital treatment and 30,000 needing continuous supervision This suggests an average prevalence of tuberculosis throughout the country of 22 cases per 1000 population During 1952 there were 1680 adult and 310 children's hospital beds in the country for tuberculous cases 19 tuberculosis clinics, 4 mass X ray centres and 2 rehabilitation units are engaged in control work B C G vaccination is available for all newborn infants and for older negative tuberculin reactors

Rakower[3] has discussed the tuberculosis morbidity and mortality of different Jewish ethnic groups

He finds that the "Yemenites," from Southern Arabia, who constitute about 5% of the Jewish population, are especially liable to tuberculosis The rapidly progressive, massive, exudative types of the disease are almost limited to Yemenites, and Rakower estimates that in this group the average interval between diagnosis and death is 1 7 years

Yemen was virtually free of tuberculosis until its people revolted against Turkey early in the present century Turkish troops sent to Southern Arabia to suppress the revolt first introduced the disease Even now the agricultural mountain areas are still relatively free The recent migration from a pastoral or desert life where tuberculosis is almost unknown escape detection by radiography, usually because they are very small or their shadow is obscured by bone or intestinal contents. There is perhaps still a place for the use of the wax-tipped catheter, but it is awkward to handle and seems to be out of favour.

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[1] See *Lancet*, 1951 i, 517
[2] The Health Services of Israel Ministry of Health Jerusalem 1952
[3] Rakower J *Amer Rev Tuberc* 1953, 67, 85

We have in fact insufficient evidence about how long a calculus may remain harmlessly in the ureter and still pass on spontaneously. DIX mentions a case in which a calculus stayed in the ureter for 14 months until non-medical reasons necessitated its removal. Some urologists interpret a diagnosis of ureteric calculus as an indication to remove it at once, but this is by no means the general view in this country. If a calculus is to be given ample time to pass spontaneously, it is, of course, important to keep a careful watch on renal function by excretion pyelography at, say, three-monthly intervals—unless symptoms or complications demand a shorter interval.

The passage of a ureteric catheter may in itself be sufficient treatment. DIX's impression, without figures or controls to prove it, is that the stone may then move—a view long held by most urologists. The injection of oil up the catheter may also help, and sometimes papaverine is dissolved in the oil with the idea of relaxing the spasm of the ureteric muscle. But the simple and passive catheter has blossomed into a variety of complex devices for grappling with the stone and pulling it out. With these ingenious instruments dexterity and perseverance have had their reward in the premature delivery of ureteric calculi, many of which might have emerged naturally if left alone. On the other hand, there is no doubt that some stones may be removed in this way which would otherwise have required open operation. Even the enthusiastic advocates of these methods have, however, reported serious complications. Of 59 patients "subjected to extraction" with the looped catheter,[2] 1 died, and there were 4 cases of ruptured ureter, 4 cases in which surgical drainage became necessary, and 1 in which nephrectomy had to be performed. In another series of 16 patients[3] there was a case where clot retention, which subsequently necessitated nephrectomy, followed perurethral diathermy-loop resection for stones in the intramural ureter. Again, epididymitis developed in 2 patients treated with the Johnson extractor (a variant of the Councill "basket"), but no other complications followed in a series of 70 cases.[4] All these reports are from North America; for in England the perurethral extraction of ureteric calculi has not proved popular. AINSWORTH-DAVIS[5] made a plea for the use of Howard's (corkscrew) extractor; and SWINNEY, at a meeting of the Royal Society of Medicine last year, said that he was having encouraging results with endoscopic methods. When the stone is held up in the intramural ureter in such a way that it produces œdema of the orifice, DIX advocates enlargement of the orifice with diathermy; and he reports only 5 known failures in 38 cases. In the remainder the stone was passed in an average time of eleven days.

Ureterolithotomy is still the standard treatment for calculi impacted above the intramural ureter, and the most enthusiastic endoscopists must resort to it occasionally. ELLIK and NEWTON[2] did 15 ureterolithotomies against 59 extractions; and MIDDLETON and GRUA[4] operated only twice in 70 cases. On the other hand, at the Cleveland Clinic,[6] "surgical interference" was used in 477 out of 857 cases; but in the last 256 cases the operation-rate had dropped to 30% and the extraction-rate had risen considerably to 58%. In DIX's series of 464 cases of proved calculi there were 177 ureterolithotomies. There are many different incisions for exposing the various levels of the ureter, and every surgeon will use the one to which he is accustomed. For stones above the pelvic brim DIX favours an approach through the flank in the line of the lower end of an extended oblique kidney incision, and for stones below the brim a paramedian incision. HIGGINS and WARDEN,[6] of the Cleveland Clinic, prefer a muscle-splitting approach for both upper and lower ureter, and in the female they remove the stone per vaginam. In dealing with the ureter itself DIX advises an incision directly on to the stone. The orthodox advice is to make the incision through the normal ureter above the stone and then to milk the stone up to this incision; but this method takes no account of the fact that operation is not, or should not, be undertaken until there is no prospect of the stone moving further—that is to say, until it is jammed. The attempt to milk an impacted stone upwards is likely not only to fail but to damage the ureter. Surgeons still disagree on whether the incision in the ureter should be sutured or not. DIX sutures it and describes a technique which, he believes, minimises the risk of stricture.

A common complication of ureterolithotomy is a temporary urinary fistula. This developed in 23 (13%) of DIX's 177 cases, and it was commoner after dealing with stones above the pelvic brim. The fistulæ persisted for from four to thirty days, with an average of eleven days. One fistula was "permanent" and was treated by nephrectomy. Fatal complications of ureterolithotomy are uncommon; but any series of major operations, candidly reported, will show a few deaths from non-specific causes such as pulmonary embolism, which were responsible for 3 of the 4 deaths in DIX's series. The 4th was due to infection—at a time when even the sulphonamides were not available. As the mortality of ureterolithotomy is mainly due to factors inherent in the open operation on the abdomen, it might be reduced by extending the use of endoscopic methods as far as their disadvantages and limitations will allow.

Bowel Action after Spinal Lesions

THE residual paralyses of the limbs after spinal injury cause patients less distress than the damage to sphincter control. As Dr. DONALD MUNRO[7] points out, reablement is hardly a matter of practical politics until the patient can be certain he has control of his bowel in all ordinary circumstances, and so need not fear soiling himself unexpectedly. Among 310 civilian patients admitted to the Boston City Hospital, whose cases MUNRO reviews from this aspect, the lesions included spinal abscess, disseminated sclerosis, and tumour, but by far the most of them (289) were the result of injury. The lesion was cervical in 161, thoracolumbar in 76, and lumbosacral in 40. Abnormal bowel reactions at the time of admission were most

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[2] Ellik, M., Newton, L. A. *J. Urol.* 1951, 65, 532.
[3] Ratner, M., Schneiderman, C. *Canad. med. Ass. J.* 1950, 63, 453.
[4] Middleton, R. P., Grua, O. E. *J. Urol.* 1952, 68, 125.
[5] Ainsworth-Davis, J. C. *Brit. J. Surg.* 1943, 31, 34.
[6] Higgins, C. C., Warden, J. G. *Ann. Surg.* 1948, 127, 257.
[7] *New Engl. J. Med.* 1953, 248, 43.

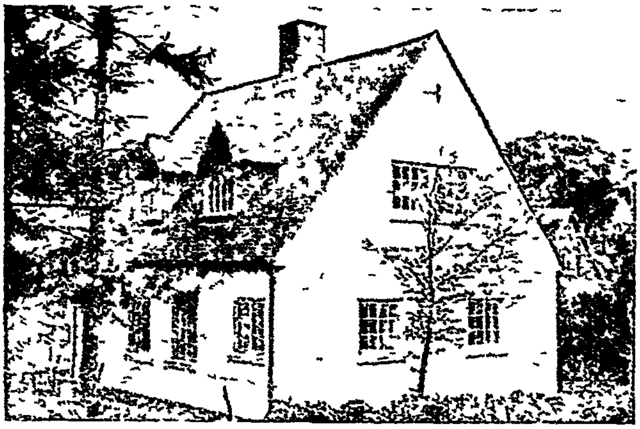

Fig 1—The building and its surroundings

berry Down serves 6 doctors, so it seems logical to suggest that it might be better to spend our money on providing units like this for some 50 doctors (leaving £50,000 for ancillary services) rather than on a Woodberry Down for 6

I joined a rural practice after the war, and six years ago, being dissatisfied with the traditional waiting-room and consulting-room, I planned a self-contained unit, based on experience of Naval and R A F sick-bays Although a building licence was granted readily enough, the cost was limited to £1200 Knowing that every building exceeds its estimated cost, we started to build, and continued until the licence money ran out There was then two months' delay for official inspections and suggestions, but we had spent the money on what was structurally unalterable So the building was completed as originally designed one year after the licence had been granted As I have said, the total cost was £2000, complete with a self-contained sewage system

The building (fig 1) is slightly larger than a council house In the long eaves there is a flat of two rooms, a bathroom and lavatory, a kitchen, and a small hall The flat was designed for a nurse or secretary There is ample storage space above the flat On the ground floor (fig 2) the doors between the various rooms were placed so as to allow patients to come and go freely without getting in each other's way Clearly much time is saved by having one patient undressing while another is being interviewed We made mistakes with some of the doors, however, and two of them opened the wrong way and had to be rehung

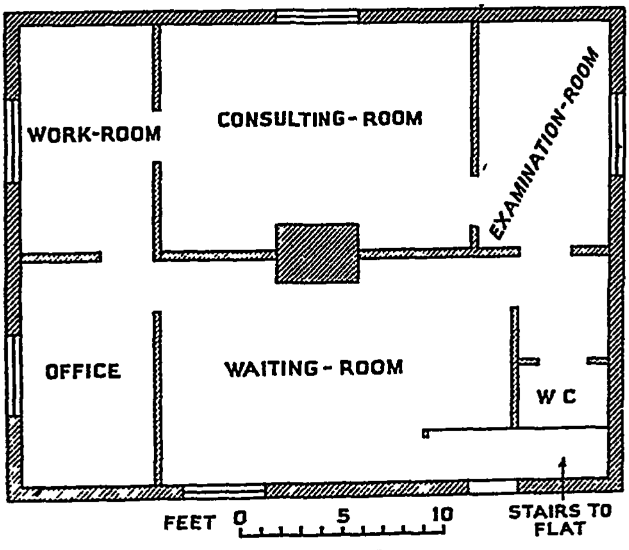

Fig 2—Plan of ground floor

In the *waiting room* (fig 3) we tried to get away from the usual waiting room atmosphere Although benches are used, they are fitted with washable chintz covers over ex Government 'Dunlopillo' cushions Pictures hang on the walls indirect lighting is included, and the walls are coloured with a white distemper, mixed with a little pink (This pink avoids the laboratory or "institution" feel of dead white walls) The distemper costs little to renew and it is therefore easy to keep the place fresh and clean The floors are 'Bitumastic with curved wainscotting for easy cleaning A fish tank stands in one corner this was installed to keep children quiet—and it does I am told that this room is a success and that it is a pleasant one to wait in

We tried to make the *consulting room* (fig 4) a place for consultations—not a hybrid minor operating-theatre cum office A separate work room, office, and examination room made it fairly easy to achieve this object

The *workroom* stores instruments and drugs for immediate use It has shelves, a bench, and a sink under the window There is cupboard space under the bench Next to the sink is a large porcelain backsplash, placed flat this has been invaluable for minor operations, for it is easily sterilised by pouring spirit over it and lighting it There are also facilities for examining pathological specimens, but the National Health Service does not offer much encouragement to this side of the work, and patients often go 15–20 miles to a hospital laboratory

In the *office*, the design and the arrangement of the filing system were left entirely to the secretary's decision This

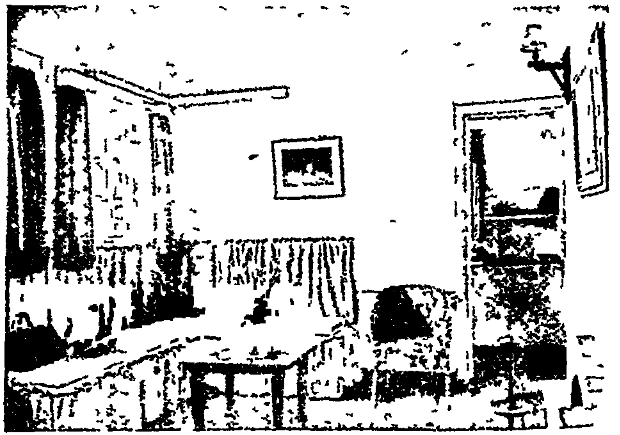

Fig 3—The waiting room

turned out to be a particularly wise move, for she is a concealed sinistral, who likes her filing system shelves, and so on arranged differently from most people Personally I am not a bit happy working there but this does bring out the point that mass produced working conditions do not always lead to efficiency

The *examination room* was also designed before it became clear that it was economic folly for N H S practitioners to do more than the bare minimum in examination and minor surgery This room can be easily blacked out, part of the wall was darkened, and the wiring was arranged so that minor E N T work could be carried out There is a small X ray set, which has proved useful, and at a rough estimate has saved the N H S about £50 a year by keeping minor fractures and sprains away from hospital

The office, workroom, and examination room are lit by fluorescent lamps, which are positioned to minimise shadows

Heating is by gas and electricity Water for the whole unit is heated by an 'Ascot' multipoint geyser

Some snags were discovered after the building came into use For one thing, there was too much storage space in the workroom Acoustics gave some trouble because of the effect of the curved edges to the ceilings and the curved wainscotting We had difficulty in preventing the high pitched female voice from penetrating outside the consulting room (a complication of plaster board ceilings) The worst mistake was not having a back door, and the doctor has to go through the waiting-room to get in matosis peritonei: each was given an injection of tritium-labelled water, either intraperitoneally or intravenously, and samples were then removed at intervals up to 24 hours. Whatever the route of administration, equilibrium between the ascitic fluid and the plasma was reached in 8–10 hours. From the slope of the equilibration curves it was calculated that between 40% and 80% of the total volume of the ascitic fluid entered and left the peritoneal cavity each hour. A simple calculation shows that a patient with 6 litres of ascitic fluid—a by no means uncommon amount—turns over 58–115 litres per day.

The remarkable absorptive capacity of the peritoneum is confirmed by both investigations. The difference in the turnover rate of protein and water, as shown by these experiments, is undoubtedly a function of molecule size. This is further suggested by the recent experiments of Whipple et al.[3] who used labelled albumin and globulin in dogs with ascites. The rate of transfer of the relatively smaller albumin across the peritoneal membrane was, in terms of weight, at least three times as fast as that of the larger globulin.

It is evident, as Prentice et al. point out, that with a turnover capacity of more than 100 litres per day the balance between inflow and outflow from the peritoneal cavity must be delicately controlled. A 1% deficit in outflow could rapidly lead to a clinically significant degree of ascites. Moreover, since ascites was present despite the apparently unimpaired absorptive capacity of the peritoneum, it is clear that the formation of ascites was probably due to greatly increased inflow. This conclusion agrees with that reached by workers at the Mayo Clinic[4] who attribute ascites formation to the grossly excessive production of hepatic lymph caused by intrahepatic sinusoidal congestion. Moreover, as Prentice and his colleagues emphasise, this conclusion leads to the conception of a reabsorption threshold which must be exceeded before ascitic fluid can accumulate. Factors such as the renal retention of sodium and water, and changes in the osmotic pressure of the plasma proteins, which are known to influence the development of ascites, may operate through their effect upon this threshold, as well as upon the direct formation of the fluid by filtration in the highly permeable hepatic sinusoids.

NOTHING BUT THE TRUTH

At the trial in Belfast this month of a young R.A.F. clerk who was charged with murder, statements made by the accused man while under the influence of sodium thiopentone were put forward by a psychiatrist who was called as an expert witness by the defence. This medical evidence was accepted by the court, and the jury, after deliberating for two hours, found the accused guilty but insane.[5] In Britain such evidence has not previously been accepted in a murder trial.

Sodium thiopentone is a quick-acting barbiturate commonly administered for anæsthesia during minor surgical operations or for inducing anæsthesia. Like sodium amylobarbitone ('Sodium amytal') it has been increasingly used in psychiatry during the past twenty years, for during the precomatose stage or during emergence from unconsciousness inhibitions are abolished or lessened, and this phase can be prolonged by slow intravenous injection of the drug. As in hypnosis, there is some dissociation and the subject is more than ordinarily suggestible; the intravenous administration of barbiturates for "narco-analysis"[6] and for "narco-synthesis"[7] is based on this. Sargant and Slater[8] approve of this use of barbiturates for diagnosing psychoses, both in depressives and catatonic schizophrenics, and for diagnosing and treating neuroses. In the acute neuroses of war they found it valuable in treating functional amnesias and conversion symptoms of recent and abrupt onset, and for the abreaction of emotionally charged experiences.[9] Henderson and Gillespie[10] suggest that the value of narco-analysis has been overrated:

> "Its chief usefulness is in the rapid recovery of memory in psychogenic amnesia. It is more certain to work than hypnosis and gives, therefore, more confidence to the doctor, but with sufficient patience and time, the same and probably better results can nearly always be obtained with persuasion, without either hypnosis or narcotisation. The method gives the patient something tangible that he understands more easily than the purely psychological method of approach, and it has in consequence considerable value as a vehicle of suggestion."

They admit, however, its value in discriminating between hysterical and epileptic fugues and between psychogenic amnesia and amnesia due to brain injury.

Prof. Jean Lhermitte[11] favours the use of thiopentone in criminal cases only for the detection of malingering ("narco-diagnosis") but not for obtaining information about the guilt of the accused ("narco-analysis"). There seem to be two main problems connected with the use of a "truth drug" in criminal investigations: the question of medical ethics, and the question of the reliability of evidence thus elicited. Probably few would object to its use for the purposes of the defence only, though the accused might be at some disadvantage if it was revealed at his trial that he had refused to submit to narco-analysis. The question of reliability is usefully discussed by Gerson and Victoroff.[12] Using intravenous sodium amylobarbitone, they investigated the possibilities and limitations of narco-analysis in 17 male neuropsychiatric patients who had refused to admit to crimes or antisocial conduct concerning which irrefutable evidence was available from other sources; they pointed out to the men that no information divulged would be used in charges against them. They emphasise the importance of establishing the best possible rapport with the subject and of obtaining a full history of his past life and of the incidents and circumstances leading up to the hidden material. The men were not warned until a few minutes beforehand that they were to have amylobarbitone; it was then explained that it would make them sleepy and enable them either to remember forgotten episodes or to talk more freely to the doctor. 6 patients submitted readily, but the remainder showed suspicion or resistance. Anæsthesia was prolonged, and the most material was obtained during emergence. Confessions were obtained from all subjects, but these were subsequently repudiated in 8 cases. Gerson and Victoroff agree with Henderson and Gillespie[10] that there is often fantasy and falsehood in the material divulged; and they point out that narco-analysis may provide the subject with a welcome opportunity of "recovering his memory" or of informing on an associate. They believe that statements obtained by means of narco-analysis, with the subject's permission, could be useful in establishing guilt or innocence, weeding out those who confess falsely to crime, and exposing malingerers. They suggest that ultimately submission to narco-analysis may be mandatory in the investigation of certain crimes, just as, in the U.S.A., the taking of fingerprints, premarital Wassermann tests, the reporting of venereal disease contacts to the board of health, and blood or urine analysis of suspected alcoholics, have been enforced;

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[3] McKee, F. W., Yuile, C. L., Lamson, B. G., Whipple, G. H. *J. exp. Med.* 1952, 95, 161.

[4] Gray, H. K. *Ann. R. Coll. Surg. Engl.* 1951, 8, 354.

[5] *Manchester Guardian*, March 10.

[6] Horsley, J. S. Narco-Analysis. London, 1943.

[7] Grinker, R. R., Spiegel, J. P. Men under Stress. Philadelphia, 1945.

[8] Sargant, W., Slater, E. An Introduction to Physical Methods of Treatment in Psychiatry. Edinburgh, 1948.

[9] Sargant, W., Slater, E. *Lancet*, 1940, ii, 1.

[10] Henderson, D. K., Gillespie, R. D. Textbook of Psychiatry. London, 1950.

[11] Lhermitte, J. Report of the Société International ede Criminologie. Paris, 1951.

[12] Gerson, M. J., Victoroff, V. M. *J. crim. Psychopath.* 1948, 9, 359.

held that the child had indicated pain on the right side, the hospital doctor should have detected signs of acute appendicitis, and the child should not have been sent home The hospital was liable for his negligence

A Transfusion Accident

The death of a 54-year-old man after a postoperative blood-transfusion was the subject of an inquest at Preston on Feb 27[1] Two pints of blood were given without mishap, and during the transfusion of the second pint the registrar in charge of the case gave instructions to the nursing staff that a third pint should be given later on if necessary A staff nurse wrote in the ward report that there was a third pint of blood in the laboratory At the inquest she explained that she did so because there was no blood in the ward refrigerator, and she concluded that it must be in the laboratory During the night, a nursing sister was called to see the patient, and she decided to give him the third pint She had read the ward report, and when she went to the laboratory she found a bottle of blood bearing the patient's name, Moon The bottle did not have the usual compatibility label, but she did not notice this The blood was given, but it proved to be incompatible, and the patient died It was stated at the inquest that the name on the bottle was in fact that of the donor Recording a verdict of death by misadventure, the coroner said that it would be unfortunate if the case should shake anybody's confidence in the hospital, which was doing first-class work

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Parliament

QUESTION TIME

Supplies of Aureomycin

Dr Santo Jeger asked the Minister of Health whether, now that aureomycin was manufactured in this country and the limitations on its efficacy were so well known among general practitioners, he would make it more freely available to doctors so that delay was avoided when its use was indicated —Miss M P Hornsby Smith replied The manufacture of aureomycin in this country still involves bulk importation of the crude drug at considerable dollar cost and the Minister thinks that its issue ought still to be subject to the present safeguards He is not aware that, under these arrangements, there is any undue delay in supplying this drug to general practitioners in cases where its use is indicated

Replying to a further question by Dr Jeger, Miss Hornsby-Smith said that 896 applications by general practitioners for aureomycin had been granted It was estimated that about 5% of the applications were refused

Tuberculosis Among Immigrants

Mr Kenneth Robinson asked the Minister how long his Standing Tuberculosis Advisory Committee had been considering the problem of tuberculosis among persons taking up residence here from abroad and what recommendations the committee had made on the subject —Mr Iain Macleod replied The actual reference to the committee was made in December I understand it is to be discussed in a few days Mr Robinson Is the Minister aware that there are at least indications that tuberculosis is being imported into this country to a disturbing extent, and that the problem is not confined to aliens but extends to British subjects from parts of the Commonwealth and Ireland? Will he introduce some measure of urgency into this matter? Mr Macleod I do not quarrel with what the hon member has said The wider questions he raised are under discussion with the Ministry of Labour and the Aliens Department of the Home Office

Fluorine Gas Inhalation

Dr Barnett Stross asked the Minister of Health what information he had of the ill effect on health from the inhalation of fluorine gas as a by product of industrial processes —Mr Macleod replied I have no evidence that such ill effects are occurring Dr Stross Is the Minister aware that, in my constituency, in the neighbourhood of at least two factories the glass of the factories is etched and rendered opaque, as is also the glass of many of the houses round about, as a result of fluorides which come from the industrial processes? Would he consider going further into this matter and seeing that some research work is done so that we know what is happening to human beings as well as to cattle?—Mr Macleod I am aware of the recent incident in which four or five cattle were poisoned in the constituency of the hon gentleman, but that seemed to me to confirm the investigation in 1949 by the Medical Research Council into an incident in Inverness, which showed that though there may be, and indeed is, danger to animals, there is no danger, so the M R C advised the Minister then, to human life

Dr Stross But may I ask the Minister to go further into the matter because there is a good deal of circumstantial evidence, which we cannot term strictly scientific, that harm comes to human beings? The right hon gentleman has a council, will he ask them to look at it again?

Mr Macleod As I have said, the M R C have looked at it, but I will draw their attention to what the hon gentleman has said

Smokeless Zones

Replying to a question Mr Harold Macmillan, Minister of Housing and Local Government, said that 12 local authorities had obtained powers by local Acts for establishing smokeless zones, but so far only 2 zones were in operation—at Coventry and Manchester The 2 zones were limited in extent and sufficient time had not elapsed to enable the full effects to be assessed

Dentists Bill

Dr Stross asked the Minister of Health when he proposed to reintroduce the Dentists Bill —Miss Hornsby Smith replied As soon as Parliamentary time permits, but I am afraid that will certainly not be this session

Spastic Children

In answer to a question Miss Florence Horsbrugh, the Minister of Education, said that there was no general register of spastic children, and she did not collect separate figures for spastic as distinct from other physically handicapped children Educable spastic children might be sent by local education authorities to ordinary schools or to special schools for the physically handicapped There were four special schools in England, of which three were maintained by voluntary organisations and one by a local education authority, specifically for children suffering from cerebral palsy, and a number of others made special arrangements for them

Juvenile Crime

In answer to a question Sir David Maxwell Fyfe, the Home Secretary, stated that provisional figures for 1952 showed that at all courts in England and Wales 26,212 children under the age of fourteen and 18,866 young persons aged fourteen and under seventeen were found guilty of indictable offences The comparable figures for 1951 were 28,578 and 18,895

Voluntary Help for Hospitals

Sir Guy Lloyd asked the Minister what success was being achieved by the encouragement he was giving to the greater use of voluntary help for the hospitals —Mr Macleod replied It is too early to attempt to assess results, but signs of development are most encouraging, and I am confident that the hospitals and voluntary workers will continue to cooperate further to the great advantage of the patients

Dental Estimates

Mr Edward Wakefield asked the Minister how many estimates per week were received on the average from dentists by the Dental Estimates Board, and what was the number of staff employed by the board to deal with these estimates —Miss Hornsby Smith replied On the average 160,000 new estimates are received each week together with 40,000 estimates submitted for a second time The staff numbers 926, some of whom are employed part time Mr Wakefield Does the Minister agree that these figures indicate an excessive degree of centralisation?—Miss Hornsby Smith There is a large sum of public money involved and the Minister feels that the service is better controlled under one organisation

Deaths from Coal-gas Poisoning

Replying to a question Mr Macleod said that during the twelve months ended Sept 30, 1952, 2356 deaths were registered as due to poisoning by gas in domestic use The trend in post war years has been upwards, but an enormous proportion of the figures given—namely 1900—were suicide deaths where site and type of electrical discharge suggest grand mal or psychomotor epilepsy. Treatment of petit mal has been greatly improved by the introduction of troxidone ('Tridione'), aloxidone ('Malidone'), and paramethadione ('Paradione'); and occasionally the attacks do not recur after these drugs have been given for a limited period. On the other hand they may aggravate petit mal and even apparently produce grand mal; and thus they are commonly administered in combination with drugs of the hydantoin group. Furthermore, they tend to cause blood dyscrasias, so that regular blood-counts are necessary. Despite these new drugs Keith,[1] at the Mayo Clinic, still regards the ketogenic diet, now rarely used in this country, as the most effective remedy.

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[1] *Manchester Guardian* Feb 28, 1953

POTENTIALS IN MYOCARDIAL INFARCTION

ABNORMAL electrocardiographic Q waves are an important sign of cardiac infarction. These abnormal waves are most obvious over anterior lesions, where precordial leads usually show also reduction or abolition of the R wave with either QR or QS ventricular complexes. Wilson and his followers, believing that an active left ventricular muscle always caused an R wave in an epicardial lead, regarded QS complexes as evidence that cavity potentials were being transmitted to the surface through a window of electrically functionless muscle. Recently Prinzmetal and his associates [1] have found in dogs that ligation of the left anterior descending coronary artery produced transmural infarcts which were generally alike in showing a QS complex on epicardial electrocardiograms, but were otherwise strikingly different. Some of these infarcts were completely functionless; but in others there were signs of muscular activity—stimulation gave rise to a current of injury with ST deviation, and wrinkling and shrinkage were seen on a high-magnification fast-moving cinematograph in contrast to the balloon-like protrusion of the dead areas. Electrocardiograms taken at a high paper speed showed that leads from partly active areas differed from the others and also from cavity leads by having a deeper and later downward deflection, often with a notch indicating the remains of an R wave. Intramural leads differed from both surface and cavity leads, and finally histological examination showed islands of healthy muscle tissue surviving in the infarct. These observations, which clearly suggested that the "window" concept was not always justified, prompted a study of intramural potentials in normal animals. Fine silver needle electrodes, insulated except for a chloride-coated tip, were plunged for measured distances into the wall of the left ventricle and the septum. Immediately below the surface the R wave diminished rapidly with a corresponding increase in S; QS complexes were nearly always recorded from the inner surface of the ventricle, while R was sometimes almost absent at a depth of 3 mm. A curved electrode passed through the free wall of the right ventricle into the septum showed an R wave increasing until approximately its mid-point and thereafter diminishing as the left ventricle was approached. Prinzmetal and his associates conclude that an epicardial R wave is due not to the sum of the depolarisation potentials of the whole underlying ventricular wall but almost entirely to the activity of the epicardium and the immediate subepicardial muscle. The potential from the septum, they think, is chiefly of left ventricular origin. This work may be criticised on technical grounds, but most of the objections seem to have been anticipated.

These findings apparently contradict the view, based on the work of Wilson and earlier of Lewis, that the heart behaves electrically as a single muscle strip. Probably Wilson,[2] working only with cavity and single surface electrodes, oversimplified it. The left ventricle, especially at the apex, is a complex of muscle-bundles; and there is evidence [3] suggesting that these are repolarised in different directions. It would not be surprising if they were depolarised in the same way.

The practical implications of the subject are important. A QS complex in a left ventricular lead does not always indicate complete transmural infarction, whilst a QR pattern is more likely to be the result of incomplete superficial than of subendocardial damage. There is already clinical support for this view in the good prognosis and the transitory character of some QS lesions, and in the absence of electrocardiographic changes over known subendocardial infarcts. Closer scrutiny of the electrocardiogram in association with pathological examination, as well as greater attention to the radiological signs of localised muscular inactivity, are obviously needed.

ISONIAZID WITHDRAWAL SYMPTOMS

THE rapid tempo of modern research often means that, whenever a new drug is discovered, the claims made by its sponsors are promptly followed by reports of alarming reactions from other sources. And isoniazid has gone through these phases particularly quickly. The American Trudeau Society has invited anyone encountering toxic manifestations during treatment with isoniazid to send them the details so that a consolidated report may be published in due course.[4] Meanwhile, a succession of individual reports have appeared. The toxic reactions that have been described include liver damage, alimentary disturbances, agranulocytosis, reactions in the nervous system, and difficulties with micturition. Mental changes have attracted considerable interest, and euphoria during treatment is an almost constant feature.[5] Frank psychoses, however, have occasionally appeared.[6] [7] There may well be some direct pharmacological relation between these changes and the action of the drug on the central nervous system. But the so-called "withdrawal symptoms" that come to notice only when treatment has to be stopped are more difficult to explain. According to Selikoff et al.,[8] these symptoms are headache, insomnia (or sometimes sleepiness), dizziness, excessive dreaming, irritability and nervousness, and an increase in hyperreflexia. They seem to be commoner after iproniazid (the isopropyl derivative) than after isoniazid itself, for they appeared in 39 out of 56 patients who had had iproniazid, but in only 2 out of 9 patients treated with isoniazid.

In this country, experience with iproniazid is extremely limited, but, so far as isoniazid is concerned, the Medical Research Council's latest report [9] is reassuring: "there has been virtually no toxicity from isoniazid with the dosage used" (100 mg. twice a day). Moreover, though there must be a comparatively large number of patients in this country who have been treated with isoniazid and have now ceased to take it, no examples of a withdrawal syndrome have yet been reported. After all, headaches, insomnia, dreaming, nervousness, and so on are common enough symptoms; and it is perhaps premature to label them as specific to isoniazid withdrawal, especially since Selikoff et al. do not definitely say that there were no other changes in the patients' régime which might have been responsible.

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Letters to the Editor

REGISTRATION OF FEVER NURSES

SIR,—In recent correspondence emphasis has been placed on the importance of retaining the Fever Register for nurses, and it seems to me that the arguments put forward by those working in large fever hospitals are irrefutable It is probably true that in many hospital management committee groups it has been possible to arrange for the appropriate staffing of the smaller fever hospitals irrespective of the enlistment of student nurses, and, to a degree, some secondment of student nurses from associated general hospitals has been possible This has, however, proved to be completely impossible in the case of large fever hospitals, of which there is at least one in each hospital region

It is this point that should be impressed on the General Nursing Council, and agreement should be secured to the retention in each region of at least one large fever hospital as a training school for student fever nurses Only in this way can we ensure an adequate supply of nurses suitably trained in fever work in such important diseases as poliomyelitis, gastro enteritis, dysentery, smallpox, and other virus diseases This arrangement would of course ensure also that these hospitals could be properly staffed so that the community is provided with a suitable hospital and nursing service in these conditions

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T LLOYD HUGHES
Senior administrative medical officer

SIR,—The present parlous position of the staffing of infectious disease hospitals has already been emphasised by other correspondents At this hospital less than half the beds are in service because of shortage of nurses, whereas during most of the year we could fill two or three times the number with ease

The mistake was made primarily in high places before the appointed day, when it was naïvely assumed that the success of diphtheria immunisation and the advent of the antibiotics had rendered superfluous the ad-hoc infectious-disease hospital, thenceforward it was to form a block in the comprehensive hospital of the future The emergence of epidemic poliomyelitis, together with the obstinacy of the common infections in refusing uniformly to yield to the new remedies, showed this forecast to be unduly optimistic Meanwhile, presumably on the strength of this same assumption, it was decided to close the Fever Register

The General Nursing Council has so far hesitated to take this decisive step, perhaps because experiments in secondment have been made with indifferent success At intervals when difficulties become acute, meetings are held with responsible nursing officials at which grievances are ventilated, and invariably the "comprehensive training" is held out as the coming solution of all our troubles The General Nursing Council *continues blandly*, if correctly, to point out that its duties are concerned entirely with nursing education and disclaims any responsibility for the supply of nurses or the staffing of hospitals In the result, fever hospitals today are often forced to rely on sisters, a few part-time staff nurses, and as many ward orderlies from Central Europe as they are allowed to employ Many of these, although untrained, do an amazingly good job of work, but in the circumstances one is astonished that results should be as good as they are If the supply dries up, as one gathers it may, then there would seem to be no alternative but to close down, and what would happen if we were to have an epidemic of poliomyelitis on the scale of that in Denmark is best left to the imagination

What solutions are practicable ? The retention of the Fever Register would help and ought to be insisted on But more than that is required There is need of some body, composed of experienced persons with a knowledge of the realities, to foster the adequate staffing of the hospitals, not only from the nursing but, also, as you have pointed out, from the medical, point of view It is curious that, among so much planning, this should have been omitted The restoration of the "differential," so disastrously abolished by the Rushcliffe Committee, will ultimately have to be considered, it lies at the root of the matter, and with the public appetite for litigation growing daily it may prove cheaper in the long run But quite apart from this there is the denial of hospital facilities to those who need them to an extent far greater than before the war—truly an ironic reward for all the upheaval we have undergone Surely we can do better than this

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Isleworth

G E BREEN

DEATHS IN THE FOG

SIR,—Professor Macdonald's letter in your issue of March 7 raises the interesting question as to whether the exceptionally high mortality experienced in London after the December fog might in part have been due to an epidemic previously under way I entirely agree that some of the increased deaths in the week ended Dec 13 would have resulted from the rising level of sickness in the preceding weeks, irrespective of the fog, but I consider that reliance on the Emergency Bed Service applications has led Professor Macdonald to overestimate considerably the extent of this sickness and I would contend that Dr Logan's figures of death due to fog are substantially correct

The weekly number of new claims for sickness benefit, figures of which are published by the Ministry of National Insurance, is a measure which over the last few years has been very sensitive to winter epidemics In the Administrative County of London, the number of new claims for the four weeks preceding and including the fog were 9099, 10,606, 11,678 and 12,553, in that order, during the influenza epidemic of 1951 the new claims rose above 30,000 a week and they again did so in late February of this year There is no indication in these figures of any particularly acute epidemic in early December In the week after the fog the claims rose to no more than 17,000 odd, well below severe epidemic level However, these figures do show that there was a definite if slow increase in sickness in late November and early December, and it is possible to utilise the remarkably constant winter relationship between the new sickness claims in a week ending on Wednesday and the deaths registered in the week ending the *following* Saturday to make some estimate of the deaths in the week ended Dec 13 which would be attributable to the increasing sickness Using the experience of the 1951 influenza epidemic and allowing for seasonal effects, the estimate from the new sickness claims is 1100 deaths in this week in the Administrative County The actual number registered was 2484 This gives an excess of 1384, the excess above five-year average is 1619 and above the week ended Dec 6, 1539 On this basis, therefore, the deaths due to fog are only 10% below Dr Logan's lower estimate, and there seems to me to be no great inaccuracy in the round figure of 4000 for Greater London

The effect of the fog upon mortality appears to have been out of all proportion to its effect upon morbidity as reflected in the sickness-benefit claims An analysis of the winter deaths in the period 1873–80, the last time that fogs of comparable severity occurred with and without accompanying epidemics, gives no reason to suppose that a fog combined with an epidemic causes deaths on a scale greater than the sum of what would be expected from each separately Winter fog will raise mortality

HOW FAR ARE THE NEEDS MET ?

In our earlier survey we pointed to some unmet needs, and on this occasion we have tried to measure them. Over two-thirds of the men and seven-eighths of the women were living alone in the sense that they had their own distinct accommodation and maintained a separate economic existence. A fifth of the men and over a third of the women were alone at night. These latter proportions are conservative measures, since, if the old person shared a dwelling with another family, she was not counted as alone at night even though she maintained a solitary existence, economically and socially—we considered her to be at least within talking or calling distance of others, if need be. But it has been found, unfortunately, that help and companionship from other residents in the house is not always assured. In this one area alone there were more than 500 people, many of advanced age, without night companionship.

Inquiries were made as to the extent to which these old people were visited. Some four-fifths of women and nearly two-thirds of men received visits from near relatives, and as these proportions tallied with the numbers of near relatives who were separately alleged to be living, it must be presumed that the response from relatives was satisfactory when one takes into account the fact that about one-third of these relatives lived outside the Borough of residence of the old people, and one-sixth of them outside London. Friends as visitors were fewer in number, covering a third of males and nearly half of females, and we formed the impression that more could be done. Churches in the main managed to cover only those who were members of church organisations and came to notice in that way. Most of those few (12 men, 36 women) who were without visitors did not seek them; presumably there were individual temperamental difficulties which may have been the direct consequence of this isolation, but this does not mean that they would not benefit from social intercourse even at this late stage.

Comparatively few of the old people claimed to have any link with outside social organisations such as old people's clubs. More than 80% of both sexes had no such link, and, since the majority of these people are ambulant, there appears to be considerable scope for further development of Darby and Joan clubs, which must be an integral part of any scheme for the care and welfare of the aged.

How did these people amuse themselves ? We found that reading (60%) and radio (70%) were the mainstays. The proportion of women who occupied themselves with needlework or knitting (10–15%) was small, partly, no doubt, because of failing sight. Generally there was little mention of home activity, and, though possibly there was some understatement due to diffidence, there is an indication that these people have drifted into inertia from which they need to be extricated by stimulation of interest. Cinema-goers were unexpectedly few (4% of men and 7% of women) and television sets rare (3% of both sexes). Inquiries were made as to unserviceable wireless sets which fortunately were uncommon (16 in all) ; and into the need for deaf-aids ; but there were only 18 cases where a deaf-aid was needed and had not been obtained and only 2 cases where a deaf-aid was in need of repair. These points need watching, however, among old people who sometimes "do without" rather than ask for help.

ASSISTANCE AND MEALS

The total volume of domestic assistance given to the household either by home helps or by relatives and friends was examined. The home helps do general cleaning in all cases, some shopping (39% of households), a little cooking (9%), and some light washing (25%). It should be emphasised, however, that the ideal home help is not merely a paid domestic servant but becomes a friend and companion to the old person whom she serves. In a quarter of the cases—i.e., those where the old people were not alone—another member of the family (spouse, son or daughter, or lodger) was able to help with household chores.

Assistance from relatives and friends was limited, on the whole, to shopping and companionship, which was extended to about a fifth of the households. No help was forthcoming for heavy washing.

In those instances where relatives existed but gave no assistance, inquiries were made as to the reason for this failure to help. Nearly one-third of these relatives lived too far away, one-tenth were too preoccupied with their own affairs, and one-twentieth were ill or too old. Only a dozen of them could but would not help. It seems that there is not a great deal of extra help which could be sought from relatives nowadays and that the alleged negligent "spirit of the age" is in reality a factor of minor importance.

Where the domestic help service was providing assistance an attempt was made to assess the additional services which were most badly needed. As might be expected, the main need was for washing (18%). In a few instances, the interviewers stressed the need for companionship, and in 22 cases there was a need for someone to take the old person out. Surprisingly enough, there was no significant pressure for weekend service, perhaps because the interviewers had become accustomed to regard it as impossible. It is important to remember that the needs indicated were really serious needs, assessed by experienced domestic help supervisors, and had not necessarily any relation to personal pleas by the old people.

An important aspect of the care of old people in their homes is the preparation of meals. In the 933 households covered by the domestic help service, meals were prepared by the home help in 79 cases (8·5%). Fortunately in only 11 of these would withdrawal of the home help have resulted in a failure to obtain any meals. Of the remainder, 21 would have been able to call on relatives and friends, and 3 could obtain meals from the L.C.C. Meals Service ; but there would still be 44 cases where only inadequate snacks could be contrived by the old people themselves. The 91·5% of households for which the home helps did not prepare meals were made up as follows : 70·9% obtained adequate meals on their own resources, 17·6% were provided with meals by relatives or friends, and 3·0% used the L.C.C. Meals Service or restaurants. Even if the meals-on-wheels service is much extended, it cannot replace adequately meals cooked in the home by a relative—or, failing her, a home help—to suit the tastes and the fads of the aged person.

HOUSING, MONEY, AND COST

With regard to housing, it was found that 25·6% of the households were in houses, 31·0% in flats, and 43·4% in rooms in divided accommodation. Only 4 dwellings were regarded as unduly crowded and in only 16 dwellings were sanitary defects reported. A more important feature was that in 72 households (6·7%) there was difficulty of access—i.e., the old person was living in the top floor of a tenement and the climbing of the steps was a deterrent to going out of the dwelling.

It is of interest and importance that 44·5% of households had been resident in their present accommodation for more than ten years, and 25·1% for more than thirty years. These deep roots complicate the problem of rehousing, although it is evident that much improvement could result from readjustments of existing accommodation.

9·9% of all households were judged to be financially comfortable, 67·1% just managed, and in 23·0% there was a definite shortage. Among the households covered by the domestic help service only 4·5% paid the charges often dangerous to remove the appendix We differ, however, from the Newcastle group in our treatment for gangrenous intussusception We had 5 such cases in this series of 106, and resected all of them with no death We believe that resection is the procedure of choice provided a very long segment of proximal dilated gut is removed and the gut is anastomosed end-to end with interrupted mattress sutures of silk This technique takes time, but is, in our opinion, the only safe type of anastomosis in pædiatric surgery We notice that you state that ileoascending colon anastomosis is invariably followed by death We performed this anastomosis in 1 of the 5 cases, the patient made a perfect recovery, and we have had other recoveries not included in this series

In conclusion we should like to emphasise again that the mortality in most of the recent accounts of intussusception appears too high and could be considerably reduced if these children were treated in hospitals where surgeons, anæsthetists, and nurses are acquainted with the special problems of pædiatric surgery

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ISABELLA FORSHALL
P P RICKHAM

MENTAL ACTIVITY IN INFANCY

SIR,—We have read with interest Mrs Collis's paper (Feb 28) in which she describes tests designed for the early recognition of mental defect in children with cerebral palsy

Though mental development depends on physical development, especially in early life, motor tests such as those described by Mrs Collis cannot detect mental defect in cases of cerebral palsy They can show the severity of the motor defect but cannot separate innate mental deficiency from mental retardation caused by the motor and sensory handicap

Most of the tests—1(b), 1(c), 1(d), 2(a)—are tests of both motor and mental functions These are, therefore, unsuitable for the differentiation of mental from motor deficiency This leaves tests 1(a), 3(a), 3(c), and 3(d) for the assessment of mental progress

Test 1(a)—Pronounced asymmetrical tonic neck reflexes in the brain damaged child are release phenomena from damage to higher motor centres Furthermore, persistence of excessive flexor tone, especially in the prone position, is due to released tonic labyrinthine reflexes which prevent the development of extensor tone, and make the raising of head and shoulders in the prone position impossible Therefore, test 1(a) can only be used to assess motor defect, and the persistence of these tonic reflexes only proves that the case is severe, and that treatment will be longer and more difficult than in cases where modification has already taken place The fact that asymmetrical tonic neck reflexes may persist in patients of normal intelligence is well known, and we have seen children and adults who, though unable to stand and walk, made use of the excessive flexor tone in sitting, and of the tonic neck reflex patterns in voluntary movements of their hands for skills such as typing

Test 3(a)—The absence of resistance to passive handling in the cerebral palsied child can only prove that the motor defect is not severe In such cases extensor spasticity has not yet developed, and excessive flexor tone has already become modified In these mild cases extensor spasticity appears later when the child is made to stand

Test 3 (c)—In this test Mrs Collis mentions the palmar grasp as "less easily elicited on the right side in most infants," and says that "the plantar grasp shows little modification" As both palmar and plantar grasp are still present at this age, accurate results cannot be expected from this test

Test 3 (d)—The rolling of the trunk to the side to which the head is passively turned (neck righting reflex) is an unsuitable test for mental advance It may be totally inhibited by the persistence and abnormal strength of the tonic neck reflexes On the other hand, the neck righting reflex is normally active up to the age of 7 months and becomes modified by the body righting reflexes acting on the body between 7 and 12 months of age (Schaltenbrand)

These tests may usefully be employed for assessing the severity of cases They will help in the selection of the milder cases which will respond quicker and more easily to treatment, but they are of no value for detecting mental defect Whether an infant can modify these early reflex patterns depends on the severity of the handicap rather than on mental endowment If such modifications occur they do so at a much later age, especially in the severe case Used for the diagnosis of mental defect in cerebral palsy, these tests would class the severely handicapped child as both mentally and physically defective They would exclude from treatment the severely motor-handicapped children, who are in special need of early and intensive treatment

London, W 1

KAREL BOBATH
BERTA BOBATH.

SIR,—The article by Mrs Collis answers a need of all health workers and pædiatricians However, in reading the article a number of questions present themselves

Of the 2000 infants with cerebral palsy who were examined, how many have been diagnosed as mentally defective? At what ages were these infants examined? Have follow ups borne out the findings? How many of the normal and palsied infants were examined at 4 months old?

Of these children how many, other than those with abnormalities confined to the reflex motor apparatus, have a history of asphyxia livida at birth? How many of the normal infants had a history of asphyxia livida at birth? On what criteria were the diagnosis of asphyxia livida based? It is well known that infants may be quite blue for varying periods following a normal birth and yet may cry lustily and breathe and suck vigorously thereafter

This article suggests that very vital decisions as to the future handling of an infant may be made at the 4th month by the results of a few simple tests, and I therefore feel justified in asking for more detailed information

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C R DONIGER

VITAMIN B_{12} AND ACETYLCHOLINE SHOCK

SIR,—Traina[1] found that vitamin B_{12} had a protective action in anaphylactic and histamine induced shock in the guineapig, and he thought that vitamin B_{12} was, weight for weight, more effective in histamine than in anaphylactic shock Although the release of histamine plays an important rôle in anaphylactic shock, there have been several reports suggesting that acetylcholine also takes part We therefore gave vitamin B_{12} to mice (mean weight 12 g) and then observed the effects on them of histamine and acetylcholine

The minimum lethal dose (M L D) of histamine hydrochloride for mice was 900 mg per kg body weight by intravenous injection Each mouse was injected intraperitoneally with 15 µg of vitamin B_{12}, and 15–90 minutes later 1 M L D of histamine was given intravenously None of the mice died and very slight signs of shock were observed However, mice given vitamin B_{12} 120 minutes before the M L D of histamine were not protected from shock and death

Mice kept for a week on a diet consisting of polished rice, vitamins A and D, calcium lactate, and salt showed less resistance to histamine—the M L D was 450 mg per kg body weight A number of these mice were injected intraperitoneally with 15 µg of vitamin B_{12}, and 15 minutes later received 1 7 M L D of histamine None of them died

As the M L D of acetylcholine for mice was 14 mg per kg by intravenous injection, each mouse in the following experiments was given 15 mg per kg of acetylcholine intravenously to produce shock The mice were first injected intraperitoneally with 15 µg of vitamin B_{12}, and the acetylcholine was given 15 minutes later All the animals died of shock Death from shock also followed when double the quantity of vitamin B_{12} was given 15 minutes before the acetylcholine On the other hand, mice injected intraperitoneally or intravenously with 15 µg of vitamin B_{12} *at the same time* as the acetylcholine recovered immediately from the slight signs of shock that developed But mice given only 6 µg of vitamin B_{12} were not protected from acetylcholine shock, and even 15 µg of vitamin B_{12} simultaneously did not prevent shock to urban communities where the disease is endemic is held by Rakower to account for the susceptibility and lack of resistance of Yemenites to this disease.

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[1] Traina V *Nature, Lond* 1950 165, 139

HOSPITALS

The hospitals division of the health ministry plans, provides, and maintains the government hospitals. It also supervises other hospitals and distributes government grants-in-aid to municipal and private (non-profit), university, and Workers' Sick Fund hospitals.

A State-sponsored lottery was recently inaugurated to provide funds for building new hospitals. The large pre-war Hadassah Hospital near the university on Mount Scopus is now, under the terms of the prevailing armistice, not in use as a hospital. Of the 5009 general and maternity hospital beds in use in Israel at the beginning of 1952, 45% were in government institutions, 13% were in local-authority hospitals, 12% were maintained by the Workers' Sick Fund, and 30% were maintained by private agencies. In addition there were 4500 hospital beds (half in government institutions) for mental, tuberculous, and "chronic" cases.

HADASSAH MEDICAL ORGANISATION

The Haddasah Medical Organisation, a voluntary agency financed by the Women's Zionist Organisation of America, has provided medical services in Palestine and Israel for the past forty years. It maintained the 450-bed university hospital on Mount Scopus which, since it became inaccessible in 1948, has been replaced by temporary quarters in Jerusalem. The Hebrew University and Hadassah jointly established a medical school in 1949. The Lasker Mental Hygiene and Child-Guidance Centre in Jerusalem and the 100-bed Negev Hospital at Beersheba are also Hadassah enterprises.

SICK FUNDS

All workers and 60% of the whole population in Israel are insured for free medical services, and some for sickness benefits through contributory membership of one of the five sick funds. the oldest of which has been operating since 1912.

NATIONAL HEALTH INSURANCE

A plan to introduce, by stages, a compulsory comprehensive social insurance scheme is about to be presented in a series of Bills to the Israeli parliament. This would provide free hospital services, unified expanded preventive services, dental care for children, medical care for the destitute, family allowances, unemployment benefits, occupational injury benefits, maternity benefits, and old-age pensions.

CLERGY AND DOCTORS

At Torbay Hospital on Feb. 26 the Torquay and District Medical Society held a joint meeting with the local clergy. Dr. G. T. Allerton, the president, was in the chair, supported by the Bishop of Exeter, who opened a discussion on the Place of Clergy and Doctors in the Ministry of Healing. Forty-five clergy and forty-one doctors attended.

The **Bishop of Exeter** said that there was a great need for coöperation between clergy and doctors, for they were both serving in the same ministry. Human nature was a unity composed of body and soul, and because of this unity priests and doctors must work together: their spheres might be distinct and each might have his own expert knowledge, but their objectives were closely interrelated. There was a great temptation for both to arrogate to themselves healing power that belonged to God, whereas at best, in both the spiritual and physical sphere, they were merely channels of grace. The first requirement was a profound humility, realising that their duty was to create conditions favourable for the operation of the Divine power. The Bishop then proposed three topics for discussion. In regard to the views he expressed, he said he was speaking for himself and not for the Church. Of *euthanasia* he said it was wrong to take life; but it was a doctor's duty to relieve unnecessary pain and it might well be that the drug needed to achieve this might shorten life. Of *abortion* he said that the doctrine of the Roman Church was that from the moment of conception the embryo had equal rights with the mother. He himself thought that the problem hinged on whether we regarded the unborn baby as having a distinct personality. The infant in the womb certainly had a claim to life: but had it a greater claim than its mother? He thought that if there was good reason for believing that the continuance of pregnancy would be fatal for the mother, to kill the fœtus might be the lesser of two evils and therefore justifiable, especially when to do nothing would mean the death of both. On *telling the patient* that his end was near, the Bishop thought that it was unfortunate that in recent times the clergy had ceased to consider it their duty to include in their ordinary course of religious instruction the preparation for death. It was so much easier to tell the truth to patients so prepared, and so the best use could be made of their last few days of life. It was of the utmost importance that chaplains should be kept informed of those on the danger-list and be allowed free access to those who were likely to appreciate their administrations.

Dr. G. M. **Tanner** said he was always ready to coöperate with the clergy and had often obtained great help from them for his patients. It was remarkable how often a suggestion from him that their priest might be asked to visit them had been welcomed.

Many clergy and doctors took part in the discussion which continued for about two hours. A strong feeling became evident that some means should be provided for maintaining a liaison between clergy and doctors in the area. The Bishop welcomed this idea and closed the meeting by charging the Rural Dean to collaborate with the council of the Medical Society in selecting a small committee of clergy and doctors to consider how this purpose could best be achieved.

Reconstruction

A DESIGN FOR FAMILY PRACTICE

Robert Howard

M.B. Brist.

Workrooms and working conditions have a fascination for those who are inclined to be slothful: their eye is caught by the amount of unnecessary physical movement and mental effort that goes on, whether in kitchens, garages, factories—or doctors' surgeries.

The large health centres that have been proposed (and built in a few places) since the late war aim to provide working conditions which would enable more patients to be seen more comfortably and efficiently by each doctor. But some members of the profession feel that the advantages of health centres are offset by the way in which they whittle down the personal family side of general practice—the importance of which is seen more clearly now that hospital clinics and local health authorities, with their impersonal peripatetic doctors, deal with so many patients.

There is another disadvantage to the health centre—it costs so much. The result (fortunate or not, according to how you look at it) is that not many have been built. The figures are staggering: for example, the only comprehensive centre so far attempted, at Woodberry Down in North London,[1] accommodates 6 general practitioners, 2 dentists, and a large number of ancillary services; and the initial outlay for the whole centre was over £150,000. It is hard to reach a figure for the cost per professional person, but a conservative estimate must approach five figures. The "family practitioner's unit" in which I have been working for the past four years makes an interesting comparison. Like Woodberry Down, it was designed to give good working conditions—in this case for one doctor—and in 1948 it cost £2000. Now, production in bulk is usually cheaper, and Wood-matters In any case further information is clearly desirable and may lead to the avoidance of some dangers of present therapy Gould's work has been done on infections of the urinary tract I suggest that the skin should also provide a valuable field for observation in this work

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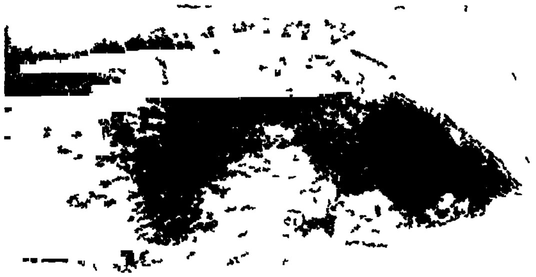
[1] See *Lancet*, 1952, ii, 772.

Leeds JOHN T INGRAM

DEPIGMENTATION OF HAIR BY OXIDISED ADRENALINE SOLUTIONS

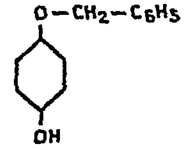
SIR,—The revival of interest in the oxidation products of adrenaline—its most recent expression being the metabolic investigations on adrenochrome by Van Cauwenberge and Lecomte[1] and by Srinivasan[2]—prompts me to report some very preliminary data on a phenomenon which may be attributable to some substance arising from the non-enzymatic oxidation of adrenaline

The subcutaneous injection of unbuffered, partly oxidised, solutions of adrenaline (4 mg per 100 ml of saline solution) into pigmented rats resulted in the following sequence of events at the injection site (a) alopecia, and (b) regrowth of hair lacking in black pigment (see figure) Neither pigmented nor albino rats receiving saline alone nor albino rats treated with oxidised adrenaline solutions showed changes in hair colour after the localised hair loss It would appear that the trauma induced by the needle could account for the transient alopecia in all cases, and that the oxidised adrenaline solutions contain one or more substances that inhibit melanin formation Observations on these animals for almost a year after the last of a series of injections indicate that the greying is permanent That the action is on melanin formation and not on melanin itself is supported by (a) the observation that depigmentation occurs in the new hair only, and (b) the failure of either adrenaline or its oxidised solutions to decolorise hair removed from the body

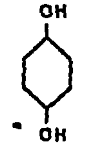


Non pigmented hair in treated area

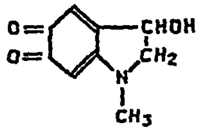
Substances that are known to inhibit melanogenesis in vivo are sodium molybdate in cattle,[3] possibly because of its ability to combine with orthodihydroxy groups, and benzylhydroquinol and, more recently, hydroquinol, both in man[4,5] The two other in-vivo inhibitors of melanin formation that may be mentioned in this connection are phenylthiourea,[6] which may act by binding copper ions, and ascorbic acid in Addison's disease,[7] where it behaves as a reducing agent Oxidised adrenaline has been shown to augment pigmentation of human skin in vitro[8] As with some of the reports just quoted, this preliminary investigation does not establish whether it is a specific cellular process that is inhibited or whether direct pigment-cell destruction takes place Nor is it known at this time whether the action is due to adrenaline or to some of its oxidation products That adrenaline may be the agent seems unlikely, for so striking an effect would have surely been recorded in the half century of the drug's history Obviously this point should be settled by further trials



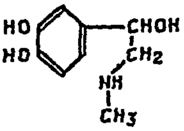
BENZYLHYDROQUINOL



HYDROQUINOL



ADRENOCHROME



ADRENALINE

In view of the repeated suggestions by Kisch[9] that adrenochrome may be a biologically active substance of the adrenal medulla of perhaps even greater importance than adrenaline, one cannot help but speculate whether the hyperpigmentation in most cases of Addison's disease and the leukoderma in less than 7% of the cases may not reflect changes in the metabolic pattern of the adrenal medulla or of chromaffin tissues in general Certainly replacement therapy with adrenal cortical extracts, deoxycortone, or cortisone has thus far proved of little value in reducing pigmentation in this syndrome

lology
rsity School
D C, U S A L P MUNAN

GONORRHŒA IN ANCIENT ROME

SIR,—Since you were good enough to publish my query on this subject I have covered much ground and still find no evidence for the existence of gonorrhœa in Greece or Rome I am again obliged to Dr Geiringer (March 7), whose enthusiasm has brought forward several reputed examples To each the simple question can be applied does this passage undoubtedly refer to the *fluxus virgæ purulentus et contagiosus*? To each I should return the answer No The author of *Leviticus* makes no mention of the penis in his general instructions about septic discharges The "figs" of Martial, purple, swollen objects, are rightly regarded as hæmorrhoids by the scholars The passage in Juvenal, which has to be read *in sensu obscœno*, requires this meaning and none other will do The medical authorities of Greece and Rome use the word gonorrhœa correctly for a syndrome of spermatorrhœa, depression, weakness in the limbs, and diminished libido, called "neurasthenia" by my earliest teachers, and were by no means such donkeys as to confuse it with a contagious inflammation of the urethra

I am at one with Dr Geiringer in believing that we should look to the past, because the further away we move from the present the more remote is the chasm between medicine and scholarship By the time one reaches the reigns of George the First and Queen Anne men are encountered who are well versed in the classics and learned in the history of medicine Their conclusion is unanimous that classical literature never refers to gonorrhœa and that there is no mention of the disease until the 14th or 15th century, the earlier date being in my opinion the correct one with the *testimonium* from John of Arderne (c 1380) There is also D J Rolleston, near in time to us but a man of the true scholar's breed who covered large tracts of Greek and medieval literature and came back with the intelligence that he had found no hint of any venereal disease, not even in a Lucian nor a

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[1] Van Cauwenberge, H Lecomte J *Lancet* Jan 10 1953, p 9
[2] Srinivasan V *Ibid* 1952 ii 684
[3] McGowan J C Brian P W *Nature Lond* 1947 159 373
[4] Oliver E A Schwartz, L, Warren L H *Arch Derm Syph* N Y 1940 42 993
[5] Duffield J A *Lancet* 1952, ii 1164
[6] Dieke S H *Endocrinology*, 1947 40 123
[7] Wilkinson J F Ashford C A *Lancet*, 1936 ii 967
[8] Meirowsky, E *Arch Derm Syph* Wien 1911 163 13
[9] Kisch, B *Exp Med Surg* 1947, 5, 166

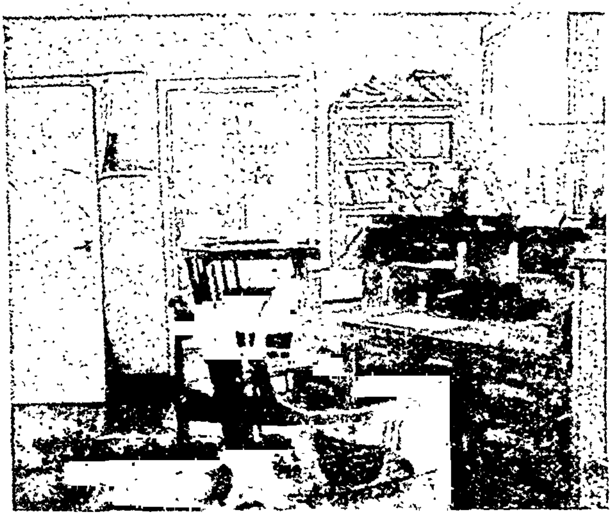

Fig. 4—The consulting-room, with the workroom beyond.

Patients' comments were sometimes illuminating. One of them observed: "The Government have built you a nice place here. It's marvellous, this Health Service." And a farmer remarked: "You get a bit of income-tax rebate on this, don't you? I do on my new piggeries." (Good piggeries, it seems, are encouraged, but there is no similar incentive to build good quarters for patients and doctors.)

The unit is in a village of about 2000 people and serves a population of between 2000 and 3000. For four years now it has proved a satisfactory place to work in. A surgery session has been set aside for antenatal examinations, and this is followed by an infant-welfare clinic. This new building has given me a feeling of confidence, of being able to do the work for which I was trained. It is possible to deal with any emergency in fairly good conditions; and the scope of my work is limited largely by the unfortunate economic pressure of time. If a doctor does more than a certain amount for his patients, his list must be smaller, and so he is poorer. Much work therefore goes to hospital, for the enlightenment of registrars and the frustration of consultants, which could well be done by the family practitioner working in such surroundings.

There should be no difficulty of principle in removing this discouragement to better work. For instance, extra fees are paid to general practitioners for obstetric work under the N.H.S.; and fees are paid to consultants when they use an electrocardiograph in domiciliary consultation. The G.P. experienced in midwifery gets higher pay for the use of his skill, but if he has any other specialised experience and training—whether in E.N.T. work, pathology, psychiatry, or some other subject—he incurs a financial penalty by using it. The College of General Practitioners will not be a real success unless it tackles this anomaly.

Medicine and the Law

A Hospital's Liability

EVEN a layman understands that Scots law and Scots procedure are different from the English. The recent case of Macdonald *v.* Glasgow Western Hospitals and Brown, heard earlier in the month in Edinburgh, provides an illustration. It was an action for damages for alleged negligence on the part of the hospital management and the house-surgeon. It was not a final hearing, nor was it a trial on the merits. In Scotland questions of the competency and relevancy of an action are decided by way of preliminary argument before the merits of the claim are examined. In Scotland, moreover, the courts still apply (notwithstanding the National Health Service Act and certain English decisions such as Cassidy *v.* Minister of Health [1]) the rule that, since a hospital board is not in a position, or not competent, to control the treatment or prescribe the operations undertaken by physician or surgeon, it is not to be held legally responsible for malpraxis.

Mr. Macdonald, a bank accountant, had been admitted to Killearn Hospital for a minor operation, successfully carried out, to his foot. He became very ill, suffering abdominal pains and continual sickness, a few days later; he was transferred to the Western Infirmary, where an operation was performed for removal of an intestinal obstruction, and died soon afterwards. His widow contended that the hospital board was vicariously responsible for the negligence of the house-surgeon who, she said, had failed to diagnose her husband's symptoms and to call in a senior doctor to examine his condition. She also maintained that the board was itself at fault in having made no provision at the Killearn Hospital for necessary and urgent operative treatment there, so that the patient had to be transferred to the Western Infirmary for operation though immediate operation was necessary.

Lord Strachan found himself obliged to follow the previous Scottish decisions which make it clear that in Scotland, if the governors of a public hospital engage competent doctors and nurses, they are not responsible for any negligent discharge by the doctors and nurses of their professional duties. He therefore dismissed the claim so far as it concerned the Glasgow Western Hospitals,[2] but allowed the case to proceed against the house-surgeon, who has already outlined his defence. The latter avers that two other surgeons examined the patient four days after the operation to the foot and found no sign of abdominal abnormality; he contends that he exercised reasonable care in his treatment of the deceased.

Not many days ago the House of Lords, in a case about the definition of a "charity," spoke of the "painful dilemma" presented where Scots and English law diverges. On that occasion there was a problem which legislation may be needed to solve. It will be interesting to see whether the liability of hospitals is to be left in so different a position in the two countries, or, if not, how harmony is to be restored.

Appendicitis not Diagnosed

The converse principle in England may be seen in Edler *v.* Greenwich and Deptford Hospital Management Committee and Another,[3] where a father recovered damages against the hospital and the doctor on a verdict of negligence. His child, aged 11, had been ill with abdominal pains and vomiting throughout a Saturday night and on a Sunday morning. His own doctor did not attend surgery on Sunday morning; he therefore took the child to the hospital. There the casualty officer asked where the pain was. The child put her hand to her stomach and moved it to and fro. She winced when the abdomen was touched. The hospital doctor thought there was nothing more seriously wrong than gastric trouble. He sent her home, saying that, if she got worse that day, the father should bring her back to the hospital; if she got worse next day, she should be taken to her panel doctor. She became much worse on the Tuesday and was hurried to hospital, where an operation was performed. There was advanced peritonitis and a ruptured and gangrenous appendix. Death occurred after the operation. Mr. Justice Finnemore a hæmatemesis and bleeding continued from the rectum and vagina

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[1] See *Lancet*, 1951, i, 468.

[2] *Glasgow Herald*, March 6, 1953.

[3] *Times*, March 7, 1953.

On my return at midday, and while preparing for blood transfusion, vitamin K (20 mg) was administered intravenously The response was immediate, and within 2 hours all external evidence of bleeding had disappeared except for small quantities of altered blood in infrequent stools over the next 24 hours Whole blood was withheld Recovery was satisfactory with vitamin K and anti anæmic treatment (vitamins B_{12} and C and iron)

The severity of the hæmorrhage and the delay of 5 days after the administration of the aureomycin seem noteworthy The possibility of hæmorrhage after administration of oral antibiotics, it would appear, should be borne in mind especially with patients whose circumstances predispose to vitamin deficiency The blood-prothrombin time was not estimated in this case owing to lack of facilities

Chibambo,
Elisabethville Belgian Congo

EDWARD McCOLL

RELIGIOUS ILLUSIONS

SIR,—Sir Ernest Kennaway (March 14) would maintain that all doubt is honest doubt If a judge has a doubt as to what his verdict is going to be neither he nor anyone else is concerned as to whether it is an honest doubt it is a judicial doubt If a doctor doubts whether an operation should be advised, no-one questions the honesty of his doubts they are real enough and occasioned by the innumerable factors to which he is trying to give appropriate weight, he has a purely medical doubt If an engineer has some doubt about the supports of his bridge, his doubt is a technical doubt and no-one wonders whether his doubts are honest If there is any doubt about the desirability that this note should be given space in your columns the doubt is an editorial one

Bognor Regis

SIDNEY RUSS

AN UNUSUAL TYPE OF HERNIA

SIR,—In your issue of Feb 21 Mr Howard described an unusual type of hernia Last year I observed a similar case, the only difference being that the hernia was not reducible These hernias are known under the name of hernia of the linea semilunaris Spigelii, and are most common where this line crosses the linea semicircularis Douglasii Margarucci[1] has studied the subject fully

Lokeren Belgium

A VAN DEN BAVIERE

BACT COLI IN THE CAUSATION OF INFANTILE DIARRHŒA

SIR,—Since Bray[2] reported his findings concerning *Bacterium coli* 0 111 B4 as a pathogenic agent in infantile diarrhœa, the relationship between serologically homogeneous strains of *Bact coli* and infantile diarrhœa has attracted much attention in Britain[3-5] and other countries[6,7]

We have attempted to reinvestigate this problem in infants with diarrhœa and in normal infants In three months between June 25 and Sept 20, 1952, 1144 infants were examined, in the following three groups

Group A comprised 968 infants who were brought to one of twelve health centres in Nagoya Of these, 94 61% were under 1 year of age, 52 16% were breast fed 4 85% were fed with cow s milk 23 35% were breast fed with supplementary feeds of cow s milk, and the remainder were in the weaning period Of the whole group 11% had mild diarrhœa, the others were all healthy In this group we detected *Bact coli* 0 55 B5 in 1 infant with mild diarrhœa In all the others bacteriological examination of the fæces was negative no shigellæ or salmonellæ were found

Group B consisted of 20 infants who were at an infants home attached to the medical school Of these, 18 were below 1 year of age, and 2 were below 2 years, all were fed with cow's milk Of this group 10, all below 1 year of age had mild diarrhœa, the other 10 were healthy *Bact coli* 0 55 B5 was isolated from the fæces of 7 infants with mild diarrhœa, in the remainder of the group bacteriological examination was negative

Group C was composed of 149 infants, 142 were hospital outpatients, and 7 were admitted to hospital In this group 50 of the outpatients and 1 inpatient had diarrhœa, and in this 1 case *Bact coli* 0 111 B4 was isolated from the fæces

Thus it appears from these observations that homogeneous strains of *Bact coli* may play an important part in the pathogenesis of infantile diarrhœa in Japan

TOHRU OGAWA
Professor of Microbiology
JIRO OGAWA
Professor of Pædiatrics

Nagoya City University,
Japan

HALLUX VALGUS

SIR,—Surgeon Captain Pollard points out in his letter last week that walking with the toes turned out may be a cause of both hallux valgus and flat-foot The conventions seem to demand this way of walking, which as children we were taught to follow, but a strong case can be made against it and in favour of walking in the natural way with the long axis of the foot fore and aft, as he states, or even by over correction with the feet slightly pigeon-toed

A distinguished anatomist, now retired, well known to surgeons all over the British Commonwealth whom he prepared for the primary fellowship examination, always walks pigeon toed, and he used to explain to his classes that this was out of consideration for the locking mechanism of the knee-joint If the foot is constantly turned outwards, unnecessary strain is thrown on the knee joint and its associated musculature—still another reason against walking with the toes turned out

Should we not cease, then, from developing in children this unphysiological and unnatural "civilised habit" of walking with the toes turned out ?

Surgical Unit
Royal Infirmary
Cardiff

LAMBERT ROGERS

DISCLAIMER

SIR,—My attention has been called to the literature which accompanies a current advertisement of 'Persomnia'

It quotes remarks made by the "Bedford Coroner," on Sept 23, 1952, and the suggestion is made in an accompanying letter from the medical director of Clinical Products Ltd., that he is entitled to use the remarks of the "Bedford Coroner" as testimony of the advantages and safety of the tablets in question

I wish to make it clear that I did not take up office here until Oct 1, 1952 The verdict was not mine, and I cannot associate myself with the opinions expressed

M G L LUCAS
H M Coroner, Borough of Bedford

STANDARDISED SENNA

SIR,—I am prompted by the comments of Dr Phatan and Dr Weeden (March 7) to report briefly on a trial of 'Senokot' in obstetric cases

The preparation was given as the routine aperient to 100 puerperal women, and results were compared with those in a similar number given castor oil and in a control series of patients to whom no aperient was given Compared with castor oil, which is still used as a routine in some obstetric units and is still advocated in some textbooks, senokot proved preferable Fewer patients had colic or discomfort the majority had 1 or 2 satisfactory movements after the standardised senna, whereas in the castor-oil series more than half had 3 or more (sometimes many more) movements Many of the patients given castor oil had relative constipation afterwards, whereas with senokot normal bowel habit was more quickly resumed The patients themselves

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[1] Margarucci O *In scritti di chirurgia erniaria* Padva, 1935, vol 2 p 339
[2] Bray J *J Path Bact* 1945 57 239
[3] Taylor J Powell B W Wright J *Brit med J* 1949 ii 117
[4] Rogers K B Koegler S T *J Hyg Camb* 1951 49, 152
[5] *Lancet* 1952 ii 324
[6] Braun O H *Mschr Kinderheilk* 1951 99 86
[7] Ferguson W W June R C *Amer J Hyg* 1952 55, 155

In England Now

A Running Commentary by Peripatetic Correspondents

"You be one and I'll be all the rest," Alice was driven to say to her sister, who complained that two were not enough to pretend to be Kings and Queens. These young pretenders should have had the chance to visit Burlington House[1] just now, where they would have found their models set out for them—from King Peada, who died in A.D. 656, looking (on a pale electrum sceat from the 7th century) unexpectedly like an American taxi-driver, to our own Royal Family, looking agreeably like themselves. All the early kings and queens are very large or very small, appearing either on coins or on tombs; and they provide a good many surprises. King Offa, who built that dyke to keep out the Welsh, is, a long-necked wide-eyed youth; St. Edward the Confessor wore his hair in two short plaits each terminating in three small knobs in the manner of the arms of Lombardy; King Henry II, full length on his tomb, looks incapable of inspiring murder in any cathedral.

Once the portraits begin, however, the historical pageant comes to life. Here is that Bolingbroke who so painfully destroyed poor Richard II, looking just the character that Shakespeare made him; and here is Prince Hal looking decidedly different. The ill-fated Henry VI has the sensitive kindly face to be expected of a scholar unfitted for his destiny. Crook-back Richard, since Josephine Tey washed off the Tudor mud,[2] has to be examined searchingly to see whether he was, after all, as snowy as she found him: from that secret face it is hard to be sure. Passing from the merchant-like presence of Henry VII we burst suddenly into the cloth-of-gold society of his much-married son, and can once again acknowledge our debt to Holbein. Here are the wives, too—Catherine of Aragon, a natural president for a Women's Institute, Anne Boleyn less beautiful than reported, the charming little Flemish mare, and the obstinate Jane Seymour. Mary Tudor is shown as she was before Philip of Spain and a broken home in childhood turned her into something less attractive; and if our first Elizabeth is done less than justice in the portraits chosen here, the Stuarts are better served, and moving—particularly Henrietta Maria before and after life had done its worst with her. The Hanoverians, too, almost step out of their frames.

Some of this long royal line were caught by their painters in childhood—Edward VI as a rosy long-skirted baby, George III playing tents with four chairs, Queen Victoria, a pretty insipid little girl beside her handsome dominating mamma, and Edward VII, delightful in a sailor-suit.

In the uneasy modern world it is beginning to look as though the best of the better things in life are still here with us at home. No other country has a richer history, or can show more beautiful or better-cherished records.

* * *

During the forty years that I have known King's Cross, I have never associated it with cleanliness. True I have often sensed a whiff of the sea as I boarded the Scarborough Flyer; or I have settled into my sleeper knowing that I shall wake in Glen Falloch as the train approaches Crianlarich. But I have never associated the terminus from which I started with anything faintly beautiful or nostalgic. But now that denial of any æsthetic claims must go, for today I saw King's Cross Station anew beneath a March sun and in a biting wind. The outside has been cleaned. Has this ever happened before? The bricks revealed were in that sunlight an ochre colour, the two great windows might have belonged to the apse of some cathedral buried in the country, and the blue sky made a convincing harmony with the refurbished stone. The petty, ill-adapted structures that surround the underground station lost all their tawdry insignificance. No Turner or Girtin dismissed a foreground as summarily as the surprise and cleanliness of the big station dismissed with an aristocratic air its Edwardian furbelows of cafés and counters. There will be many magnificent sights in London during this Coronation year. Will any give me such a fillip as the rejuvenated façade of King's Cross? It is man's fate (or his blindness) to concentrate on ugly realities, often as dirty as the historical King's Cross. Yet it is not only poets who sometimes see ladders rising from Charing Cross. Busy doctors have their visions too.

* * *

"Look," said the physiotherapist, wielding her inch-tape, "you started off three feet from the lamp, and now you are only twenty-six inches away. Staff are always the same, doctors worst of all." A heated discussion ensued in which I described the difficulties of treating physiotherapists, inventing instances as I went along. Distracted by the argument, we both forgot to watch the clock, and I got a full erythema dose. What I didn't realise until the following morning was that I had turned half-right to observe the effect of my diatribe. Seen from the north-west I was bright red, seen from the north-east my usual pallid self.

As it happens, the single rooms on the female wing are so arranged that as I entered each room the patient saw me off-white; as I left, I was red. Later that morning, Sister told me that roughly half of the patients asked her what they had said that had annoyed me; the other half, what had embarrassed me. These patients can thus be classed as recessive and dominant respectively. Follow-up studies at five-yearly intervals will show how many of the first group develop frank paranoia, and how many of the second delusions of grandeur.

* * *

I grew tired of having my hair cut at the village barber's. The countryman *will* talk disease and he will talk *at* you. When you are shrouded in the chair you are in the witness-box.

"I hear old Tom be rare bad." (My patient.)
"Ar."
"Terrible sick he wor last night."
"Ar." (Pause).
"Spec they'll gie him somethin' for it." (They means me.)
"Ar." (Another pause.)
"Minds me of old Harry. Died last Michaelmas."
"Ar."

The assembled company wait for my evidence, but I am a bad witness. Mute of malice.

Then I made a haircutting pilgrimage to a small town ten miles away, hoping to be unknown. There the shop was on village club lines, with the barber, a fat chubby man, as chairman and master of ceremonies. The club did not like anonymous members, and when my turn came the chairman was out to get me properly enrolled.

"Nice weather now, Sir. Take your holidays soon?"

"Ar." (Revenge was sweet.)

"Take them when you like or when you have to?" (i.e., employer or employee?)

"Ar. Depends on a lot of things." I ask him to pass me the *Farmer and Stockbreeder* and go through it critically. "I see store pigs are fetching a nice price. Mornin' all." I said putting on my hat.

On my next visit I read the *Guardian* and told the chairman a lot he didn't know about the parish church. He craned his neck trying to read my name inside my collar. It was not there.

"Come from near here, Sir?"

"Not so very far. Hereabouts. Morning all."

For a few happy months I kept the club on its toes. Once I took the *Poultry Farmer* with me to read. Another time the *Teachers' World*. I buried my face in the *Law Journal*, and once I spent the time in an abstraction of poetic inspiration, scribbling verses under the chairman's nose. But it was too good to last. Ten miles is not far in the country. Not far enough.

"Hullo doctor," said an acquaintance, poking his head through the door. "Didn't know you came here."

"Ar" breathed the waiting members, relieved and satisfied.

I had had my holiday.

* * *

News from School.—Yesterday we played —— School. They were not allowed to swear and the number of times when they were accidently tripped up to see if they would swear was unbelievable.

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[1] Kings and Queens, A.D. 653–1953. Exhibition in the Diploma Gallery, Royal Academy of Arts, London. Open until June 28.

[2] The Daughter of Time. London, 1951.

by the bureau, but mainly to the immense technical advances in methods of suppressing and removing dust Artificial ventilation and the axial water-feed drill have been particularly successful in this respect

Now that several Rand gold mines are producing uranium concentrates, the effect of uranium dust may be another danger But observations made in three mines in 1947 indicated that there was no trace of radon gas present, and the dust samples taken showed no signs of dangerous radioactivity Further investigations are being made to ensure safe working conditions

Agriculture (Poisonous Substances) Regulations

The purpose of the Agriculture (Poisonous Substances) Regulations, 1953, which come into force on March 31, is to protect employees against poisoning by dinitro compounds and by organic phosphorus compounds used as weed-killers and insecticides The regulations apply to the dinitro compounds, *dinitro-ortho*-cresol (D N O C) and 'Dinoseb,' and to the phosphorus compounds, 'Parathion,' 'Schradan,' 'Dimefox,' 'Mipafox,' and tetra-ethylpyrophosphate (T E P P) The use of these compounds in agriculture and horticulture will be prohibited unless the employees working with them are wearing protective clothing The clothing to be worn varies according to the operation being performed for example, for wet spraying in a greenhouse the regulations require rubber gloves and boots, hood, face-shield, and either an overall or a mackintosh The regulations will also restrict working hours, and, for example, not more than ten hours in any one day or sixty hours in any seven consecutive days may be spent on work with these substances A leaflet summarising the main provisions of the regulations and giving a number of additional precautions is being issued to users of these chemicals

Obituary

GORDON ALEXANDER RYRIE

M A, M B Edin

Dr Gordon Ryrie, who died at Kirkcaldy on March 9 at the age of 53, was superintendent of a leper settlement at Sungei Buloh, Malaya for almost twenty years During the late war he refused to leave his patients, and his health never fully recovered from the rigours of the occupation and his subsequent imprisonment

He was born in Montrose, his father being a missionary in the fishing village of Ferryden, and he went to school at Montrose Academy After serving in the 1914–18 war he entered Edinburgh University, where he graduated first in arts and then in medicine Having qualified in 1926, he entered the Colonial Medical Service in 1928 and soon afterwards he was appointed medical superintendent of the Sungei Buloh Leprosy Settlement Here, by his work and his contacts in many lands, he quickly won the reputation of a sound and careful clinician, and an honest critic not only of others' work but also of his own. His contribution to the literature of leprosy, particularly in the clinical and therapeutic fields, was considerable

When the Japanese entered the war in 1941 Ryrie insisted on remaining at his post, and during the next two years he did all he could to mitigate the suffering caused by the callousness of the occupying forces To his sensitive nature this suffering must have been mental torture, apart from his own personal privations Actively associating himself with the underground movement, he was continually under suspicion and supervision, and in 1943 when he was found to have treated wounded members of the guerilla bands he was moved to the concentration camp at Changi During his imprisonment he was greatly weakened by attacks of malaria and dysentery, and when Singapore was liberated he was officially refused permission to travel But he succeeded in making his way back to his patients at Sungei Buloh, whose appalling plight he afterwards described in the *Leprosy Review* for January, 1947 "When the end came the hospital wards were empty, for no one was left able to care for the sick Like wraiths over the untended paths, the patients came out of their houses with uncertain eyes and wavering gait, to welcome thei liberators"

But in 1945 illness forced Ryrie to return to th country After a long period of treatment he was abl to start work again, and in 1947 he was appointe medical secretary of the British Empire Leprosy Relie Association Despite growing ill health he undertool his duties there with the same characteristic courage, an he continued to show in his writings the independenc of thought which had always gained the respect an admiration of his colleagues

R G C writes "*Gordon Ryrie lived courageousl* and throughout his all too short professional career h displayed tenacity of purpose and determination to wi despite overwhelming difficulties To those who knew the warmth of his nature, his deep sensitiveness fo suffering will remain an inspiration and challenge Hi patients were devoted to him, and will miss an under standing friend, and his colleagues have lost a courageou and undaunted champion"

His wife, who survives him, continued after thei marriage her work as a teacher in a mission school a Sungei Buloh

ALEXANDER JAMES MacDOUGALL OF MacDOUGALL AND DUNOLLIE

C M G, M B Edin, D L, J P

Colonel MacDougall, who retired from the Roya Army Medical Corps in 1922, died at Dunollie Hous Oban, on March 13 at the age of 81 He was 29t hereditary chief of the Clan MacDougall

His father, the 28th chief, was Surgeon-genera H R L MacDougall, and he was born at Poona i India in 1872 Educated at Clifton and Edinburg University, he qualified in medicine in 1894 and wa appointed surgeon lieutenant in 1896 After six years service in India he became adjutant of the Glasgow R A M C Volunteers in 1905, and later had four years in Ceylon In 1914 he went to France with the 5t Division and in 1915 he was given command of th 11th Field Ambulance At the end of that year h mobilised the 35th Casualty Clearing Hospital, whic he commanded in Egypt and Macedonia In 191 he became A D M S 52nd Division in France, and h remained with this division till 1919 when he was appointed C M G After retiring to Dunollie he was made honorary sheriff substitute for Argyllshire, and from 1939 to 1945 he served in the Home Guard In 1901 he had married Colina Edith MacDougall, wh survives him with three daughters

Births, Marriages, and Deaths

BIRTHS

Clark—On March 15, at Kendal, to Jean, wife of Dr A M Clark—a daughter

Mulholland—On Feb 13, at Sydney Australia, to Mary (née Duckett), wife of Dr Gerald Mulholland—a daughter

DEATHS

Mason—On March 12, at 79, Willes Road Leamington Spa Harold Mason, M B Lond, J P, aged 87

Appointments

Brilger Johanna, B A M B Camb asst chest physician (S H M O), Rhymney and Sirhowy Valleys H M C

Craig J A M B, B SC N U I, D P H M O, co Louth

Crowley Daniel, M B N U I D M R T first asst (S H M O) radiotherapy department Royal Free Hospital London

Hughes, M S M R C S registrar in surgery, Rookwood Hospital Cardiff

Milne J C M B Aberd D I H D T M & H asst M O H Portsmouth

Morgan, C Naunton M B Lond F R C S consultant surgeon Royal Masonic Hospital London

O Donnell B A M D N U I D P H M O co Leitrim

Phillips H T, M D Lond D I H D I H D C H chief asst M O Central Health Clinic Bristol by a large amount depending on the severity of the fog but irrespective of the prevailing level of morbidity and mortality.

J. A. SCOTT
Medical Officer of Health,
County of London.

County Hall, S.E.1.

PAID SICK-LEAVE

SIR,—It may not be generally known that the Ancillary Staffs Council for the Whitley Council for the Health Service of Great Britain have fairly recently come to a very important decision concerning entitlement to sick-pay of ancillary staffs. This states quite clearly that, as from Jan. 1, 1953, before becoming entitled to benefit under the scheme an employee shall (*a*) complete six calendar months' continuous service, and (*b*) submit, *if so required* (by the employing authority), to a medical examination by a registered medical practitioner nominated by the employing authority, and be recommended by such medical practitioner for admission to the scheme.

It will be appreciated that if the hospital management committee decides that all "ancillary staffs" appointed after Jan. 1, 1953, must undergo such a medical examination, one important point must be decided—i.e., who is the best medical practitioner to undertake the examination ? Should it be the employee's general practitioner, who knows the employee well, or should it be an independent practitioner who may be a member of the hospital staff ?

There is no doubt that the Ministry of Health, through the Whitley Council, are well aware that the sick-pay scheme is open to abuse, and are trying to overcome the inherent difficulties. The recent circular forwarding the decisions of the Whitley Council also suggests that it may be useful to calculate the approximate average amount disbursed weekly in sick-pay, whether certified or uncertified; and this information will be very revealing.

Pontefract and Castleford Hospital
Management Committee,
Pontefract.

W. BOWRING.

VITAMIN E AND INTERMITTENT CLAUDICATION

SIR,—Three years ago, in a paper[1] from Professor Boyd's department, it was reported that, of 41 patients suffering from intermittent claudication and treated with vitamin E, 34 showed improvement after only three months' treatment, as compared with 5 out of 25 "controls." The vitamin E was given in smaller doses than we have used.[2] In limiting the duration of treatment in our trial to three months we were partly influenced by these claims. Professor Boyd and his colleagues (March 7) now advocate six months' continuous treatment, despite their previous experience.

An increase in exercise tolerance of patients suffering from intermittent claudication is generally accepted as indicating a dilatation of previously existing vessels, or alternatively the development of new collateral channels. If it is accepted that vitamin E acts by either of these methods then vascular changes resulting from its administration should occur independently of any test used to measure progress. If a patient is grade II by Professor Boyd's testing, even though he may be grade III on our test, then he should be expected to respond to treatment with vitamin E, if it is effective.

Moreover, we have analysed the results for the 20 patients in our trial who were less severely affected (grade II). The mean increase in the average number of circuits walked during the treatment period, compared with the pretreatment period, was 1·05 ± 1·38 for 11 patients treated with vitamin E, and 1·84 ± 1·52 for 9 controls. The mean increase in the average number walked during the three months following the end of treatment, compared with the pretreatment period, was 0·66 ± 1·34 for the vitamin-E group and 1·76 ± 1·48 for the controls. Thus, even in this group of less severely affected patients there is no evidence that vitamin E was effective in increasing the exercise tolerance.

We would remind Dr. Shute and Mr. Shute (March 7) that in a therapeutic trial conducted on the "double blind" principle, such as we advocated for vitamin E, effective remedies will still prove effective as compared with an inert substance, even though neither patient nor clinical observer is aware of the substance received by each patient. We have no doubt that both insulin and liver would have proved their value in the treatment of diabetes and pernicious anæmia respectively under these conditions. The fact that vitamin E did not survive this test in the treatment of intermittent claudication is our reason for claiming that it is an ineffective remedy in this condition.

Nor do we doubt that ten observers have claimed it to be an effective treatment; as we pointed out in our paper, many trials of this drug have been reported but unfortunately these have been characterised by the absence of controls, and have not been conducted along the lines which we advocate. Had they been so conducted the controversy mentioned by Professor Boyd and his colleagues need not now exist.

M. HAMILTON
G. M. WILSON
P. ARMITAGE
J. T. BOYD.

London, W.12.

INTUSSUSCEPTION

SIR,—We have read with interest your leading article (Jan. 31) and the critical comments by Mr. Jones and his colleagues (Feb. 21). We have recently completed a review of 106 cases of acute intussusception in childhood admitted under our care during the past 3½ years. In this series there was 1 death.

In our opinion, the operative mortality for reducible intussusceptions should approach zero. Occasional deaths will occur in two types of cases :

1. Where reduction is very difficult and time-consuming and the surgeon has to decide whether to persevere with his efforts or proceed to resection.
2. The moribund case with gangrenous bowel, extreme distension, and pronounced dehydration and electrolyte imbalance which does not respond to intestinal decompression and intravenous infusion therapy carried out over several hours. Here the surgeon has to decide between continuing medical therapy in the hope of making the patient fit for operation, or risking operation in order to remove a length of gangrenous intestine.

In both these types of case applying hydrostatic pressure will only cause delay and do harm, and we can therefore see no point in using this method.

We agree with Mr. Jones and his colleagues that the main reason for the fall in the mortality from intussusception (to 1% in their series) is the better management of preoperative and postoperative fluid and electrolyte deficiencies. We consider that a general fall in the mortality to a level of 1% will only be achieved when children are treated in hospitals specially equipped and staffed for pædiatric surgery. We in Liverpool have not been so fortunate as the Newcastle workers in getting cases early. The average duration of symptoms in our series was 34 hours, and 27·3% of the children were admitted with symptoms of over 48 hours' duration.

We too have found that the symptoms are surprisingly constant. In our series vomiting occurred in 82·1%, pain in 83%, and attacks of pallor in a further 13·2%. Blood was passed in only 67·9% of cases.

As regards surgical technique, we too are of the opinion that a right lower paramedian incision just long enough to admit two fingers is better than an incision in the right iliac fossa, and that it is unnecessary and

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1. Ratcliffe, A. H. *Lancet*, 1949, ii, 1128.
2. Hamilton, M., Wilson, G. M., Armitage, P., Boyd, J. T. *Ibid*, Feb. 21, 1953, p. 367.

Royal College of Surgeons of England

At a meeting of the council on March 12, with Sir Cecil Wakeley, the president, in the chair, Mr R S Corbett (*St Bartholomew's*) and Mr N C Lake (*Charing Cross*) were re elected members of the court of examiners

The Hallett prize was presented to A T Matheson (Cape Town), and the Handcock prize to A H Tooley (King's College Hospital) A diploma of membership was awarded to D B Fox

International Hæmophilia Society

The annual general meeting of this society will be held at 2 P M on Sunday, March 22, at the Seymour Hall, Seymour Place, London, W 1

Register of Orthoptists

The Board of Registration of Medical Auxiliaries have now published the 1952 register of orthoptists Copies may be had from the secretary of the board, B M A House, Tavistock Square, London, W C 1

Chadwick Public Lecture

Prof S E Finer, M A, will deliver a lecture at the Walker Art Gallery, William Brown Street, Liverpool, 3, on Thursday, April 30, at 7 30 P M He will speak on Public Health—a Comparison Between the Age of Chadwick and Our Own

European Symposium on Cortisone

From Aug 31 to Sept 2 a symposium on cortisone and the suprarenal cortex will be held in Milan It is sponsored by the Società Italiana di Reumatologia Further particulars may be had from Prof C B Ballabio, secretary of the congress, Clinica Medica dell'Università di Milano, via F Sforza 35 Milan, Italy

Australasian Research Fellowships

The Life Offices' Association for Australasia has established a fund for the promotion of scientific and medical research in Australia and New Zealand The fund is offering fellowships, ranging from £1250 to 1500 a year, for research into cardiovascular function and disease The fellowships are tenable either in Australia and New Zealand for a year in the first instance, or for three years only one of which will be spent in Australia or New Zealand Applications should reach Dr John Halliday, medical director of the fund, 87, Pitt Street, Sydney, New South Wales, by March 31

Ophthalmological Society of the United Kingdom

The annual congress of this society will be held at 1, Wimpole Street, London, W 1, on Thursday, Friday, and Saturday, April 23, 24, and 25, when Dr A MacRae will deliver a presidential address on Prognosis in Malignant Melanoma of Choroid and Ciliary Body Sir Geoffrey Jefferson, F R S, will deliver the Bowman lecture on the Syndromes of the Cavernous Sinus The programme *also includes a discussion* on the Scope of Antibiotics and Chemotherapeutic Agents in Ophthalmology, which will be opened by Prof Robert Cruickshank, Prof Arnold Sorsby, and Mr Derek Ainslie

Queen Elizabeth College, London

Speaking at a luncheon, held in London on March 11, to commemorate the granting of a royal charter to this college, formerly known as King's College of Household and Social Science, Lord Horder recalled that the college was opened nearly 50 years ago when a home science department was instituted in King's College for Women at Kensington Square He went on to trace its steady growth till in 1928 it became an independent school of the University of London In 1916 the university granted a diploma in household and social science, and in 1920 a degree of B SC in these subjects In 1933 the postgraduate diploma in dietetics was instituted This year the old university degree of B.SC had been replaced by two new degrees—a B SC in household science and a B SC in nutrition To me," he added "no more significant step could have been taken at Queen Elizabeth College than this addition of the subject of nutrition to its curriculum I have quite recently said, in reviewing the developments in medicine during the past 50 years, that I put the science and practice of nutrition in the foremost place I believe it holds within its scope more potential gain to human progress—and I bear in mind moral as well as physical progress—than any other single contribution that the science and art of medicine can make

Chairmanship of Hospital Boards

The Minister of Health has lately made the following new appointments to the chairmanship of regional hospital boards and boards of governors of teaching hospitals

Mr E F COLLINGWOOD, C B E, J P Newcastle Regional Hospital Board, Hon JOHN FREMANTLE, North West Metropolitan Regional Hospital Board, Mr A G LINFIELD, O B E, J P, South West Metropolitan Regional Hospital Board Mr N M AGNEW, Manchester Regional Hospital Board and Board of Governors of the United Manchester Hospitals, Mr EVAN NORTON, Board of Governors of the United Birmingham Hospitals

EMERGENCY BED SERVICE —In the week ended last Monday applications for general acute cases numbered 1336 The proportion admitted was 87 2%

Diary of the Week

MARCH 22 TO 28

Monday, 23rd

MEDICAL SOCIETY OF LONDON, 11 Chandos Street, W 1
8 30 P M Dr T H Hills Mr Murray Falconer Value o
ROYAL is Southwark, S E 1
5 15 P ology of Accommodation

Tuesday, 24th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
8 P M *Section of Medicine* Dr J F Wilkinson Prof Alexander Haddow, Dr J D N Nabarro Chemotherapy of the Reticuloses
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street W C 2
5 30 P M Dr W N Goldsmith Vegetating Dermatoses
WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane W 1
5 30 P M Dr N G Hulbert Neurological demonstration

Wednesday, 25th

ROYAL EYE HOSPITAL CLINICAL SOCIETY
8 P M Mr Falconer Visual Field Changes in Compressions of the Optic Nerve, Chiasm, and Tract
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28 Portland Place W 1
Alexander Treatment of Pulmonary
Adult
Lichenoid Eruptions
INSTITUTE OF UROLOGY St Paul's Hospital Endell Street W C 2
5 P M Mr H G Hanley Disorders of Micturition in Females
EUGENICS SOCIETY
5 30 P M (Burlington House Piccadilly, W 1) Miss Gertrude Willoughby, D UNIV PARIS Population Problems and Family Policy in France
UNIVERSITY OF WALES
8 P M (Reardon Smith lecture theatre, Park Place Cardiff) Sir Cecil Wakeley, P R C S Modern Trends in Treatment of Cancer (William Sheen lecture)

Thursday, 26th

ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P M Dr E R Cullinan East African Interlude
INSTITUT
5 30 P M emiology of Fungus Infections
LONDON SOCIETY
8 30 P W 1) Dr M H Papworth
MIDDLESEX COUNTY MEDICAL SOCIETY
3 P M (Central Middlesex Hospital Park Royal, N W 10) *Clinical Meeting*
4 45 P M Dr F Avery Jones Australian Journey
CAL PATHOLOGISTS
College of the South West, Exeter) Start
general meeting
NORTH WESTERN TUBERCULOSIS SOCIETY
4 30 P M (Manchester Royal Infirmary) Mr J F Dark Mr P Jewsbury Results of Lung Resection in Pulmonary Tuberculosis
LIVERPOOL MEDICAL INSTITUTION, 114 Mount Pleasant Liverpool, 3
8 P M Dr Lennox Johnston Cure of Tobacco smoking

Friday, 27th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray's Inn Road W C 1
3 30 P M Mr Maxwell Ellis Nasal Catarrh
ROYAL SOCIETY OF MEDICINE
5 P M *Section of* n Prematurity
8 15 P M *Section of* Mr J B Blaikley Mr C D Read, vic Exenteration
INSTITUTE OF DERMATOLOGY
5 30 P M Dr L Forman Lichen Planus
BIOCHEMICAL SOCIETY
11 A.M (University College, Gower Street W C 1) Scientific papers
BRITISH PHARMACOLOGICAL SOCIETY
9 30 A M (193 Euston Road N W 1) Start of two day symposium on Anticholinesterases
MEDICAL SOCIETY FOR STUDY OF VENEREAL DISEASES 11 Chandos Street W 1
7 30 P M Dr A H Harkness Non-gonococcal Urethritis

EFFECT OF VITAMIN B_{12} ON ACETYLCHOLINE SHOCK IN MICE

Time of vitamin B_{12} injection	Dose of vitamin B_{12} (µg.)	Dose of acetylcholine (mg. per kg.)	Fate of mice
15 min. before acetylcholine	15 p.	15	Died
„ „ „	30 p.	15	Died
Same time as „	15 p. and v.	15	Survived
„ „ „ „	12 v.	15	Survived
„ „ „ „	6 v.	15	Died
„ „ „ „	15 v.	20	Died

p. = intraperitoneally ; v. = intravenously.

when the dose of acetylcholine was raised to 20 mg. per kg. The results are shown in the accompanying table.

The effect of vitamin B_{12} on the low blood-pressure produced in rabbits by acetylcholine was also observed. Rabbits injected with 5–30 µg. of vitamin B_{12} per kg. intravenously showed no appreciable change in blood-pressure. 5 minutes after the injection of the vitamin, each rabbit received 5 mg. of acetylcholine per kg. The blood-pressure fell as usual, and in this dosage vitamin B_{12} does not seem to modify the action of acetylcholine on the blood-pressure.

Two mixtures—0·5 ml. of 'Fresmin' (a preparation of vitamin B_{12} containing 15 µg. per ml.) with 5 mg. of acetylcholine, and 1·0 ml. of fresmin with 100 mg. of acetylcholine—were left in an incubator for 3 hours at 37°C. Strips of guineapig intestine were placed in Tyrode's solution at 37°C and connected to a Marey drum to record contractions. The mixtures were then added to the Tyrode bath in turn. The strips of intestine showed no appreciable difference in contraction in either of the vitamin B_{12} and acetylcholine mixtures or in control solutions of acetylcholine alone. But the ratios of the concentrations of acetylcholine to vitamin B_{12} in the Tyrode bath were less than those reached in vivo in the mice experiments.

Naranjo[2] reported that vitamin B_{12} could not prevent histamine shock in the guineapig ; but he used doses of vitamin B_{12} as low as 15–30 µg. *per kg.* Our results show that larger doses of vitamin B_{12} can protect mice against histamine and acetylcholine shock.

Department of Bacteriology,
School of Medicine,
Nagoya University.
Department of Pharmacology,
Medical School,
Nagoya City University, Japan.

KAZUO OGASAWARA
SANESHIGE ATA.
SIRO HISADA.

GOUT, LEUKÆMIA, AND POLYCYTHÆMIA

SIR,—The interesting syndrome of gout followed by polycythæmia and leukæmia was described by Dr. Hickling in your issue of Jan. 10. We have lately studied a case with some of the features of this syndrome ; in this case, however, the polycythæmia was apparently induced by the administration of vitamin B_{12} and extract of hog's stomach.

A woman, aged 74, with a four-year history of gout was admitted on account of anæmia : Hb 44% ; red cells 2,120,000 per c.mm., showing anisocytosis and some poikilocytosis ; leucocytes 3100 per c.mm. (neutrophils 55%, lymphocytes 41%, monocytes 4%) ; thrombocytes 122,000 per c.mm. Repeated biopsies of the sternal marrow showed intense marrow hyperplasia, with normoblasts preponderating but a few megaloblasts and 5–7% reticulum cells. There was hypoferræmia and hypoprothrombinæmia ; free HCl was secreted by the stomach after injection of histamine. Serum-uric-acid was constantly high at 16·1–16·4 mg. per 100 ml.

For experimental reasons the patient was given each day by mouth vitamin B_{12} 80 µg. and hog's stomach extract 2 g. This dosage had previously been used successfully in ordinary cases of pernicious anæmia. There ensued a characteristic reticulocyte response and a considerable increase in hæmoglobin level and erythrocytes ; after $2^1/_2$ months the patient had developed polycythæmia, the peak of which was reached 2 weeks after this treatment was discontinued, when the blood-count was as follows : red cells 7,600,000 per c.mm. ; Hb 121% ; leucocytes 26,000 per c.mm. (neutrophils 84%, lymphocytes 14%, eosinophils 2%) ; thrombocytes 316,000 per c.mm. Sternal marrow biopsy now showed intense hyperplasia with a pronounced shift to the left and no megaloblasts suggesting polycythæmia. Moderate splenomegaly had developed.

During the next 3 months no treatment was given ; hæmoglobin and red cells gradually fell to normal values, whereas the leucocytosis persisted. Further treatment for 1 month with vitamin B_{12} and hog's stomach extract was tried ; but although the bone-marrow showed the same picture as when the patient was first seen, it was impossible to reproduce the polycythæmia and even the splenomegaly gradually receded.

We have here a patient with : (1) gout : (2) hyperplasia of the bone-marrow with temporary polycythæmia (and splenomegaly), induced by the administration of vitamin B_{12} and hog's stomach extract ; and (3) polymorph leucocytosis without manifest leukæmia.

The induction of temporary polycythæmia by several different agents—iron, liver extract, X-ray treatment to the enlarged spleen (Hickling), or vitamin B_{12} and hog's stomach extract (our case)—seems to be a specific feature of this syndrome in which gout appears to play a central, though hitherto unexplained, rôle.

Blegdamshospitalet,
Copenhagen.

K. KJERULF-JENSEN
M. SCHWARTZ.

OSTEOPATHY

SIR,—I should like to correct any false impression created by Dr. Stoddard's letter last week. He states that training in manipulation is virtually unobtainable outside reputable schools of osteopathy. In so far as he is referring to England he is mistaken, even if one grants his premise that such osteopathic schools as do exist over here are reputable. This was not the House of Lords' opinion in 1935.

For twenty years before the war Dr. J. B. Mennell taught spinal manipulation to the physiotherapists at St. Thomas's Hospital. For the past ten years I have continued this instruction, with emphasis on the reduction by manipulation of a displaced fragment of annulus at a cervical, thoracic, or lumbar intervertebral joint. Many hundreds of our physiotherapy students have learned these methods, which form part of their routine work. I am in the process of trying to persuade the teachers at other physiotherapy training schools of the efficacy and importance of these measures, with a view to their widespread adoption.

In the end, given success in this endeavour, it should become possible to replace the lay manipulator by the trained ethical physiotherapist. I hope that Dr. Stoddard will support the chartered physiotherapist and myself in this reasonable aim.

London, W.1.

JAMES CYRIAX.

DOSAGE OF ANTIBIOTICS

SIR,—In dermatology it has always been my practice to prescribe small doses of sulphonamides, chiefly because the clinical results have been eminently satisfactory and because the toxic effects of these drugs are serious and seem particularly to paralyse the natural defence mechanisms of the body. The dramatic cessation of the gonococcal urethral discharge—without cure—following massive chemotherapy in the early days was a case in point. It has also seemed important to relate the course of treatment to the natural history of the disease rather than give short, sharp, and heavy courses of the drug. It has not been evident that this practice has favoured drug resistance in the organisms or drug sensitisation in the patients, though many such cases have been seen following the more usual courses of therapy.

It is comforting to have laboratory support for clinical practice, but it is important that we should not seek such security by too slavish a servitude to test-tube directives. As your leading article of March 7 suggests, the important work of Dr. Gould and his colleagues (Feb. 21) must make us hesitate and consider whether we are keeping a proper sense of proportion in these study the whole system and be ready to help a man to readjust whatever part of his balance has gone astray Properly instructed, doctors are likely to be as well *able to do this as any other class of the community* Indeed, I see no way of making them satisfactory doctors simply on the "structure and function," or plumbing basis I would stress again that language which compares the body with a machine fails to pay attention to features of the greatest practical importance in human life—namely, the cerebral and social ones

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[2] Naranjo, P. *Proc. Soc. exp. Biol., N.Y.* 1952, 81, 199.

The machine analogy has a very strong effect on the procedure both of research and practice in medicine Since the emphasis is on a structure, when something "goes wrong" in human life we try, using the analogy of the machine, to "mend" the body Much can be done in this way, but a more powerful approach is possible The simple machine-view assumes *the presence* of the organism, ready manufactured, as a going concern But a living organism is being made all the time Recent work, *especially* since the advent of isotopes, has shown more and more the weakness of the conception of the body or the cell as having a fixed framework What is fixed is the *organisation*, *the way of doing things*, of taking in materials and making them serve to maintain the organism in balance with its surroundings Surely any biological study must be centred on examination of how this balance is maintained In the case of medicine, when the balance is upset we have illness, and the doctor is called in If he is to be effective he must know as much as possible *of the factors that are at work influencing* the balance These include a whole set that at present he is hardly taught to consider at all—namely, those responsible for the daily manufacture of the machine (if we must use that analogy) The hereditary mechanism of the nucleus, controlling all metabolic processes, is *presumably working with the doctor and patient* all the time in re establishing homeostatic balance, though as yet we know little of the details Seldom (if ever) does the doctor diagnose a complaint by saying "I'm afraid there is something wrong with the organisation of your nucleoproteins" If he does refer to a condition as "hereditary" it is only to dismiss it as "incurable" But as we *learn to speak effectively* of the *organisation* of the life of a person, and all that controls it, this aspect will surely give much greater power to medicine than does our present concept of the body as a *ready-made machine*

Animism and Dualism

The human brain functions by making comparisons Every individual, faced with a particular situation, deals with it by comparison with other situations through which he has passed, which have left their imprint on the memory system of the brain *Each new situation is* matched by this memory system, until an adequate response is produced Obviously there is no brief way of describing the method by which this matching and selection are achieved, indeed we do not know how it is done When we make a real effort to find out we shall have made a tremendous step forward

Yet, we can see already that there is something cognate between the aspects of any situation that we select for attention and observation, and the motor response by which we deal with it The *brain* reacts to those features of environmental change that have produced effective motor responses in the past In particular, it selects features that it can call to the attention of others by a name This is the activity which gives language its central importance in determining both the observations a doctor makes and the actions he takes on behalf of his patient, and that is why it is impossible for science or medicine to proceed with the motto *nullius in verba* To a large extent words determine observations We see what we can name and speak about, neglecting the rest Anyone who studies the fashions and conventions of a science at any epoch must be struck by this fact For example, at present many physiologists make observations on nerve impulses and the excitation of one nerve cell by another Few try to study the processes by which organisms *discriminate visual forms* Most physiologists would probably say that the time is not ripe for this, and that we have no language adequate to deal with such complex processes But how are we to make the time ripe? Does language develop automatically? The matter has been so little investigated that it is difficult to be sure, but it seems that a science goes on finding out more and more detail within one language system until new comparisons are introduced—usually as a result of the discovery of a new technique or invention in a different field

All sciences in their early stages made much use of the description of phenomena by comparison with the *behaviour of human beings Among the first memories* to be printed upon our brains are the facial expressions of others We early learn to distinguish and react to their finest shades, and to give names to these The names for facial expressions are therefore close to the centre of our conventional language system Surely this simple *fact explains the influence of animism in all its various* forms In order to describe what any occurrence is like, the simplest method—usually—is to compare it with the actions of a human person From this it is but a short step to suppose that the object in question is tenanted by some entity who is like a person and produces the action in question

In the particular case of human behaviour this leads to the familiar terminology in which we describe each person as if there were within him some other entity, also like a person, and called his "spirit" or "mind" If this is but a special case of a general human method of description, then we may reasonably hope to grow out of this use of animistic language, and begin to describe the individual in words that shall treat him as one entity rather than as two, one within the other

Some Rewarding Analogies

One way of examining the matter is to study the words used by people in writing about the nervous system during the modern period Before the 17th century the language of animism held such firm sway that no other was possible Then gradually other comparisons were introduced, and it is interesting to see how their effect has developed, though even today the old system still holds chief place

Vesalius's account already seeks to get away from the dualist approach

> "But how the brain performs its functions in imagination, in reasoning, in thinking and in memory (or in whatever way, following the dogmas of this or that man, you prefer to classify and name the several actions of the chief soul) I can form no opinion whatever Nor do I think that anything more will be found out by anatomy or by the methods of those theologians who *deny to brute animals all powers of* reasoning " (Foster 1924)

Notice that the conception of the brain acting and performing functions as a machine was already *taken for* granted, indeed Vesalius wished to express himself sceptical about this well established approach

When he comes to the nerves his account of them is even more mechanistic They serve the same functions to the brain as the great artery does to the heart, and the vena cava to the liver, inasmuch as they convey to the instruments to which they ought to be sent the spirits prepared by the brain, and hence may be regarded as the "busy attendants and messengers of the brain" The method used for description is here very clear The vessels and hence the nerves are tubes for transport But there is a very personal account of what circulates—namely, "messengers" Vesalius like everyone else had to call upon comparison with human activities for most of his description of the actions of the nervous system

Boccaccio. The conclusion seems inevitable: that during the span of eleven centuries between Galen and John of Arderne, an ample length of time, the gonococcus changed its habits. Dr. Geiringer will not agree, I expect; but

Scimus, et hanc veniam petimusque damusque vicissim.

Orpington, Kent. H. ST. H. VERTUE.

POLIOMYELITIS

SIR,—I was interested to read Mr. Capener's excellent survey (Feb. 14) of some of the effects of poliomyelitis on structure and function. In connection with his remarks on "muscle spasm," if by this he means pain and inability to obtain full length on stretching, then it is interesting to note that, on this continent, it can be found even in muscles which appear to be completely paralysed both on clinical examination and on electromyography with a needle electrode.

It is a pity for the sake of completeness that Mr. Capener has not included two other members in his suggested team for the investigation of methods of treatment in poliomyelitis. Firstly, the specialist in physical medicine; after all, so much of the treatment of the average case of poliomyelitis is nothing but physical medicine. Secondly, the occupational therapist; there is undoubtedly a place for this therapy in the actual physical treatment, in the prevocational preparation, and in work assessment of some of these patients; we need to determine its exact place, and what better opportunity than in such a team?

Division of Physical and
[illegible]

ANDREW ZINOVIEFF
Director.

ACUTE RESPIRATORY INSUFFICIENCY

SIR,—While agreeing entirely with the remarks by Dr. Donald in his letter of March 7, in which he emphasised the necessity of oxygen therapy in emphysematous patients with an acute respiratory infection, we would suggest another and simpler means of avoiding carbon dioxide narcosis. Barach[1] has described this in detail.

He believes that the mental symptoms in an oxygen tent are due not so much to the height of the arterial carbon dioxide level as to the speed with which it is produced with consequent alteration in the arterial pH. He therefore advises that oxygen be given in *gradually* increasing concentration by nasal catheter, starting with a flow of 4 litres per minute. In this way mental symptoms are avoided or minimised, and when the patient is fully oxygenated a tent can be substituted for the nasal catheter.

There are occasions when we use the oxygen tent rather than the nasal catheter. The severely ill, deeply cyanosed, patient, often mentally dulled or even disorientated, will die if not given oxygen. We put such a patient at once into an oxygen tent and keep him in it, even though mental symptoms or coma supervene. It is too often assumed that this coma will inevitably lead to death. This is certainly not true, and we feel that more lives are saved than lost by using the tent in this way. We have, in such cases, tried the "intermittent" method as used by Donald, but prefer ours.

The severely anoxic emphysematous patient can die suddenly and unexpectedly, even after apparent recovery from an acute respiratory infection. We believe, therefore, that it is wrong to attribute death in the oxygen tent always to carbon dioxide narcosis.

Congestive cardiac failure in the emphysematous patient is usually precipitated by an acute respiratory infection. As the infection improves so the heart-failure improves, and no specific treatment is required for the latter. In other words, the treatment for this acute congestive cardiac failure is antibiotics, antispasmodics, and oxygen.

Since antibiotics are proving successful in combating respiratory infections we may, in the future, see more cases of congestive cardiac failure due to emphysema alone. Such cases, which are not commonly seen at present, respond to digitalis, low sodium diet, mercurial diuretics, and therapy directed specifically against the emphysema. There is, however, as with congestive cardiac failure due to rheumatic heart-disease, a "point of no return" when œdema persists despite therapy.

Chase Farm Hospital,
Enfield, Middlesex.

THOMAS SIMPSON
E. K. WESTLAKE.

COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS

SIR,—The report by Dr. A. F. Foster-Carter and others[1] on collapse therapy in pulmonary tuberculosis, and your comments on prognosis (March 7), are of great interest and undoubtedly very timely.

Progress in chemotherapy and thoracic surgery in recent years has distracted attention from ordinary medical collapse therapy; so some turn to thoracic surgery for early and minimal disease, while others rely entirely on chemotherapy. The results reported by the Brompton team confirm again the value of treatment by artificial pneumothorax, and they are the more significant because they refer to the era before chemotherapy.

It is interesting to note that the presence of adhesions does not prejudice the therapeutic result. The results of artificial pneumothorax in this series compare favourably with those of thoracoplasty. The report, I feel, can be taken as a warning against too much reliance on chemotherapy alone or on early major surgery before sufficient time has been given to medical collapse therapy. An artificial pneumothorax can be satisfactorily maintained without recourse to surgery even where the adhesions cannot be entirely freed, if there is sputum conversion and cavity closure.

The time has come to review the place of artificial pneumothorax aided by modern chemotherapy.

Dagenham Hospital, Essex. M. WEINBERGER.

ORAL ANTIBIOTICS AND SPONTANEOUS HÆMORRHAGE

SIR,—The letters of Dr. Payling Wright[2] and Dr. O'Driscoll (Jan. 10) have already attracted attention to the danger of spontaneous hæmorrhage after oral administration of antibiotics. A case which has been observed here differs somewhat from that described by Dr. O'Driscoll.

A Bantu woman was admitted to hospital with a history of a difficult labour 3 months previously, since when she had had complete urinary incontinence. She appeared to be healthy. The pelvis was of good shape but generally small. The bladder and vagina were in communication as a result of gross destruction of the adjoining walls; the pelvic aspect of the pubic symphysis was completely exposed in the rent.

Prophylactic aureomycin was started (500 mg. 6-hourly) the day after admission. At operation the next day both ureters were implanted into the sigmoid colon. Aureomycin was continued, apart from a short break on the day of operation, until the 5th postoperative day. Progress was satisfactory until the 10th day (by which time the patient was taking normal native food) when bleeding of darkish blood from the rectum was observed. I was absent on a hundred-mile trip, and penicillin and sulphaguanidine treatment was started by the nursing staff. Later in the day bleeding started from the vagina. During the night there were frequent small stools containing blood; the stools later became copious and consisted of almost pure blood-clot. Intravenous saline was commenced. On the morning of the 11th day the patient had which latter accentuate the tendency to the alterations produced by the special causes. These general dispositions include all the conditions which he observes to influence the occurrence of nervous diseases, including weather, time of year, and heredity.

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[1] Barach, A. L. Physiologic Therapy in Respiratory Diseases. Philadelphia and London, 1948.

[1] Foster-Carter, A. F., Myers, M., Goddard, D. L. H., Young, F. H., Benjamin, B. *Brompton Hosp. Rep.* 1952, 21, 1.

[2] Payling Wright, H. *Lancet*, 1952, ii, 1180.

When it comes to treatment he follows the plan laid down by his description. Since the chief predisposition is in too great or little sensitivity of the viscera, "the best remedies are such as not only strengthen the stomach and bowels, but the whole body or alternatively lessen for a time the too great sensibility of the whole system." The list of remedies that will alter the general disposition includes bitters and bark, steel for strengthening, cold baths, air, diet, wine, exercise, friction, and amusement. For weakening the nerves there is opium. The particular causes to be dealt with include wind, phlegm, worms in the stomach or bowels, improper aliments, obstructions of the viscera, and "sudden and violent afflictions of the mind." These last were to be dealt with (*a*) by avoiding them, (*b*) by strengthening the nerves as above, (*c*) by exciting other sensations or passions of a superior force (e.g., firing a gun by the bed of a girl as she recovered from epileptic fits—or whipping for the same).

The influence of the system used for describing the diseases upon the treatment is clear, though not in all cases completely dominant. For example, opium, the only real specific in the list, is an ancient remedy discovered by who knows what accident, aided or not by language. But the emphasis on the symptoms that can be described by simple comparisons and the introduction of a whole system of treatment by "strengthening" and "weakening" shows the limitations imposed by the language used.

New Names and New Notions

Study of the nervous system with the microscope at first made little progress, because there was no model for comparison. By contrast, looking at sperms seventeenth-century spermatists were able to see homunculi because of their interpretation of Aristotle's view that the male contributes form to the embryo. But there was no clear expectation as to what would be seen in a piece of brain. Malpighi reported that he saw little glands, but could make no progress. Indeed it was not until well on in the 19th century that a large development of new ways of speaking about the nervous system took place. This was the result partly of the finding of a terminology by which the microscopical structure could be described. Schwann took a big step in 1839 by showing how the cell theory could be applied to nerve-trunks, though he was wrong in supposing that the cells that carry his name were the units of which a peripheral nerve-fibre is made up. It was only with the development of the neuron theory that a really powerful language for description of the nervous system appeared. Accident played its part, as in the discovery of the Golgi technique for staining nerve-cells, but it could perhaps be shown that language was very important even in the interpretation of these "accidents." The steady application of the method of looking for cells was the clue that led in the end to the neuron theory and to all its modern growths, including the interpretation of the action potential as a surface phenomenon.

Towards the end of the 19th century it began to be possible at last to apply Descartes's analogy of the reflex arc in earnest. Sherrington and others were so successful in this that physiologists have been dazzled by the power of the language ever since. Armed with words like axon, dendrite, synapse, and nerve impulse we can indeed do a great deal better than Descartes with his water pipes and fountaineer. Use of electrical analogies has given us more and more powerful ways of speaking about transmission along nerves and from cell to cell by synaptic excitation.

The Need for New Comparisons

With our current terms we can now say a great deal about the functions of nerve-fibres and nerve cells. But no one can feel that we can say all that we wish about the activities of the brain. We teach every medical student to speak about the nervous system in this language of impulses and reflexes, and the result is that it leaves him puzzled. Essentially the language carries us very little further than that of the 17th century. Although it enables us to speak so fully about the activities of the spinal cord and brain stem it fails for those of the cerebrum. The result in practice is that we have to continue to use person language to speak of the higher activities. Most of us are so used to doing this that we hardly imagine that there is any other method. We speak of a mind interacting in some mysterious way with a body—with all the difficulties that this method entails. It leaves the neurologist not quite sure how far up the brain-stem his domain extends. After many chapters on the spinal cord and cranial nerves his text book gives one or two chapters on psychoneurosis and disorders of speech. All the rest of human nervous activity (much the most important part) is handed over to another set of specialists with another language—or rather with the several other languages of the various schools of psychology.

Is it necessary for this state of affairs to continue indefinitely? Of course, no one reasonable would deny that there are considerable differences between what may be called "reflex" and "mental" phenomena, and a case can be made for treating them separately. But what we have been progressively learning is that they also have much in common and that the boundary between them is not sharp. The trouble is that the words that are adequate for describing the lowest or reflex activities seem at first sight to break down completely in dealing with the highest ones.

In order to talk about the brain we need to use comparison with something very much more complicated than any simple machine. Until recently no useful method has presented itself and we have had to regard brain function as something unique. The new features of the situation that have emerged in recent years are (1) the better understanding of the nature and limitations of all language, and (2) the invention of machines that perform some of the actions hitherto characteristic only of the brain. As has happened so often before in history, man makes a tool to assist his living activities and then learns to describe his own actions by comparison with his tools. The language used by those who make machines to assist with communication and computation has provided further means for talking about the brain.

Anyone who has to work on the brain will agree that the lack of adequate comparisons is a serious barrier to research and therefore also to treatment of nervous diseases. This is certainly true so far as the histology and histopathology of the brain is concerned. The methods of preparation available, such as those of Golgi and Cajal, provide us with magnificent pictures of the cells and their processes, but we do not know how to set about describing what we see. We do not know what differences to look for between the brains of idiots and normal men, still less can we succeed in finding, by histological or other methods, signs of the print of memory which determines so much of behaviour. Yet without means of describing this memory system it is only tantalising to suggest that a unified language is possible.

This is surely just the situation in which we should encourage people to try to make new comparisons in order to suggest hypotheses that can be tested. Only in this way can we concentrate attention on the problem and find a satisfactory language. This indeed is what is happening; much attention is devoted to the found the senna more acceptable. Since this trial some months ago, senokot has been used as a routine in my unit and has proved suitable during pregnancy as well as in the puerperium.

A more detailed trial is being conducted, but I am already satisfied of the value of this preparation in obstetric practice.

I wish to thank Westminster Laboratories Ltd. for supplies of senokot.

Western General Hospital,
Edinburgh.
A. S. DUNCAN.

Public Health

London Fog

London County Council, at a meeting last Tuesday, agreed to ask the Minister of Housing and Local Government, the Minister of Fuel and Power, and the Minister of Health to set up a scientific and medical committee: (1) to investigate the causes and effect on health and property of atmospheric pollution and fog, and suggest remedies; and (2) to inquire into the general problem of emissions of oxides of sulphur from large installations consuming coal, including electricity-generating stations, with special reference to the desirability of installing gas-washing plants to reduce sulphur emissions.

The rivers and drainage committee reported that the meteorological factors that gave rise to the intense fog last December were the almost complete absence of air movement and the low surface temperature which produced an inversion whereby the normal upward air circulation was arrested. The problem of fog, says the committee, is more serious in London than anywhere else in the country. The county, with an area of 120 square miles, contains twenty power-stations, consuming between them 3¼ million tons of coal a year. In 20 square miles of south-west London about 65% of the coal burnt is burnt at the Battersea, Fulham, and Lots Road power-stations. With temperature inversions and little air movement there is a danger of sulphur dioxide becoming concentrated in the neighbourhood of the power-stations; and during the weekend of Dec. 6–8 the concentrations of smoke and sulphur dioxide were the highest in the council's records.

The committee remarks that for the past eight years a working group set up by the Department of Scientific and Industrial Research has been investigating means of removing sulphur compounds from flue gases; but "any reports which they may have made to the Lord President of the Council have not been made public."

Smallpox

A man living in Bacup, Lancashire, and working in a cotton mill in Todmorden, West Riding, has died of variola major. He was admitted to hospital on March 12 with what was thought to be scarlet fever. Petechiæ appeared later, and he died next day. The diagnosis of smallpox was confirmed in the laboratory. Two other men working in the same mill also have smallpox, and the wife of one of them seems to be in the prodromal stage. The man and his wife were admitted to hospital on March 15: the husband fell ill on Feb. 28, and a rash, thought at first to be that of chickenpox, appeared on March 4. The patient who died had been ill with quinsy since Feb. 28, but the probable date of onset of smallpox was March 9. The third man became ill on March 3, and the rash appeared on March 7. The Ministry of Health points out that the outbreak will probably continue because of the time which elapsed before the cause was recognised.

The M.S. *Batory*, sailing from India to Southampton, landed a patient suffering from smallpox at Gibraltar on March 3. When the ship arrived at Southampton on March 6 all her passengers were found to be in good health and, with one exception, they had all been vaccinated recently. Medical officers of health of the areas to which passengers have gone have been notified.

Influenza

The number of deaths from influenza in the 160 great towns of England and Wales continues to decline sharply. In the week ended March 7 there were 193 deaths, compared with 314, 521, and 530 in the three preceding weeks. The total for the London and south-eastern region fell to 47, as against 90 in the week ended Feb. 28, and there were comparable decreases elsewhere. The number of deaths from influenza (including influenzal pneumonia) in the great towns this year is now 2571, compared with 360 at this time last year, and 7150 in 1951.

Sickness Absence in the Metropolitan Police

In 1949 Bransby [1] compared the rates of sickness absence among regular Metropolitan policemen before and after the late war. He found that there was considerably more absence in 1946 and 1947 than there had been in the years 1936–38—a difference which was only partly accounted for by the older average age of the post-war police force. This analysis has now been brought up to date [2]; and the latest figures show that in the period 1949–51 the rate of sickness absence was still considerably above the pre-war figure, though it had decreased slightly since 1946–47. The rate was 4·67% in 1951 and 2·66% in 1938. The number of spells of sickness absence per man was 52% greater in 1949–51 than before the war, and it was among the younger policemen that the increase was greatest. The average length of sick leave increased by 16%, and this was almost entirely the result of longer absences by men over the age of 40. Among the younger men who were ill more than once, the length of time off duty for each illness was remarkably constant, but among the older men the more frequent the illness the shorter the average period of absence. Respiratory illnesses were responsible for more than twice as much absence as any other group of illnesses. The average time off duty for the common cold was just over 10 days, which is a surprisingly long time, as the report remarks; and it was also surprising that there was little variation between the prevalence of colds in summer and in winter. Influenza was nearly as common as colds, and accounted for slightly more absence.

Lead Oxide Dust in Birmingham

A three-inch layer of grey dust covering the roof of a tram depot in Birmingham has been found to contain 1·3% of lead oxide.[3] The lead has presumably been discharged from a factory chimney, and nearby premises are being investigated. The dust also contained zinc and copper oxides, and it is known that these metals came from the chimney of a factory near the depot, but the source of the lead has not yet been identified. Inadequate sorting of metals before melting, and neglect of precautions to prevent the escape of metallic vapours are thought to be likely causes of the exceptionally high lead content of the dust.

Health of Gold-miners

The South African gold-mining industry had been trying for fifty years to prevent silicosis, and it has been partly successful. Figures issued by the government mining engineer show a substantial decline in the prevalence of silicosis. In 1927–28, of every 1000 miners in a dusty occupation 19·41 were shown by strict periodic examinations to have silicosis. By 1947–48 the rate had been reduced to 7·29. Moreover, the comparatively few who do get silicosis today work, on the average, much longer before its onset. In the 1917–20 period, of every 1000 employed in a dusty occupation the 21·95 persons who contracted the disease worked an average of only 9 years and 9 months before it showed itself. In 1947–48 the 7·29 silicotics per 1000 in a dusty occupation worked an average of 21 years and 8 months before getting silicosis. This deferment of onset reflects, firstly, general improvement in working conditions and, secondly, better selection by the Silicosis Medical Bureau of candidates for work. Another encouraging feature is that the type of disability is now less severe than it was when the Silicosis Medical Bureau was founded. As a recent report of the Silicosis Medical Bureau pointed out, the position is being steadily improved: this is partly due to the way in which recruits for the mines are selected

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1. Bransby, E. R. *Mon. Bull. Minist. Hlth Lab. Serv.* 1949, 8, 31.
2. Bransby, E. R., Thomson, D. *Ibid*, 1953, 12, 32.
3. *Birmingham Gazette*, March 5, 1953.

Within the past few years, however, some doubt has been cast on the validity of such statements. Vaughan (1946) said that he had observed kernicterus in two premature babies in circumstances where there was no possibility of rhesus immunisation. Parsons (1947) cited two similar cases, and Aidin, Corner, and Tovey (1950) reported twenty-five cases of kernicterus in premature babies without any pathological or serological evidence of hæmolytic disease.

We report here a further ten cases of kernicterus in which there was no possibility of rhesus incompatibility between mother and fœtus. We also consider the pathogenesis.

Clinical Picture

In the histories and the symptoms and signs of the ten infants there were many similarities. All were premature, the average birth weight being 3 lb. and the average duration of pregnancy 32 weeks. In each case there was some complication either during pregnancy or at the time of birth. In four cases there had been antepartum hæmorrhage due to placenta prævia. Severe pre-eclampsia affected the mothers of another two infants. The cord prolapsed in one case during labour and had to be replaced. Another infant was the second of twins presenting as a breech, and version had to be undertaken before delivery could be effected. A spontaneous but rather precipitate breech delivery occurred in another case. In the tenth case the labour was prolonged for 86 hours.

The infants were feeble at birth, cyanosed, and difficult to resuscitate. All were admitted to the sick-nursery and treated by the usual methods for premature babies. Heat and oxygen were supplied, and each received 'Synkavit' and penicillin. The babies were œdematous, and fluids were therefore restricted initially. After 76 hours three of the babies were able to suck, but by the 4th day they were all considerably weaker and had to be tube-fed. Jaundice appeared on this day, and three babies who had been very weak since birth died. On the 5th day a further three had cyanotic attacks and died. Pyrexia developed in two others at this time, and despite treatment with penicillin and aureomycin they died on the 6th day. One infant died on the 7th day, and the last on the 9th day. It was noteworthy that in all the cases for several hours before death, sometimes 24, there was a bloodstained mucous discharge from the nose.

These ten cases have been chosen from a larger series because they exhibited the typical changes and the time range as we have found them. In addition there was no question of blood incompatibility. All were Coombs-negative, and the blood-groups of mother and child, as regards both ABO and rhesus factor, were similar.

Findings Post Mortem

Necropsies were made within 12 hours of death. The babies had lost weight, probably owing to loss of œdema fluid, and they appeared rather dehydrated. Jaundice was severe, particularly in those infants who had lived longest. No gross abnormality was found in the heart, but the right ventricle tended to be dilated. A patchy hæmorrhagic bronchopneumonia was common to all the cases. There was much bile staining of the liver; in nine cases this was green, but in the infant who lived for 9 days it was bright yellow. No sign of biliary obstruction was found. The spleen was normal. Many uric acid infarcts were seen in the kidneys, but apart from this these organs appeared to be normal. No gross abnormality was found in the intestinal tract. The adrenals were rather small and lipoid was confined to the deeper cortex. The brain in every case was rather "wet," but this was most evident in the infants that died earlier. There was an apparent increase of cerebrospinal fluid. Virchow's encephalitis was present around the posterior and inferior horns of the lateral ventricles in every case, but especially in the babies dying on the 4th day. In these babies there was much injection of the vessels in these areas, and the appearances suggested that petechial hæmorrhages were also present. The striking feature in all the cases, however, was the presence of circumscribed jaundiced areas typical of kernicterus. This staining affected the grey matter of the caudate nucleus, corpus striatum, hippocampus, subthalamic nuclei, nuclei in the floor of the fourth ventricle, inferior olives, and dentate nuclei. The umbilicus showed no gross evidence of infection.

HISTOLOGY OF BRAIN

In the present communication the description will be confined to the changes in the brains. It will suffice to say that no evidence of erythroblastosis was found in the spleen or liver.

The histological changes in the brain varied somewhat from case to case, but there was a rough chronological order, with vascular phenomena predominating in the earlier deaths and degeneration of the neurones in the later deaths. In the babies dying on the 4th and 5th days there was conspicuous congestion of the vessels, and many small perivascular hæmorrhages were present in the white matter. These changes were greatest near the lateral ventricles, especially those parts showing Virchow's encephalitis. In addition some of the smaller vessels were thrombosed. Damage to the nerve cells varied and was not confined to the jaundiced areas. Intracellular œdema was widespread (fig. 1), but more positive signs of degeneration were found in the jaundiced areas. The earliest sign of injury appeared to be a flocculation of the Nissl substance to form larger masses. Further development of the degenerative process took different forms in individual cells. In some, cytoplasmic vacuolation occurred, and this increased in degree while the nucleus, which had moved to an eccentric position, underwent karyolysis. Ultimately only a vacuolated "ghost" cell remained (fig. 2). In other cells there was a loss of Nissl substance until the cytoplasm had a homogeneous hyaline appearance (fig. 3). The nuclei of these cells often showed karyolysis, but some were pyknotic. In the final stage of this change a round and faintly eosinophilic mass was formed.

Only a few tiny perivascular hæmorrhages were seen in the brain of the baby dying on the 7th day. Thrombosis was not found. Œdema was still present, and the perivascular spaces were distended. Many of these spaces contained one or two large cells of macrophage type filled with brownish pigment. Histological evidence of

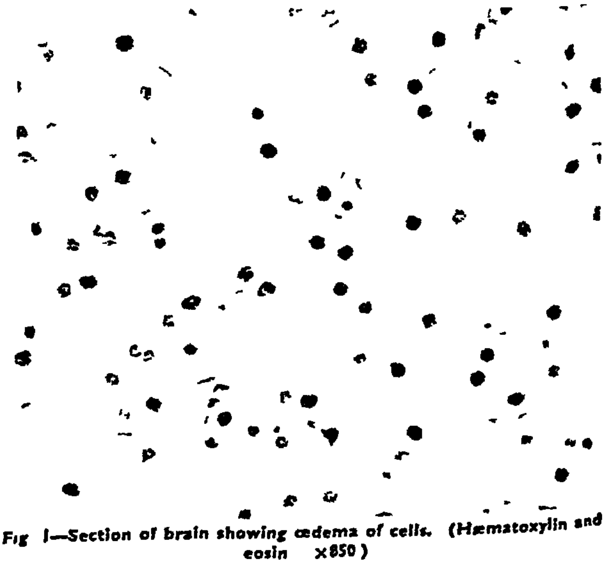

Fig. 1—Section of brain showing œdema of cells. (Hæmatoxylin and eosin ×850.)

Notes and News

A GIFT FROM CANADA

WHEN Sir Stanford Cade and Prof. B. W. Windeyer were visiting Canada last year, they discussed with their Canadian colleagues the use of radioactive isotopes in the treatment of malignant disease. They were particularly interested in Co^{60}, the isotope of cobalt with a mass number of 60, which has proved a valuable source of radiation in this work. The isotope is prepared by exposing natural cobalt to the reactions going on in an atomic pile. Natural cobalt is relatively scarce, but there are considerable deposits in Canada; and Dr. O. H. Warwick, executive director of the National Cancer Institute of Canada, suggested a gift from Canada to help British research in this subject. Mr. J. W. McConnell, of Montreal, who has contributed generously to the cause of medical research in Canada, offered to pay for a complete cobalt-beam unit which would be given to this country.

The news of the gift was announced by the Duke of Gloucester at a meeting of the British Empire Cancer Campaign on March 10.[1] The unit will be ready in June, and it will go first to Copenhagen for the International Congress of Radiology in July. It will then be installed at Mount Vernon Hospital, Northwood. Sir Stanford Cade said that the new unit would be nearly 200 times more powerful than radium units at present in use, and the depth-dose delivered by it would be about the same as that given by 3MeV X rays. A cobalt beam, he said, was more stable, more reliable, and simpler to control than that from a high-voltage X-ray unit. The new unit would be used primarily for the treatment of deep-seated growths that had proved beyond the range of existing radiotherapy apparatus. Professor Windeyer described how a cobalt-beam unit could be rotated around the patient with the beam constantly directed upon the tumour. A higher tumour dose could be achieved with relatively little damage to normal tissues or disturbance to the general health of the patient. The cost of the new unit is £25,000: a radium unit of comparable energy would cost over £1 million.

A cobalt-beam unit has lately been installed at the Montefiore Hospital, New York.[2]

BRITISH RHEUMATIC ASSOCIATION

THE annual report of this association describes some of the developments that have arisen from its work during 1952. Probably of the most immediate importance is the series of medical hostels which will enable industrial workers suffering from rheumatic complaints to receive prompt and expert attention. The first hostel will be at Northwood, in Middlesex, and when funds become available similar hostels will be set up in Scotland, the industrial North, and the Midlands. The building for the hostel at Northwood has been bought, and it is hoped to adapt, equip, and open it within the next year. A housing society, B.R.A. Homes Ltd., has been formed to manage the hostels when they are established. As the report points out, the new hostel service should achieve a considerable saving in national expenditure and man-power.

The association has continued its vigorous efforts on behalf of "the vast army of home-bound rheumatic sufferers" in many other ways. It has emphasised the plight of those whose livelihood is threatened by rheumatism; and the Ministries of Labour and of Health have decided to review the whole position of the handicapped unemployed in this country. The association's parliamentary committee is pressing for a debate. Social surveys and inquiries have been set going to support the campaign with evidence of the economic burden of rheumatism: and a national programme to teach the public about rheumatism has been undertaken with the coöperation of the National Federation of Women's Institutes.

Membership of the association costs 10*s*. a year, including the subscription to the *B.R.A. Review*, the official journal of the association. The address is 5, Tite Street, London, S.W.3.

INSTITUTE OF ALMONERS

STARTING in autumn this year the Ministry of Health is to make a number of grants to help student almoners to attend the special year's course in medical social work organised by the Institute of Almoners. Prof. A. A. Moncrieff, chairman of the council of the Institute, explained at the annual meeting in London on March 13 that last year only 87 students qualified—a much smaller total than previously because the Ministry had withdrawn an earlier subsidy and fees had had to be raised above a level that many students could afford. Even so the rise did not meet the cost; the treasurer reported a deficit of £1823 on training courses. A selection committee is about to sit to make the first grants under the new scheme.

The annual report shows that 95% of all almoners belong to the institute. In 1952 those engaged in hospital work numbered 993, distributed among 481 hospitals, and roughly half were in one of the four Metropolitan regions. At least 54 new posts were created during the year, and at the end there were over 100 unfilled vacancies. Clearly therefore the profession is still expanding, and Government grants to help more people to take special training are likely to be very valuable. The institute is also exploring the possibility of getting university social study departments to offer courses leading to a university qualification specially for medical social casework. If this comes about it is likely to enhance the almoner's status as a social worker by raising the standard of entry.

The annual meeting heard Mr. L. Farrer-Brown speak on Professionalism in the National Health Service. We hope to publish the text of his address.

GEORGE OLIVER: 1841-1915

THE Harveian Librarian of the Royal College of Physicians of London asks us to inquire of readers whether any can tell him of the existence of a portrait or photograph of Dr. George Oliver, founder of the college's Oliver-Sharpey lectures. With E. A. Sharpey Schäfer, Oliver, in 1894, demonstrated for the first time the presence of a pressor substance in the suprarenal gland, and in 1895 he reported on the physiological action of extracts of the pituitary gland. In the thirty-three years ended in 1908 he practised in Harrogate as a physician, but in the winter months he did much of his investigation at University College as well as in his private laboratory. He early developed the bedside testing of urine, and his devices included a hæmocytometer, hæmoglobinometer, arteriometer, and sphygmomanometer. On his death in 1915, we wrote: "He it was among British physicians who chiefly *insisted on the importance of estimating blood-pressure in* diagnosis, and the instruments of precision he introduced for this purpose will live long to keep his memory green."

Before going to Harrogate in 1875 Dr. Oliver practised for a few years at Redcar. His last years were spent at his home in Surrey.

University of Oxford

At a congregation, held on March 10, a resolution was passed by 153 votes to 89 to promote legislation raising the retiring age for holders of university posts from 65 to 67. A second resolution to promote legislation to abolish the power of the visitatorial board to extend the normal retiring age was defeated by 150 votes to 86.

University of Cambridge

On March 7 the following degrees were conferred:

M.D.—H. C. Churchill-Davidson, J. H. Dean, Margaret H. Pond.
M.B., B. Chir.—* J. R. Kirkup.

* By proxy.

University of London

Dr. D. A. McDonald, senior lecturer in physiology at St. Bartholomew's Hospital Medical College, has been appointed to the university readership in physiology at the college.

Mr. J. A. V. Butler, D.SC., physical chemist at the Chester Beatty Research Institute of the Royal Cancer Hospital, has been appointed to the university chair of physical chemistry at the Institute of Cancer Research at the hospital.

University of Edinburgh

At a special graduation ceremony on May 22 the honorary degree of LL.D will be conferred on Surgeon Vice-Admiral Sir Sheldon Dudley, F.R.S. At the summer graduation on July 3 the honorary degree of LL.D will be conferred on Dr. Charles McNeil, professor emeritus of child life and health in the university, and on Dr. S. L. A. Manuwa, director of medical services in Nigeria.

Association of Clinical Biochemists

The inaugural meeting of this association will be held at 2.30 P.M. on Saturday, March 28, at the Postgraduate Medical School of London, Ducane Road, W.12. The secretary of the interim committee is Mr. A. L. Tárnoky, PH.D., Pathological Laboratory, Royal Berkshire Hospital, Reading.

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[1] *Times* and *Manchester Guardian*, March 11, 1953.

[2] *New York Times*, Feb. 9, 1953.

hæmorrhages Thrombosis of small vessels was common around the ventricles but was not confined to these regions Changes in the nerve-cells were not so well developed as in the babies with kernicterus but they followed the same general pattern. Cellular œdema was widespread The earlier phases of cell damage, such as loss of Nissl substance and vacuolation, were very common, but in addition necrosis of cells similar to that seen in kernicterus was seen (fig 4) These changes had the same anatomical distribution as those found in kernicterus Apart from damage to nerve cells, occasional small areas of necrosis were found in the white matter, mostly in the corona radiata

Discussion

Our findings are in agreement with those of Aidin et al (1950) kernicterus can occur in the absence of rhesus incompatibility In our series, in view of the serological findings, there seems to be no possibility of a blood-group dyscrasia Occult erythroblastosis can be ruled out on the same basis and also because of certain differences which are evident when these infants are compared with others dying of kernicterus due to erythroblastosis Children with kernicterus due to erythroblastosis are usually mature (Zimmerman and Yannet 1933, Claireaux 1950) Jaundice is an early feature in erythroblastosis, whereas in our series it was delayed till the 4th day Death usually takes place within the first 48 hours in erythroblastosis, whereas in the premature babies with kernicterus the earliest death recorded was on the 4th day and in one case death was delayed until the 9th day

Despite these clinical differences, however, the microscopical changes were almost identical in both groups There is less vascular disturbance in the erythroblastotic type, but the features reported by various workers (Zimmerman and Yannet 1933, Dereymaeker 1949, Putnam and Alexander 1937, Wolff 1937) were the same as those found in our series of premature infants This immediately brings us to consider the pathogenesis of kernicterus in these two groups and whether there is any possible connection between them

Our study of the brains from non-jaundiced premature infants indicates that similar lesions can occur in the absence of liver dysfunction, and that the pigment is merely deposited in areas already damaged As indicated above, the same appears to be true of the erythroblastotic infant (Cappell 1947) It is interesting also to note that, although there have been many instances of death in adults following a rhesus incompatible transfusion, there has never been any report of kernicterus in these circumstances

Since it seems that hepatic damage can be ruled out as a cause of the brain lesions, it is necessary to consider the factors common to both groups of premature infants The only significant feature common to all of these infants was difficulty in resuscitation at the time of birth This would inevitably lead to anoxia Many workers have claimed that brain lesions are produced by anoxia at birth (Schreiber 1938, Stewart 1942, Darke 1944, Stevenson and Stuart 1950), but no direct proof can be obtained from a study of pathological material Of more direct significance probably are the studies made of changes in the central nervous system in known states of anoxia Rotter (1929) described brain lesions in cases of respiratory failure due to poisoning by morphine, by carbon monoxide, and by potassium cyanide Lesions have also been found in diabetic coma (Riggs and Dyer 1935) and in asphyxia due to nitrous oxide anæsthesia (Courville 1936) The pathological changes described in these conditions are very similar to those found in kernicterus, and the distribution of the lesions is identical An experimental approach to fœtal asphyxia has been made by Windle (1944), Windle and Becker (1942 1943), and Windle et al (1944), who produced temporary asphyxia of animal fœtuses in utero by interfering with the placental circulation, and demonstrated both functional and structural changes in the central nervous system after birth The focal distribution of asphyxial lesions has been studied by Spielmeyer (1925, 1929), who states that the vulnerability of certain areas of the brain is related to the vascular supply, and according to Ushimura (1927) these vulnerable areas have fewer blood-vessels than do other regions

From a consideration of the changes described and the findings in comparable conditions reported by other workers there appear to be reasonable grounds for assuming that the main factor in the production of the lesions in our cases of kernicterus in premature infants is anoxia There is no direct evidence which will allow us to make the same assumption regarding kernicterus of erythroblastotic origin Nevertheless, in view of the similarity of histological changes and anatomical distribution of lesions, and the absence of any correlation between the occurrence of brain lesions and the titre of antibody or degree of erythroblastosis, it seems probable that anoxia is an important factor Cappell (1948) states that he is more impressed by the difficulty in establishing respiration than by either the hæmoglobin level or the antibody titre in cases subsequently found to have kernicterus

Summary

Ten cases of kernicterus in premature infants are described No evidence of blood-group incompatibility between child and mother was found

Jaundice appeared on the 4th day in these children, and the time of death varied from the 4th to the 9th day of neonatal life

The brain lesions found had the same anatomical distribution and histological appearance as those found in kernicterus due to erythroblastosis

Similar lesions have been found in premature infants dying during the first 3 days of neonatal life before jaundice appeared, indicating that pigmentation of the lesions is a secondary feature

From a comparison with lesions found in known states of asphyxia we are led to the conclusion that damage to the brain occurs at the time of birth and is due to anoxia

The lesions of erythroblastosis are probably of similar origin

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THE INFLUENCE OF LANGUAGE ON MEDICINE *

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IT may seem strange to introduce a course on the scientific basis of medicine with a discussion of the influence of language. Indeed it might be thought to be treachery for a scientist to discuss these subjects at all; the motto of the Royal Society is *nullius in verba.* Is it possible, as the motto seems to suggest, to escape from the pervasive effect of language on our observations and instruments, our diagnosis and prescription?

In the study of the actions of the nervous system the language currently used certainly presents severe difficulties to the student, research-worker, and practising doctor. It leads to the absurd situation that those who advise us about the disorders of the nervous system are divided into several camps, which have separate languages and are often antagonistic to each other.

Since the nervous system occupies a central part in our life this weakness in our language for dealing with it is reflected throughout medical science. It is largely because we find it so hard to say what we are, whether mind or body, that we have no central approach to medicine. It is often lamented that our students are taught a mass of detail but are given no general framework in which the facts can be set. I propose to try to show how this framework can be provided if we approach the problem directly and simply, as biologists should.

We all have the aim of describing man, and assisting men to live their lives. Specialists may feel anxious to hurry on from such apparently familiar ground to whatever particular subject they regard as more exciting. But let us pause to consider the implications of the fact that medicine is a special aspect of man as a social animal.

Good practitioners of an art often tell us that any study of method is unnecessary and even harmful; and those who teach, or have taught, well, often say that there is no profit in studying how to teach. This is especially true in medicine, where much teaching is practical. That good teachers do not like discussing how to teach is surely a sign that they have appreciated the essence of the use of language—namely, that being conventional it must be used uniformly throughout the group. What the student has to learn is the current methods of practising his art. But by a curious tradition, we take pains to disguise from him this central fact of social activity: we tell him instead that what he is studying are the "facts"—say of anatomy—without pointing out that all we can teach him is the current way of describing the phenomena. When we recognise that the central "fact," or item of knowledge, is that human beings communicate, a surprising clarification sets in.

In the 17th century there was a revolution in practice, springing from the recognition that words are but counters, as Hobbes put it. *Nullius in verba:* the scientist was determined not to care for words for their own sake, but to recognise that they were but an instrument, comparable to the other instruments he used. Perhaps this lesson was never fully learnt, or has been forgotten; so that a new absolutism has come among us, where the "facts" of science are as tyrannical as were the dogmas of religion. Particularly there are signs of this in medicine, where the strict discipline of method, necessary for the protection of the patient, is all too apt to degenerate into dogma. The corrective—which frees the scientist or the physician, and yet leaves him able to use his tools with confidence—is to understand the nature of the tools, to learn the significance and dangers of language. If we neglect this necessary task, we fall into the dangers awaiting those who use tools they do not understand. Surely this is the answer to the common complaint that we are narrow specialists, and the more serious one that we have no general system within which to place the separate pieces of knowledge we acquire about man.

The Man and the Machine

The neurologist has a special reason for studying language. Words used for description condition to a remarkable extent the amount of attention directed to objects in the world around us, and also condition the actions we perform in response to our environment. Further understanding of those operations of the brain that are involved in speaking would give us clues as to how that organ performs its remarkable computations. Some day we may, I hope, be able to understand the pattern of activities in the brain in a way that will show how all the seemingly disconnected actions of a man are knit together into one pattern. The fact that so much of what passes through our brains is symbolised in words may give us a powerful hint as to *what* it is that is passing through them. For this reason it may prove to be easier to study the brains of men than those of other animals. There is perhaps a clue in the fact that languages as different as Icelandic and Hebrew share many sounds that can be related to gestures. Jóhannesson (1949) has developed the thesis of Paget (1930) that speech is "gesturing with the tongue." Further analysis on these lines might help in the search for unit processes of the cerebral speech mechanism, and hence of cortical action in general.

The influence of language appears as soon as we begin to try to define medicine, or the sciences of anatomy and physiology which are its foundations. A biologist examining our society might say that medicine is an activity by which individuals help each other to maintain homeostasis or the balance of life. Since man's special homeostatic machinery is mainly social, medicine may often be called upon to assist in correcting some social incapacity. All too often the doctor, not having been trained to recognise this characteristic of his charges, limits his activities to correcting what we may call the lower homeostatic machinery. Is this a result of the deep-seated linguistic convention that uses the analogy of a machine, and starts by introducing to students a "body" (in anatomy) with "functions" (in physiology)? We are so used to talking like this that many people are unable to see that it is but a verbal device, a first attempt to describe a man by means of a very crude comparison.

It might be held that a doctor is justified in restricting himself to the "machinery" of the body, and has no responsibilities for the social lives of his patients. Clearly he cannot advise on all aspects of man's homeostasis; he is no expert, for instance, on coal-mining or cooking. Why, then, should he deal with social relations? At this point a biologist might notice another aspect of doctors in our civilisation—that they are experts. They are called upon to give precise advice in relatively limited and defined circumstances. The doctor is called in when needed; although he may regulate our lives for long periods we do not ask him to devise a system for the whole conduct of life. In other communities, however, the medicine-man has much wider functions. The question of where the doctor's functions should best end is debatable and difficult. If he is an expert, what is he to be expert at? Is he just to attend to the plumbing of the body, or is he to be the expert of experts, who attends to the whole man? You cannot have it both ways. If you are to be the chief experts you must

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* Based on a lecture delivered to the British Postgraduate Medical Federation on Oct. 7, 1952, to introduce a course on the Scientific Basis of Medicine.

TABLE I—HÆMATOLOGICAL FINDINGS BEFORE AND AFTER LIGATION OF SPLENIC ARTERY

Case no	Time	Red cells (million per c mm)	Hæmo globin (g per 100 ml)	White cells					Platelets (thousand per c.mm)	Sternal marrow
				Total (thousand per c mm)	Differential count (%)					
					Poly morphs	Eosino-phils	Lympho cytes	Mono cytes		
1	Before operation	2 7	7 1	2 7	75		24	1	115	Marrow hypercellular, hyperplasia of erythroid and myeloid elements normoblastic erythropoiesis increased megakaryocytes
	1 Month after operation	3 5	8 6	6·8	60	14	26		77	
	2 Months " "	3 7	9 5	3 2	50	1	47	2	91	
	6 " " "	3 3	9 6	2 1	55	1	43	1	95	
	9 " " "	3 2	9 1	2 5	42	2	53	3	119	
2	Before operation	3 1	8 0	2 8	68		30	2	124	
	1 Month after operation	3 6	9 8	7 2	60	9	31		151	
	2 Months " "	3 5	9 6	4 0	Not done				115	
3	Before operation	3 6	9 4	2 7	42	2	54	2	193	
	1 Month after operation	4 7	11 4	2 1	40	5	52	3	125	
	3 Months " "	4 4	12 2	3 2	39	2	55	4	110	
	4 " " "	4 7	12 8	2 2	Not done				75	
4	Before operation	4 4	11 5	3 1	52	5	43	5	92	
	1 Month after operation	4 2	12 1	7 5	60	19	20	1	117	
	2 Months " "	4 5	12 5	2 7	45	3	51	1	96	
5	Before operation	3 5	9 8	1 9	72	2	26		70	
	1 Month after operation	3 7	10 0	2 2	64	5	31		85	

operation free fluid was detected in the abdomen, but this rapidly disappeared with salt restriction alone The general condition was good The liver was not felt, but the spleen was palpable 4 cm below the costal margin Large lumbar and abdominal collateral veins were present

Case 5 —A Chinese male house servant, aged 35, had an attack of severe melæna and a moderately large hæmatemesis in the 2 months before operation Variable ascites had been present for 6 months but after the hæmatemesis it had become tense Restriction of salt intake to 1 g daily and diuretics produced a reduction in the quantity of free fluid There was considerable wasting The liver was not felt, but the spleen was palpable 8 cm below the costal margin

The artery was approached through the lesser sac via an incision in the gastrocolic omentum, isolated at the upper border of the pancreas, tied, and divided

RESULTS

After operation there was a rapid reduction in size of the spleen by 3–6 cm, but in all the cases the spleen remained palpable

Case 5 did not attend for examination after discharge 6 weeks after the operation and could not be traced Cases 2 and 3 had massive repeated hæmatemeses 9 and 18 weeks respectively after operation and died of them Case 4 had a moderate hæmatemesis 10 weeks after operation and a further attack 1 week later, he recovered but refused further treatment and returned to his village in China Case 1 remained well for 12 months, when he had melæna for 3 days, followed by a severe hæmatemesis This patient accepted further treatment and is the same person as case 12 (see below)

During the follow-up no change was seen in the radiological appearance of the œsophageal varices When present the visible collateral veins persisted unchanged

Cases 1, 2, and 5 had ascites before operation In cases 1 and 5 this could be controlled by restriction of salt intake to 1 g daily and by diuretics, but in case 2 paracentesis had been required in addition to these measures in the 2 months before operation In case 1, after operation free fluid persisted in the abdomen, but increase could be prevented by restriction of daily salt intake to 2 g After 2 months free fluid could no longer be shown in the abdomen, and return to a full salt intake did not provoke recurrence The patient remained free from ascites until the recurrence of hæmorrhage 12 months after operation In cases 2 and 5 there was reaccumulation of fluid after operation, and restriction of daily salt intake to 1 g and diuretics continued to be required

The effect of ligation of the splenic artery on the hæmatological findings is set out in table I, from which it will be seen that, before operation, all the cases showed thrombocytopenia and leucopenia, and 4 of them (cases 1, 2, 3, and 5) a significant degree of anæmia After the operation there was no significant change in the platelet-count, the leucocytes were increased in cases 1, 2, and 4, but this increase was transient and within 2 months the white cell count returned to the preoperative level, cases 1, 2, and 3 showed an increase in the red cell count but in case 5 it was unaffected In cases 1 and 2, within 1 month, the red-cell counts rose from 2,700,000 and 3,100,000 per c mm to about 3,500,000 per c mm respectively, and then rose no further In the same period in case 3 the red-cell count rose from 3,600,000 to 4 700,000 per c mm and was maintained there for a further 3 months

DISCUSSION

Watson (1935) tied the splenic artery in a patient with severe ascites and repeated hæmatemeses In a follow-up of more than 3 years there was no recurrence of the hæmatemesis Berg and Rosenthal (1942) did the operation on 3 patients with cirrhosis and a history of hæmatemesis, 2 of the patients died within a year, 1 of them after a splenectomy done 10 months after the ligation, and the 3rd patient died 3 years later from a massive hæmatemesis Everson and Cole (1948) reported 3 cases in which ligature of the splenic artery was combined with omentopexy, 1 patient only had a history of hæmatemesis 4 years before, and this patient died of a massive hæmatemesis 3 months after operation Of the 5 patients reported by Blain and Blain (1950) 3 had cirrhosis and only 1 a history of hæmatemesis, this last patient was well 10 months after the operation According to Rosemond (1951) Sweet followed up, for 11 years and 2 years, 2 cases of cirrhosis in which the splenic artery had been tied, and there had been no bleeding in these periods It is not stated whether there had been preoperative hæmorrhage

So far as the prevention of hæmorrhage is concerned our experience has not been happy Of our 5 patients the 4 who could be followed up had recurrence of the bleeding, which proved fatal in 2 The recurrence took place 9, 10, and 18 weeks and 12 months after the operation In none of the cases were œsophageal varices or visible collateral veins altered by the operation This is in keeping with the finding of Julian and Dye (1951), who found no immediate drop in portal venous pressure after the ligation of the splenic artery in 8 patients with portal hypertension Sweet, according to Rosemond (1951), considered ligation of the splenic artery as possibly a complete preventive of further hæmorrhage from œsophageal varices The operation has had no such effect in the present series

In the case reported by Watson (1935) ascites persisted after operation but paracentesis was required less

Descartes, writing about the transport along the nerves, dispensed with "person language" and used instead the analogy of hydrodynamics:

> "You may have seen in the grottos and fountains which are in our royal gardens that the simple force with which the water moves is sufficient to put into motion various machines and even to set various instruments playing or to make them pronounce words . . . . External objects, which by their mere presence act upon the organs of sense of the machine may be compared to strangers, who entering into one of the grottos tread on certain tiles—which are so disposed that if they approach a bathing Diana, they cause her to hide in the rose bushes, and if they then try to follow her. they cause a Neptune to come forward to meet them, threatening them with his trident."

But simple comparisons like this do not provide satisfactory means for describing all human behaviour. For the more complicated parts Descartes, like everyone else, had to use person language—the rational soul being compared to the fountaineer of the system, who takes his place in the reservoir, the pineal gland.

Throughout the 17th century a wide variety of new comparisons was made in the attempt to speak more clearly about the nervous system and its activities. Thomas Willis (1684) from his contacts with the physicists of the Royal Society, divided the corporeal soul into

> "a part which glides into the blood after the fashion of a lighted flame, while the other half seems diffused through the animal fluid after the manner of light, like the rays emanating from that flame, rays which, taken up by the brain and nerves as by dioptic glasses and manifoldly reflected or refracted form various figures according to the workings of the animal faculties."

This particular analogy has often been ridiculed, but it at least *tries* to cover the more complex activities of the brain—which is more than can be said even of some very modern physiological treatments of the subject. Willis was typically of the 17th century in that he was prepared to attempt a variety of new analogies.

> He elsewhere describes "the ducts of the nervous structures like cords lightly strung and so actuated by a certain continuity of the soul that if either extremity be struck the blow is forthwith felt throughout the whole." Again, "the same spirits rush at once from one goal to another as in a race game or a circus, and then rush back again." Or "its particles, that is to say the spirits, are arranged touching each other, drawn up as it were in line, so these in military fashion, perform their functions [and thus] obey the commands of the brain."

Borelli tried another analogy:

> "The nerve fibres are . . . filled with a certain spongy material like elder pith . . . and may indeed be saturated to turgescence, as we see sponges are saturated by water in contact with them." Then "the acts of the command of the will . . . by concussing the whole length of the nerve can squeeze out and discharge from their extreme orifices some spiritous droplets into the appropriate muscle."

It is interesting that such analogies do not seem today to be so useless as they may have looked twenty years ago. Of course they ignore the electrical activities of nerve, which could not then be known, but they bring to our attention other aspects, which electrical analogies at present neglect. Every part of a nerve-fibre depends on its cell body, and certainly some entity passes down the fibre to maintain its trophic integrity. Weiss (1944) and others have shown that there is an actual transport of material along the nerve-fibre and that this may become dammed up behind a constriction. I have suggested (1945) that the breaking up of a nerve-fibre during degeneration is comparable to the segmentation of a column of liquid under surface tension (note once again the use of analogy). It may be that the normal cylindrical shape of the fibre is maintained by a turgor pressure within. Of course, the axoplasm is not exactly comparable to pure water, it is not a "true" liquid. Some people are very ready to condemn analogies because they are not complete or exact. We should not expect them to be. A new comparison is useful if it suggests new observation and measurement, and enables us to talk about the subject more effectively.

What travels along the nerve-fibre may well partake also of the nature of a change in molecular orientation; each section influences the next rather in the manner that Willis hinted with his analogy of the soldiers. Professor Causey (1952) has recently shown that the degeneration of a nerve-fibre spreads steadily away from a cut surface towards the periphery. To use person language, the command from headquarters in the cell has been cut off and the troops fall into disorder. Even the transmission of information along nerve-fibres may partake more of the "transport of spiritous droplets" than a purely electrical view of it suggests. It has been shown that excitatory material is passed along certain axons of insects and crustaceans and in the supra-optic-hypophyseal tract to the posterior lobe of the pituitary gland. Of course there is also considerable evidence of secretion at nerve-endings, histologically as well as physiologically detectable. Surely we see here the advantage of the use of several analogies as methods of comparison. The phenomena in nerve that resemble those commonly called electrical are so conspicuous that they have perhaps hypnotised us and caused us to neglect other aspects.

Certainly the analogies used in speaking about the nervous system are still numerous and varied. Even the chemical and electrical information that we acquire is based upon analogy. What we need is more general language by which to put all these descriptions into their place as part of a system for talking about the whole human being. I believe that it can be done, and indeed that unless we do it soon our age may well come to be recognised as one which is concerned only with lesser problems. Perhaps this is an uncomfortable and stimulating thought.

The analogies of Descartes, Willis, and Borelli did not immediately lead to any great developments in method for management of diseases of the nervous system. Throughout the 18th century the methods of description, diagnosis, and treatment made use of a combination of the old "person language" with new and more "objective" methods of description. Thus Robert Whytt in his treatise on *The Nature, Causes and Cure of Nervous Disorders* (1768) gives descriptions of symptoms which are mainly visceral. They begin with wind in the stomach and intestines, sudden flushings, palpitations, giddiness, and so on. He is able to describe only those things that have simple physical analogues ("wind," "flushings of heat"). Then he tries to refer these to equally simple changes in nerves whose "coats may be obstructed or inflamed, compressed by hard swellings or irritated by acrid humours." In order to describe the actions of nerves, however, he uses a different idiom:

> "We know certainly that the nerves are endued with feeling, and that there is a general sympathy which prevails through the whole system, so there is a particular and very remarkable consent between various parts of the body."

Here he is comparing parts of the body with actions of the human whole—they "feel," have "sympathy," and "consent." When the nervous canals become obstructed "the sentient power of the nerves may be either weakened or quite destroyed." Here he uses the two analogies combined. Again if the feeling of the nerve is too acute then there will be "no firm or long-continued state of health, but almost constant succession of greater or less complaints." On the other hand, when nerves are deprived of a proper degree of sensibility, actions will be imperfect: "when sensibility of the retina is impaired objects are seen less distinctly."

He thus divides the influences acting on the nervous system into special causes and general dispositions, Death is due to a massive necrosis of the liver the cause of which is uncertain Ellis and Dragstedt (1930) attributed the necrosis in the dog to extensive infection by a spore forming anaerobic bacillus, which Wolbach and Saiki (1909) had demonstrated in the livers of normal dogs Andrews and Hrdina (1931) and Boyce and McFetridge (1937), however, reported that autoclaved dog liver would produce death when introduced into the peritoneal cavity They attributed the death of the animals to absorption of autolytic products, inferring that death following ligation of the hepatic artery was also due to absorption of products of autolysis in the necrosed liver

Markowitz et al (1949) showed that dogs survive ligation of the hepatic artery distal to the origin of the right gastric artery if given massive doses of penicillin postoperatively Davis et al. (1949) and Grant et al (1950) confirmed these findings, and the latter showed that parenteral aureomycin was equally effective Chau et al (1951) found that penicillin or aureomycin afforded complete protection to dogs which had the arterial supply to the liver interrupted

Successful ligation of the hepatic artery in man had been reported, at the time of our observations, on three occasions All the ligations were done for aneurysm of the hepatic artery Kehr (1903) ligated the artery distal to the point of origin of the gastroduodenal artery, and Sudeck in 1915, according to Kading (1919), and Colmers (1921) ligated it proximal to all its branches

It seemed to us that under cover of antibiotics the hepatic artery could be safely tied close to its origin from the cœliac axis As the result of experience gained later, the hepatic artery was tied distal to the point of origin of the gastroduodenal artery Such an operation would be relatively simple and would lead to a significant reduction of the portal pressure Further, it appeared from perfusion experiments that the rate of flow of the portal blood through the liver would be increased—a point of major importance, since Mann et al. (1931) have shown that portal blood is necessary for regeneration of the liver On the other hand, Karn and Vars (1951) have shown that regeneration of the liver in rats is not impaired by ligation of the hepatic artery

Simultaneous ligation of the splenic artery was considered desirable First, there was the theoretical consideration of maintaining the anastomotic channels while denying to the portal system blood previously distributed to the spleen Secondly, although our previous experience with ligation of the splenic artery alone rendered it very unlikely, there was the possibility that simultaneous ligation of the hepatic and splenic arteries might correct the hypersplenism and prove a simple substitute for splenectomy

We were unaware of the extensive observations of Berman et al (1950) on ligation of the hepatic artery in dogs (summarised by Berman et al 1951a).

These workers confirmed that the dogs survived the operation when given penicillin and streptomycin. They showed that ligation of the hepatic artery reduced the portal pressure by 10–20 mm H_2O and that subsequent ligation of the splenic artery reduced it further by 40–50 mm Ligation of the splenic artery alone reduced the portal pressure by 5–10 mm H_2O, and subsequent ligation of the hepatic artery reduced it further by 40–60 mm They demonstrated radiographically the development of an extensive collateral circulation through the left gastric artery anastomosing with the right gastric artery and thence into the hepatic artery In some cases there was also a blood supply through the accessory hepatic artery

From their experimental findings, coupled with a review of published perfusion experiments, Berman et al concluded that ligation of the hepatic artery in cirrhosis of the liver parallels ligation of the arterial component of a cavernous hæmangioma The operation would force arterial collaterals to form which would allow a capillary bed to arise within the liver, thereby permitting nourishment of the starved liver cells They argued that a simultaneous reduction in portal flow was desirable so that the lateral pressure within the portal vein might not be great enough to occlude the new hepatic artery capillaries Reasoning thus they tied the splenic artery simultaneously They reported (1951a) that they had performed the operation of simultaneous ligation of the hepatic and splenic arteries on 10 occasions, and they described 1 case in detail (1951b)

MATERIAL AND METHODS

All our patients were Chinese adult males with diffuse hepatic fibrosis of cryptogenic origin, the diagnosis being established by biopsy As the operation was still untried, only cases with advanced cirrhosis and a very poor prognosis were considered All had a history of two or more hæmorrhages from œsophageal varices, which were demonstrated radiographically in each case All had tense ascites

Case 6 —A Chinese male shop-assistant, aged 27, had seven massive hæmorrhages in the 12 months before operation

TABLE II—HÆMATOLOGICAL FINDINGS BEFORE AND AFTER LIGATION OF HEPATIC ARTERY AND LIGATION OF SPLENIC ARTERY OR SPLENECTOMY

Case no	Time	Red cells (million per c mm)	Hæmoglobin (g per 100 ml)	White cells: Total (thousand per c mm)	White cells: Differential count (%): Polymorphs	Eosinophils	Lymphocytes	Monocytes	Platelets (thousand per c mm)	Sternal marrow	Operation
6	Before operation	2 8	7 5	2 1	52	3	45		79	Marrow hypercellular, hyperplasia of erythroid and myeloid elements, normoblastic erythropoiesis, increased megakaryocytes	Ligation of hepatic artery proximally and of splenic artery
	1 Month after operation	2 9	8 1	3 4	67	2	30	1	57		
	3 Months „ „	3 6	9 5	2 9	53	2	45				
	6 „ „ „	3 3	8 9	2 0	58	12	30		44		
	7½ „ „ „				Splenectomy done						
	9 „ „ splenectomy	4 1	10 5	10 2	52	12	32	4	410		
7	Before operation	3 1	7 9	2 6	54	2	44		111		„
	1 Month after operation	3 8	10 0	7 2	68	12	28	2	99		
	3 Months „ „	3 7	10 5	3 1	50	3	45	2			
	8 „ „ „	3 5	10 1	3 0	48	5	47		100		
8	Before operation	3 8	11 0	3 1	60	6	34		78		„
	3 Weeks after operation	4 0	10 8	11 2	82	2	16		112		
9	Before operation	3 4	7 9	2 9	58	2	38	2	82		
	1 Month after operation	4 0	10 6	6 2	58	12	30		98		
	3 Months „ „	3 9	11 7	2 5	47	5	46	2	112		
	6 „ „ „	4 2	12 0	2 1	45	3	49	3	97		
10	Before operation	3 9	10 8	3 3	67		33		61		Ligation of hepatic artery proximally and splenectomy
	1 Month after operation	4 4	11 4	9 9	45	32	23		470		
	4 Months „ „	4 9	12 9	11 7	47	6	47		320		
11	Before operation	4 0	11 4	2 2	62	6	30	2	86		Ligation of hepatic artery distally and splenectomy
	1 Month after operation	4 7	12 8	6 7	43	27	29	1	346		
	3 Months „ „	5 1	12 1	7 8	54	18	28		370		
12	Before operation	2 7	7 8	2 2	48	2	47	3	44		„
	1 Month after operation	4 0	10 9	10 2	62	15	23		360		
	3 Months	4 6	12 2	7 8	70	5	25		2		

comparison of brains and machines and the construction of analogues such as those of Grey Walter (1951) and Ashby (1952). It may be some time before the fruits of such endeavours become apparent, and we must be prepared for many absurd analogies and false starts. The methods of information theory used by engineers are already beginning to provide terms by which we can speak about systems in which there is a complex input, memory, and output. But, as we should expect, the language cannot be taken over unchanged and applied to the brain. Communication engineers deal mostly with systems in which much information is carried in a single channel by very precise physical changes. The brain on the other hand uses a vast number of imprecise low-information channels, which all together carry a great deal of information. In order to be able to speak about this we need to look for other comparisons, for combination with those of communication engineering. For example, a population of organisms also carries its information in many distinct channels. We may be able to combine the methods of information theory with those of the mathematicians who have studied natural selection. The acid test of any comparison is whether it suggests the making of measurements which lead to verifiable forecasting—in fact to control of phenomena.

The case for trying to develop new analogies is that the old ones have proved inadequate. No-one could suggest, I think, that the person language has been as successful as we could wish in describing behaviour or in the handling of nervous diseases. Until the late 19th century insanity was not only incurable but a disgrace to the individual and his family. Was there no connection between the language used and the fact that the insane were kept in the filthiest conditions, usually in chains? As Dana (1925) put it in the introduction to his textbook, "German psychiatry was naught but windy speculation in the top-heavy jargon of German philosophy." Kant (1798) felt that he was qualified to describe insanity and claimed it as the province of the philosophical not the medical faculty. Of course the person language has developed considerably in recent years; modern psychiatry represents the extreme development of this verbal technique. Ways have been found of talking about the more elaborate aspects of human behaviour in terms of entities such as id and super-ego; these provide more complete descriptions than anything that the neurologist can offer at present. Yet one cannot but feel that the whole system lacks power because its method is description of human behaviour by comparison of man with his own image. Our tools are also such images, but they are made of non-living material. When we speak in terms of them we gain generality and power of forecasting.

All our talk of neurons, action potentials, and synaptic transmitters has not produced a satisfactory set of methods for dealing with nervous disease. But it has provided a set of words with which we can at least speak somewhat better than a hundred years ago. The pace of change of language suggests that we shall do very much better still a hundred years hence. But what we still need is a greater unification of our approaches. I should be the last to suggest that we should try to operate with one analogy only. The essence of the scientific approach is the realisation that for each purpose we should use a different analogy—that language and instrumentation are equally tools, useful only within their limits. *Nullius in verba*, yet one of our chief aims is to find ways of speaking by which much information can be compactly conveyed. This, surely, is the nature of the grand generalisations, such as those of physical theory that apply to a wide range of phenomena. It is these which we lack in biology and medicine. What I am suggesting is that we shall find them by first recognising that all our methods are but attempts to describe man and his behaviour. Sometimes we speak about some part by comparison with fire, saying it is inflamed; later we compare a part with a machine, as having structure and functions. Then again, when we can think of no better comparison, we say that in his head there sits an entity which shows some actions analogous to those we name in each other's faces and call love, anger, and so on. All of these are but attempts to describe to each other what we see, and particularly to speak about our forecasts of what will be, and of the actions we propose to take to meet the future.

Surely this shows the secret of how to set about teaching and speaking of the whole man. We are all dissatisfied with the attempts to say that he *is* a machine or he *is* a mind. If we want to tell our students what he is, we should be quite simple about it and start with the "fact" that he is a social animal and a great talker. The question then becomes how we can best talk about man. Our central theme should be to study the balance by which human life is maintained and all the factors that influence it. Such study can be thorough, profound, and exact, and includes all the separate subjects under which we now group our knowledge of medicine. All of these investigate the way in which human life is maintained. If they are to reach to the root of the matter they must go beyond the influences that bear upon the organism every day. Whatever balance we now enjoy is the result of the powers of forecasting learnt during millions of years of evolutionary history, allied to the forecasts each of us has learnt during our lives. The memories of all these past years are retained in the organisation of the nuclei of our cells and in our brains. Knowledge about the nature of these memory stores will provide a proper scientific basis for medicine.

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KERNICTERUS AND PREMATURITY

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KERNICTERUS was first described by Orth in 1875, but until comparatively recently the ætiology remained obscure. With the discovery of the rhesus factor by Landsteiner and Wiener (1941) a reassessment became necessary.

Hitherto kernicterus had been attributed to sepsis (Beneke 1907, Knoepfelmacher 1910, Pfältzer 1914, Thorling 1922), hepatitis (Hoffmann and Hausmann 1926), or an undetermined toxin (Schmörl 1903), as well as to erythroblastosis. As a result of serological investigations following the discovery of the rhesus factor, de Bruyne and van Creveld (1948) demonstrated a relation between kernicterus and rhesus immunisation. Similarly Claireaux (1950) declared that "nuclear jaundice is always associated with icterus gravis neonatorum resulting from hæmolytic disease"; and this is the view commonly held today.

time showed œsophageal varices which, when compared with films taken before operation, showed no change 14 days later the patient developed petechial hæmorrhages over both legs and had melæna for 48 hours The platelets numbered 80,000 per c mm, clot retraction was impaired, and there was increased capillary fragility The bleeding-time was normal. Table II shows that pancytopenia had persisted after ligation of the hepatic and splenic arteries Splenectomy was done, and the patient made an uneventful recovery In the 5 months following operation there was no recurrence of bleeding but the œsophageal varices persisted unchanged

Before operation the ascites, present in all the cases, could not be controlled adequately by medical measures, and in 5 cases paracentesis was required From the 4th day after operation the intake of salt was restricted to 2 g a day After 14 days all the patients were given a full diet and the salt intake was not restricted With unrestricted salt intake in cases 8 and 10 the fluid in the abdominal cavity increased, but in both cases after a further 4 weeks of restriction of salt to 2 g a day a return to a normal salt intake was not followed by reaccumulation of fluid Throughout the follow-up in all the cases, except case 12, a little free fluid has persisted in the abdominal cavity. This has shown no tendency to increase, is unknown to the patient, and constitutes no handicap No free fluid can be demonstrated in the abdomen of case 12

The hæmatological findings are set out in table III which shows that all the cases had pancytopenia before operation In the group in which ligation of the hepatic artery was combined with splenectomy the leucopenia and thrombocytopenia were corrected and there was a significant increase in the hæmoglobin levels and red-cell counts This includes case 12, in which the splenic artery had been tied 12 months before without effect on the hæmatological findings In the group in which the splenic artery was tied the hæmatological findings persisted substantially unchanged save for a transient correction of the leucopenia in cases 7, 8, and 9 In case 6 splenectomy 7½ months after ligation of the hepatic and splenic arteries corrected the leucopenia and thrombocytopenia and raised the hæmoglobin level and red-cell count

In all 6 surviving patients the appetite returned rapidly, weight was gained progressively, and muscular strength returned All 6 are now fully employed, 2 of them in heavy manual labour

DISCUSSION

From the literature available to us it seems that ligation of the hepatic artery in the treatment of cirrhosis of the liver with portal hypertension has been performed on 30 occasions.

Rienhoff (1951) reported 2 personal cases and referred briefly to 4 other cases—1 by Markle and 3 by Lupo In an addendum to his communication he reported that the operation had been done in 6 further cases—4 by Thorek and 1 each by Hunt and Kunkel Berman et al (1951a) indicated that they had done the operation on 10 occasions, but Berman et al (1951b) reported 1 case only in detail Leger et al (1952) reported 5 personal cases and referred to a *further* case by Thorek, and 1 each by Darmalhacq and Jackson For many of the cases no details are available, but those available and relevant to this discussion are set out in table III

Table III shows that there were 2 deaths, both in the series reported by Leger et al (1952) One resulted from secondary hæmorrhage, and the other took place 3 weeks after operation from, possibly, hepatic coma In our series there was 1 death, due to thrombosis of the portal vein about 3 weeks after operation

Thrombosis of the portal vein in cirrhosis of the liver seems to have an exceptionally high incidence in Hong-Kong McPherson (1951) reported an incidence of thrombosis of the portal vein in 6 of 98 cases of cirrhosis, whereas here in 174 cases we have encountered 16 The diagnosis in these cases was established either at necropsy or by the appearance of an unmistakable clinical syndrome This does not represent the actual incidence, for in some cases a thrombosis may develop without clinical manifestations Though complete occlusion of the portal vein can readily be detected at operation, partial occlusion cannot be determined, and we are doubtful whether radiography would assist Such a partial occlusion, as in case 7, seems to predispose to further thrombosis The occurrence of portal vein thrombosis constitutes a definite hazard, and, because of this, the portal pressure was not measured, for we have encountered thrombosis following this procedure

McPherson (1951) provocatively defined the place of surgery in portal hypertension as the treatment of bleeding—a contention made by Welch (1951) To this opinion we subscribed throughout our observations, and operation was restricted to patients who had two or more hæmorrhages from œsophageal varices Further, we held that the effectiveness of the operation in preventing hæmorrhage could only be assessed in those who had already bled Table III shows that hæmorrhage was the indication in 6 of the 19 cases of which records are available In these cases in the follow-up of 5–12 month there was no further hæmorrhage

In the present series, except case 6, there has been no further hæmorrhage from the gastro intestinal tract in a *limited follow-up of 6–11 months* Further, 6 weeks after operation radiography showed the disappearance of œsophageal varices in cases 10, 11, and 12 In cases 7 and 9 the varices, although still present 6 weeks after operation, were considerably reduced Examination 3 months after operation showed complete disappearance of varices in case 7, but in case 9 no further change was noted Visible collateral veins which were present in 3 cases before operation disappeared within 3 weeks Berman et al (1951b) reported disappearance *of both* œsophageal varices and collateral channels in their case

Case 6 had a symptomless melæna for 2 days following an attack of severe gastro enteritis At that time there was a hæmorrhagic tendency associated with thrombocytopenia Although large œsophageal varices were still present, it is difficult, in our opinion, to ascribe the bleeding to them After splenectomy the tendency to bleed ceased, and in the ensuing 2 months there has been no further bleeding from *the gastro intestinal tract Radiography 2 months* after splenectomy still showed the œsophageal varices virtually unchanged

In 2 of the 3 surviving patients treated by ligation of the hepatic and splenic arteries close to the cœliac axis œsophageal varices persist In the 1 case treated by ligation of the hepatic artery in the same position and splenectomy, and in the 2 cases in which the hepatic artery was tied distal to the gastroduodenal artery and a splenectomy *done, the varices disappeared* within 6 weeks

Berman et al (1951a) thought that establishment of an anastomotic circulation via the right gastric artery is of importance, consequently they tied the hepatic artery close to the cœliac axis This was the operation done by Leger et al (1952) Rienhoff (1951), and presumably those workers referred to by him, tied the artery immediately distal to the origin of the gastro duodenal artery One of Rienhoff's *patients* had an abdominal aortogram, which showed no filling in the region of the liver Of our patients 4 have undergone splenectomy in 2 it was combined with ligation of the hepatic artery close to the cœliac axis, and in 2 with ligation distal to the gastroduodenal branch In the latter 2 there was prompt disappearance of œsophageal varices, whereas in the former the varices persist in case 6 These results, coupled with the aortogram reported by Rienhoff (1951), *suggest that the* development of the anastomotic circulation, described by Berman et al (1951a) is to be avoided, and that ligation degeneration was now well developed, and necrosis was advanced. Vacuolated and non-vacuolated "ghosts" were common, although a few vacuolated viable cells could still be seen in the affected areas.

Similar changes were found in the brain of the infant dying on the 9th day. In addition, however, there were areas in the grey matter from which all nerve-cells had disappeared. This gave a patchwork appearance to the brain tissue. Perivascular œdema was still present, and pigmented macrophages were common. In the white matter near the lateral ventricles reaction appeared to be taking place with small round cells streaming in columns into the surrounding brain tissue.

For comparison the brains from three fatal cases of kernicterus associated with erythroblastosis due to rhesus factor were examined. Apart from the fact that congestion was less, hæmorrhage not so common, and paraventricular reaction absent, the changes were identical with those described above. Loss of Nissl substance, vacuolation, and necrosis were all found in the affected areas, and the anatomical distribution of the lesions was similar.

OBSERVATIONS ON PREMATURE INFANTS

It is thus apparent that kernicterus can occur quite apart from erythroblastosis, and the lesions in the two conditions are indistinguishable from one another. At first sight there appears to be a ready explanation of the lesions in erythroblastotic infants. It is obviously possible that the nerve-cells are directly attacked by the maternal antibody, but there are many objections to this theory. The damage to nerve-cells is almost certainly done after or just before birth, since there is little histological change in the brains of infants dying shortly after that time (Cappell 1947). Similarly there is no report of kernicterus in stillbirths due to the most severe form of erythroblastosis—i.e., hydrops fœtalis.

Kernicterus is never found apart from jaundice—a fact which naturally raises the question of the relation of hepatic function to the development of this lesion. If such a relation does exist it is obscure, for there is no apparent connection between the degree of liver damage in erythroblastosis and the development of kernicterus. It is, however, a point which must be considered, and it seemed to us that some indication of the answer to this question might be obtained, particularly in the non-erythroblastotic case, if we could examine the brains of premature infants dying before the onset of jaundice. At the same time it was necessary to choose material from infants who had lived long enough to allow histological changes to develop. Eventually we studied the brains from three premature infants who had died 48–72 hours after birth. All three had a history of difficulty at birth similar to that obtaining in the series described above. Asphyxia with cyanosis was present in each one. After admission to the sick nursery they remained feeble. Treatment was applied as in the ten other babies. There was no response, however, and these babies were never able to suck and had to be tube-fed. By 48 hours they were perceptibly weaker, and all died within 72 hours without showing any sign of jaundice.

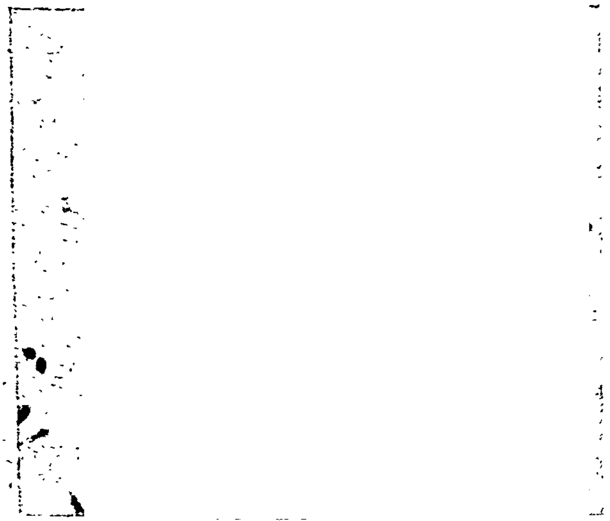

Fig. 2—Ganglion cells showing vacuolation of cytoplasm. (Hæmatoxylin and eosin. ×850.)

Fig. 3—Necrotic "ghost" cells. (Hæmatoxylin and eosin. ×850.)

The brains from these babies showed congestion of the superficial vessels, and there appeared to be an excess of cerebrospinal fluid. Patchy congestion was present in both the white and the grey matter. A severe degree of Virchow's encephalitis was present in each, and many small petechiæ were seen, particularly around the ventricular system but also in other parts of the brain. In addition there were tiny discrete opaque areas whose appearance suggested necrosis. These areas were found in the basal nuclei and in the nuclei of the brain stem, and also in the white matter, where their appearance was more distinct. Microscopically the impressions gained at necropsy were confirmed. There was much congestion and œdema of the brain, with numerous perivascular of the hepatic artery might in some cases deprive the liver of its main or only blood-supply have been realised

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INTRA-AORTIC BLOOD-TRANSFUSION

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THERE is now much evidence that, for blood-transfusion in severe oligæmic shock, the intra-arterial route offers important advantages over the intravenous Experimental work (Wiggers and Werle 1942, Kohlstaedt and Page 1943, 1944, Glasser and Page 1948, Negovsky 1945a, Mallet Guy et al 1949, Jones et al 1950, Holden et al 1950) has demonstrated the following facts

(1) Dogs which have been exsanguinated to the point of respiratory and cardiac arrest can be revived by intra arterial but not by intravenous transfusion Indeed, rapid intravenous transfusion hastens death

(2) In partially exsanguinated dogs the quantity of blood required to restore the blood pressure to normal is only half as large if it is given by the intra arterial rather than the intravenous route

The reason why the intra arterial route gives greater success is that rapid intra arterial transfusion raises the general systemic arterial pressure and with it the coronary artery pressure (Veal et al 1952) Consequently the coronary blood-flow is increased and the myocardium can recover from its depressed state Rapid intravenous transfusion, on the other hand, increases the venous return and so throws an added strain on the heart muscle, without at the same time improving its blood supply

These findings are amply supported by clinical observations Several workers (Negovsky 1945b, Porter et al 1948, Robertson et al 1948, Bingham 1952) have reported series of cases, up to 100 in number, in which intra-arterial transfusions were given They are unanimous in the conclusion that oligæmic shock can be combated more quickly and effectively in this way than by intravenous transfusion

Hitherto infusions have been made into peripheral arteries either the radial (Page 1949, Porter et al 1948 Bilsland 1951, Brown 1951, Bingham 1952), femoral (Liaras et al 1949), dorsalis pedis (Bingham 1952), iliac (Lugarisi 1949, Devitt and Wigderow 1951) or common carotid (Constantini et al 1951) Often a cut down operation with insertion of a cannula has been required and the artery has had to be tied afterwards or undergoes obliteration by thrombosis There is serious danger to the lower limb when this happens in the femoral artery (Liaras et al 1949) and gangrene of the hand, in whole or part, has followed the use of the radial artery (Porter et al 1948, Bingham 1952) Discoloration of the skin of the forearm and hand, with blistering, has been reported after transfusion into the radial artery Furthermore, there may be difficulty in entering the lumen of a contracted peripheral artery in severe shock, and the vasoconstriction may interfere seriously with the transfusion (Porter et al 1948)

These risks and difficulties act as deterrents and cause intravenous transfusions to be made when the arterial route would be more effective There is, therefore, need for a method which is free from complications Such is intra-aortic transfusion (Haxton 1952), which has now been in use for more than eighteen months It was conceived from experience with some hundreds of lumbar paravertebral sympathetic blocks, in which I found that the aorta could be easily punctured from the left side and that no sequelæ resulted From this observation the technique of intra aortic transfusion has evolved

METHOD

The patient lies either fully on the right side, or midway between this and supine, supported by sandbag under the pelvis and left scapula A skin weal is raised with 2% procaine at a point opposite the third lumbar vertebra (just above the level of the umbilicus) and in the line through the tip of the 11th rib and the highest point of the iliac crest In practice, this point is rather more than a hand-breadth from the dorsal midline, and is about 3 5 cm lateral to that used for lumbar sympathetic chain block (Haxton 1953) The reason is that the needle must be inserted more nearly transversely to reach the aorta as it lies on the anterior surface of the vertebral body

A track down to the front of the vertebral body is infiltrated with 2% procaine through a 12 cm needle and then the skin is nicked with a fine knife A special stepped needle, with a stem 14 5 cm long and 2 8 mm in diameter terminating in a section 1 cm long and 1 5 mm in diameter, is inserted along this track The step on the needle is made fairly abrupt so as to prevent the passage of the thicker section into the aorta, and this arrangement necessitates a moderate amount of pressure to get the needle through the lumbar fascia The needle is manipulated until its point slides on to the anterior surface of the vertebra There a resistance is felt when the point encounters the aorta, and insertion for a further 1 cm results in a pulsating flow of blood

The needle is then connected to a transfusion apparatus which may consist simply of the standard equipment found in hospitals, with the addition of a pressure bulb and air reservoir (conveniently the bulb and cuff from a sphygmomanometer) It is advisable, however, to use a

LIGATION OF THE SPLENIC AND HEPATIC ARTERIES IN PORTAL HYPERTENSION

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The incidence of cirrhosis of the liver among the Chinese in Hong-Kong cannot be correctly estimated but seems to be high; for of 3532 consecutive cases admitted to Queen Mary Hospital 174 were of cirrhosis of the liver.

The pathogenesis of the cirrhosis has been investigated for the past four years by McFadzean, Wong, and Hou (1953), of the departments of medicine and of pathology in the University of Hong-Kong, whose findings are summarised here: cirrhosis in association with infestation by *Schistosoma japonicum* is encountered, as is also postnecrotic scarring. A history of jaundice may be obtained, suggesting a virus hepatitis. Occasionally there is a history of alcoholism. In most cases, however, the pathogenesis is obscure. The cases reported here all belong to this last category. In these the liver is usually small and is the seat of a diffuse hepatic fibrosis. The spleen is enlarged, commonly grossly so, and there is invariably some hypersplenism.

Himsworth (1950) emphasised the part played by protein deficiency in the pathogenesis of "tropical" cirrhosis. Such deficiency is regarded as producing severe prolonged fatty infiltration of the liver which is followed by diffuse hepatic fibrosis. Though the Chinese diet in this area is such as to lend credence to the view that the cirrhosis may be due to protein deficiency, the mechanism of production is not that described by Himsworth. Extensive investigations in all age-groups, both by aspiration liver biopsy and by determination of total fat contents of livers obtained at necropsy, have failed to show a significant incidence of fatty infiltration either in cirrhosis of this group or in the hospital population in general. This is in sharp contrast to cirrhosis of the liver in Chinese with a history of alcoholism, in which gross fatty infiltration is encountered. For convenience the cirrhosis of obscure pathogenesis will be called cryptogenic cirrhosis.

A major problem in the management of established cirrhosis of the liver is to prevent death from the direct or indirect effects of hæmorrhage from œsophageal varices, and this is the primary purpose of any operation designed to reduce portal hypertension. Secondary considerations are that a favourable effect should be exerted by the operation on the ascites and that it should correct the hypersplenism. Ideally the operation should have a beneficial effect on the disease in the liver, either halting or retarding its progress.

There is no doubt that portacaval shunts prevent recurrence of hæmorrhage in most cases and exert a favourable effect on the ascites. Unless the operation is combined with splenectomy, hypersplenism is, at best, only partially corrected (Blakemore 1951). Blakemore said that evidence was accumulating to suggest that portacaval shunts slow the advance of the disease in the liver, but his evidence was equivocal. There is experimental evidence which indicates that this is unlikely. Mann et al. (1931) have shown that the liver does not regenerate after partial hepatectomy in dogs which have an Eck's fistula or in which an anastomosis has been made between the portal vein and the inferior vena cava. Perhaps the greatest defect of portacaval shunts is that they are technically difficult to make and even in the most expert hands are associated with a significant mortality.

In an effort to provide a technically simpler operation with a low mortality the following procedures have been investigated: (1) ligation of the splenic artery alone; (2) ligation of the hepatic and splenic arteries; and (3) ligation of the hepatic artery combined with splenectomy. These operations have been assessed as regards their effectiveness in preventing recurrence of hæmorrhage from œsophageal varices and their effect on the varices, on ascites, and on hypersplenism. In the case of operations involving ligation of the hepatic artery, liver-function tests and aspiration liver biopsies have been carried out at intervals to determine the influence exerted by the operation on the disease in the liver. Because of the absence of an adequate preoperative base-line, and because of the short duration of the postoperative follow-up, our observations on the effects on the liver and liver function are incomplete and are therefore not reported here.

Ligation of Splenic Artery

According to Watson (1935) the splenic artery was first tied by Long in 1905, for a "floating" spleen which had become firmly fixed by adhesions. The operation was repeated by Lantz (1914) for a floating spleen which had become adherent to the bladder; after the operation bimanual examination failed to reveal the presence of an abnormal mass. Blain (1918) tied the artery of a grossly enlarged adherent spleen in a Greek labourer diagnosed as having Banti's syndrome; the patient was reported later as alive and well thirty-four years after the operation. Since then the splenic artery has been tied in most of the conditions for which splenectomy is indicated.

McNee (1931) suggested ligation of the splenic artery in the management of portal hypertension. The rationale of this procedure is based on the fact that the splenic artery furnishes 25–40% of the blood in the portal system, a contribution which is probably increased when the spleen is abnormally large. On theoretical grounds splenectomy should reduce portal pressure by denying to the portal circulation the blood previously distributed to the spleen. Ligation of the splenic artery should be superior to splenectomy because the veins and rich anastomoses therewith are preserved and assist in carrying the blood round the block in the portal system. Everson and Cole (1948) and Blain and Blain (1950) revived the operation as a substitute for splenectomy or lienorenal shunts in poor-risk cases.

MATERIAL AND METHODS

All 5 patients were Chinese adult males with diffuse hepatic fibrosis of cryptogenic origin, the diagnosis being established by biopsy. All of them had a history of at least one attack of severe hæmatemesis from œsophageal varices, which were demonstrated radiographically. The main clinical details are as follows:

Case 1.—A Chinese male labourer, aged 31, had two severe hæmatemeses in the 10 months before operation. Ascites had been present for 3 months and had been prevented from becoming tense by restriction of salt intake to 1 g. daily and by diuretics. There was moderate wasting. The liver was not felt, but the spleen was palpable 5 cm. below the costal margin. Abdominal collateral veins were present.

Case 2.—A Chinese male labourer, aged 35, had two severe hæmatemeses in the 10 months before operation. Ascites had been present for 4 months, and in the last 2 months paracentesis was required twice in addition to salt restriction to 1 g. daily and diuretics. Wasting was moderate. The liver was not felt, but the spleen was palpable 5 cm. below the costal margin. Large collateral veins were present in the lumbar region.

Case 3.—A Chinese male shop-assistant, aged 25, had a massive hæmatemesis 6 weeks before operation. There was no history of ascites. The general condition was good. The liver was not felt, but the spleen was palpable 7 cm. below the costal margin.

Case 4.—A Chinese male tailor, aged 32, had a severe hæmatemesis and three attacks of melæna in the 5 months before operation. On admission to hospital 1 month before emboli Experiment has shown, however, that the relatively fine point used will pass quite easily through the ordinary atheromatous plaque without causing any detachment

The vertebral level at which the needle is introduced is important Above the third lumbar vertebra there is a danger of damage to the left kidney, and below it the aorta bifurcates and could be missed The possibility of puncture of the descending colon by a needle inserted too far anteriorly must also be borne in mind

In selecting the type of needle to be used there are two conflicting considerations the bore must be large enough to allow a rapid flow of blood, but the puncture in the aorta must be small if leakage is to be minimised A compromise is reached in the stepped needle, in which there is only a short length of relatively small bore With this needle a pressure difference of 200 mm Hg between the two ends gives a rate of blood delivery of 180 ml. per minute With a 12-cm Labat needle 1 1 mm in diameter, on the other hand, this pressure gives a rate of flow of only 13 5 ml per minute

The stepped needle can also be used, with advantage, for aortography, because 20–40 ml of 70% diodone can be injected quickly without great force If fine needles are used, a pressure of 45 lb (2326 mm Hg) per square inch may be needed for even moderate rates of injection (Doss 1944)

As has been pointed out (Haxton 1952) the aorta is directly accessible when the thorax or abdomen is open, and transfusion into it can be made easily and quickly should the need arise during operation As an example a patient of mine was recently operated on by the resident surgical officers H A Simmons and J P Flanagan, for recurrent severe hæmatemesis from a large duodenal ulcer After the abdomen was opened, a pint of blood was rapidly transfused through a stepped needle inserted, under vision, into the aorta The patient's general condition was greatly improved and partial gastrectomy was safely carried out It is now our practice to keep the necessary apparatus sterilised in a drum so that an intra-aortic transfusion can be set up at very short notice If all hospitals did likewise, it seems certain that some lives could be saved which would otherwise be lost

SUMMARY

Experimental and clinical evidence indicates that, in states of severe shock and exsanguination, the intra-arterial route for blood-transfusion is superior to the intravenous route

Transfusions into peripheral arteries are subject to difficulties due to spasm and to dangers from subsequent ligation or thrombosis

Transfusion into the abdominal aorta at the level of the third lumbar vertebra with a special stepped needle has proved simple and free from complications in 20 cases

In cases with repeated gastro-intestinal hæmorrhage this method has rapidly restored the general condition and has allowed the safe performance of early operation In other cases with acute oligæmia rapid improvement with transfusions of moderate size has been the rule

Transfusion can be made under vision into the aorta during thoracic and abdominal operations, should the need arise

A plea is made for keeping the necessary apparatus sterile and at hand, ready for immediate use

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A TRIAL OF ISONIAZID IN RAT LEPROSY

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RAT leprosy occurs as a natural infection in various parts of the world It is a slowly progressive fatal condition which may be predominantly musculocutaneous or glandular In the musculocutaneous form the animal is emaciated, the skin becomes atrophic and ulcerated, and the deeper layers are replaced by a greyish white granular material In the other form the inguinal, axillary, cervical, and other glands are enlarged, hard, and white The causative organism is an acid fast bacillus, *Mycobacterium lepræ murium*, which has so fa not been definitely cultivated, though claims have been made from time to time Recently Hanks and Soule (1949) failed to confirm such claims made by Ashbel and Poljakoff (1948) In the diseased rat, enormous numbers of bacilli are found in the corium and subcutaneous tissue, mostly in the cells of the granulation tissue, and in large cells with much cytoplasm, resembling the lepra cells of human leprosy, but without vacuole They are also found in large macrophages densely packed in the sinuses of the glands The mode of natural infection is not known but the organism probably enters through cutaneous abrasions

Rat leprosy can be reproduced experimentally by the intraperitoneal inoculation of infected material The animals usually die in four to ten months with gross lesions The omentum is converted into a huge hard mass of opaque pale yellow material, consisting of collections of cells containing very large numbers of acid fast bacilli The diaphragm is replaced by similar material and the mediastinal and other glands are grossly enlarged, hard, and pale-yellow in colour

Rats cannot be infected from human cases of leprosy It is therefore probable that the human leprosy and the rat leprosy bacilli are different, although a few observations suggest that some cases at least of human leprosy are caused by the rat leprosy bacillus (Wilson and Miles 1946) The similarity between the two diseases suggested, however, that it would be worth investigating the effect of isoniazid on the course of experimental rat leprosy

EXPERIMENTAL METHOD

The strain of rat leprosy bacillus used in this work was provided some years ago by Dr A Q Wells, and has been maintained by intraperitoneal passage in rats The inoculum was obtained from a rat infected two

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frequently. All 3 patients reported by Everson and Cole (1948) had tense ascites. The ascites reaccumulated in the patient who died from hæmatemesis 3 months after the operation. One of the 2 remaining patients continued to require frequent paracentesis after operation, but the other, after a transient reaccumulation of fluid, remained free from ascites and a year later was fully employed. All 3 patients with cirrhosis in the series reported by Blain and Blain (1950) had ascites. In 1 of these the ascites reaccumulated within 7 weeks of the operation and the patient died a month later. The remaining 2 patients were free from ascites 10 months and 2 years later.

Before operation 3 of our patients had ascites, which in 2 was controlled by restriction of salt intake to 1 g. a day and diuretics, but in the 3rd, in addition to these measures, paracentesis was required. One of the former, case 1, showed improvement following operation. Free fluid was present in his abdomen for 2 months, but accumulation was controlled by restriction of the daily salt intake to 2 g. After 2 months a return to a normal salt intake did not provoke recurrence of the ascites. The patient remained free from ascites for 10 months, when it reappeared following recurrence of the hæmorrhage. The operation in the remaining 2 cases exerted little effect. Case 2 required no further paracentesis, but rigid salt restriction and diuretics were required to control the ascites. Case 5, when last seen 6 weeks after operation, also required this régime. In view of the notoriously fluctuating course of ascites it is difficult to attribute any improvement to the operation. Certainly, if the operation has an effect, this is by no means uniform.

Everson and Cole (1948) and Blain and Blain (1950) claimed that ligation of the splenic artery produced a result similar to that of splenectomy. Their claim, so far as the effect in cirrhosis of the liver with portal hypertension is concerned, seems to be based on the postoperative diminution of the spleen, because these workers do not give postoperative hæmatological findings.

In our series the operation had no effect on the thrombocytopenia which was present in all the cases. In only cases 1, 2, and 4 was an effect observed on the leucopenia, and this was transient. Two months after the operation the white-cell counts had fallen to the preoperative levels. The effect on the red-cell count is rather more difficult to assess because, except in case 4, the red-cell count had not become steady after the hæmorrhage before operation. Significant anæmia persisted in cases 1, 2, and 5, and the rise in the red-cell count in cases 1 and 2 after the operation may be attributed to regeneration following the hæmorrhage. In case 3 a significant rise in the red-cell count was encountered; but, in view of the persistent leucopenia and thrombocytopenia, again the rise may probably be attributed to regeneration following hæmorrhage rather than to a selective effect of the operation on a pancytopenic hypersplenism. The contention of Everson and Cole (1948) and Blain and Blain (1950) that ligation of the splenic artery acts as a "functional splenectomy" seems to be untenable, since the operation leaves the hæmatological findings virtually unaltered. Further proof that the spleen continues to function after ligation of the splenic artery is afforded by case 1, in which splenectomy and ligation of the hepatic artery later corrected the pancytopenia (see case 12 below).

Learmonth (1951) on anatomical grounds raised objection to ligation of the splenic artery because a collateral circulation is provided through the right gastro-epiploic artery. He tied and divided the splenic and right gastro-epiploic arteries. This he reported as producing an initial improvement in the blood picture, but later there was return of the pancytopenia. It therefore seems that any elaboration of the operation of ligating the splenic artery is doomed to failure.

It may be concluded from the present series that ligation of the splenic artery alone failed to prevent recurrence of bleeding from œsophageal varices; it exerted at most a doubtful effect on the ascites but no significant effect on the hypersplenism. We can find nothing in the literature accessible to us which negates these conclusions. Learmonth (1951) thought that, with very rare exceptions, the operation need not be retained. Milnes Walker (1952) referred to the operation as useless, a viewpoint with which we agree.

Ligation of Hepatic Artery with Simultaneous Ligation of Splenic Artery or Splenectomy

During the greater part of our observations we were unaware of the work of Berman et al. (1951a) on ligation of the hepatic artery in dogs and the report of Rienhoff (1951) of its use in man. For the sake of clarity we shall present the evidence which first led us to attempt the operation.

Wakim and Mann (1942), using a transillumination technique, made exhaustive microscopical studies of the circulation in the livers of living animals and demonstrated the existence of interconnections between the branches of the hepatic artery and those of the portal vein. These interconnections were present both in the interlobular spaces and between the sinusoids. The former consisted of side-to-side anastomoses between arteries and veins and arteries terminating end-to-side in veins. The sinusoidal connections consisted either of a terminal branch of the hepatic artery and a terminal branch of the portal vein entering into the same sinusoid or of cross-communications between the arterial and portal sinusoids.

The histological observations of Cameron and Mayes (1930) on the effects of ligation of the hepatic artery on the liver had indicated the existence of these communications between portal vein and hepatic artery at arteriolar level. According to Moschcowitz (1948), Sabourin in 1885 demonstrated shunts between branches of the hepatic artery and of the portal vein in cirrhosis of the liver, an observation which has been confirmed by Epplen (1922) and Popper et al. (1950).

Herrick (1907) first noted the effects of these shunts in arterial perfusion experiments on excised normal and cirrhotic livers. He found that in normal livers there was a rise in portal pressure of 1 mm. Hg for every 40 mm. Hg rise in arterial pressure, whereas in the cirrhotic liver it was 1 mm. Hg for every 6 mm. Hg rise in arterial pressure. Dock (1942), using kerosene as the perfusing fluid, showed that, if the portal vein and the hepatic artery were perfused simultaneously at a pressure of 20 and 100 mm. Hg respectively, in the normal liver the rate of flow through the portal vein was 30% less than if the portal vein was perfused alone. In a case of alcoholic cirrhosis he found that the rate of flow was reduced by 78%. One of us (A. J. S. M.), using Dock's technique, repeated his observations on excised cirrhotic livers of cryptogenic origin in Hong-Kong and found the average reduction in flow in 3 cases to be 56%.

That these shunts, which can be demonstrated anatomically and by perfusion experiments, are operative in vivo can be readily shown at laparotomy in cases of cirrhosis of the liver with portal hypertension. If the portal vein be temporarily occluded by pressure, the portal pressure falls only slightly in the segment of vein between the liver and the point of occlusion. This observation has also been reported by Blakemore (1952). If the hepatic artery is then occluded, the portal pressure falls precipitously in this segment. Temporary occlusion of the hepatic artery alone leads to a prompt and significant fall in portal venous pressure.

From these considerations it seems that the pressure within the hepatic artery is a main contributing force to the production of portal hypertension in cirrhosis of the liver.

Ligation of the hepatic artery is usually fatal in guineapig, rabbit, cat, dog, and man. According to Loeffler (1936) the liver of rats and rabbits can survive on portal blood alone. Haberer (1905) emphasised the importance of the position of the ligature and concluded that ligation beyond the origin of the right gastric artery invariably caused massive necrosis. Huggins and Post (1937) showed in dogs that, though ligature of the hepatic artery immediately proximal to its bifurcation caused rapid death, multiple-stage ligations beginning proximally and proceeding distally were safe.

INFECTED ARTERIOVENOUS FISTULA IN THE LUNG

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The association of multiple hereditary telangiectasia with polycythæmia, clubbing, cyanosis, and a shadow in the lung with murmur and sometimes a thrill is well known, and many cases of pulmonary arteriovenous aneurysm have now been described (Crane et al 1949, Baker and Trounce 1949, Hayward and Reid 1949, Duisenberg and Arismendi 1949) Yater et al (1949) give a useful survey of the published cases but prefer the term arteriovenous fistula, indicating a direct communication between artery and vein without interposition of capillaries and a "false aneurysm"

The only previously published case claimed to be infected (Maier et al 1948) was very doubtful The patient, a young woman aged 20, had at the time an abscess at the right ankle and a left sided empyema both caused by a non-hæmolytic streptococcus, which was also obtained by culture from the blood She was cured with intramuscular penicillin, instillations of penicillin into the empyema, and sulphadiazine by mouth Subsequently she underwent lobectomy and the inside of the aneurysmal sac had, on its wall, a thickened area which was thought to represent the site of previous vegetations The scanty evidence of infection of the sac and the presence of other severe localised sepsis quite likely to cause a septicæmia make the diagnosis doubtful Thickening will occur from organisation of non septic clot Our own case even shows some calcification radiologically in the wall of the sac

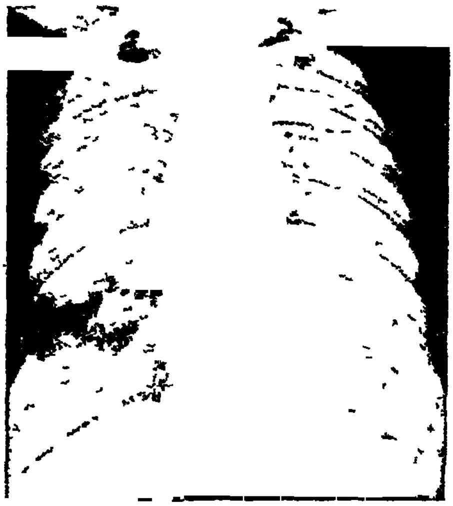

Fig 1—Anteroposterior view, showing arteriovenous fistula in lower zone of right lung

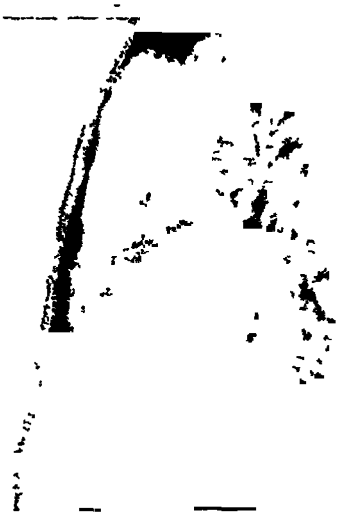

Fig 2—Lateral view, showing arteriovenous fistula in middle lobe of right lung

CASE-RECORD

A thin, plethoric, and cyanosed man, aged 58, had in the past been known at times to be polycythæmic and at times to have had an iron lack anæmia His liver was moderately enlarged and his spleen just palpable He had clubbing of the fingers, was hypertensive, and had multiple telangiectases on lips, face, and tongue, with flecks under his nails There was a family history of this condition affecting his maternal grandmother, his mother, himself, and, to a slight extent, his two children, one male and one female He was admitted to the Bushey and District Hospital in late September, 1950, with a history of two weeks' high temperature (99°–102°F) and pain in the back He had no cough but was found to have a *Bacterium coli* infection of the urine, although there were only about 10 pus cells per one sixth field in centrifuged deposit A blood culture made at the same time was reported as growing a *Staphylococcus pyogenes*, which the laboratory regarded as "probably a contaminant"

Treatment and Progress—Shortly after admission the patient's auricles began to fibrillate, and he was given digitalis After three days his heart returned permanently to regular rhythm His *Bact coli* infection was treated with streptomycin, and his temperature, which had risen to 103°–104°F, fell during the next few days After he had been apyrexial for a week on the cessation of his chemotherapy his temperature rose again to the same heights By this time stool cultures had been shown to be normal and to contain no microscopic abnormality Widal tests were negative except for a rise in titre which was finally concluded to be due to previous inoculation in the Army His white blood cell count had risen from 7000 to 16,000 per c mm (polymorphs 95%)

On Oct 12 he was very sick, with a very high temperature, pulse rate 110, and no signs of pulmonary consolidation his spleen was not felt , his liver was just palpable There were normal heart sounds in the precordial area, but a systolic murmur with a doubtful early diastolic addition was audible in the front of the *right* lower chest and in the *right* axilla Radiography of the chest disclosed in the right lower zone a shadow (figs 1 and 2) which in lateral views was shown to be in the middle lobe A second blood culture again produced a *Staph pyogenes* sensitive to penicillin, aureomycin, and chloramphenicol As soon as this was known, the patient was given penicillin 1 mega unit four hourly

The diagnosis of arteriovenous fistula of the lung associated with his telangiectasia was now clear, and the *Staph pyogenes* septicæmia was thought to be due to an infection in the aneurysm The murmur changed somewhat, and by Oct 19 there was a complete round-the clock machinery murmur with a palpable thrill in the left axilla It was loudest during full inspiration Despite 6 mega units of penicillin a day the patient's temperature remained about 100 F until Nov 4 Aureomycin 500 mg six hourly was then added for four days, and then, owing to nausea and vomiting reduced to 250 mg six hourly The patient's temperature gradually settled, and he had no further pyrexia after Nov 12 He refused lobectomy

Follow up—The patient was seen again in October 1952, two years after his septicæmia He was then slightly anæmic from repeated bleedings from his nasal telangiectasia but otherwise well He was not dyspnœic, and there was no evidence of cardiac embarrassment The murmur in his right lower chest was now absent on full expiration, systolic on half inspiration, and a full round the clock machinery murmur with thrill on full inspiration Radiography in two planes showed no change in the size of his middle lobe shadow

SUMMARY

A typical case of pulmonary arteriovenous fistula associated with multiple hereditary telangiectasia is described

The patient had a *Staph pyogenes* septicæmia with no apparent localised sepsis, and infective endarteritis of his fistula is thought the most likely explanation He was cured with penicillin and aureomycin and is well two years later

Only one similar case with infection has been previously published, but it was associated with other possible and even likely sources for the septicæmia

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TABLE III—RELEVANT AVAILABLE DETAILS OF PUBLISHED CASES IN WHICH HEPATIC ARTERY WAS TIED

Reference	No. of cases	Indication for operation	Results	Duration of follow-up	Operation
Rienhoff (1951)	2 { 1	Ascites	Resolution	3½ Years	Ligation* of hepatic and splenic arteries]
	1	Hæmorrhage	No recurrence	1 Year	,,
Markle (Rienhoff 1951)	1	,,	,,	8 Months	? ,,
Lupo (Rienhoff 1951)	3	Ascites	Resolution	Unknown	? ,,
Berman et al. (1951b)	1	,,	,,	6 Months	Ligation† of hepatic and splenic arteries
Leger et al. (1952)	5	,,	2 Deaths 3 Resolution	5–9 Months	Ligation† of hepatic artery (3); ligation† of hepatic and splenic arteries (2)
Jackson (Leger et al. 1952)	1	,,	Resolution	3 Months	Ligation of hepatic and splenic arteries
Darmaillacq (Leger et al. 1952)	1	Hæmorrhage	No recurrence	5 Months	Ligation† of hepatic artery
Thorek (Rienhoff 1951 and Leger et al. 1952)	5 { 2	Ascites	Resolution	Unknown	Ligation* of hepatic and splenic arteries
	3	Hæmorrhage	No recurrence	,,	,,

* Distal to origin of gastroduodenal artery. † Close to cœliac axis.

The last two hæmorrhages had precipitated hepatic coma. In the first 6 months after the onset of bleeding there was a variable ascites, but in the second 6 months the ascites became tense and, in addition to restriction of salt intake to 1 g. daily and diuretics, paracentesis was required about once in 14 days.

Wasting was marked. The liver was not felt, but the spleen was palpable 9 cm. below the costal margin. Pressure sores were present over the occiput and sacrum at the time of operation; these had developed 2 months before, during the hepatic coma following the last hæmorrhage.

Case 7.—A Chinese male labourer, aged 32, had five attacks of melæna and two severe hæmatemeses in the 10 months before operation. Ascites had been present for 9 months and followed the second attack of melæna. In the last 4 months paracentesis was required about once in 22 days in addition to salt restriction to 1 g. daily and diuretics.

Wasting was moderate. The liver was not enlarged, but the spleen was palpable 8 cm below the costal margin. Large lumbar collateral veins were present.

Case 8.—A Chinese male cook, aged 45, had two massive hæmatemeses in the 4 months before operation. Ascites had been present for 6 months, and before admission to hospital five paracenteses had been done, but after admission restriction of salt intake to 1 g. daily and diuretics partly controlled the ascites and, although much free fluid persisted, the abdomen was not tense.

Wasting was severe. The liver was not felt, but the spleen was palpable 5 cm. below the costal margin.

Case 9.—A Chinese male shopkeeper, aged 49, had two severe hæmatemeses in the 2 years before operation, but there was a history of five minor hæmatemeses extending over 5 years. Ascites had been present for 7 months, and for 2 months before operation, in addition to restriction of salt intake to 1 g. daily and diuretics, paracentesis was required about once in 16 days.

The liver was not felt, but the spleen was palpable 6 cm. below the costal margin. Large abdominal collateral veins were present.

Case 10.—A Chinese male messenger, aged 30, had two massive hæmatemeses in the 6 months before operation. Ascites had been present for 2 months, and before admission to hospital paracentesis had been done twice. After admission the ascites could be prevented from becoming tense by restriction of salt intake to 1 g. daily and mersalyl.

Wasting was severe. The liver was not felt, but the spleen was palpable 10 cm. below the costal margin. Large abdominal lumbar collateral veins were present.

Case 11.—A Chinese male cobbler, aged 21, had two massive hæmatemeses in the 6 months before operation, and repeated attacks of melæna of varying severity for 8 months. Ascites had been present for 3 months, and, in addition to salt restriction and diuretics, paracentesis was required twice in this period.

Wasting was moderate. The liver was not felt, but the spleen was palpable 7 cm. below the costal margin.

Case 12.—A Chinese male labourer (the same as case 1), aged 32, had three severe hæmatemeses in the 22 months before operation. The splenic artery was tied after the second hæmatemesis. At that time ascites had been present for 3 months. After the operation the ascites resolved and he remained moderately well for a year, when he had melæna for 3 days and then a massive hæmatemesis. After the bleeding, ascites reappeared and became tense and paracentesis was required in addition to restriction of salt intake to 1 g. daily and diuretics.

Wasting was moderate. The liver was not felt, but the spleen was palpable 2 cm. below the costal margin.

The hæmatological findings immediately before operation are set out in tables II and III. It must be emphasised that the red-cell counts and hæmoglobin levels cannot be regarded as a base-line, because in all the cases there had been recent severe hæmorrhage, and recovery from its effects may not have been complete.

Paracentesis was done in all the cases 48 hours before operation. For 12 hours before operation and 7 days thereafter penicillin 5 mega-units and streptomycin 3 g. a day were given intramuscularly in divided doses. In cases 6–9 the hepatic and splenic arteries were defined and tied close to their origin from the cœliac axis. In case 10 the hepatic artery was similarly tied and the spleen was removed, but in cases 11 and 12 splenectomy was combined with ligation of the hepatic artery distal to the origin of the gastroduodenal artery. No attempt was made to measure the portal pressure at operation.

No dietary restrictions were imposed in the immediate postoperative period, but from the 4th day, for 14 days thereafter, the salt intake was reduced to 2 g. a day. At the end of that time salt restriction was removed, and it was reimposed only in those cases where there was evidence of reaccumulation of ascitic fluid.

RESULTS

There was 1 death in the series (case 8). In this case the immediate postoperative period was satisfactory, but on the 22nd day after operation the patient refused food and became drowsy. Next day he was comatose and jaundiced. He remained in coma until his death on the 26th day. At necropsy a thrombus was found partially obliterating the lumen of the portal vein and extending into and obstructing the left branch. The liver showed extensive necrosis, but there was no evidence of infection.

The remaining 6 cases have been seen and investigated at intervals of from 6 to 12½ months after operation.

Except in case 6 there has been no further bleeding. Radiography 6 weeks after operation showed that œsophageal varices were no longer present in cases 10, 11, and 12, whereas in cases 7 and 9 the varices were still present but much less conspicuous than before operation. Further radiography 3 months after operation showed disappearance of the varices in case 7 but no change in case 9. The visible collateral veins in cases 7, 9, and 10 rapidly regressed after operation and could no longer be detected 4 weeks after operation.

Case 6 was readmitted to hospital 6½ months after operation with severe gastro-enteritis, from which he made a satisfactory recovery. Radiography at this however, was the disappearance of the bundle branch-block pattern from the electrocardiogram, that recorded on March 7, 1950, showing a Q R S lasting 0 06 sec (see figure) The pattern of left ventricular hypertrophy was present

Follow up—After discharge from hospital the patient resumed work as a secretary and did not complain of shortness of breath She continued at work for a year with a blood-pressure about 250/150 mm Hg, but with normal conduction in the electrocardiogram In December, 1950, she was readmitted to hospital with a severe attack of pneumonia affecting the right lower lobe, which responded somewhat slowly to treatment with antibiotics Electrocardiography on Jan 23, 1951, still showed a Q R S lasting 0 08 sec (see figure) After her second discharge from hospital she was never fit enough to work again, and died fifteen months later

DISCUSSION

The relief of hypertension produced at times by the removal of a diseased kidney is familiar, and numerous examples have been reported. In one case the patient is still fit after eight years (Petch 1947) Only too often, however, other hypertensive mechanisms have developed, perhaps in the sounder kidney, and permanent recovery is impossible Such improvement as takes place is attributed to the removal of a pressor substance secreted by the damaged kidney, and presumably a similar mechanism produced the electrocardiogram described in the present case The first blood-pressure recordings were made in the presence of severe cardiac failure, and with improvement the pressure rose It is not known what levels obtained before failure developed The severity of hypertensive disease in general is often best inferred from its indirect effects rather than by direct measurement, and it seems reasonable to suppose that the disappearance of the abnormality was mediated by a fall in the basal blood-pressure from some previous high level rather than by any direct effect on the conducting tissue

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CONGENITAL ABSENCE OF THE GALL-BLADDER

WITH STONE IN THE COMMON BILE-DUCT

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Congenital absence of the gall-bladder in man is a rare anomaly It may occur without any other variation from the normal in the remaining extrabiliary system The fossa of the gall-bladder is commonly absent, but occasionally a shallow fissure or dimple is visible on the under surface of the right lobe

This anomaly is twice as common in females as in males The ages of the patients when the anomaly is discovered, at operation or at necropsy, varies from a few days to 65 years, with an average of about 35 years Its absence has no effect on the health or digestive functions When the extrahepatic ducts are dilated, the presence of one or more gall-stones makes it virtually certain that the increased size is due to the obstruction from the calculus, rather than from the absence of the gall-bladder Gross (1936), who reported 38 cases of total absence of the gall bladder, said that this anomaly was rarely associated with any compensatory dilation of the hepatic or of the common bile ducts Other workers have confirmed this

Aristotle (384–322 B C) did not agree that the gall bladder gave rise to certain sensations, or that the absence of the gall bladder gave long life He said that in some people there was apparently a gall-bladder attached to the liver, whereas in others there was none He observed that some animals (mule, ass, deer, camel, dolphin, and sea calf) have no gall-bladder.

Pliny (A.D 23–79) added the wild boar to Aristotle's list of animals without a gall bladder The gall bladder is also absent in badgers and some species of sharks but in other species of sharks an intrahepatic gall bladder has been found The horse and the rat have no gall-bladder, whereas the cow and the mouse have Scammon (1911) states that the pigeon is the only bird without a gall-bladder, but its embryo has one

According to Gross (1936), Stolkind (1939), Muir (1941), and others, the absence of the gall bladder is a developmental abnormality, whereas Gaultier de Claubry (1829), and Lémery (1701) regard it as a result of inflammation

Virenque (1923), who made a great number of post mortem examinations of children and adults never found a single case of congenital absence of the gall bladder Knox (1922) found 2 cases in 2000 necropsies Mentzer (1929) and Nagel (1926) each found one instance of congenital absence of the gall-bladder in 100 necropsies At the London Hospital 9 cases of congenital absence were found in 21,631 necropsies from 1908 to 1939 At the Hospital for Sick Children, Great Ormond Street, 20 of these cases were met in 5395 necropsies on children in 1909–35 Stolkind (1939) published 31 cases of congenital abnormalities of the gall-bladder, of which 11 were absence thereof

Huber (1749), Vergne (1826), Canton (1847), Rambault and Schachmann (1882), and many others have reported cases of adults who died from other reasons and were found at necropsy to have no gall-bladder

CASE RECORD

A multiparous married woman, aged 64, was referred to the surgical clinic at Leigh Infirmary with five months history of recurring abdominal pain After her first attack of pain she became jaundiced, and the discoloration persisted for three weeks There was no previous history of indigestion or flatulence, but she had lost her appetite recently and almost 2 stone in weight

On examination a barium meal showed no abnormality A cholecystogram showed no filling of the gall-bladder

At operation, on June 11, 1952, a small cirrhotic liver was exposed The common bile duct was easily identified because it was grossly dilated No gall bladder or cystic duct was present, and there was no fossa or fissure on the under surface of the right lobe of the liver The dilated duct was incised, and a single spherical stone, 0 75 cm in diameter, was extracted from its lower end The duct was drained with a T tube

After operation a choledochogram on the tenth postoperative day showed no filling defect in the duct The tube was removed, and the patient discharged from hospital Since then she has gained weight and has had no recurrence of the pain

DISCUSSION

The outgrowth from which the liver is formed is a ventral outpouching from the entoderm covering the abdominal aspect of the septum transversum During the development of the liver bud, the region of the liver in front of the hilum comes into existence as a projection from the ventral aspect of the gland originally embedded in the septum The future gall bladder is a short diverticulum, actually embedded in the mesoderm of the septum at its ventral limit Later, when the gland extends beyond the ventral mesentery, it carries the gall-bladder with it, stretching its stalk in so doing The fundus of the gall bladder appears in this mesoderm below the liver Thus the gall bladder is formed from the lower part of the hepatic diverticulum distal to the origin of gastroduodenal artery may be the operation of choice. That the development of the anastomosis is unnecessary is indicated by the observations of Huggins and Post (1937) on the effects of removal of the hepatic artery in dogs. These workers showed radiographically that the only arterial supply in dogs subjected to this operation was by way of the phrenic arteries; yet no histological changes were observed in the liver.

From table III it will be seen that ascites was the indication for operation in 13 of the 19 published cases, and that the response was satisfactory. There was no recurrence in a follow-up ranging from 3 months to $2^1/_2$ years. The effect of the operation in the present cases confirms these findings. The control of ascites, which may be regarded as resistant to medical measures before operation, has so impressed us that we now consider the operation indicated in ascites which cannot be readily managed by medical measures. This is of great importance in Hong-Kong, where ascites has a higher incidence than hæmorrhage and where the poor economic status of our patients renders medical treatment difficult. The persistence of small amounts of free fluid in the peritoneal cavity is of interest and is being investigated.

In the published cases no reports are available of the hæmatological findings before and after operation. In the present series the preoperative and postoperative findings are set out in table II, which shows that a significant difference emerges between those cases in which ligation of the hepatic artery was combined with splenectomy and those in which it was combined with ligation of the splenic artery. Apart from a transient effect on the leucopenia in cases 2 and 4, the latter operation did not correct the hypersplenism, whereas this was achieved in the 3 cases subjected to splenectomy. Further, in case 6 splenectomy done 8 months after the first operation brought the platelet and white-cell counts back to normal and raised the red-cell count and hæmoglobin level significantly. Case 12 is also of interest, in that splenectomy and ligation of the hepatic artery 12 months after ligation of the splenic artery alone corrected the hypersplenism which had persisted despite the earlier operation. We agree with Learmonth (1951) that the hypersplenism must be corrected, and in our opinion this can only be achieved by splenectomy. Berman et al. (1951a) considered that ligation of the splenic artery with conservation of the collateral channels arising from the splenic vein was desirable to reduce lateral pressure in the portal vein and to permit the development of a new capillary bed in the liver. The results in the 3 cases subjected to simultaneous ligation of the hepatic artery and splenectomy suggest that this is unnecessary.

After operation all the patients showed an increase in appetite, a rapid gain in body-weight, and progressive return of muscular strength. The happiest aspect is that they are now fully employed.

Though it would be premature to comment on the effect of the operation on the disease in the liver, it may be stated that in the 6 surviving patients the operation had no deleterious effect on the liver microscopically or on liver function. Indeed, the evidence which is accumulating suggests that liver function may be improved.

A major worry throughout our observations had origin in the perfusion experiments reported by McIndoe (1928), who showed that, if the portal vein of the cirrhotic liver was perfused at a pressure of 20 mm. Hg, 86–100% of the perfusing fluid could be collected from collateral channels and, at most, 14% from the hepatic vein. Since the collaterals are given off at presinusoidal levels, ligation of the hepatic artery would cut off the main, or in some cases the only, blood-supply, unless the collateral channels closed, and ischæmic necrosis would result. Though this has not been encountered, the reported cases of ligation of the hepatic artery are few, and we feel it must be regarded as a definite risk. Further, we have assumed that, in cirrhosis, the flow of blood through the hepatic artery greatly reduces the flow of portal blood through the liver, but the perfusion experiments of Dock (1942) showed that this reduction varied widely; indeed in some cases of cirrhosis the reduction in portal-vein flow produced by simultaneous perfusion of the hepatic artery was less than in normal livers. In view of these considerations it is our opinion that the operation should be restricted for the present to cases of advanced cirrhosis with poor prognosis.

Summary

In an effort to provide a technically simple and effective substitute for portacaval shunts, two operations —ligation of the splenic artery and ligation of the hepatic artery—have been assessed as regards their effectiveness in preventing further hæmorrhages from œsophageal varices and their effect on the varices, ascites, and hypersplenism.

LIGATION OF SPLENIC ARTERY

This operation was performed in 5 cases with a history of one or more hæmorrhages from œsophageal varices. The 4 patients followed up had recurrence of bleeding, which in 2 cases was fatal.

No effect was exerted on the varices and other collateral channels when present. Ascites was present in 3 cases, and in 2 it was uninfluenced by the operation; a doubtful effect was exerted in the 3rd case. The operation failed to correct the hypersplenism which was present in all the cases.

Other published cases are discussed, and it is concluded that the operation is useless.

LIGATION OF HEPATIC ARTERY

This operation was performed in 7 cases with a history of two or more severe hæmorrhages from œsophageal varices. In 5 cases the artery was tied close to the cœliac axis, and in the remaining 2 immediately distal to the origin of the gastroduodenal artery. In the first 4 cases the splenic artery was tied simultaneously, and in the last 3 the spleen was removed.

There was 1 death, some 3 weeks after the operation, due to thrombosis of the portal vein. In a follow-up ranging from 6 to $12^1/_2$ months in the 6 surviving cases there has been no further hæmorrhage from œsophageal varices. The varices have disappeared in 4 cases, have been substantially reduced in 1 case, and persist unchanged in 1 case. The ascites has been controlled.

Hypersplenism was corrected in the 3 cases in which the spleen had been removed, but persisted in the 3 remaining cases in which the splenic artery had been tied. Splenectomy in 1 of these cases, $7^1/_2$ months after the first operation, corrected the hypersplenism.

All the surviving patients, previously invalids, are now fully employed.

Of the modifications used, ligation of the hepatic artery distal to the gastroduodenal branch, combined with splenectomy in the presence of hypersplenism, is the operation of choice. This operation has proved satisfactory in the limited period of follow-up.

We wish to thank Mr. John Gray, who operated on 1 of the patients and gave us much valuable advice and criticism.

ADDENDUM

Since this paper was written ligation of the hepatic artery has been performed in 8 further cases. In 2 of these it was done in the course of repeated massive hæmatemesis; after the operation there was no further bleeding. Among the remaining 6 cases there have been 2 deaths from massive necrosis of the liver; in 1 the portal vein was thrombosed, but in the other the vein was patent and there was no evidence of infection. In this last case it would appear that our fears that ligation women which affect the offspring Two of the contributions are from non American authors J Mulder, of Leiden, discusses influenza and J Waldenstrom, of Lund, the abnormal proteins in multiple myelomatosis A glance through the five volumes published since 1942 reveals how thoroughly the growing edge of medical knowledge is surveyed in this series The price, however, is a high one for nine articles

John Abernethy

A Biography JOHN L THORNTON, A L A, librarian, St Bartholomew's Hospital Medical College, London London Distributed for the Author by Simpkin Marshall 1953 Pp 184 25*s*

IT is unfortunately true that Abernethy is remembered for his eccentricities rather than for his sterling qualities, and an assessment of his contributions to surgery is overdue

His life was covered roughly by the reigns of George III and IV He first made his reputation by his ability as a teacher and, because his fame spread far and wide, he became the founder of the great medical school attached to St Bartholomew's Hospital He was also the founder of the British school of surgery based on physiology rather than anatomy, and he was the first of the great English surgeons of the last century to treat patients by expectant means rather than by operation These very attributes make him a less colourful and exciting personality than his contemporary Astley Cooper He has never been described as a brilliant operator, and he had little opportunity to become one, for he was a full surgeon for a few years only His dread of operating, in the days that knew not anæsthetics, was due to a sensitive nature that abhorred the infliction of pain His writings have little value today though they were considered vital additions to the literature of his period Thus it is that the most interesting parts of this biography are those which describe his rudeness to patients, and his quarrel with the Editor of the *Lancet*, who printed his lectures without his permission and in the embarrassingly exact words that he used His finer qualities were admired by his successors who reaped the benefit of his teaching and later appreciated the full significance of his work for surgery

Statistical Method in Biological Assay

D J FINNEY, M A, SC D, lecturer in the design and analysis of scientific experiment, University of Oxford London Charles Griffin 1952 Pp 661 68*s*

AS bacteriology and pharmacology become increasingly sophisticated there is a growing need for a rigorous statistical approach to the quantitative assessment of, for example, bacterial count or drug strength From the central themes of the analysis of variance and experimental design has developed the technique known as bio-assay at a speed which has called forth this companion volume to Dr Finney's *Probit Analysis* which was published last year Some overlap between the two is inevitable but the suggestion of duplication is more apparent than real

This volume gives a more general account of the relevance of different experimental designs to particular problems in the interpretation of quantal responses in potency estimation, and discusses the merits and limitations of the rapid analytical methods proposed by various authors Enough of the mathematical background is given for the book to be an intelligible introduction for someone who is statistician rather than biologist, but the sections are so arranged that a laboratory worker, prepared to take a certain amount on trust can extract the experimental plan and computational procedure which he needs for a specific problem To do that intelligently, however, he would need some background knowledge of statistical method and would be well advised to read through the chapters on the general arguments involved

Methods in Medical Research

Vol 5 Editor A C CORCORAN, M D, assistant director, Research Division, Cleveland Clinic Foundation, Cleveland. Chicago Year Book Publishers London Interscience Publishers 1952 Pp 394 57*s*

LIKE the previous volumes in the series, this book consists of short monographs on research methods in a small number of broad fields The emphasis is on technical detail, but naturally varies from one contribution to another, and applications of the methods described are given

The fields covered in this volume are methods for separation of complex mixtures of higher molecular weight substances, methods of renal study, and immunochemical methods for determining homogeneity of proteins and polysacchari- The first section contains useful monographs on chromatography, electrophoresis, and ultracentrifugation The methods of renal study range from bio assay of antidiuretic substances through clearance techniques to the production and measurement of experimental hypertension There are 26 monographs in this section, and the main trends of renal research are well represented on the level of methodology The third section, edited by Melvin Cohn, consists of three detailed monographs on the production, separation, and assay of antibodies

This volume should fulfil the hopes of its editor by finding its place " in laboratories rather than in libraries " The monographs are authoritative and clearly written for the most part, and the value of many of them is enhanced by editorial comment at the end

Practical Management of Pain in Labour

W D WYLIE, M B Camb, M R C P, D.A, anæsthetist, St Thomas's Hospital, London London Lloyd Luke Medical Books 1953 Pp 148 18*s* 6*d*

THERE can be few anæsthetists who can write about anæsthesia in labour with the confidence and understanding which Dr Wylie shows here He has produced what must be one of the best practical books on the subject available today He not only deals with the practical difficulties encountered and the apparatus used for analgesia and anæsthesia in normal and abnormal labour but also gives just enough about the anatomical and pharmacological parts of the subject to assist the reader in using the techniques intelligently A short list of helpful references is included at the end of each chapter, so that if the text is insufficient the reader can refer to original papers for detailed descriptions of the various methods The last two chapters are devoted to local anæsthesia and to therapeutic blocks for conditions such as venous thrombosis Caudal anæsthesia is dealt with adequately, but perineal and vulval blocks and local infiltration for cæsarean section are described more briefly, for these techniques are more within the province of the surgeon than of the anæsthetist the illustrations are clear and useful, and the pictures of apparatus are grouped together in the middle of the book Every doctor who looks after women in childbirth will find this book of value

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Biochemistry in Relation to Medicine (2nd ed Lond Longmans, Green 1953 Pp 524 30*s*)—It is n long since we welcomed the first edition of this exce elementary text for medical students by Dr C W Car and Prof R H S Thompson The new edition is as l as the old, and it contains new chapters on the metabol of lipids and proteins, and the accounts of carbohydra metabolism, sterols and steroid hormones, plasma prot electrolytes, vitamins, hæmoglobin, and acid base equilib have been largely rewritten The approach is simple a essentially empirical while the inclusion of exercises a methods for the estimation of important chemical subst (some not commonly included in elementary books) en that the more strictly chemical aspects of the subject re their fair share of attention The number of references more than doubled and now exceeds 1200, and the p of the book has increased only in proportion to its size

Poliomyelitis *Papers and Discussions presented at Second International Poliomyelitis Conference* (London J Lippincott 1952 Pp 555 60*s*)—In September, 1951 published a short report of the second International ference on Poliomyelitis, held that month in Copenh This volume presents, with every grace which fine typ paper and skilful blockmaking, can supply, a full accou the occasion In his preface Dr Morris Fishbein, chair of the committee on publications, notes that the procee of the first conference held in 1948, have been widely c lated, and are to be found in most of the medical librar the world This handsome volume will take its place b them as a permanent record of the stage our knowledge reached when the speakers met modified filter and to reverse the attachments to the glass tubes which enter the bottle, so that it may be used in the upright instead of inverted position (fig. 1). This reduces the possible mess should the stopper blow out of the bottle, but actually a simple clip is used to prevent this happening. A more elaborate apparatus can easily be made up from ordinary transfusion sets, with the addition of a Y-tube, a three-way tap, and a sphygmomanometer (fig. 2). With this, blood or saline solution can be run in at will, and continuity in the administration of blood is more easily maintained. Furthermore, readings of the intra-aortic blood-pressure, and also of the pressure at which blood is delivered to the needle, can be made.

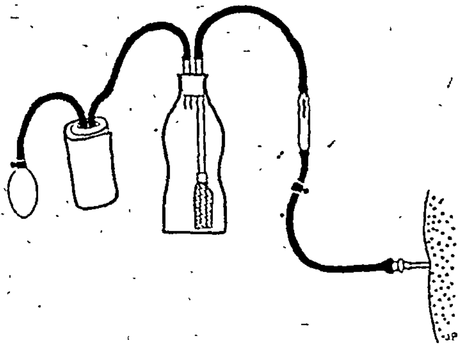

Fig. 1—Simple apparatus, with bottle upright, for intra-aortic blood-transfusion.

If the manometer pressure is kept 200 mm. Hg above the mean aortic pressure, a pint of blood can be delivered in three minutes. In most cases a rate of about one pint in five minutes was used, and two pints was the largest quantity required to restore the blood-pressure to normal and to give a pulse of good quality. The blood-flow through the drip chamber usually has a pulsatile character which confirms that the needle is in the aorta. If there is any doubt, the needle is momentarily disconnected and the retrograde flow inspected.

At the completion of the transfusion the needle is withdrawn about 1 cm. to allow the blood which escapes from the puncture in the aorta to leave the body instead of forming a hæmatoma. When the flow ceases, as it does in a minute or less, the needle is withdrawn.

In children and infants smaller and shorter needles without the step are used.

RESULTS

In all, 20 patients, ranging in age from 2 days to 84 years, have been transfused by the intra-aortic route, and in 3 of these the transfusion has been repeated. Owing to the serious nature of the illness, there have been some fatalities; but in only 1 case did the transfusion appear to have a deleterious effect. In this case, an infant with recurrent intestinal obstruction, a temporary improvement in the blood-pressure was followed by a fall despite continued transfusion, and the infant died with signs of heart-failure. It was thought that possibly too large a transfusion had been given, though necropsy provided no evidence of this. Another patient, moribund from a perforated peptic ulcer combined with hæmatemesis and superimposed on advanced phthisis, rallied only temporarily. In all the others there was a dramatic and rapid improvement in the general condition. The blood-pressure rose quickly, even with as little as 200 ml. of blood; the pulsations became stronger, and the colour of the lips and face improved rapidly. Several patients stated immediately that they felt very much stronger.

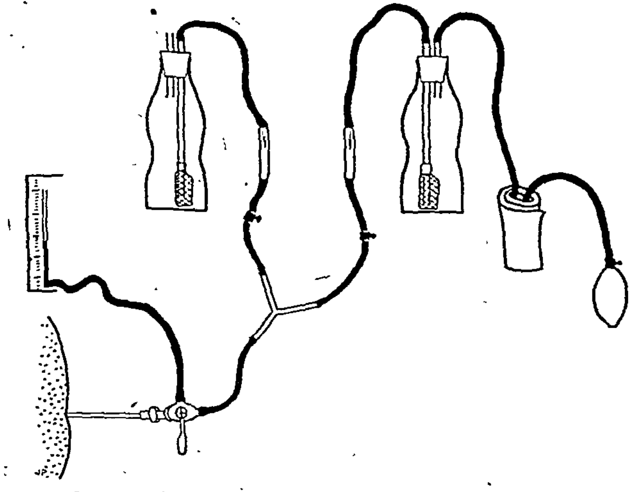

Fig. 2—More elaborate apparatus for intra-aortic blood-transfusion.

No pain in the back was experienced, apart from the transient discomfort during the insertion of the needle and slight backache for a few days in a few patients. The commonest complaint was a tingling in the legs and feet, which passed off as soon as the transfusion ended. This was at first attributed to the use of cold blood, producing vasospasm either in the lower limbs or spinal cord; and, indeed, the first case showed much pallor of the skin of the thighs and buttocks, followed by hyperæmia when the transfusion ended. But the symptoms are felt even when the blood is warmed before infusion. My colleague, Dr. M. D. Milne, has drawn my attention to the paræsthesia experienced with high concentrations of citrate in the blood, and it seems very probable that while infusion is in progress the blood in the lower limbs will contain enough citrate to produce tingling.

Some examples may serve to illustrate the use of the method.

The first case was that of a baby 2 days old and moribund from congenital obstruction, in whom attempts to introduce blood into veins and into the superior sagittal sinus had failed. An aortic transfusion of 50 ml. was given quickly and easily, and was repeated after an exploratory operation.

A woman had a hæmoglobin level of 2 g. per 100 ml. owing to continued hæmorrhage from an inoperable carcinoma of the bladder. After rather heavy premedication her blood-pressure fell and her pulse became impalpable, with the result that blind needling of the femoral artery proved impossible. She had gasping respiration and appeared on the point of death when the aortic transfusion was set up. At that stage the mean aortic pressure was 40 mm. Hg. After 250 ml. of blood had been given quickly, the pressure rose to 60 mm. Hg, and the pulses were palpable; and after 500 ml. the pulses were of good volume, the blood-pressure was 90 mm. Hg, and the lips had regained a fair amount of colour.

In 4 cases repeated hæmatemesis from peptic ulcer had reduced the patient to a poor general condition, with low blood-pressure and a rapid thready pulse. After the transfusion of $1^1/_2$–2 pints of blood their blood-pressure, pulse, and general condition were so much improved that immediate partial gastrectomy was considered feasible and was successful.

All the other patients felt and looked greatly benefited by the intra-aortic transfusion.

DISCUSSION

The aorta has many advantages over the peripheral arteries as a site for transfusion. It is constant in position and is relatively fixed by the lumbar arteries. It contains little muscle tissue and so cannot go into spasm, and its width and the rapidity of its blood-flow are sufficient to preclude any chance of obstructive thrombosis resulting. The aorta can usually be entered in a few seconds, and its depth from the surface and the elasticity of its walls prevent the needle from shifting once it is in position. It has been argued that in older patients atheromatous plaques might impede the passage of the needle or might be detached and become selection is desirable. The new *British Pharmacopœia* provides a reminder that the proportions of the components of mixed vaccines such as TABC (typhoid and the three paratyphoid groups A, B, and C) are already officially defined. In the past the criteria considered in determining the composition of mixed vaccines were the relative severity of the various diseases concerned and the frequency with which they occurred. It is now evident that with a mixed prophylactic other factors, such as the comparative immunising potency of the constituents and the immune state of the population, should be considered. The practitioner will need guidance on the choice of a suitable mixture of prophylactics; and the conclusion seems inescapable that an expert committee should tackle the difficult task of advising on the composition of approved combined prophylactics. Perhaps the biological products committee of the British Pharmacopœia Commission is the appropriate body, since it already defines the composition of official biological preparations. In any event information from all sources should be collated in order to prevent further unsuitable mixtures being brought into general use.

Exit Extrapleural Pneumothorax?

In pulmonary tuberculosis the results of treatment cannot be assessed quickly. Even with a definitive procedure such as thoracoplasty or resection, several years must pass before a balanced estimate can be made. With such operations as intrapleural or extrapleural pneumothorax, the success of which depends not only on the initial operation but on maintaining pulmonary collapse by repeated air refills, the time required is yet longer. The well-being of many patients while the lung is kept collapsed is very pleasing, but this limited success does not necessarily betoken final victory. With both methods the collapse obtained is, as a rule, temporary; and sooner or later either the lung must be allowed to re-expand or some further step must be taken to secure its permanent collapse.

Patients treated by extrapleural pneumothorax often have to submit to subsequent thoracoplasty. In some centres[1] efforts have been made to avoid such a sequence by resorting to oleothorax; but this operation has not become generally popular, principally because of the fear of late fistula formation. Nor has the introduction of plastic materials directly into the extrapleural space[2] proved a satisfactory alternative. Apart from the long-term problems, extrapleural pneumothorax has caused much concern on account of the high incidence of postoperative complications; even with skilled surgery, hæmorrhage and tuberculous infection of the space have been disturbingly common. Attempts to prevent or minimise the consequences of severe bleeding into the space have had some success,[3-5] and chemotherapy has helped to counter both tuberculous and non-tuberculous infection; but even so the method clearly has only a limited value, and most surgeons have concluded that thoracoplasty gives a much more satisfactory result and that extrapleural pneumothorax should be undertaken only when thoracoplasty is contra-indicated. This has led to the employment of extrapleural pneumothorax in two quite different types of case where intrapleural pneumothorax has failed: first, where deformity is especially undesirable as in the growing adolescent; and, secondly, in the patient with bilateral disease where major surgery is either required or has already been done on the other side. It seemed that here extrapleural pneumothorax, because it preserves the integrity of the chest wall and thus causes little impairment of respiratory function, really had a sure place in treatment; but since the introduction of subcostal, extraperiosteal plombage the question has been whether it should have any place at all.

Strieder and Gaensler,[6] of Boston, suggest that extrapleural pneumothorax is the procedure of choice only for "patients with pulmonary insufficiency due to previous collapse or resection on the opposite side and for patients for whom surgical treatment of the other lung is anticipated in the near future." The Boston workers divide their series of 47 cases from the point of view of indications into two groups; but unfortunately they do not specify clearly the relative incidence in these two groups of complications and poor results. Baldry et al.[7] have shown that this information is essential for assessing the value of the operation, since fibrosis or otherwise unsuitable disease greatly increases the incidence of serious complications and diminishes the chance of a satisfactory result. Nor is it manifest why Strieder and Gaensler chose extrapleural pneumothorax rather than extraperiosteal plombage. Plombage might seem the happier choice for several reasons, including the slighter risk of hæmorrhage, easier postoperative management, and more permanent control of the disease; and the limitations of plombage regarding fibrotic lesions and unsuitable cavities apply at least equally to extrapleural pneumothorax. As regards effect on respiratory function, it seems unlikely that extrapleural pneumothorax can claim any significant superiority. Its one possible advantage is its very impermanence; but this is contingent on overcoming all the hazards and on maintaining satisfactory healing after re-expansion—a tenuous basis on which to retain it as a modern therapeutic weapon.

Extrapleural pneumothorax is still commonly practised on the Continent[8]; but in this country it is rapidly being replaced by subcostal, extraperiosteal plombage, the immediate results of which are more reassuring, and which also offers better hope of permanent control of the lesion. Laird and Stephens,[9] for example, have abandoned extrapleural pneumothorax in favour of the 'Polystan' sponge operation. Plombage, it is true, has its own problems as regards indications, technique, postoperative management, and complications; and the long-term results are still awaited with some trepidation. Nevertheless confidence in it is increasing so rapidly among both doctors and patients that it is invading the field not only of extrapleural pneumothorax but also of the standard thoracoplasty and, less firmly, of ordinary intrapleural pneumothorax.

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months previously. The animal was killed, and a piece of infected omentum, removed with sterile precautions, was homogenised in the Waring blender. The material was then diluted with saline and 1·5 ml. was injected intraperitoneally into each of 40 rats. Films of the suspension showed about 20 acid-fast bacilli per field ($^1/_{12}$ in. oil-immersion objective and × 6 eyepiece).

The animals were female white rats weighing about 160 g., divided into four groups, each of 10 rats. The mean weights of the four groups did not differ appreciably. Observations made before the start of the experiment determined the average amount of a standard diet (M.R.C. diet no. 41) normally eaten each day by a group of rats. This amount, pulverised and throughly mixed with the drug, was reconstituted into cubes and fed to the animals under treatment. The preparation of isonicotinic acid hydrazide used was 'Pycazide.' The daily dose was 20 mg. per kg. body-weight.

The groups were lettered as follows:

Group A.—Untreated controls.

Group B.—Those receiving isoniazid for four weeks, starting on the day of infection.

Group C.—Those receiving isoniazid for twenty weeks, starting on the day of infection.

Group D.—Those receiving isoniazid for four weeks, starting four weeks after infection.

RESULTS

All the rats that died were fully examined, and microscopic preparations were made from the omentum and other organs showing lesions. The results are shown in the accompanying table. Intercurrent disease appeared in groups B and D, and the table therefore shows separately deaths due to rat leprosy and deaths due to other causes. All the rats that died from causes other than rat leprosy had large abdominal abscesses from which proteus or *Bacterium coli* was isolated. The occurrence of this lesion in 12 rats in groups B and D may have been assisted by cannibalism of the animals first succumbing to it. It is possible that these lesions are not entirely independent of rat leprosy and that they may represent leprosy lesions which regressed and later became secondarily infected with gram-negative bacilli; but a careful microscopic search of the walls of these lesions revealed only an occasional acid-fast bacillus in some of the animals. The absence of these "non-specific" lesions in group C might, on this hypothesis, be correlated with the longer period of treatment with isoniazid; but clearly this question requires further investigation. The rats that died of rat leprosy all had very extensive lesions, as described above, and films from these lesions showed hundreds of acid-fast bacilli in every field.

CAUSES OF DEATH IN RATS DYING AT VARIOUS TIMES AFTER INFECTION WITH RAT LEPROSY

Weeks	Group A		Group B		Group C		Group D	
	Rat leprosy	Abdominal abscesses	Rat leprosy	Abdominal abscesses	Rat leprosy	Abdominal abscesses	Rat leprosy	Abdominal abscesses
0–4	..	..	..	..	..	..	..	..
5–9	..	..	..	1	..	..	..	1
10–14	..	..	..	1	..	..	..	2
15–19	..	..	..	..	..	..	..	1
20–24	..	..	..	3	..	..	..	1
25–29	2	..	..	..	..	..	..	..
30–34	4	..	..	..	..	..	..	1
35–39	2	..	2	..	..	..	..	..
40–44	1	..	..	1	..	..	..	..
45–46	1	..	..	..	..	..	..	..
Totals	10	..	2	6	..	..	..	6

At the beginning of the experiment there were 10 rats in each group.

In the forty-six weeks that have elapsed since infection, all the untreated rats have died of rat leprosy. All the rats that received isoniazid for twenty weeks are alive and appear to be in good health so far. In groups B and D respectively, 8 and 6 rats died at various times from the 9th week onwards, but only 2, both in group B, showed signs of rat leprosy. No deaths from rat leprosy occurred before the 25th week. Of the 20 rats that had some treatment and survived to the 25th week, only 2 died of rat leprosy, compared with 10 out of 10 in the untreated control group.

DISCUSSION

Comparison of the results observed in groups A and C makes it clear that the prolonged course of treatment with isoniazid had had a beneficial effect on the course of the disease. The experience of the other two groups suggests that shorter courses may also be effective. Observations made during the treatment of tuberculosis with isoniazid show that resistant organisms may appear. For this, among other reasons, the surviving rats will have to be observed for many more months. The results, along with other work work in progress, will be reported later.

A preliminary report on the present stage of the experiment has seemed justified, because Goulding et al. (1953) have recently published the results of a trial of isoniazid and other drugs on mice infected with *Myco. lepræ murium* by the intracorneal route, and others will probably contemplate making further tests of isoniazid in rat leprosy. Goulding et al. found that the drug showed a striking suppressive effect on intracorneal infection. Perhaps the trial now reported, in which a systemic infection was produced in the natural host by intraperitoneal inoculation with a massive dose of rat leprosy bacilli, provides a more impressive test of the effect of isoniazid.

Since this work reached its present stage, two other reports on the effect of isoniazid on rat leprosy have appeared. Chaussinand et al. (1953) found that the drug suppressed the infection in rats injected subcutaneously, treatment being started either the following day or, delayed until the 17th day. Barnett and Bushby (1953), who inoculated white mice intravenously and observed them for 180 days, found that isoniazid given throughout the experiment almost completely suppressed the infection. They give their reasons for considering that the action of drugs on *Myco. lepræ murium* may be of value in forecasting their activity in human leprosy.

SUMMARY

Preliminary results in a trial of isoniazid in experimental rat leprosy indicate that the drug has a beneficial effect on the course of the disease.

I wish to thank Dr. D. McAnally, of Herts Pharmaceuticals Ltd., for a generous supply of 'Pycazide,' and Mr. B. Madge for his efficient technical assistance.

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"One should remember also that everything that we value is connected with the transference of energy from places where there is much to places where there is little, and that this process is irreversible. When energy has become evenly distributed throughout the universe there will be no more life, and therefore no more philosophers. I leave it to each reader to decide whether this will be the millennium."—BERTRAND RUSSELL, *Manchester Guardian*, March 14, 1953, p. 4.

cautiously suggest the possible need for reassessing some of these pensioners in later life

"An important effect of our further studies is to suggest that amongst amputees and other classes of wounded there are some individuals who with the lapse of time reach a stage deserving of reconsideration. *In any such reconsideration* careful discrimination would be needed, as our conclusions are based on average tendencies and do not necessarily apply to any particular individual"

Of immediate relevance are some studies, by Dr Verne T Inman and his colleagues[2] in San Francisco, of the energy expended in displacing the centre of gravity of the body through space While the below-knee amputee is relatively normal from this point of view, the thigh amputee has to expend some 27% more energy for the same physical performance Such a man, in effect, walks 5 yards to a normal man's 4

An interesting point that emerges from the analysis is that major sepsis was also associated with a reduced liability to subsequent death from cancer, even allowing for the effect of an earlier average age of death on the incidence of malignant disease This obviously calls for further study

Dr A Hope Gosse, in a minority report supported by Dr W E Lloyd, denies that the evidence shows that the strain of wearing an artificial limb for thirty years increases the risk either of cardiovascular disease or of earlier death, and doubts whether one and the same statistical survey can show any true relation between previous sepsis on the one hand and cardiovascular or malignant disease on the other And he takes the robust commonsense view—on a matter in which his opinion carries great weight—that there is no reason why life assurance should not be offered to these patients and to amputees in general at normal or near-normal rates

For the present, therefore, the matter cannot be regarded as entirely decided Further investigation is called for by the committee, whose work is one more instance of the interesting and sometimes unexpected findings that may emerge from the statistical analysis of large numbers of detailed case records

INCREASES IN MATERNITY BENEFITS

THE changes in maternity benefits set out in the National Insurance Bill, presented to Parliament on March 17, give effect to the recommendations made a year ago by an advisory committee[3] One of the most important principles which the committee urged was that the woman who wished to have her baby at home should not lose by this decision, and the Bill introduces a new home confinement grant of £3 which will do something to meet the extra expenses which a domiciliary birth always entails The grant will be paid to mothers who are confined at their own expense and who do not occupy an N H S hospital bed

The Bill continues to offer different benefits to meet the differing needs of the housewife and the employed woman The first is the larger group, for six out of every seven who claim maternity benefits are housewives At present they receive a grant of £4 and a weekly attendance allowance of £1 a week for four weeks after the birth In future they will receive a lump grant of £9 (plus the £3 home confinement grant when appropriate), and this sum will be paid before or after the birth as the mother chooses

For the employed woman the changes are even more advantageous The advisory committee thought that maternity benefits, like sickness or employment benefits, should be payable only to women who chose to pay their own contributions, and that an employed married woman should no longer be eligible by right of her husband's contribution The committee hoped that the money saved in this way would go to enlarge the grant made to contributors The Bill gives effect to this restriction of claims, but safeguards for a transitional period the rights of women who have not yet had time to qualify The basic grant which an employed woman receives is increased from £4 to £9 (£12 if the confinement is at home) It also provides that her maternity allowance, now 36*s* a week, will in future be paid at the standard benefit rate, which at present stands at 32*s* 6*d* a week She will receive this allowance for eighteen weeks (instead of thirteen) and it will start eleven weeks before the expected date of her confinement (instead of six weeks). This allowance may be increased when the mother has dependents The effect of these changes will be that a woman who is doing paid work will receive £38 5*s* (or £41 5*s* if her confinement takes place at home) instead of £27 8*s* as at present

Minor changes in the number of qualifying contributions are also designed to bring maternity benefit into line with sickness and unemployment benefits But here, too, the woman who wishes to give up work earlier is offered help, for she may complete her qualifying contributions by paying the last thirteen at the non-employed reduced rates

A LONG-ACTING LOCAL ANÆSTHETIC

IN the treatment of pain, analgesics only stop a gap until the cause is disposed of, and the so-called "local anæsthetics" may perhaps be regarded in the same way With a duration of activity normally measured in hours, they allow ample time for various surgical manœuvres, and their effect may be prolonged, if need be, by giving with them vasoconstrictor drugs which delay dispersion from the site of injection A new preparation, 'Efocaine,' has now been devised, however, in which the span of local anæsthetic action has been considerably extended First developed in the United States,[1,2] it is a solution of 1% procaine base, 0 25% procaine hydrochloride, and 5% butyl *p* aminobenzoate at a critical level of saturation in propylene glycol, polyethylene glycol, and water It will remain stable at room-temperatures for more than three months Even after repeated intramuscular injections, the solvents used have produced no apparent local damage or systemic toxic effects

Dilution of this preparation with body-fluids at once brings about deposition of the aqueous insoluble anæsthetic base When this occurs after intramuscular injection an in-vivo microcrystalline depot is formed Absorption then takes place slowly and anæsthesia may be prolonged for days or even weeks In fact, the solution has the advantages of an insoluble suspension without the disadvantages in manipulating a suspension with syringe and needle It is claimed, but not completely confirmed, that injection of efocaine produces no local pain In the dosage recommended, only the medium and small nerve-fibres, with comparatively thin myelin sheaths, are blocked, thus pain and tactile sensibility are lost without interference with motor innervation Permanent nerve damage has never been detected

Acknowledging its efficacy and relative safety, what is the place in clinical practice for this remarkably long acting local anæsthetic? It is perhaps most useful for the relief of postoperative pain When the anæsthetic was given to 54 patients after a variety of operations, the results were "unsatisfactory" in only 3 cases[1] No examples of systemic toxicity or local tissue reaction were encountered The doses given did not exceed 15 ml Roualle[3] reported good results after operation in 8 out of 14 patients, and in another 3 the results were fair He considered that an accurate nerve block was more effective than local infiltration, because it was important to achieve adequate concentration in close proximity to the nerves supplying the area He suggested that the

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[2] See *Lancet* 1952, ii, 80

[3] *Ibid* i, 201

[1] Ansbro, F P Iason A H Shaftel, H F Halpern, A, Latteri, F S Bodell B *Anesthesiology* 1952 13, 306

[2] 'Efocaine' is now manufactured in this country by Me Crookes Laboratories Ltd

[3] Roualle, H L M *Brit med J* 1952, ii 1293

THE KIDD (ANTI-Jk^a) HÆMAGGLUTININ

A THIRD EXAMPLE

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A previously unidentified blood-group antibody, which was found to agglutinate the red cells of 77% of white inhabitants of Boston, Mass., was described by Allen et al. (1951). The antigen present in such red cells is known as the Kidd, or Jk^a, antigen, and the antibody as anti-Kidd or anti-Jk^a. Hunter et al. (1951) have reported the finding of an antibody of apparently identical specificity. The discovery of a third example is now reported in a Scotswoman.

When her blood was examined on Sept. 15, 1950, Mrs. C., aged 29, was found to belong to group O, R_1r (CDe/cde). She was suffering from debility and gross anæmia after giving birth to apparently healthy twins a few weeks before. Her previous obstetric history showed six full-term normal births and one stillbirth, the latter with no signs of hæmolytic disease of the newborn. She had never received a transfusion or injection of blood.

Irregular antibodies were discovered on routine direct matching of donor bloods against the patient's serum, and it appeared that at least two such antibodies were present in the serum. One of these agglutinated saline suspensions of red cells of all bloods carrying the Rh antigen E and was most active at 37°C. Of the panel of cells which were not agglutinated in saline suspensions by the patient's serum the majority gave a positive indirect anti-globulin (Coombs) test, but a few gave clear negative results. These antibodies were best detected at 37°C. In addition to these two antibodies the patient's serum contained anti-P active only at temperatures about 4°C.

The patient's complete blood-groups were:

ABO	*Rh*	*MN*	*S*	*P*	*Lu*	*Kell*	*Le^a*	*Le^b*	*Fy^a*
0	R_1r (CDe/cde)	M	–	–	–	–	–	+	+

Her serum was examined against an extensive panel of cells by the anti-globulin technique. The frequency of negative reactions was about 10%, and the unidentified antibody detectable by this technique did not appear to conform to any known antibody.

At this time some serum from Mrs. Kidd (Allen et al. 1951) became available. Mrs. C. was found to be Kidd-negative, whereas her husband and all her children were Kidd-positive. At the same time most of the members of the staff of the Lister Institute were tested with anti-Kidd serum by Dr. R. R. Race and Dr. Ruth Sanger. Dr. Race and Dr. Sanger also absorbed the anti-E from some of the serum of Mrs. C., using E-positive Kidd-negative red cells, and tested some of the same staff members with the resulting serum; they have kindly allowed us to make use of their results. We also tested some E-negatives with the unabsorbed serum. In both cases some individuals were selected because they were Kidd-negative. The numbers given, therefore, do not represent the true frequencies of the Kidd groups in the British population. In all, 54 unrelated persons were tested with anti-Kidd and with the absorbed or unabsorbed serum of Mrs. C.: 39 were positive with both and 15 negative with both; there were no discrepancies. The chance of such a situation occurring accidentally with two unrelated sera is infinitesimal, and there can be no doubt that Mrs. C.'s serum contains anti-Jk^a in addition to anti-E and anti-P.

In addition to the tests mentioned above, the serum of Mrs. C. was used to test samples from 105 Africans (all E-negative), of whom all but 5 gave a positive reaction (Ikin and Mourant 1952).

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ELECTROCARDIOGRAPHIC CHANGES AFTER NEPHRECTOMY

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Bundle-branch block (intraventricular block), at one time regarded as irreversible, may appear transiently in many forms of heart-disease, and may be temporarily induced in diseased hearts by such factors as tachycardia, infection, and anæmia (Sandberg et al. 1951). The electrocardiographic tracings reproduced here show that normal conduction replaced left bundle-branch block after nephrectomy in a patient with hypertensive heart-disease. This seems an unusual event, though electrocardiographic changes after sympathectomy for hypertension have been widely studied. Cardiac failure, for the relief of which the operation was planned, was only temporarily improved, but normal conduction persisted to the last tracing taken.

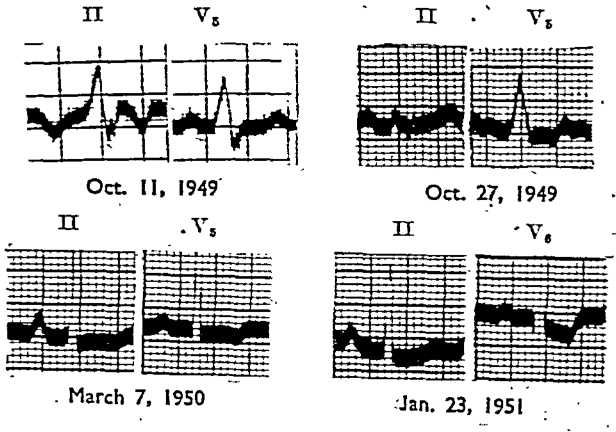
CASE-RECORD

A single woman, aged 35, was admitted to hospital on Oct. 8, 1949, with a history of shortness of breath for eleven months, anginal pain for five months, and œdema and orthopnœa for a week.

Examination showed a blood-pressure of 185/130 mm. Hg, cardiac enlargement with triple rhythm, numerous crepitations in the lungs, a palpable tender liver, and some sacral œdema. The diagnosis of hypertensive cardiac failure was supported by the radiological appearance of the heart. Electrocardiography on Oct. 11, 1949, showed left bundle-branch block with a QRS lasting 0·16 sec. in the standard limb leads (see figure), and delayed intrinsicoid deflection in the left precordial leads. Further investigation indicated that all that remained of the left kidney was a hydronephrotic sac.

Treatment and Progress.—Rest and digitalisation improved the cardiac failure to some extent, but an electrocardiogram on Oct. 27, 1949, showed little change (see figure). A left nephrectomy was done by Mr. Terence Millin on Oct. 31, 1949.

Postoperatively there was further improvement in the cardiac failure: triple rhythm was no longer audible, and the blood-pressure rose to 205/130 mm. Hg. Most striking,



Oct. 11, 1949 Oct. 27, 1949
March 7, 1950 Jan. 23, 1951

gallamine, or decamethonium iodide may be administered to inhibit reflex activity, or pentamethonium iodide or hexamethonium iodide as a ganglion paralysant, together with, say, thiopentone to bring about unconsciousness With the components of anæsthesia divided in this way, no single series of stages can give a reliable guide Indeed, the balance is not always smooth In a fully curarised patient the "anæsthetic" drug may be reduced so much that pain stimuli reach the higher centres of the brain and cause reflex vasomotor disturbance, which are *not* inhibited by a neuromuscular paralysant This may lead to blood-pressure changes, sweating, and circulatory disturbances, while the nightmare return of consciousness with the operation still in progress has occasionally been reported

No knowledge of the stages of anæsthesia will avert such mistakes Yet, presumably because it illustrates these different stages, ether is still commonly used for teaching Only a sound knowledge of the capabilities and limitations of each of the modern drugs will enable the administrator to choose wisely and to anæsthetise skilfully The actual administration calls only for venepuncture, but the subsequent care of the patient, in whom unconsciousness and reflex inhibition are achieved almost immediately, requires perhaps even more skill than does the continued administration of an anæsthetic by inhalation It would seem prudent to concentrate on teaching the sound use of intravenous anæsthetics with special emphasis on the care of the unconscious patient, in whom vital reflexes have been obtunded or inhibited

THE SECOND WORLD FOOD SURVEY

As soon as F A O was established by the United Nations it set about the task of assembling all the information in the world about agricultural production, and comparing this, country by country, with the food requirements of the people judged according to physiological standards The World Food Survey published in 1946, showed how much the war had disrupted agriculture and gave quantitative assessments of the gap, in many countries, between food needs and food supplies Six years later these balances have again been drawn up and are set out in the Second World Food Survey[1] This gives no ground for satisfaction or complacency, but is rather a challenge to activity World food production has indeed expanded since the war, but much of this achievement is merely a recovery from war-time devastation, and it is insufficient to meet the increasing demands of growing populations The number who are underfed increase Before the war 38 6% of the total population of the world lived in countries which did not receive sufficient food to allow a daily distribution of 2200 calories per head Now this proportion has risen to 59 5% This majority of human kind also receives less than 15 g of animal protein per head There is no doubt that at least three-fifths of the world do not get enough food to supply the physiological minima for health

On the bright side the report points out that "in the last few years consciousness that the world is one has grown space There is increasing realisation that the better off countries must assist the comparatively poorer nations, not merely from humanitarian motives, but also to safeguard their own living standards" Most men of sense and good will now realise the urgent need for developing agricultural resources in all countries, but most especially in the tropics further, it is widely appreciated that this can only be done by some temporary sacrifices by the better off The problems are essentially technical Here the report gives a few pointers It is optimistic about the possibilities of great increases in crop yields Rice yields, in particular, could ri 15–20% if the gap between modern scientific knowledg and primitive agricultural practices could be narrowed

The report is cautious about the possibilities of expanding crop areas There have been impressive succe in bringing new land under the plough, but such schemes need immense capital investment Finance must often be a major limiting factor There is a wide scope for spreading modern techniques in animal husbandr and in fishing The enormous amount of food waste is also pointed out Rats alone are said to eat 7 million metric tons of human food each year in the U S A., and insects perhaps double this amount Then again, farmers need to be offered proper incentives, but so far few countries have overcome the difficulty of encouraging the farmer to produce by paying him high prices and at the same time protecting the consumer in the towns

Although the survey presents a thoroughly disturbing picture of the world food-supply today, there are signs that the future may be brighter—what is being done in overcrowded Hong-Kong and Israel[2] shows that man has not lost his ingenuity

ABO BLOOD-GROUPS AND FERTILITY

RARELY a number of alternative genetic factors each of them not uncommon, may occupy a particular locus on a chromosome, and one would then expect one of the alternative forms to have some selective advantages and to replace the rest by natural selection, except for a small proportion maintained by mutations The best examples of such polymorphism in man are the blood-groups Death due to hæmolytic disease of the newborn from rhesus incompatibility tends to lower the frequency of whichever is the least frequent gene in the community—that for D or that for d The present dimorphism in the population of England and Wales might be due, as suggested by Haldane[3] and also Wiener,[4] to a recent mixture of predominantly rhesus positive and predominantly rhesus negative races This suggestion gained weight from the discovery that the Basques were predominantly rhesus-negative It is also possible, however, that the present position arises from a balance between the tendency for d to be lost through deaths from hæmolytic disease and a tendency for the gene for it to become more common from an increased fertility of those who possess it

In 1947 Waterhouse and Hogben[5] suggested, from an analysis of the recorded information on families in which the groups of mother, father, and child were given, that there was a pronounced deficit of A children of O mothers They attributed this to the early loss of A fœtuses from blood group incompatibility of mother and child Boorman,[6] however, in personal observations with Daley and Dodd, was unable to confirm this Struthers[7] suggested that the discrepancy might be due to the loss of A children not prenatally but in infancy He claimed that in a sample of children coming to necropsy in a Glasgow hospital there was a distinct excess of group A children, in all of whom there was post mortem evidence of bronchopneumonia

If selection of this kind is taking place against the gene for the A antigen, the population may not be in equilibrium, and the present proportions of A and O may be due to a recent mixture of a predominantly O race and a predominantly A race, but more probably the loss of genes for the A antigen is balanced by some countervailing advantage conferred by this gene Kirk et al[8] claim to have discovered in Australia some remark

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[1] Food and Agriculture Organization Rome 1952 Pp 59 Obtainable from H M Stationery Office 2s 6d

[2] See *Lancet* March 14, 1953 p 538

[3] Haldane J B S *Ann Eugen Lond* 1942 11 333

[4] Wiener A S *Science* 1942 96 407

[5] Waterhouse J A H Hogben, L *Brit J soc Med* 1947 1 1

[6] Boorman K E *Ann Eugen Lond* 1950 15 120

[7] Struthers D *Brit J soc Med* 1951 4 223

[8] Kirk R L, Kirk M Stenhouse N S *Ibid*, 1953, 7, 1

The absence of the gall-bladder may be explained in two ways:

(1) The hepatic diverticulum arises from the foregut to form the liver, the extrahepatic ducts, and the gall-bladder. The gall-bladder and the cystic ducts normally originate from this diverticulum as an outpocketing, but the failure of the latter development would cause complete absence of the gall-bladder and cystic duct.

(2) Alternatively, the absence might be explained by the failure of the gall-bladder bud to resolve from its solid embryological stage. In early embryonic life the gall-bladder is a hollow structure, but it has its lumen temporarily obliterated during the so-called solid phase through which such structures pass. The lumen is re-established in the normal organ, but an arrest in the obliterated stage would leave a structure invisible to the naked eye.

The literature supports our belief that congenital absence of the gall-bladder causes no alteration in function nor any symptoms. The symptoms that arise if cholangitis supervenes or a stone forms are similar to those of these complications when the extrahepatic system is normal.

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Reviews of Books

Local Analgesia: Abdominal Surgery

R. R. MACINTOSH, D.M., F.R.C.S.E., D.A., Nuffield professor of anæsthetics, University of Oxford; R. BRYCE-SMITH, B.M., D.A., first assistant, Nuffield Department of Anæsthetics, University of Oxford. Edinburgh: E. & S. Livingstone. 1953. Pp. 94. 22*s.* 6*d.*

VERY few teachers have the gift of understanding their pupils' difficulties. Professor Macintosh and his colleagues possess this rare faculty and they are demonstrating it to advantage in their series of books on local analgesia. The latest one makes no bones about explaining with crystal clarity to the surgeon or anæsthetist long past his student days, what is really simple anatomy to the 2nd M.B. student. Local analgesia is essentially a practical art, but seeing Miss M. McLarty's illustrations is the next best thing to being in the operating-theatre. All the classical blocks of the abdominal wall, the abdominal sympathetic system, and the hernia region are clearly and simply described. With such a combination of text and illustrations, the reader is almost assured of success even if he performs local analgesia but rarely.

Understanding Children's Play

RUTH E. HARTLEY, LAWRENCE K. FRANK, ROBERT M. GOLDENSON. London: Routledge & Kegan Paul. 1952. Pp. 372. 21*s.*

THESE authors are concerned to show in detail the contribution made by play to the development of personality and character on the one hand, and of the intellect on the other. They also want to show that, without turning themselves into amateur psychiatrists, teachers can extend their capacity to observe and interpret children's play.

> "This understanding is essential if teachers are to have insight and be helpful in what they do—and proof that it can be acquired is shown by the increasing number of teachers who have learnt to think of their function in more understanding ways."
>
> "Teachers have usually accepted expressions of pleasant and happy emotions, but there are other emotions that are equally strong and real. These other emotions have been almost universally banned from the class room . . . but no normal child is completely free of the adjustive devices that are labelled 'problem behaviour.'"

It is asking a great deal of ordinary adults to ask them to accept expressions of unpleasant emotions directed at themselves. If, however, the children can express these in play, the adults can learn to understand what is being expressed and to tolerate what they understand. Play serves many therapeutic and educational functions, and these are examined in detail. The book is valuable in that it sets the reader thinking about ends rather than means and in that it will provoke thought even in those who do not agree with its basic principles. It is addressed to teachers, but all workers with young children, including parents, will find it well worth reading.

Thoracic Surgical Management

J. R. BELCHER, M.S., F.R.C.S., consultant surgeon, London Chest Hospital; I. W. B. GRANT, M.B., M.R.C.P.E., assistant physician, Edinburgh Northern Hospitals. London: Baillière, Tindall, & Cox. 1953. Pp. 196. 16*s.*

MOST modern textbooks on thoracic surgery are concerned with the higher flights of technical achievement, devoting little space to the problems of preparation and after-treatment which play a vital part in this branch of surgery. Mr. Belcher and Dr. Grant set out to give a conscientious and accurate account of methods of investigation and of postoperative treatment and complications, leaving out all reference to operative technique and selection of cases. Theirs is therefore a specialised book, but one which will appeal to the large group of people—from housemen upwards—who are called on to look after patients undergoing thoracic operations. Admittedly, not everyone will agree with all the details, but the experiences of the authors can be taken as representing the basic teaching and practice of the London chest hospitals.

The accounts of bronchial anatomy, bronchography and bronchoscopy, and the technique of pleural aspiration are particularly well done. There is perhaps some unnecessary detail in such lists as those describing apparatus, and on occasions the authors have found it difficult not to go into technical details which, a priori, they wished to avoid. The list of operative complications makes formidable reading; but these events can and do occur, and must be remedied as speedily as possible along the lines the authors suggest.

The line drawings make effective illustrations, with one or two small exceptions. For example, in fig. 33 the drainage tube projects too far beyond the safety-pin, and in another place the operator's hand shows polydactyly.

If the authors have found it difficult to limit the scope of their thesis or to obtain an ideal balance, they can rest assured that they have provided a work which is full of common sense. It is the only book which gives full details and guidance on the management of thoracic surgical cases and indicates the thorny passages along which this branch of surgery has evolved—a feature that is often forgotten by the surgeon who is not continually operating on the chest.

Advances in Internal Medicine

Vol. 5. 1952. Editors: WILLIAM DOCK, M.D., Long Island College of Medicine, Brooklyn; I. SNAPPER, M.D., Mount Sinai Hospital, New York. Chicago: Year Book Publishers. London: Interscience Publishers. 1952. Pp. 464. 80*s.*

THIS fifth volume maintains the standard of its forerunners.

Richard Bing discusses the complicated subject of cardiac catheterisation, A. H. Blakemore reviews portal hypertension and its treatment, and A. B. Gutman gives an interesting account of the derangement of purine metabolism in gout. Two subjects of topical interest are an account by Lyons and Love of the clinical aspects of ganglionic and adrenergic blocking agents and one by M. H. Bass on those diseases of pregnant

The Wider World

OBSERVATIONS ON THE EPIDEMIOLOGY OF STONE IN THE BLADDER IN THAILAND*

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THE medical visitor to Thailand is soon informed that stone in the bladder is a common complaint in parts of the country But precise information about the epidemiology of the condition is hard to obtain and the only literature in English which I could find was a report of an address given to the Thailand Research Society in 1940 by Dr Pyn Muangman, director of the radiology department in the Siriraj Hospital in Bangkok In this he records that large numbers of persons come to Bangkok for operation, especially from the north-eastern provinces, Korat and Ubon He sums up local opinion as to ætiology thus "Every factor ideal for stone formation, seems to be present (1) deficient food, (2) excessive calcium intake from drinking water, and (3) vitamin D excess from the sun's rays"

The opportunity arose to visit Ubon province during November and December, 1951, in company with Dr Amara Chandrapananda, a nutritionist from the Thailand department of public health I had already spent some time in Bangkok and toured peninsular Thailand (fig 1), going as far as Yala near the Malay border, and had satisfied myself that there was no undue incidence of bladder stone either in the capital or in the south

Ubonrachatani is the capital of the most easterly province of North-East Thailand The population of the province in 1947 was recorded as 850,000 The total area of the province is 2,221,900 hectares, but less than 10% of this is cultivated The soil is poor and there is much shifting cultivation, with land left fallow for many years, the large area of uncultivated land, together with a sparsity of people, gives the countryside an appearance reminiscent of parts of Africa and quite unlike that of neighbouring countries in South-East Asia Rice is the principal crop and according to official figures accounts for 99 5% of the area shown Tobacco, maize, and cotton make up the tiny remainder Visits to farms and villages did not cause me to dispute this figure Rice and only rice can be seen growing in the fields There are still considerable areas of uncut forest, which provide minor industries for the people Trees are tapped and supply a variety of resins, which are used for making torches, for waterproofing, and so on Cattle are kept as beasts of burden and raised for export to central Thailand they are never milked and seldom killed and eaten Goats are seldom seen Should they be introduced and flourish, the effect on the countryside is likely to be disastrous and the parallel with Africa soon complete Cattle manure is collected under the houses and used to fertilise the mulberry gardens and the tobacco patches Cotton does not grow well and the people are too poor to buy it, perforce many must wear homespun silk During the rains there is an abundant supply of fish

Ubon has three seasons The hot weather lasts from March to May, the monsoon from May to October, and a cold season from November to February There is no meteorological station in the province, but in Udomthani, which is nearby, a yearly rainfall from 1000 mm to nearly 2000 mm is recorded This is often concentrated into a short space of time and may give rise to widespread floods, isolating many districts for weeks together The cold weather is delightful the days are dry and sunny and at night the temperature drops to about 12°C In the hot weather there is little or no rain, temperatures rise to over 40°C, and it is easy to imagine that much of the landscape is reduced in appearance to a desert

The peasants are nearly all Thais who migrated from the North generations ago In the town many of the merchants are recent immigrants from China They rarely suffer from stone The Thais themselves are a cheerful people, who perpetually seem to put a brave face towards their poverty They are Buddhist by religion, and the saffron-robed priests are a feature of every village The monastery compound usually provides a school many of the village temples are fine examples of rural craftsmanship and taste The people suffer from few, if any, dietary prohibitions Although rice (and in season fish) is their sole real food, it may be garnished with almost anything which is either animal or vegetable Nothing else is systematically cultivated, but almost anything that the countryside presents may be eaten A full account of local agriculture with beautiful illustrations has been given by Pendleton (1943)

UBONRACHATANI HOSPITAL RECORDS

Ubon town has a hospital containing 100 beds and is well equipped for surgery It is the only government hospital serving the 850,000 inhabitants of the province There is a well-kept operation register Dr Chovit Chutikom, the surgeon-in charge, had been through the register for the period 1936–42, and in the seven years 1250 operations for vesical calculus were recorded Through the courtesy of Dr Chutikom, I went through the register for 1948–51 and found that during the four years 610 operations had been performed on persons resident in the province in addition there were a few

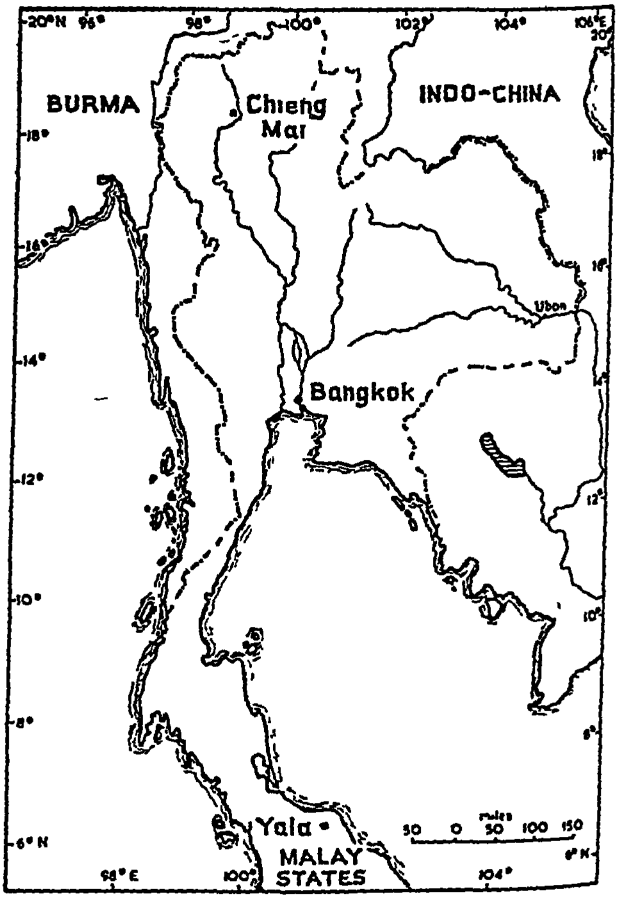

Fig 1—Map of Thailand.

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* This study was made whilst on a visit to Thailand as a nutrition consultant on behalf of the Food and Agriculture Organisation of the United Nations

THE LANCET

LONDON: SATURDAY, MARCH 28, 1953

Combined Prophylactics

SUCCESSFUL protection from the cradle to the grave against infectious diseases, once a pipe-dream of the immunologist, is rapidly becoming feasible. In a single decade immunisation has eliminated diphtheria as a major cause of death and disease among children; and clinical trials are proceeding now to discover the best form of vaccine for the prophylaxis of another scourge of young children—whooping-cough. Likewise B.C.G. vaccination will, we hope, lessen the incidence of tuberculosis. During the late war many servicemen were immunised against tetanus, typhoid, paratyphoid A, B, and C, cholera, and yellow fever. The list of successful prophylactics is growing, but if each is to be given in a separate immunisation course childhood will be punctuated with needle-pricks. As an alternative to turning children into pin-cushions there is the blunderbuss method by which the syringe is loaded with a mixture of immunising agents in the hope that a single shot will be effective against all diseases. The advantages of using a combined antigen are not confined to the person receiving the injection. Both the doctor who has to give the inoculations and the administrator who has to plan the immunisation campaign, make the arrangements, and record individual immunisation histories will appreciate any relief that can be afforded them.

It is necessary, therefore, to inquire into the efficacy of multiple prophylactics. The first question is whether some constituents of a combined antigenic mixture interfere with the immunising effects of others, or whether the presence of other antigens stimulates antibody production. Some of the first answers to this question were very encouraging. RAMON[1] concluded that the addition of typhoid-paratyphoid vaccine to tetanus toxoid enhanced the tetanus immunity, and this finding was confirmed by MACLEAN and HOLT.[2] Similarly, synergistic effects have been noted with various mixtures of diphtheria, tetanus, and staphylococcal toxoids, and typhoid and pertussis vaccines; each antigen was found to be more effective in combination than alone. HEKTOEN and BOOR[3] used a mixture of 35 different antigens and observed the formation of precipitin against almost all of them. The enhancement of antigenicity by the addition of other antigens may be due to various factors. Adjuvants such as alum increase the immunising potency of diphtheria toxoid[4] either by entraining the antigen and preventing its rapid elimination or by stimulating antibody-forming elements of the body. In recent years the influence of hormones on antibody production and sensitisation has been recognised, and some of the non-specific effects of antigens on antibody production may be traced to pituitary adrenocortical stimulation.

Unfortunately, however, the use of multiple antigen mixtures has its pitfalls, and the evidence is not fully in its favour. One of the important points in immunisation is the avoidance of side-reactions, and it seems possible that toxic reactions are commoner with combined prophylactics; the combined subliminal reactions of some immunising agents might be expected to add up to appreciable effects in some people. Little is yet known on this point, and it is important to gather further evidence. A further disadvantage of combined prophylactics that needs further exploration is the possibility that the presence of some antigens may interfere with the immunising effects of others. There must obviously be a limit to the antibody-forming capacity of the body, and one potent antigen may swamp the effects of relatively feeble antigens in the same mixture. In a combined diphtheria/scarlet-fever prophylactic excess of scarlet-fever toxin interfered with the development of diphtheria immunity,[5] and the responses to a combined diphtheria-tetanus prophylactic were found to be lower than to the two prophylactics administered separately.[6] With a combined diphtheria-tetanus-pertussis-typhoid preparation development of diphtheria immunity was unsatisfactory.[7] Thus the components of a combined prophylactic need to be chosen with care, and both the quality of the components and the relative amounts of each are important. Some of the factors involved have been examined by BARR and LLEWELLYN-JONES[8] in work with guineapigs immunised with a mixed diphtheria-tetanus prophylactic and with a combined tetanus-typhoid-paratyphoid prophylactic. These workers emphasise that it is important not only to select carefully a suitable batch of each component for incorporation into a combined prophylactic and to blend appropriate amounts of each, but also to match the composition of the blend to the previous immunisation history of the population to be treated. If an individual already has an established primary immunity to one component of the combined prophylactic, the immune response to the secondary stimulus may be so overwhelming that the effects of other antigens will be swamped. A blend of prophylactics suitable for some members of the population may prove unbalanced for others who are already partly immune. For mass-immunisation it is obviously impossible to determine the probable immune response of each individual to each antigen and to prescribe for each an appropriate blend of prophylactics. Yet the premature use of inappropriate blends is likely to result in inadequate immunity and the subsequent discrediting of immunisation in general.

Various mixtures of toxoids and vaccines are already on the market, and some guidance in their

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softer than Thames water Water can never contribute an excess of calcium to a diet beyond physiological tolerance It must be emphasised that McCarrison (1927), in his experimental production of stone in the bladder of rats, used a highly artificial mixture of foods devoid of vitamin A and with a great excess of calcium No natural diet possesses this combination

Swift Joly (1929), in his great review of the distribution of bladder stones throughout the world, has shown that in Western Europe and in the the United States of America there has been an enormous change in the incidence of vesical calculi since the 17th and 18th centuries, when the great itinerant lithotomists flourished Bladder stone in childhood is now a rare disease That an all-round improvement in the diets of children has been an important general factor in this decline is not improbable But the absence of a factor of proven prophylactic value need not by itself cause the onset of a disease The widespread distribution of deficiency diseases throughout South-East Asia contrasts with the restricted foci of bladder stones and makes a direct causal relationship unlikely A similar argument applies to climate effects Ubon, like other stone areas such as parts of the Punjab and Persia, has a hot dry season Urinary outputs must inevitably be reduced and some concentration of urinary constituents result This might predispose to stone formation But most hot countries are free from stone and in the past it has been common in such places as Iceland

An interesting speculation is that a positive noxious factor in the diet might be the responsible agent Undoubtedly the children of Ubon province eat many strange foods One such, consumed only on occasions, might contain a poison which upsets the delicate balance of urinary colloids which, as Butt and Hauser (1952) show, help to keep the supersaturated electrolytes in solution An interference with surface tension within the bladder might follow and allow the stone to form An up-to date review of this work has appeared in the *Lancet* (1953)

Another possible mechanism is that a poison might interfere with either the production or the excretion of citric acid by the kidney Shorr (1945) has brought forward the claim that " citric acid is not a waste product but a useful urinary constituent by virtue of its capacity to enhance calcium solubility " He has shown that in certain circumstances, notably in hyperparathyroidism, there is a close parallel between levels of urinary calcium and urinary citric acid Œstrogens are also able to raise the urinary output of citric acid Further, Scott et al (1943) report that " non-infected recurrent renal stone formers excrete subnormal amounts of citric acid in their urine " That plant poisons can upset citric acid metabolism is well known The poisonous South African plant *Gifblaar* is responsible for the deaths of sheep and cattle Its botanical name is *Dichapatalum cymosum* The poison in the plant is potassium fluoracetate and this exerts its lethal action by preventing the kidney from removing citric acid, which accumulates in that organ in concentrations 56 times above normal (see Peters 1949) Might not another plant poison prevent the normal excretion of citric acid in the urine and so break up a mechanism for keeping supersaturated salts in solution ? But this is pure speculation

That stone formation in the bladder is due to the disturbance of a complicated biochemical mechanism is certain The nature of this mechanism awaits discovery Should any clues with a practical consequence be forthcoming from biochemistry laboratories, the children in the villages of Nong Kai Nog and Loi Bog in North-East Thailand provide suitable material for testing their validity Until such a biochemical advance takes place, these children must continue to rely upon their surgeon to relieve them of their pain and suffering

I owe a great debt to Dr Chovit Chutikom and Dr Amara Chandrapananda Without their ready and cheerful assistance it would have been impossible for a stranger to undertake these field studies

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Special Articles

DERMATOLOGY IN LONDON

Past and Present

FROM A CORRESPONDENT

THE year 1714 is one which commands no little space in the larger history books In its early months the matter of the Hanoverian succession had been settled, and clinched by a proclamation (June 23) which warned the citizens that if the son of James II arrived in England he was to be apprehended forthwith Early on July 28, John Arbuthnot, the friend of Swift and Pope, and physician extraordinary to Queen Anne, was summoned to the Palace, and on Aug 1 the Queen thankfully relinquished forever the cares of her great office " Sleep was never more welcome to a weary traveller than death was to her "

Possibly, as Arbuthnot penned these words, there was in his room a copy of the new book *De Morbis Cutaneis, a Treatise of Diseases Incident to the Skin* written by his colleague, Daniel Turner, of the College of Physicians, London For Arbuthnot was at least as much interested in literature as he was in medicine, the written work of a colleague was always of interest to him, and this was the first attempt in English to *bring some order to the chaos of dermatology*

A portrait of Turner shows a man about forty years of age, with a firm mouth and well-moulded chin, a large nose, wide-set eyes, and a lofty brow He looks resolute and stern Obviously he was not a man to be trifled with, pioneers seldom are His book was widely read in England and the Colonies A second edition was published in 1723 In the same year he received from Yale College the first medical degree given in English speaking North America

In 1757 Robert Willan was born It is said that he came to London in 1782 and the next year was appointed to the Public Dispensary in Carey Street, where he established the bedside method of teaching Doubtless it is a mistake to compare the portraits of two men in an attempt to judge their characters, but we can say that Willan had more kindly lineaments than Turner The chin was less pronounced, the lips more full, more ready to smile, the nose aquiline, the eyes larger but the gaze very direct, the brow broader but less high, a very intelligent face tinctured with understanding and kindliness This was the man who, in 1785, submitted to the Medical Society of London a plan for the classification of skin diseases, for which five years later he received the Fothergillian medal In 1808 the first volume of his work *On Cutaneous Diseases* was published by J Johnson of St Paul's Churchyard

As Pusey has written, " Willan's reputation cannot be separated from that of his faithful associate, Thomas Bateman (1778-1821) ", for when Willan died, at the age of 55, before his treatise could be completed, his work was continued by the man who had been his colleague for ten years at the Public Dispensary Bateman published an important work entitled *A Practical*

Communication

Exploding any naïve belief that in science we use precise terms, Prof. J. Z. Young this week reminds us that, on the contrary, our language is largely that of analogy. The difficulty of the scientist in describing his material is, in fact, exactly the difficulty of the poet and the mystic—the necessity of finding which words, and in what order, will best convey to another person some even remotely accurate idea of what he is talking about. The poet, being born with some facility—which he can improve by practice—for arranging these counters, has perhaps the least exacting problem of the three. He proceeds, as the scientist does, by the method of analogy and comparison, using verbal images to rouse in other minds echoes of the emotion he feels in his own. The mystic, with no vocabulary whatever to express his experiences, encounters the greatest difficulty of the three. If he attempts exact description he is driven either to the spineless " ineffable " or to such humdrum mineral images as gold, jasper, and sardonyx. For him, too, the only profitable means of communication is the language of analogy and symbol. The scientist, though he can mint new counters as he needs them, has his own peculiar problem: once he has described his objects he has to measure them; and the terms and analogies he uses, as Professor Young points out, will decide what objects he measures. If he is not inventive enough, not rich enough in rewarding analogies, he may hinder the development of his study and cut it off from allied lines of research.

Professor Young is particularly concerned with the lack of a common language between neuro-anatomy and psychology. For though he favours an abundance of new analogies, from which new hypotheses might spring, he nevertheless thinks the current analogies used in speaking about the nervous system are too numerous and varied. The neurologist has equipped himself well with words to describe the functions of nerve-fibres and nerve-cells, but cannot find words to say all he would about the activities of the brain. Meanwhile psychologists have a totally different set of terms to describe events in human consciousness, and find they have little need to use or refer to neurological terms. Some psychologists talk of the more elaborate aspects of human behaviour in terms of entities such as the " id " and the " super-ego "; and these, Professor Young admits, at least provide more complete descriptions than anything the neurologist can offer at present. What we need, he feels, is a common language in which both neurologists and psychologists can express their concepts—some set of terms which compares the brain with something more complicated than any simple machine, and which offers means of describing the memory system. This general language, he suggests, might put all the descriptions of the nervous system—structural, chemical, electrical, psychological—into their place as part of a system for talking about the whole human being. He believes it could be done, and that unless we do it our age may come to be regarded as concerned only with trivia.

That such a synthesis is needed, and ultimately inevitable, no-one will doubt; yet it may be that at present it is beyond us. The nature of the material we are examining may prevent us, for the moment, from describing it in any common set of terms. Physicists find that light behaves in some respects like waves and in some respects like particles, and they have to put up with this peculiarity of light and adapt their language accordingly. Neurologists and psychologists who are unable to find a common language can at least behave like good citizens of the world and acquire each other's. Some have already done so, learning, in the process, something of each other's methods and achievements, and finding approaches to their joint study in which they can collaborate. From such combined endeavour may be expected to grow new terms, new analogies, new hypotheses and experiments, and, finally, a common language; and the two disciplines would be in harmony for the theme to which Professor Young invites us all—the study of the balance by which human life is maintained, and all the factors that influence it.

Annotations

THE FATE OF THE AMPUTEE

In 1950 the director-general of medical services, Ministry of Pensions, set up, under the chairmanship of Sir Ernest Rock Carling, an advisory committee[1] to consider whether limb amputation and the subsequent wearing of a prosthesis could initiate or aggravate cardiovascular disorder, and whether mortality-rates were higher in amputees than in equivalent non-amputated persons. A somewhat inconclusive interim report, based on a statistical study of amputee pensioners from the first world war, was published in 1951, and revealed in those still living no abnormal incidence of cardiovascular disease but a slight elevation of mean blood-pressure. Amputation, in itself, did not appear to influence mortality-rates during the period 1930–50, but the rate was higher in pensioners who had suffered severe wounding, whether accompanied by amputation or not. However, a more detailed study of certificates of deaths in 1945–49 did suggest—though not to the point of statistical significance—that patients with leg amputations died earlier, and more commonly from cardiovascular disease, than comparable pensioners with leg wounds not requiring amputation.

The final report now being laid before Parliament describes further investigations, which have shown that thigh amputees and double leg amputees have a reduced expectation of life compared with normals or men with single below-knee amputations; and also that, within the average figures for amputees as a whole, expectation of life was particularly lessened for those who had suffered serious prolonged sepsis after wounding. In this class of case also there was a greater than normal probability that certain cardiovascular disorders would be certified as the underlying cause of death; and, unexpectedly, when cases of fractured femur and other leg wounds which had not led to amputation were analysed on the basis of whether major sepsis had occurred or not, it was found that this complication was again associated with a higher late incidence of cardiovascular disease and an earlier average age of death.

The factors involved are complex and difficult to separate. Possibly the overweight and sedentary living consequent on limb amputation predispose to cardiovascular disorder; and the committee, recognising that the strain of carrying an artificial leg may become an increasing physiological burden with advancing years, specialised in discomfort and inconvenience At Hill End, as in so many of our great mental hospitals, some of the wards used by St Bartholomew's open endlessly from each other like picture-galleries, others are so large and low that even ample windows would not dispel the central gloom, while corridors like symbols of despair, daunt the heart with interminable perspectives Yet a great deal has been done to mitigate these and other drawbacks at relatively little cost Dr Harold Palmer the medical superintendent, and the management committee have achieved this by a policy which combines æsthetics, humanity, and reasonable economy

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[1] Since the interim report appeared in April, 1951, the members of the committee have been: Sir Ernest Rock Carling, F.R.C.S., Dr. A. Greig Anderson, F.R.C.P., Prof. G. R. Cameron, F.R.C.P., F.R.S., Dr. T. F. Cotton, Prof. J. L. D'Silva, M.R.C.P., Prof. K. J. Franklin, F.R.C.P., Dr. A. Hope Gosse, Dr. W. E. Lloyd, Dr. W. P. D. Logan, the late Mr. P. H. Mitchiner, F.R.C.S., and Dr. E. Livingstone (secretary).

ÆSTHETICS

We have often had occasion to speak of the influence on the spirits of the colour of paintwork in hospitals Dark brown paint on the walls and varnished pine woodwork were a passion among Victorian builders of institutions, and this curiously distasteful form of interior decoration has been maintained in many of our mental hospitals At Hill End it is being steadily obliterated There are still outcrops (the superintendent's office and the doctors' library are still honourably waiting their turn for redecoration), but in the wards, the secretarial departments, and the corridors pastel colourings of walls and wood have changed the aspect and spirit of the place Professional artists have chosen most of the colour schemes which aim at breaking up long vistas, drawing attention to intersecting planes or interesting recesses, and resting the eye with a pleasing variety of colours This has been specially successful in some of the long corridors and in a once dingy concert hall, now entirely beautiful The effect on the mood of the staff has been considerable: staff dances are now packed, and the social clubs have funds in hand No doubt the effect on patients has been equally good We may recall Dr L Z. Cosin's experience, at Orsett Lodge Hospital of the effect on the chronic and aged sick of agreeable colouring and energetic murals[1] and sick people do not need to be aged to profit from such things In particular the low dark wards at Hill End have been improved by the great gain in light from shell-pink walls or aquamarine ceilings

HUMANITY

All this has been achieved with a very moderate outlay, and with no structural alterations whatever This does not mean, of course, that structural alterations would not be desirable. many of the wards would benefit from a revision of their design on the lines indicated in the report of the Nuffield Job Analysis Team[2] Sluice rooms, bathrooms and washbasins are often awkwardly placed Patients' water-closets may be divorced from washing facilities by the length of half a ward, screens are scarce, and some of them are of old-fashioned and heavy design But since the spirit of a place is what determines the standard of the work done in it, it is well to begin by making surroundings cheerful even if they are not ideally equipped The convenience of the staff is considered too They are well supplied with public telephones (one being in the nurses' home), their uniforms are nicely cut and in particular, their food is nourishing, various, and served hot A noticeable result of this kind of consideration is that the staff are contributing their share to the general good on their own initiative, nurses have been found weeding flower-beds electricians have woven a garland of coloured lights round the chandelier of the dance hall and male nurses and porters have made a lawn from a derelict stretch of grass, sparing, in the process, a watery depression in which birds like to bath Things of this kind do not happen in hospitals where the staff are disgruntled

Patients' visitors—sometimes a nuisance and too often made to feel it—are here treated with courtesy and kindness A large room, charmingly decorated and well warmed, has been set aside for them to use if they need to wait any length of time Small simple bedrooms open from it, where those who have to stay a night, or longer, can sleep, and hot meals are served to them at very low rates Sometimes relatives may need to stay a fortnight or longer, but they do not find themselves outstaying their welcome

These are all the sort of things which help to build up a society of service rather than a society of contract

ECONOMY

It has been said already that lavish outlay is not attempted; on the contrary, Hill End offers an example of economy and retrenchment Thus the staff of porters has been cut down, though the number of patients has been increased The hospital operating-theatres have an old-world look, with walls of painted brick and a network of pipes and girders overhead that seem designed for trapping dust, but the St Bartholomew's surgeons use them regularly and successfully The X-ray equipment is good, but housed in a nondescript room with a makeshift darkroom near at hand There is no drier for the films—they hang on a clothes line fanned by a small electric fan It is all very amateur and inglorious, but reasonably efficient

INTEGRATION

The staffs of the two hospitals work together in amity Miss V.M Houghton, the matron, Mrs. I C. Thacker, the St Bartholomew's assistant matron at Hill End, and Dr Palmer are colleagues collaborating successfully in a joint enterprise and they are creating an integrated hospital in which there is a sense of partnership between all members of the staff The same good relationship extends to the family doctors of the neighbourhood, who feel they *can turn* to Hill End on behalf of any of their patients, and their patients—including those who are mentally sick—share this confidence Nothing could be more effective in removing the "stigma" of treatment in a mental hospital than the reunion—now gradually being achieved—of mental and general medicine When the patient with a mental or emotional disorder knows he can go to his usual hospital for treatment he is greatly reassured and feels little hesitation in presenting himself as a voluntary patient

The fact that the association with St Bartholomew's has had particularly happy results of this kind suggests strongly that Hill End could be made the centre of a new experiment in nursing St Bartholomew's has student nurses in plenty, and usually a waiting list, Hill End, like other mental hospitals, is short of nurses Surely here is a most fortunate opportunity to give nurses in general training a short term of experience in mental nursing The prejudice in the nursing profession against mental nursing springs very largely from fear and ignorance—useless attributes in a nurse Those who work with the mentally sick know how quickly any preliminary apprehension fades in the presence of patients These sick people are no more alarming than their counterparts in medical and surgical wards in fact, they appeal, perhaps more strongly than any other type of patient to the parental instinct It seems highly probable that, if nurses in general training were allowed to see something of mental patients they would not only gain in professional insight but some of them would seek a career in mental nursing when they had qualified, and there is no branch of nursing where they are more greatly or urgently needed method might reduce the number of complications due to inhibition of the cough reflex and retention of urine, but his series was too small for any conclusions to be reached on this point.

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[1] *Lancet* 1947 i 840

[2] The Work of Nurses in Hospital Wards London The Nuffield Provincial Hospitals Trust 1953 see *Lancet* Feb 21 1953 p 379

Leriche[4] said that the idea of pain having a protective quality "is an extraordinary error . . . which has no shadow of justification"; and if this is so there are neither moral nor clinical objections to the complete relief of pain. On the other hand, postoperative pain, or, more especially, changes in the postoperative pain in the incision, are signals on the patient's road to recovery, upon which the surgeon and the houseman have come to rely. Clearly the utmost relief should be assured, provided the patient's ultimate welfare is in no way jeopardised. Although the anæsthetising of an incision does not interfere with pain sensation from distended viscera, the removal of pain entirely and for a considerable period may allow complications to develop in sinister silence. Indeed, before any long-acting local anæsthetic can be widely and confidently used for postoperative pain it may be necessary to modify the standards by which postoperative progress is normally judged. Moreover, only further experience will show whether tissue healing does in fact proceed unhindered in the presence of these deposits of drugs—a point that is of particular importance after anorectal operations.

STRUCTURE OF STREPTOCOCCI

IN 1948 Maxted[5] demonstrated that culture filtrates of a strain of *Streptomyces albus* lysed β-hæmolytic streptococci. The group-specific C carbohydrate was liberated undamaged by this process, which is now widely used in preparing streptococci for serological grouping. More recently McCarty[6] has investigated the formation and mode of action of the enzymes produced by *Streptomyces albus*, and has used these substances to investigate the structure of the cell-wall of group-A streptococci.

Filtrates of *Streptomyces albus* are strongly proteolytic. Known proteolytic enzymes such as trypsin and pepsin, however, do not disrupt streptococcal cells; this process seems to depend on some other enzyme in the filtrate. McCarty has shown that the formation of this enzyme coincides with sporulation of the fungus; and he has separated it from the proteolytic component by chemical fractionation. Complete clearing of a streptococcal suspension apparently requires both components. The "disruptive enzyme" alone causes only partial lysis; the cells become gram-negative and have an indistinct outline. Lysis is completed by the addition of the proteolytic component or any other non-specific protease. This resembles the effect of lysozyme, which renders many gram-positive organisms susceptible to lysis by trypsin.[3]

McCarty[4] has also investigated the structure of group-A streptococci as revealed by the action of streptomyces enzymes. By means of a mill containing stainless-steel balls, he prepared a suspension of ground-up streptococcal cells. This suspension was treated with trypsin, chymotrypsin, and ribonuclease, and was then repeatedly washed; and electron microscopy showed that the residue comprised only the cell-walls of the cocci. These cell-walls were highly resistant to the action of such enzymes as trypsin, pepsin, papain, and lysozyme and were unaffected by various organic solvents. The "disruptive enzyme" of *Streptomyces albus*, however, caused almost complete solution of the material, suggesting that it acts on intact cells by dissolving the cell-wall with resultant release of cellular materials into solution. Chemical analysis of the cell-wall preparation showed that much of it consisted of carbohydrate, which was identified serologically as the group-specific C carbohydrate of group-A streptococci. The streptomyces enzyme seems to act on this carbohydrate, which, McCarty concludes, makes an important contribution to the structural integrity of the cell-wall. This conclusion is not original, but the work is important since it illustrates the use of a relatively new technique to investigate bacterial structure.

HOSPITAL COSTING

THE Hospital Costing Returns for 1951–52 have now been issued by the Ministry of Health.[1] When the first of these returns was published last year, we remarked on the inadequacy of the existing method of compiling the figures.[2] The deficiencies are recognised by the Ministry itself; and the reports by the Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund[3] originated in the Minister's desire to improve the usefulness of the costing analysis.

Hitherto the emphasis has been mainly on the production of figures for inter-hospital comparisons, in order to expose local extravagance. It is generally agreed, however, that there is no large-scale extravagance to be exposed, but only different degrees of housekeeping efficiency; and the costing returns so far published show the difficulty of drawing useful conclusions about moderate differences in the cost per patient per week. Costing analyses should surely relate cost to the adequacy or quality of the services provided. Otherwise a hospital which fails to provide various desirable services, or provides service of poor standard, may nevertheless earn full marks for economy when its figures are taken at their face value. A complete unit costing system may overcome this difficulty. On the other hand, such an approach may lead to over-complication: the figures which are of most use, to laymen and executive officers alike, are the simplest figures—the figures behind which lies little calculation and "treatment." One of the major items of expenditure is salaries and wages; because salaries are determined on a national basis, there is no point in elaborating the data. The most useful index to the adequacy of staff in any department is not financial: it is a statement of the number of people of different grades who are employed, related to equally simple numbers of patients, or tests, or examinations, or items of service.

There is a danger that the elaborate methods of costing that have served industry well will be too readily retained in the wholly different context of the hospital service. The need is to re-examine each type of costing return with a view to simplification and the abandonment of those for which the cost of ascertainment is not balanced by enough useful information. The hospitals have still to forge their own measuring-rods.

STAGES OF ANÆSTHESIA

MANY anæsthetists learned the basic principles of their specialty with ether as the sole anæsthetic agent and the signs of Guedel's stages as their guide. Today, however, ether has been very largely replaced by other agents; and with none of these are Guedel's stages clear-cut. Laycock[4] rightly remarks that the 2nd stage, of excitement, which he terms "unconsciousness with reflex activity," should now hardly ever be seen. Similarly, the reflex depression of the 3rd, or "surgical anæsthesia," stage (termed by Laycock "unconsciousness with reflex depression") is commonly replaced by deliberate reflex inhibition through neuromuscular paralysis. Nowadays separate drugs are given for motor paralysis and for unconsciousness. Thus *d*-tubocurarine, by a physician is increased from 25 to 40 guineas, with a similar increase for a surgeon in cases not involving an operation There are also changes in the maximum fees in other specialties, and the scale for radiotherapists has been completely revised The maximum fee payable to a general practitioner attending a patient privately in hospital has been increased from 15 to 20 guineas

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[4] Leriche, R. The Surgery of Pain. English translation by A. Young. London, 1939.

[5] Maxted, W. R. *Lancet*, 1948, ii, 255.

[6] McCarty, M. *J. exp. Med.* 1952, 96, 555.

[7] Webb, M. *J. gen. Microbiol.* 1948, 2, 260.

[8] McCarty, M. *J. exp. Med.* 1952, 96, 569.

[1] Hospital Costing Returns: Year ended March 31, 1952. H.M. Stationery Office. Pp. 123. 10*s*.

[2] See *Lancet*, 1952, i, 1243.

[3] *Ibid.* ii, 1067.

[4] Laycock, J. D. *Anæsthesia*, 1953, 8, 15.

The over all fee of 75 guineas to be charged by all the practitioners concerned in the patient's treatment is retained as the normal maximum, but provision is now made for this maximum to be increased to not more than 125 guineas (at the discretion of the hospital board or committee) in the following circumstances

(*a*) when the treatment of the patient in accommodation provided under Section 5 of the Act has lasted four months, or

(*b*) when the patient needs at least two major operations or at least three major or intermediate operations as part of the same course of treatment during the same stay in such accommodation as aforesaid, or

(*c*) when the patient requires excision of lung, an operation on the heart or œsophagus, or the excision of a tumour of the brain or spinal cord, or otherwise requires specialised operative techniques involving complicated team-work

Provision is retained for the maximum charges laid down in the regulations to be exceeded in cases where the patient so agrees

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COLLEGE OF GENERAL PRACTITIONERS

IT is proposed that the peripheral activities of this new college shall be organised by a number of regional faculties

HEADQUARTERS OF REGIONAL FACULTIES

Ideally the headquarters of these regional faculties should be situated near the offices of the undergraduate and postgraduate deans or directors of the medical schools and the university research departments, for educational purposes and to facilitate arrangements for postgraduate study and research But in some places this may not be possible, or headquarters may be offered to the college elsewhere, as has already happened in Birmingham and in Edinburgh It is felt that a close link like this with the universities will underline the academic nature of the college's work

In London, the Director of the British Postgraduate Medical Federation has offered the college accommodation at his headquarters (2, Gordon Square, W C 1) This arrangement will lead to close cooperation between the two bodies, and it is hoped that similar cooperation may be arranged between the college's regional faculties and the postgraduate deans or directors of other university cities

In the British Isles and Republic of Eire there are 19 universities with medical schools—Aberdeen, Belfast, Birmingham, Bristol, Cambridge Cardiff, Cork, Dublin, Durham, Edinburgh, Galway, Glasgow, Leeds, Liverpool, London, Manchester, Oxford, Sheffield, and St Andrews Pilot faculties will be formed at once in London, Birmingham, Bristol, Cardiff, Edinburgh, Belfast, and Dublin After the first annual general meeting, to be held next autumn, a further 12 or more regional faculties may be set up in the British Isles plans for these will be made soon In areas far away from these university cities faculties may be needed in a few cities or towns that have no medical school (e g, Plymouth and Inverness) Other regional faculties may be developed in parts of the Commonwealth Further details will be published next month

The foundation council has approved the establishment of a "Council of the College in Scotland" to coordinate the regional faculties and other local organisations in Scotland, and to maintain liaison with the council of the college It is proposed to open an office in Edinburgh at once

A meeting of general practitioners in Eire, held in Dublin on March 15, decided to form a faculty of the college in Dublin, and an interim committee was set up to study this Dr John Fleetwood of Dublin (chairman of this interim committee) has been elected to the foundation council of the college in London

A meeting of the full foundation council, held in London on March 18 agreed that the college provisional by-law 1 (B) should be altered to read

"A 'Registered medical practitioner' means a person holding a medical qualification which has been registered with the General Medical Council or with the equivalent organisation of a country or state within the British Commonwealth of Nations and the Republic of Eire"

STATUS

The status of all regional faculties will be equal Those in Scotland, Wales, Northern Ireland, and Eire will be free to form colleges of their own in the future if they wish to do so

DUTIES

In general the duties of these regional faculties will be to relieve the college's central council of local responsibilities connected with the activities of the college in the regions concerned

For the first few years the main concern of the faculties will be to help (1) in the teaching of certain aspects of general practice to final year students and those newly qualified (2) in the postgraduate education of general practitioners in the region, and (3) in research in general practice Later many other functions of the college may devolve upon the regional faculties Members of the board of each faculty will work in liaison with the local medical school, the postgraduate departments of the university and the university research departments, the local medical committees of the executive councils, the local divisions of the British Medical Association, and the local medical societies

THE BOARDS OF THE REGIONAL FACULTIES

Each board will have up to 21 members

It will have a chairman (who may be a member of the college council or coopted to the council), a deputy chairman, a member for undergraduate instruction a member for postgraduate study, a research member, and an hon secretary The secretary will keep in touch with members and associates of the college who work in the region, receiving information from them and providing them with information, so that the college and its regional faculty can give them all possible help in the academic field There will be up to 15 other members, including two associates, and the boards will have power to coopt further members from the university and elsewhere

Members of the boards of the faculties will be elected annually by the members of the college who live in each region The officers will be elected by the boards themselves

Meetings of the boards will take place about once a month Five will be a quorum Copies of the minutes of the meetings of the boards will be sent to the college headquarters in London for filing and reference Each year an annual report from each board will be sent to the college headquarters and incorporated in the college's annual report Subcommittees on undergraduate education, postgraduate education research, &c, will be elected by the boards at any time for special purposes These subcommittees will have power to coöpt members from the university departments concerned. The secretarial expenses of the boards will be met by the college

Members or associates of the college who care to make further suggestions or comments on the development of these regional faculties are asked to write to the secretary, College of General Practitioners, 14, Black Friars Lane, Queen Victoria Street, London, E C 4

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY

ON March 16, opening the new laboratories at the Chelsea Hospital for Women and the new wing of the Institute of Obstetrics and Gynæcology, Mr IAIN MACLEOD, the Minister of Health, admitted that there were difficult days in the hospital service, for there were many competing claims on a limited purse But however urgent other claims might be, we must, he affirmed, never lose sight of the absolute necessity of holding and improving our position in the specialist fields Stressing the importance of laboratory investigation in gynæcology, able differences in the fertility of A and O mothers. The over-all fertility, they found, was slightly, though not significantly, higher in group A; but these women had notably more pregnancies between 25 and 35 years of age. The O women had more children under 25 and over 35. These workers suggest that the difference may be due to an inherently higher fecundity of O women, some of whom, however, become infertile early in their married life from blood-group incompatibility. The higher fertility of the A mothers would balance this loss of the genes for the A antigen among the children of O mothers. In a letter this week Dr. Allan suggests that further inferences may be drawn from the published figures on the relative fertility of A, B, and O women.

Nevertheless so far none of the findings and the suggestions based on them are entirely convincing. In one or two studies tests of significance may have been used incorrectly. To test a hypothesis by applying significance tests to an observed set of figures, it is necessary that the hypothesis should have been clearly formulated before the figures are examined or, better still, even collected.* By examining a random set of figures from a sufficient number of different angles it is possible to find some "significant" differences in almost any set. A hypothesis suggested by examination of a set of figures should be retested on a new independent series to which significance tests may be justifiably applied. We hope that those who work with blood-groups will collect fresh series of figures relating blood-groups to fertility and infant survival, and so test the various fascinating hypotheses that have been put forward.

THE PRIVATE BED

FROM the end of this month there will be a new and better system of calculating the charges made to private patients occupying pay-beds in National Health Service hospitals.[1] Where such beds are not in a self-contained block or wing whose running costs can be separately computed, the charge made to the patient is at present based on the average daily cost per inpatient for the hospital as a whole, to which is added 25% for a single room, 15% for a room shared with one other patient, and 5% for a room shared with more than one patient. Under the new regulations the charges will be altered, first by reducing these percentages to 15, 10, and 5 respectively, and secondly by subtracting from the "average daily cost per inpatient for the hospital as a whole" the cost of certain services from which the private patient derives no benefit (e.g., almoner's department and medical records department) and the remuneration of the medical and dental staffs. (Where admission to a private bed entitles the patient to medical care from hospital doctors—e.g., house-physicians—other than the doctors to whom he pays fees, an appropriate amount will be added to the charge for his accommodation.) In calculating the average daily cost of inpatients "no allowance can be made for the vacant bed factor," and there is at present to be no change in the procedure whereby the care of 5 outpatients is regarded as the equivalent of one inpatient day—an arbitrary estimate which sometimes makes the cost of inpatients seem higher than it is. But the regulations go a long way to meet our wish that "the N.H.S. should neither penalise the private patient, nor try to make a profit out of him, by charging him more than the true cost."[2] The charges for pay-beds will now, we hope, be a less grave deterrent to their use—though some patients may not approve as strongly as their doctors of the new and reasonable arrangement by which, in exceptional circumstances, the total of medical fees payable by them may be raised from 75 to 125 guineas. In the memorandum that we publish on p. 643 the Joint Consultants Committee express legitimate satisfaction with the results of their lengthy negotiations with the Ministry (and the Minister) but regret the continuation of the schedule which divides operations into major, intermediate, and minor. This schedule has been altered in some details, but the committee, disapproving in principle, declines any responsibility for it either in the old form or the new.

The Minister asks that steps should always be taken to ensure that patients know exactly what obligations they are undertaking in booking a private bed. They should be told of the existence of "amenity beds" (if there are any) and not be left with the impression that they can secure privacy only by paying for a private bed and medical fees. "It should also be made clear to patients who need immediate admission on medical grounds that they can be admitted at once as general patients."

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[1] Statutory Instruments, 1953, no. 420. Ministry of Health Circulars R.H.B.(53)26, H.M.C.(53)24, and B.G.(53)26.

[2] *Lancet*, 1952, ii, 229.

GAMMA-GLOBULIN AND POLIOMYELITIS

A FEW months ago we described the results of an investigation in the U.S.A. of the protective action of gamma-globulin against poliomyelitis.[1] The figures cited by Hammon and his co-workers[2] left little doubt that gamma-globulin protected against poliomyelitis; but its widespread use seemed unlikely because of the large dose required. One possible application of it would be as an "umbrella" in preliminary trials of attenuated poliomyelitis virus vaccines; another is suggested by the work of Adams et al.[3] on tonsillectomised monkeys.

It has been known for some years that tonsillectomy during a poliomyelitis outbreak carries a grave risk of bulbar poliomyelitis. Experimentally, too, it has been found that tonsillectomised monkeys show an increased rate of paralysis when fed virus for 3 to 5 days after operation. Now, Adams et al.[3] find that tonsillectomised monkeys can be protected from paralysis by an injection of human gamma-globulin before they are fed with virus. The dose of gamma-globulin was enormous (2 ml. per lb. body-weight), but it should be remembered that the monkey is a foreign species and that smaller doses of homologous globulin might suffice. Fortunately there are not many operations on the throat which cannot be postponed until a poliomyelitis epidemic has subsided, but there may be an occasional emergency case where gamma-globulin would be valuable.

FOUR members of the medical profession are among the twenty-five newly elected fellows of the Royal Society. They are: Dr. HENRY BARCROFT, professor of physiology in the University of London, at St. Thomas's Hospital medical school: Dr. G. W. HARRIS, Fitzmary professor of physiology in the University of London, at the Institute of Psychiatry; Dr. L. S. PENROSE, Galton professor of eugenics in the University of London, at University College; and Dr. DAVID WHITTERIDGE, professor of physiology in the University of Edinburgh. The following have also been elected to the fellowship: Mr. KENNETH BAILEY, PH.D., assistant director of research in the department of biochemistry of the University of Cambridge; Mr. J. W. CORNFORTH, D.PHIL., a member of the staff of the chemotherapy department of the National Institute for Medical Research, London: Mr. C. S. ELTON, director of the Bureau of Animal Population, Oxford; Mr. E. F. GALE, SC.D., reader in chemical microbiology in the University of Cambridge: and Lord ROTHSCHILD, SC.D., chairman of the Agricultural Research Council.

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[1] *Lancet*, 1952, ii, 970.

[2] Hammon, W. M., Coriell, L. L., Stokes, J. jun. *J. Amer. med. Ass.* 1952, 150, 739.

[3] Adams, J. M., Boak, R. A., Carpenter, C. M., French, J. D. Klein, S. J., Pressman, J. J., Smith, J. L. *J. Lab. clin. Med.* 1953, 41, 142.

In England Now

A Running Commentary by Peripatetic Correspondents

MY first afternoon on the river this season was blank I collected my licence at the pub, got down to the water's edge, and had hardly put up my rod before my eagle-eyed friend the bailiff was there just to make sure that I wasn't a poacher He told me that there were few fish up yet and no wonder, for we are short of rain The water, though low, was beautiful, cold and sparkling in the sunlight I fished down the Washing Pit without result, though two salmon, probably kelts, heaved themselves out of the water Down I went to try the Four Acre, and at my second cast was into a fish which gave me ten minutes' fun, agony, and exercise till I had her out on the bank an ugly kelt she was who had taken my fly half-way down her gullet In rather a middle-aged manner and cumbered by waders and brogues I ran back to fetch my disgorger—an old pair of Spencer Wells, the best disgorger ever invented—and soon tweaked the fly out

With loving care I returned the fish to the river and held her upright and upstream till she got her breath back and wobbled off slowly but surely into the deeper water Never was more trouble taken over a patient

There was a pair of yellow wagtails to watch and also a pair of dippers before I went off to try the Hurdle Pool in which, and in the Dead Hole below it, there were several large but not very silvery fish jumping from time to time None came to me and I comforted myself with the reflection that they were probably all kelts The sunshine was brilliant, and on the trees there was that wonderful reddish purple sheen that one sees in early spring Yes, a blank afternoon Or was it?

* * *

As winter epidemics are inevitable and make the doctor's life a burden, I have, over the years, evolved a plan by which I claim I can actually extract pleasure from them

The first step in Operation Sniffles, as I call it, is to allow plenty of time Chasing the clock is the chief blight of G P epidemic existence, and plenty of time means no private engagements, no cinemas, no dining-out No appointments means no disappointments

Next, answer all new calls and visit any serious cases in the daytime Leave the others till the evening Once you have your evenings free you can enjoy them Do not hurry your crowded surgeries Hurry is bad for the patients' health and for the doctor's temper You have all night before you, so take your time and enjoy yourself Besides, it is surprising how many will decide they are not bad enough to wait all that long for their turn

Remember that for publicity purposes you are *very, very* busy Accept it, revel in it—but privately To expressions of sympathy for your hard lot return a wan but heroic smile Say nothing, the sympathy will increase a hundredfold

After your leisurely (even if prolonged) evening surgery, have a still more leisurely and ample dinner Nothing sours the temper like hunger And now you are all set to enjoy the evening round Do not start before 9 P M "Good Heavens, why, at this time! You *must* be tired," will be your first greeting And at each succeeding visit you will be good-graciousd and good-heavensed more and more Sympathy will increase, and so will your self-esteem Your last four calls have been hand-picked At the first you may droop a little more wearily, and when pressed to take refreshment permit your scruples to be overcome But be emphatic that this is quite exceptional You will be assured it will not hurt you It will not At the next two visits the same attitude will serve, but be firm in the amount of restorative you accept, lest at your last and carefully chosen visit cheerfulness should inadvertently break through This last visit is technically the important one Here you may allow yourself to be cosseted and refreshed to the limit Take your fill of appreciation and admiration You will be beyond criticism hereafter, so in your own good time make your way tranquilly and peacefully homewards, and dare to say you have not enjoyed your evening

* * *

I don't care what my colleagues say, I've made up my mind I'm going to be an ologist Not a proct, not an ot, and not an ur, but a simple [illegible] plicated ologist I've had my pla [illegible] Ologist," and already I can see the patients beating a path to my door

An ologist, in case you are unfamiliar with the term, is a specialist who has not confined himself to any one subject, system, or symptom You may call him, if you wish, a general-practitioner specialist or, if you feel inclined, a specialist general practitioner Sneer if you wish, pioneering was ever thus, and I can see a great future opening up

Such a being has long been needed in these days of left-eye ophthalmologists and hair-trigger dignities What houseman has not been confronted with the horrible politics of nystagmus, for instance Who to call in? The general specialist, the ophthalmologist, the neurologist, or the industrial medical officer? In future the answer will be easy Without further thought the medical contact man—the ologist—will be summoned

In my mind's eye I can see the future version of a familiar scene "And what are you just going to do?" the old lady is asking the first-year doctor "Are you going to be an ologist or are you going to specialise?" As I have created this new field the least my regional board can do is appoint me its first consultant in ology

* * *

As every schoolboy who has failed part I of the D P M knows, the central nervous system is a structure of no little complexity But much of the difficulty arises because it is littered with Latin or Greek derivatives The whole thing is understood quite easily, I find, if one substitutes homely Anglo-Saxon terms

What an interesting organ the cerebellum becomes when we consider that in it are a toothy nut and a clottish nut, presumably growing on the tree of life, while it straddles the fourth little tummy with six little feet which are probably necessary in view of the four little hills just above it And to make it even more endearing, there are two little locks of wool underneath Passing the mid-brain we pause to feast our eyes on the red nut and black stuff, then on to the little breasted bodies Moving forwards we come to two hooks on either side of a funnel We see the reason for the hooks when we pass deep to the pear-like place and discover a sea-horse If we follow this backwards and upwards we find ourselves, possibly to our surprise, in the brothel There can be no doubt of this, for behind us we see two soft couches while below and on either side are three more little tummies We glance fearfully over our shoulders, for we are obviously in the presence of the Id Hurriedly we retrace our steps to the surface Here we find a strange trio, a hard mother, a spidery mother, and a loving mother, evidently close associates of the Super Ego Treading our way onwards over the bark we come across a hard skinned body, encircled by a girdle Could this be a stout and resolute Ego? Passing inwards again we sink down, tired but happy, on the carpet where we partake, in the light of the pale orb, of a light vegetarian meal of almond nuts, tailed (presumably monkey) nuts, and prunes

* * *

Once upon a time the governor of a prison was allowed the privilege of releasing one of his prisoners each year It was his custom to choose the most intelligent prisoner for this honour, but in this particular year there were three prisoners of equal merit He sent for them, and when they came to his room he showed them three black dots and two white dots which he had cut out of paper He then made them face the wall while he pinned a black dot to each man's back and destroyed the two white dots The prisoners, of course, did not know what kind of dot each had on his back The governor then sent them into the next room and said that the first man to come out and tell him what kind of dot he had on his back and how he had worked it out would have his freedom Presently one of the prisoners came out with the right answer and the right reasoning to support it How did he do it? Note it was all done by logic, no mirrors no contortions, no violence I wonder how many peripatetic readers would be able to claim the order for release

OPERATIONS FOR STONE IN THE BLADDER AT UBON HOSPITAL DURING 1948–51. (PERSONS FROM OUTSIDE THE PROVINCE EXCLUDED)

District from which patient came	Population of district	Number of operations	Operations per 10,000 per year
Muang	67,052	66	2·5
Varind	79,665	58	1·8
Pibulmungsahan ..	68,616	74	2·7
Amnajcharea ..	97,504	49	1·3
Yastotorn	90,620	40	1·1
Traganpunpol ..	87,740	50	1·4
Kemraj	52,458	23	1·1
Mahe-chanajai ..	42,155	39	2·3
Muangsomsib ..	50,347	39	1·7
Kuengnai	46,585	60	3·2
Loompuk	44,404	39	2·2
Kongjuen	30,405	7	0·6
Dej-udom	53,076	35	1·6
Laingnokta	39,914	31	2·2
Whole province ..	850,541	610	1·8

operations on visitors normally resident outside the province. I was told that a small but unknown number of sufferers from stone went to Bangkok for operation.

The accompanying table shows the distribution of the homes of those operated on in the various districts of the province. It will be seen that the patients came from all over the province and there is no evidence of any special focus. Fig. 2 shows the age and sex distribution of the patients. The operation-rates are calculated on a basis of population structure provided by the department of vital statistics at the Thailand ministry of health. It will be seen that males outnumber females by nearly 8 to 1. The operation is performed on persons of all ages, but there is a peak incidence in small boys with a maximum of 14·5 operations per 10,000 persons in the fifth year. Three operations were done on infants under one year. A large chest in the hospital office contains a great collection of stones. Many specimens of all the common varieties are present and no single type appears to predominate.

Dr. Chutikom records that in 25% of the patients there was a history of another member of the family suffering from stone. All the patients complained of difficult and painful micturition with frequency: about two-thirds complained of hæmaturia and about one-quarter gave a history of passing small stones or gravel on urination. Diagnosis presented no difficulty and was usually made by the patient or his parents, the significance of the symptoms being well known amongst the people. Symptoms had usually been present for six months to two years before operation, but sometimes patients came up after many years of suffering. In Dr. Chutikom's series there were only 10 cases of recurrence (i.e., less than 1%). Dr. Chutikom told me that renal calculi were rare and at the most he removed one or two a year.

OBSERVATIONS IN THE VILLAGES

At the time of our visit there were only 2 patients with stone in hospital. The rice harvest was being gathered in and this activity takes precedence over lithotomies. Accordingly we made visits to villages in the districts where the hospital records indicated that stones might be prevalent. We found a high incidence in the village of Nong Kai Nog, in the Muang Samsib district. The village schoolmaster had been forewarned of our visit and had gathered 16 sometime sufferers for us in a coconut grove around the wat or temple. Of these, 4 had been operated on, 5 stated they had previously passed a small stone, and 7 complained of present pain and dysuria. There were in the village 390 families and the population was about 2000. So approximately 1 out of 125 persons had suffered from stone at some time. On the previous day at the village of Loa Bog we had found 13 sufferers out of 2500 people (an incidence of about 1 in 200). We examined a large number of children in these and other villages in the province. By Western standards they were clearly undersized, but on South-East Asian standards they were, for the most part, a sturdy lot. Stigmata of deficiency diseases were not common. It was usually possible to demonstrate in any group an early case of xerophthalmia or of angular stomatitis. But no well-marked case was seen. Very few spleens were palpable and severe anæmia was not common. The teeth were almost all uniformly good. Yaws was endemic in the district, but we saw no evidence of syphilis. In most villages there were one or two persons with obvious goitre. In brief, the general health and nutrition of the children appeared no worse and perhaps a little better than of the children in thousands of other villages in Thailand and other parts of South-East Asia who do not suffer from stone. A much more complete study of the incidence of disease in the area has been given by Zimmerman and Vaidhyakara (1933).

Dietary histories were collected in all the villages. In addition to the rice, which is home-pounded, most families got a little fish every day (this would be impossible in the hot weather). They only have meat on rare occasions. Milk and pulse are never eaten. There is a great variety of fruit trees (notably mango) around the villages and in nearby woods which must contribute beneficially to the diet. Coconut oil is the only available edible fat, but little is eaten and food is seldom fried. The rice and fish are usually garnished with leaves or vegetables, which are gathered unsystematically. We collected the leaves of a large number of shrubs and trees which are eaten on occasion. Not a few of the children stated that sometimes they ate frogs and a variety of insects.

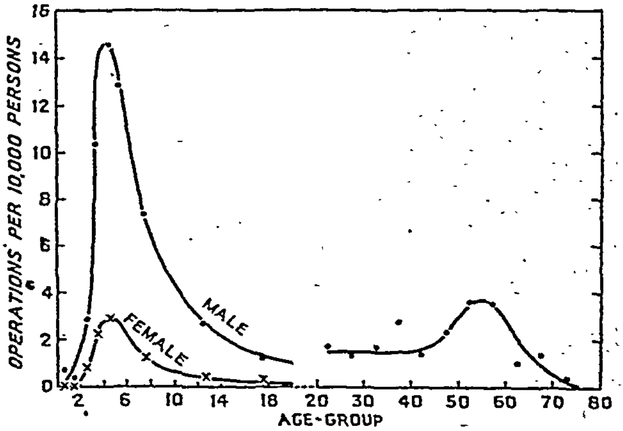

Fig. 2—Operations for stone in the bladder, Ubon Province, 1948-51. Standardised annual rates per 100,000 persons.

DISCUSSION

The high incidence of stone in small boys probably reflects the anatomy of their urethras. Presumably the basic biochemical lesion must be much commoner than the surgical complaint. Probably large numbers of the population at one time or another form deposits in the bladder; but, except in the case of small boys, such deposits are usually voided with the urine. Apparently urinary deposits rarely settle and grow stones in the kidneys: we heard no description of renal colic. That vitamin-A deficiency is a predisposing factor to stone formation is possible, but that it is an important precipitating cause is extremely unlikely. Although the diet is certainly not rich in vitamin-A activity, clear-cut clinical signs of deficiency of the vitamin are not common. An excess calcium intake is also an unlikely ætiological agent. The staple rice has a low calcium content. No other food, regularly consumed, could add an excess of the mineral. Chemical analyses of the water were not made, but on the simple shaving test it seemed to be

The clinical features of the five patients were identical with the exception of the added cerebral manifestations in the patient previously described In four of the patients an arrest in the progress of the symptoms and signs occurred with the removal of the adenoma In the fifth patient, post-mortem examination showed a pancreatic adenoma and severe and widespread degeneration of the anterior horn cells of the spinal cord Barris points out that to conclude that adenomas of the pancreas are usually responsible for the syndrome seen in progressive muscular atrophy is not warranted. It did seem important, however, to show that sufficient hormonal imbalance or altered hormonal function existed to cause ultimate damage to the anterior horn cells of the spinal cord

Blau et al[6] have reported a case which adds to the confusion The symptoms and signs in this patient were almost entirely of a neuropsychiatric nature and included changes in the psyche and in the central, peripheral, and vegetative nervous systems The patient suffered from convulsions, parkinsonism, pyramidal signs, ataxia, generalised muscular weakness with myotatic irritability, and sensory changes, and from progressive emotional and intellectual deterioration accompanied by paranoid delusions During several hypoglycæmic attacks coarse fibrillations were noted in the right forearm The outstanding features were a persistent Parkinson syndrome and evidence of progressive internal hydrocephalus as shown by several encephalograms Attention was called to the coexistence of the manifestations of chronic disease of the periventricular nuclei and the constant hypoglycæmic state The authors were not able, however, to establish whether the disease of the central nervous system or the hypoglycæmia came first

Also confusing is the fact that spontaneous hypoglycæmia, without a functioning islet-cell tumour of the pancreas, does not necessarily produce the symptoms of hypoglycæmic shock Hypoglycæmia and hypoglycæmic shock are not the same, nor is the latter always produced by the former

Practically all patients with hypoglycæmia will have neurologic symptoms The earlier diagnosis and proper treatment of such patients necessitates that the physician become more conscious of the syndrome due to hypoglycæmia

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Fort Howard, Maryland U S A
JOSEPH M MILLER

MENTAL ACTIVITY IN INFANCY

SIR,—May I comment briefly on the letters last week about my article on mental activity in infants ?

It is clearly impossible in a letter to answer all Dr Doniger's questions , she may care to know that a statistical paper on the work already done has been prepared for publication, and that the Medical Research Council is supporting further research by Dr William Dunham and myself into the problems of early diagnosis of neurological defect

The specific points raised by Dr and Mrs Bobath are dealt with in the original text of my article Their statement that mental development depends on physical development as it stands cannot be upheld If by physical development they mean neural maturation, the relationship between this and mental development is not disputed There can be no doubt that motor retardation occurs in cases of mental deficiency, though, except in amentia, motor development is in due time, attained by the mentally deficient child Indeed, many "therapeutic successes" in such cases are attributable to this process On the other hand no useful purpose is served by disregarding the fact that syndromes occurring in the presence of neural defect differ The purpose of my paper was to show that mental and motor defects both affect physical activity, though in differing ways The differences are not effaced by indiscriminate application to all abnormalities of the label "release phenomenon"

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EIRENE COLLIS

OSTEOPATHY

SIR,—I should like to correct any false impression created by Dr Cyriax's letter last week

No one would seek to deny that he has taught "spinal manipulation" to physiotherapists over a period of ten years *The point at issue, it seems to me, is that whereas* Dr Stoddard and the osteopathically trained apply very gentle forces, very strictly localised and guarded, in order to obtain a specific result at a joint, Dr Cyriax and his adherents indiscriminately mobilise the intervertebral joint systems by applying uncontrolled torsional forces *I do not seek to suggest that even this may not at times* relieve pain , but it can hardly do so by "reducing a displaced fragment of annulus," unless by the process of reductio ad absurdum The annulus fibrosus is living tissue, not dry friable matter

In cases of pain due directly to pressure upon nerve roots—a process caused by . (1) narrowing of the intervertebral distance, from (2) disc nucleus leakage which may sometimes cause (3) actual pressure on the radix by nucleus pulposus or by annulus bulging (because of nucleus pressure)—in such cases the radix will suffer from localised inflammatory reaction as a direct consequence of pressure

In these cases osteopathic methods, of gentle traction followed by specific movement, seek to relieve the pressure by altering the relationship of the affected nerve root to the [illegible] factor, relief of pressure will at once allow [illegible] and decongestion Those of us who use the gentle specific methods of osteopathy would never seek to deny Dr Cyriax and his trainees *their satisfaction in their own manœuvres,* rather do we say that we find the gentler methods we have learned effective without that element of uncontrol present in "spinal manipulation"

London W 1
DONALD TURNER

INVOLVEMENT OF AUTONOMIC NERVE-FIBRES IN DIABETIC NEUROPATHY

SIR,—It is to be expected that autonomic nerve fibres are involved in diabetic neuropathy and that this involvement produces changes in the vasomotor reflexes I think, however, that Dr Martin (March 21) too readily assumes that he has demonstrated this

The validity of his investigations depends on the reliability of skin-temperature measurements as a method of estimating skin blood-flow , and unfortunately Lewis's statement (referred to by Dr Martin) that these are most reliable cannot be substantiated Fetcher et al[1] in a most careful study compared the skin temperature of the finger with the blood flow of the same finger measured by means of a Goetz plethysmograph They demonstrated that with an ambient room temperature of 21°C (comparable to that used by Dr Martin) there is scarcely any correspondence between finger surface temperature and changes in blood flow In their experiments an increase in finger blood flow of 400% over a period of 10 minutes (i e , from 15 to 60 ml per 100 c cm per min) did not produce any significant change in skin-temperature These workers concluded that to obtain a good correspondence between skin temperature and skin blood flow "the part of the body under investigation must lose heat at a rate of at least 240 K Cal/hr/M^2"—conditions which can only be obtained in still air at room temperatures below 0 C

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[6] Blau A , Rieder N Bender M B *Ibid* 1936 10 910

[1] Fetcher E S Hall J F Shaub H G U S Air Force Memorandum March 1919

Synopsis of Cutaneous Diseases, the sole purpose of which was to present an abstract of Willan's classification of skin diseases and to elaborate that work; some seven editions of this book were printed and it was translated into French, German, and Italian. He also published *Delineations of the Cutaneous Diseases comprised in the Classification of the late Dr. Willan*, which contained a large number of coloured plates.

THE LONDON "SCHOOL"

It was through the work of these three—Turner, Willan, and Bateman—that many years ago England achieved an international reputation for the clinical study of skin diseases. There followed men such as W. C. Dendy, Jonathan Green, A. T. Thompson, and Samuel Plumbe, and later Erasmus Wilson, Tilbury Fox, Jonathan Hutchinson, Colcott Fox, and Radcliffe Crocker. Thus, starting with the impetus conferred by the work of Turner and Willan, there came into being what we may loosely term a school of dermatology, which was not only particularly English but particularly of London; and in saying this we do not wish to belittle the brilliant work performed at other centres in the United Kingdom—by, for example, J. N. Neligan of Dublin, H. G. Brooke of Manchester, W. A. Jamieson of Edinburgh, and T. McCall Anderson of Glasgow.

As is well known, the teaching of dermatology in London during the latter half of the 19th century, though competing with the work of Hebra in Vienna, Unna in Hamburg, and the flourishing French school at the St. Louis Hospital in Paris, influenced the practice of that specialty in many parts at home and abroad.

The influence of the London school was fostered by the action of Erasmus Wilson in establishing a *Journal of Cutaneous Diseases* in 1867, the foundation of the Dermatological Society of London in 1882, and the inauguration of the Dermatological Society of Great Britain and Ireland in 1894. These societies merged to form the dermatological section of the Royal Society of Medicine in 1907; and it would be difficult to overestimate the importance of the frequent meetings of that body in moulding clinical opinion in dermatology in this country.

In 1921, largely on the initiative of Dr. A. M. H. (now Sir Archibald) Gray, the British Association of Dermatology and Syphilis was founded, its first meeting being held in London, whence its journal has always been published. The association meets annually in a different town in Britain, not infrequently in London. Membership tends to be restricted to those who have become established and have made some mark in the specialty.

The London Dermatological Society was founded in 1912 and was renamed the St. John's Hospital Dermatological Society in 1926. This society also has much influence; its meetings are well attended, its discussions are often lively, and its annual oration has been given by many distinguished men, both from at home and abroad. In 1934 Dr. R. Prosser White bequeathed a sum of money to finance this oration, which was renamed the Prosser White oration.

The particular genius of London dermatology has lain in a flair for diagnosis, on which visitors from abroad have always commented; on integrity in the assessment of therapeutic measures, which more enthusiastic practitioners have found ruthless and chilling; and on a capacity for rapidly assimilating advances made elsewhere.

On the Continent, dermatology and venereology are usually combined in practice, and ample provision in hospital beds and in laboratory space and equipment is made for the two subjects in a single department. In London this arrangement is not considered rational or desirable, and few hospital beds and little laboratory space, except for histopathology, have been given to dermatology alone. This major defect may perhaps explain why London dermatologists have hitherto tended to regard the practice of dermatology as all-important and have failed to attract research-workers to a subject in which they are much needed.

POSTGRADUATE TEACHING

For many years, postgraduate students have come to London from far-distant countries, as well as from the universities at home, to absorb the practical teaching which London dermatologists could give. In this postgraduate migration, St. John's Hospital for Diseases of the Skin, with its associated London School of Dermatology, played a large part. The school was founded in 1923. Instruction in the form of lectures and clinical demonstrations was conducted by the (then) honorary staff of St. John's Hospital and the heads of the skin departments of the London undergraduate teaching hospitals, a department of special pathology being directed by Dr. J. M. H. MacLeod.

In July, 1948, the Institute of Dermatology, an institute of the British Postgraduate Medical Federation, was constituted on the foundations of this London School of Dermatology, remaining attached to St. John's Hospital, which was designated a postgraduate teaching hospital under the National Health Service Act. The Institute of Dermatology is now under the control of a director; the pathology department has been extended to include sub-departments of medical mycology and biochemistry, in addition to histopathology; a large and expanding museum of "moulages," photographs, and coloured drawings has been added, and a library has been included. Besides arranging for postgraduate teaching on the widest scale, the institute provides facilities and encouragement for clinical investigation and scientific research. An annual prize (the Chesterfield medal), which was founded in 1895, is awarded on the results of an examination.

The inpatient department of St. John's Hospital having been destroyed in 1940, a new one has been opened in North London, where the teaching activities of the Institute will be further extended. In addition, postgraduates at the Institute may sometimes obtain facilities to enlarge their experience considerably by visiting the skin departments of the general teaching hospitals; and here they may witness various methods of undergraduate instruction. Overseas students who have followed this course in the past have often said that, owing to its wealth of material and variety of teaching, London is in their opinion the most valuable dermatological teaching centre in the world. Outside the circle of schools associated with the University of London, visitors are likely to be made welcome at the London Skin Hospital and at the Skin Hospital at Blackfriars.

* * *

Though brief, these notes will perhaps suffice to show that the dermatologists of London today are endeavouring to continue the tradition founded by Turner, Willan, and Bateman, and have much to offer the postgraduate student who possesses ability and who is willing to do his best.

SYMBIOSIS AT HILL END

SOME ACHIEVEMENTS AND OPPORTUNITIES

DURING the war, Hill End Mental Hospital, at St. Albans, was called on to provide out-of-London wards for St. Bartholomew's; and the partnership thus begun has persisted. Hill End was vast enough to give such hospitality—a rambling Victorian structure, as able to accommodate guests as a Victorian house. The simile, however, must not be stretched too far; for Victorian houses were often solidly comfortable and convenient, whereas Victorian hospitals seem to have pressures rise precipitously, cardiac output rises very little or not at all, and right auricular filling pressures rise Although it is recognised that disability in mitral stenosis is not always entirely due to pulmonary vascular distension or diminished right ventricular competence, the exceptions are so few as to be unimportant

Finally it should be emphasised that mitral incompetence leads to profound changes in the hæmodynamic picture, and unless every precaution is taken to rule it out the correlation between symptoms and the hæmodynamic findings is likely to be unsatisfactory

Royal Prince Alfred Hospital,
Sydney, Australia RALPH BLACKET

BLOOD-GROUPS AND REPRODUCTION

SIR,—Kirk et al[1] have just published figures showing a highly significant difference in the reproductive pattern of women of blood-groups A and O, and have pointed out that their results are supported, though not on a significant scale, by data of Boorman[2] on 2000 mother-infant combinations They consider Boorman's data, like their own, *from the point of view of maternal age-group*, but from this point of view the difference between A and O mothers can be shown to be accompanied by an identical form of difference between AB and B mothers On the other hand, when the mothers are looked at from the point of view not of age-group but of parity, AB mothers assume the pattern of O and B mothers, and in addition the difference in pattern between A and O mothers appears as less distinct than the difference between A and B mothers (The numbers are rather too small for a comparison of individual classes) Similar tendencies can be seen in the associated *infants, AB and A infants showing an opposite trend* to B and O infants, according to both the age-group and the parity of the mothers, except when one excludes the classes A infants of A mothers, AB infants of AB mothers, B infants of B mothers, and O infants of O mothers, in which event the remaining A children assume the pattern of the O and B children (In 11 of the 14 classes of mother-infant combination the excess or shortage in Boorman's sample agrees with that of the much larger sample of Bryce et al[3])

TABLE I—RATIO OF OBSERVED TO EXPECTED MOTHERS, ACCORDING TO DATA OF BOORMAN, EXCLUDING A MOTHERS OF A INFANTS, O MOTHERS OF O INFANTS, AB MOTHERS OF AB INFANTS, AND B MOTHERS OF B INFANTS

Number of mothers	Group of mothers	Parity of mothers				
		1	2	3	4	5
259	A	0 97	1 01	1 04	1 03	0-66
266	O	1 07	0 92	0 94	1 11	0 83
53	AB	1 07	1 01	0 54	0 66	0 79
103	B	0 98	0 78	1 04	1 40	2 52

Furthermore, when one excludes the four classes mentioned, as in table I, the trend of the ratio of the remaining observed to expected A mothers, according to parity, is seen to be least unlike that of the remaining O mothers and most unlike that of the remaining B mothers The resulting order of groups—namely, A — O — AB — B—is the same as the descending order of fertility of the mothers who remain in Waterhouse and Hogben's[4] sample of 1239 families with 4139 children when one excludes the *mating classes* B × B, O × O, A × A, and AB × AB, and when these four classes are excluded the descending order of fertility of all the remaining parents in the Waterhouse Hogben sample is B father, A mother, AB father, O father, O mother, AB mother, A father, and B mother, the A mother being the only type of mother with a higher *than* average number of children per family And further evidence from fertility in support of the belief that A and O are less unlike than A and B in their reproductive characteristics can be seen in table II, which gives the average number of children per family according to the ABO group of the parents, in a sample of 7700 families with 16,371 children assembled by Hirszfeld[5] from reports published in 1927–33, the overall average number of children per family being 2 13 compared with 3 34 in the Waterhouse Hogben sample The average number of children is 1 90 in the 62 AB × AB families and 2 26 in the 1077 A × B and B × A families

In 2407 of Hirszfeld's families note was made of the sex of the 6547 children as well as of their group, and the ratio of male to female children is 1 16 for B, 1 14 for A, 1 14 for O, and 0 95 for AB In a sample of 661 families with 1539 children assembled by Hirszfeld and Zborowski[6] from reports published in 1920–24 the ratio *of male to female children* is 1 21 for AB, 1 16 for B, 0 97 for A, and 0 91 for O (A low sex-ratio in the children of the mating class O father × A mother was remarked on by the authors, and had previously been noted by Dossena[7]) *And in* Sanghvi's[8] personal sample of 2194 newborn infants the ratio of male to female infants is 1 33 for B, 1 25 for O, 1 21 for AB, and 0 98 for A The ratios for the three samples combined are 1 19 *for* B, 1 12 *for* O, 1 08 *for* A, and 1 03 for AB, but the only constant individual feature is the high sex-ratio of the B children When, however, one excludes, as in table III, B children of B mothers, O children of O mothers, A children of A mothers, and AB children of AB mothers, a second constant feature appears in the low sex-ratio of the remaining O children, the ratios for the three samples combined being 1 19 for B, 1 05 for A, 1 00 for O, and 0 99 for AB Given the B — A — O descending order of ratios in any one of the samples shown in this table, the same order would *occur by chance in both the other samples 1 in* 36 times The difference between the B and A children in the table is consistently greater than that between the A and O children

TABLE II—VARIATION OF FERTILITY WITH ABO BLOOD GROUP ACCORDING TO DATA OF HIRSZFELD (FATHER'S GROUP IS GIVEN FIRST)

No of families	Types of mating	Av no of children per family		Types of mating	No of families
301	B × B	2 28			
900	B × O + O × B	2 26	2 66	B × AB + AB × B	211
1039	O × O	2 10	2 42	O × AB + AB × O	354
2180	A × O + O × A	2 04	2 18	A × AB + AB × A	401
1175	A × A	1 85			

TABLE III—RATIO OF MALE TO FEMALE CHILDREN, EXCLUDING A CHILDREN OF A MOTHERS, O CHILDREN OF O MOTHERS, AB CHILDREN OF AB MOTHERS, AND B CHILDREN OF B MOTHERS

No of children		Data of Sanghvi		Data of Hirszfeld and Zborowski		Data of Hirszfeld	
Male	Female	Group	M/F	Group	M/F	Group	M/F
575	482	B	1 21	B	1 14	B	1 20
758	721	A	1 07	A	0 98	A	1 06
745	745	O	1 02	O	0 85	O	1 03

Hirszfeld and Zborowski's main purpose was to compare the birth weights of infants of the same ABO

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[1] Kirk R L Kirk, M Stenhouse N S *Brit J prev soc Med* 1953 7, 1
[2] Boorman K E *Ann Eugen, Lond* 1950, 15, 120
[3] Bryce L M, Jacobowicz R MacArthur, N, Penrose L S *Ibid* p 271
[4] Waterhouse J A H, Hogben L *Brit J soc Med* 1947 1 1
[5] Hirszfeld, L *Ergebn Hyg Bakt* 1934, 15 54
[6] Hirszfeld L Zborowski H *Klin Wschr* 1926, 5, 741
[7] Dossena G *Ann Ostet Ginec* 1924 46 335
[8] Sanghvi L D *Nature Lond* 1951, 168, 1077

ESTIMATES FOR 1953–54

The National Health Service estimates for 1953–54 [1] allow for gross expenditure in England, Scotland, and Wales of £487,984,040, compared with £515,381,500 in 1952–53. These totals are made up as follows:

	1953–54 (£)	*1952–53* (£)
Central Council, &c.	4500	4250
Hospital specialist and ancillary services	305,150,110	304,656,300
Grants to local health authorities ..	21,558,020	21,233,000
General medical and dental services, pharmaceutical services, and supplementary ophthalmic services	135,215,520	158,280,700
Training services, &c.	1,689,750	1,751,650
Civil Defence services	6,406,100	9,805,200
Other services	17,960,040	19,650,400

Appropriations-in-aid (e.g., from National Insurance contributions) in 1953–54 are expected to total £71,503,680, compared with £76,480,000 in 1952–53, thus bringing the net cost to £416,480,360, as against £438,901,500 in the present year. In arriving at the true cost of the service the expenditure on Civil Defence should be excluded.

The difference between the two years is mainly due to the exceptional expenditure in 1952–53 on retrospective payments under the Danckwerts award on the remuneration of general practitioners. Originally the cost of general medical services for 1952–53 was estimated at £48,500,000,[2] whereas the cost now shown for this year is £86,913,000; in the coming year it is expected to fall back to £58,217,000.

According to the estimates, the cost of the hospital services will drop slightly in 1953–54; and this will be the first year since the inception of the service in which there has been such a decrease.

The grant-in-aid to the Medical Research Council in 1953–54 [1] is set at £1,805,846, compared with £1,898,287 in the present year. Of the total £134,700 is for capital expenditure, and £1,671,146 for general expenses compounded as follows (with deduction of £117,908 for receipts): administration, £70,652; provision for general scientific purposes, £20,707; National Institute for Medical Research, £343,771; research units and external scientific staff, £984,624; special grants to institutions, &c., £187,300; temporary research grants and training awards, £182,000.

PRIVATE TREATMENT IN N.H.S. HOSPITALS

Memorandum from the Joint Consultants Committee

The Minister of Health has now laid before Parliament new Pay Bed Regulations under sections 4 and 5 of the National Health Service Act, 1946. These regulations are designed to come into operation on April 1 next, when they will supersede the existing regulations.

The new regulations, which have been the subject of lengthy discussions between the Joint Consultants Committee and the Ministry (and with the Minister himself), deal broadly with two matters:

(a) The manner in which the charges for private hospital beds shall be assessed.

(b) The maximum professional fees to be charged to patients desiring private treatment in hospital.

PRIVATE BED CHARGES

Under section 5 of the 1946 Act, patients seeking treatment in private hospital beds are required to pay the whole cost of the accommodation and services provided. Since 1948 the charges for private beds have risen to an alarming degree, and during the discussions on the new regulations, the Joint Committee sought a personal interview with the Minister of Health, and impressed upon him that unless some action was taken to reduce the charge private practice would steadily diminish. The committee reminded the Minister of the promises of previous Governments that facilities for private practice would be retained under the new service. It pointed out that it was the experience of consultants in many parts of the country that there was a falling-off in the demand for private treatment—due largely in their opinion to the high maintenance charges—and that this was bound also to affect hospital revenue. The committee therefore urged the reintroduction of a moderately priced private bed.

In reply, the Minister stated that he thought the possibility of introducing the necessary legislation during the next two or three years was extremely remote, having regard to the heavy parliamentary programme. The Minister added that while he was anxious not to place any obstacle in the way of private practice he doubted whether the falling-off in private hospital treatment was primarily due to the high charges. He agreed, however, that if this could be substantiated, the position would warrant further consideration because the provisions of section 5 were intended to implement the promise given that private practice facilities should continue.

The new regulations are still designed to secure that the charges for private beds shall represent the whole cost, but there are certain changes in the method of calculating the charges that will, in many cases, result in a reduction of the charge. Thus in hospitals where the total cost of the pay block cannot be determined separately from the cost of the public wards, the percentage increases which are added to the average daily inpatient cost to arrive at the private bed charge are reduced from 25% (single room), 15% (double room), or 5% (multiple-bedded room), to 15%, 10%, and 5% respectively. Furthermore these percentage increases are to be added to the net daily inpatient cost before the addition of the salaries of medical and dental staff instead of after the addition of these salaries as hitherto; and the cost of any service from which the private patient receives no benefit is excluded from the maintenance charge.

MAXIMUM PROFESSIONAL CHARGES

The main criticism which is likely to be levelled by the profession against the new regulations, so far as they concern the professional fees to be charged to private hospital patients, is that the detailed classification of operations is retained.

The Joint Committee made strenuous efforts to persuade the Ministry—and the Minister himself—that the attempt arbitrarily to divide operations into categories of major, intermediate, and minor, without reference to the condition of the individual patient, was unrealistic and unlikely to work satisfactorily. Unfortunately the Minister has adhered to the view that the classification is necessary as a protection to the patient, despite the repeatedly expressed view of the committee that the classification afforded no protection at all but that, on the contrary, the maximum fee for each category of operation was likely to become the standard charge, whereas in the past consultants normally related their fee to the particular requirements of the case and to the patient's circumstances.

The Ministry sought the assistance of the Joint Committee in improving the detailed classification of operations, but because of its view that any classification was impracticable the committee declined to accept any responsibility for it.

Apart from this point of major principle on which the Ministry and the Joint Committee were unable to reach any agreement, there are certain improvements in the 2nd Schedule, setting out the maximum professional fees. The maximum fee that may be charged

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1. Civil Estimates for the Year Ending March 31, 1954: Class V: Housing, Local Government, Health, Labour, National Insurance, and National Assistance. H.M. Stationery Office. Pp. 185. 6s.
2. See *Lancet*, 1952, i, 661.

relieved by hot packs We do not believe that the mere relief of pain with analgesics is enough It has never been seriously suggested that the life of a nerve cell has ever been saved by the use of hot packs On the other hand many patients have been saved from crippling deformities and on occasion from the respirator by the use of hot packs

Dr Russell suggests that muscle shortening is best countered by passive movement In our experience tightened muscles cannot be adequately stretched without hot packs or hot baths If tightened muscles are stretched without previous packing, pain is induced and the muscle tightness and protective spasm may be aggravated

I must disagree with Dr Russell on the matter of re education At all cost the correct pattern of posture and walking should be maintained and trick movements avoided It is only by the maintenance of a normal correct pattern of movement that residual unaffected muscle-fibres can be correctly exercised and encouraged to hypertrophy

Finally I disagree, too, on the early introduction of active vigorous movement to a point of fatigue In our experience this will often reactivate muscle tightness and spasm and induce deformities

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J E CAUGHEY

POLIOMYELITIS IN DENMARK

SIR,—We should like to comment on one or two points in Dr Ritchie Russell's letter (March 14) where we consider that he is seriously in error

1 "In this regard we lag behind American practice which has long ago devised methods for dealing with the type of case which caused so much trouble in Copenhagen" It is very unlikely that any European group had a greater knowledge of this "American practice," but the hard fact is that these methods were ineffective in dealing with the problem that confronted Professor Lassen and his colleagues The Danish practice seems to us to contain certain features which are an advance on previous methods of management—even in theory—and, moreover, it has been shown to work One suspects that, as in other fields, an ounce of practical experience is worth a vast amount of theorising The apparent ease with which Dr Russell finds that postural drainage in the prone position copes with the pure bulbar case makes one wonder what all the bother is about How simple it all is—in theory! Unfortunately, in practice so many cases fail to present themselves as "pure" that generalisations tend to be dangerous

2 "Cases with true respiratory paralysis of severe degree must, of course, be clearly distinguished and require different treatment which I shall not refer to here" Does Dr Russell appreciate that many of the Danish cases were of this type and that it is the ability of their method to deal with them in a highly satisfactory way that is so impressive? Indeed not the least impressive aspect of a visit to Blegdams Hospital is the obvious comfort—one might almost use the word happiness—of the patient

3 Dr Russell's remarks regarding the "mechanical student"[1] also seem to betray a lack of understanding of the problem Many people have devised valves of one kind or another but most of them are inapplicable to the Danish method of treatment What is required is something that can follow and augment the patient's own inadequate voluntary respiration, and which causes minimal interference with venous return from the lungs and with cardiac output

We believe that the Danish workers have made an important advance in the technique of handling this difficult type of case Those of us who are concerned with the management of poliomyelitis—and some of us have acquired a fair degree of experience in the past twenty years considering the small numbers of cases normally encountered in this country—are constantly endeavouring to improve our techniques One suspects that, no matter what the extent of previous study, it is when one has actually dealt with the kind of experience that Copenhagen has had that one looks back and says "As a matter of fact, when the thing started we really knew nothing" There is wisdom in regarding one's theoretical knowledge with due humility

Department of Infectious Diseases
University of Glasgow
THOMAS ANDERSON
JAMES H LAWSON
H H PINKERTON

Fazakerley Group of Hospitals,
Liverpool
A B CHRISTIE
J R ESPLEN

PERMEABILITY OF NATURAL MEMBRANES

SIR,—May I take up a point in your kind review[1] o the book on *Permeability of Natural Membranes* b Dr Davson and myself? You correctly state that we ha not attempted to survey recent work involving isotop studies and the effect of cell metabolism on the distribu tion of ions We agree that such a survey should b made as soon as possible, and we also agree that sinc the first edition of the book in 1943 there has been " considerable shift of emphasis in our whole way thinking about the distribution of ions, the properti of the membranes themselves are less emphasised an more importance is attached to active processes"

While this is true, the reason for such emphasis no being placed upon the membranes themselves is that present we have extremely little idea of how acti transport mechanisms are incorporated in cell mem branes At present, views in this field are in an extreme fluid state Each year sees one or more new theoretic approaches There would be no justification in writi a textbook in the field of active transport until a adequate theory of the relation between cell metabolis and membrane properties can be established

King's College,
London, W C 2
J F DANIELLI

SPONTANEOUS RUPTURE OF JEJUNUM

SIR,—I was interested in Mr Frederick Smith's repor (Feb 28, p 421) of a case of spontaneous rupture of th proximal jejunal loop as a late complication of gastrec tomy. Last year I had a similar case, but the ruptur occurred on the twelfth postoperative day

On July 7, 1952, a man, aged 52, underwent an anterio Polya isoperistaltic partial gastrectomy He gave a lon history of indigestion culminating in a fairly profuse hema temesis He made good progress after the operation and wa up and about the ward from the fourth day onwards

On July 18 he had some nausea and vomited small amount of fluid This persisted next day, a Ryle's tube was passed and hourly aspirations brought considerable relief A recta drip was also set up During the same night his abdomin pain became very severe, and early on the morning of July 2 he collapsed The abdomen became rigid and tender with al the signs of a perforation At no time was a swelling felt i the abdomen

After resuscitation, laparotomy revealed that the peritone cavity was full of free fluid The afferent jejunal loop could not be seen at first because it had passed to the left behind the distal loop, and actually lay a little to the left side of t distal loop It still showed some distension, and fluid wa pouring from a linear perforation, $^3/_4$ in long, situated abou $^1/_2$–1 in distal to the duodenojejunal junction The linea character of the perforation was particularly noticed at th time

The perforation was repaired, and the loop restored to its proper position and fixed by sutures to adjacent structure A Ryle's tube was then guided from the stomach down th proximal loop to ensure that it could be kept decompressed b aspirations A second Ryle's tube was left in the stomach

Convalescence was stormy at first but complete recovery followed Three months later he was fit and had had no complications

At the operation the trouble was thought to have been due to rotation of the stomach, carrying the proximal loop behind the distal one and causing an obstruction at the duodeno-jejunal flexure and at the anastomosis of this loop with the stomach Presumably, the closed loop thus formed became grossly distended without being detected and finally ruptured he added that now that women played an ever-increasing part in our national life, it was even more important to seek ways to relieve the unhappiness, discomfort, and pain that gynæcological disorders brought. He ended by drawing attention to the association of friends which the hospital had; he hoped to see the time when every hospital would have a friendly voluntary association of this kind.

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[1] Christie A B Esplen J R *Lancet* March 7 1953, p 492

[1] *Lancet* 1952, ii, 1210

Viscount WAVERLEY, chairman of the governing body of the British Postgraduate Medical Federation, recalled how in 1948 the postgraduate units of Queen Charlotte's, Chelsea, and Hammersmith Hospitals were brought together to form the Institute of Obstetrics and Gynæcology, now part of the British Postgraduate Medical Federation. As the three hospitals lay so far apart, each had to have its own laboratories. For Chelsea Hospital this was difficult owing to lack of space, but the Ministry and the South-West Metropolitan Regional Hospital Board had now found accommodation nearby at St. Luke's Hospital.

After the ceremony Mr. Macleod inspected the new premises, which are connected with the Chelsea Hospital by a bridge. The institute's wing includes a lecture-room, a students' common-room, a refectory, and administrative offices; while the Chelsea Hospital's share of the extensions comprise a photographic studio and darkroom and three laboratories for the departments of pathology and endocrinology.

Parliament

Smoking and Lung Cancer

REPLYING to an adjournment debate on this subject on March 19, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that in view of the grave rise in the number of deaths from lung cancer the Ministry of Health and the Medical Research Council were stimulating new lines of research into this disease. In their important report on the connection between smoking and cancer Dr. Richard Doll and Prof. Bradford Hill concluded that the association between tobacco-smoking and lung cancer was a real one, the effect varying with the amount smoked. A similar investigation had been carried out in America with the same conclusion. But Miss Hornsby-Smith emphasised that the information which the Ministry of Health had so far received from their Standing Advisory Committee on Cancer and Radiotherapy and from the Medical Research Council showed that they did not regard this report as wholly conclusive. While they accepted that research had shown a statistical relationship between tobacco-smoking and lung cancer, they did not necessarily accept that that statistical relationship meant a causal relationship. All the evidence so far in the possession of the Ministry indicated that the arsenical content of certain tobaccos was too small to be effective in carcinoma. All those concerned were doing their utmost to find a solution, but nothing should be done to panic the population. Research into exhaust gases of petrol and diesel engines had now been abandoned as a possible source contributing to cancer of the lung. The Standing Advisory Committee on Cancer and Radiotherapy had not yet come to any conclusion or given the Ministry any advice beyond the statement on the correlation between tobacco-smoke and cancer of the lung. Therefore the Ministry could only be non-committal for the time being in this matter. It was a long-term matter requiring careful sifting of results and highly complicated experimental work over a long period, and the collection of vital statistical data.

QUESTION TIME

Sickness-rate among Post Office Employees

Replying to a question, Mr. LEONARD GAMMANS, Assistant Postmaster-General, said that the average number of days' sick absence for non-established Post Office staff in 1938 was 8·1 days for men and 9·3 for women; in 1951, it was 15·0 days for men and 18·4 for women. This was an alarming increase, and the Government and the Post Office under successive Administrations had been disturbed about it. He estimated that if the figures were the same as before the war there would be a saving in staff of at least 6500 people.

Prescription Charges

Mr. LESLIE HALE asked the Minister of Health the estimated total net saving to the Exchequer, after making allowances for administrative costs and for the extra cost to the National Assistance Board, both direct and administrative, of the charge of 1s. on prescriptions from the time of its introduction to the nearest most convenient date for computation.—Mr. IAIN MACLEOD replied: The estimated net saving to the Exchequer from the prescription charges paid by patients in England and Wales between June 1, 1952, and Dec. 31, 1952, after the deduction of refunds made by the National Assistance Board, is about £2$^3/_4$ million. Administrative costs, though not known in detail, would not materially affect this estimate. In addition there was a saving to the Exchequer during this period of about £1$^1/_4$ million because fewer prescriptions were dispensed than would have been expected if charges had not been introduced; though it is possible that other factors contributed to this decrease.

Medical Auxiliaries

Replying to a question, Mr. MACLEOD said that, as the result of discussions with the professional bodies of medical auxiliaries, the Secretary of State for Scotland and he were satisfied that there was insufficient agreement on fundamental matters to proceed with statutory registration on the lines proposed by the Cope Committees. They intended, therefore, as soon as possible to make Regulations to prescribe qualifications for medical auxiliaries for the purpose of employment in the National Health Service. They would shortly give the professional and other bodies concerned an opportunity to comment on an outline of the Regulations proposed.

Public Health

Smallpox

BY noon on March 23 a further 6 cases of smallpox had been notified from Todmorden, where the outbreak reported last week continues. In addition a cotton operative living and working in Oldham has been diagnosed as having smallpox, bringing the total to 11. Another of the first 4 patients died on March 20—the second death in the outbreak. The 6 new patients at Todmorden are all direct contacts of the earlier cases; but so far no contact between them and the Oldham man has been established. It may be that the mill in which he works received cotton waste, or part of a consignment of raw cotton, from the Todmorden mill where the first men to be infected were employed. There have been no more cases in Bacup, the home of a man working in the Todmorden mill who died of smallpox on March 13.

Infectious Diseases Regulations

The Public Health (Infectious Diseases) Regulations, 1953,[1] which come into force on April 1, make a number of changes in the existing regulations, which were first issued in 1927. The provisions governing the action to be taken by local authorities and medical officers of health against the risk of food-poisoning apply at present to "enteric fever and dysentery": under the new regulations they will apply to "typhoid fever, paratyphoid fever or other salmonella infections, dysentery, and staphylococcal infection likely to cause food poisoning." The 1927 regulations allowed action to be taken only in the matter of a person actually suffering from one of the diseases in question; but from April 1 the provisions will be extended to cover carriers of infection. In future both carriers and people who are clinically ill may be prevented from continuing in or entering an occupation connected with food or drink. At the moment these steps cannot be taken until the medical officer of health has reported the case concerned to the local authority, which may be liable to pay compensation under the Public Health Act, 1936. A new provision will allow a local authority to sanction immediate action in cases where the medical officer of health judges the matter to be urgent.

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[1] The Public Health (Infectious Diseases) Regulations, 1953. S.I. no. 299. H.M. Stationery Office. 4d.

JAMES EDWARD HILL SAWYER

M.A., M.D. Oxfd, M.R.C.P.

Dr. J. E. H. Sawyer, who died on Feb. 22 at his Sussex home at the age of 78, had close ties with the Birmingham medical school, where his father, Sir James Sawyer, was physician to the Queen's Hospital and professor of medicine at Queen's College. He was educated at Shrewsbury School, Christ Church, Oxford, and St. Thomas's Hospital. At St. Thomas's he won the Solly and Bristowe medals and the Hadden prize. He qualified in 1900, and three years later proceeded to the D.M. and M.R.C.P.

In 1906 he was appointed casualty assistant physician to the General Hospital, Birmingham, becoming assistant physician in 1914. He was also physician to outpatients at the Children's Hospital and assistant to the chair of medicine. He published articles on cardiac and cerebral disease; he contributed to French's *Index of Differential Diagnosis*, and for a time he edited the *Birmingham Medical Review*.

In 1908 he joined the Territorial Army as registrar of the Birmingham military hospital, and he received the 1911 Coronation medal. During the 1914–18 war he was registrar and later administrator of the 1st Southern General Hospital, which was established in the buildings at Edgbaston of Birmingham University. In 1917 he became brevet lieut.-colonel. At the end of the war he decided that he would not resume his work as a consulting physician and he retired to Burwash in Sussex. In the last war, until he reached his 70th year, he served as a captain in the Home Guard.

Mrs. Sawyer, to whom he was married in 1906, is the daughter of the late Lieut.-Colonel C. W. Longstaff. She survives him with a daughter and three sons.

Births, Marriages, and Deaths

BIRTHS

BREARLEY.—On March 17, at Mill Road Hospital, Liverpool, to Joyce Mary (*née* Hewitt) and Roger Brearley, F.R.C.S., of 55, Meadow Lane, West Derby, Liverpool—a son.

LE VAY.—On March 15, at Woolwich Memorial Hospital, to Dr. Marjorie Le Vay, wife of Mr. David Le Vay, M.S.—a son (Benedict).

MORGAN.—On March 9, at Jacksonville, Florida, U.S.A., to Mildred, wife of Mr. Bernard L. Morgan, F.R.C.S.—a daughter (Lesley Cynthia).

MARRIAGES

NEWNS—CHRISTMAS.—On Feb. 28, in Norwich, George Reginald Newns, M.B., M.R.C.P., to Patricia Mary Christmas, M.C.S.P.

DEATHS

BURT.—On March 18, at 5, Springfield Place, Bath, Joseph Barnes Burt, M.D. Lond., aged 72.

Diary of the Week

MARCH 29 TO APRIL 4

Monday, 30th

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, S.E.1.
5.15 P.M. Dr. T. H. Whittington: Myopia and the Care of the Myopic Patient.

HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, 64, London Wall, E.C.2.) Dr. Keith Simpson, Dr. Robert Forbes, Dr. D. C. Norris: Professional Pitfalls.

Tuesday, 31st

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. D. O'Neill: Diagnosis and Management of Stress Disorders of the Skin.

Wednesday, 1st

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Section of History of Medicine.* Major J. B. Neal: Two Reformers of Royal Army Medical Service—Sir William Muir and Sir William Taylor (Part I). Dr. John Keevil: Leonard Gillespie (1758–1842), Naval Surgeon and Physician to Lord Nelson.

INSTITUTE OF UROLOGY, St. Paul's Hospital, Endell Street, W.C.2
5 P.M. Dr. W. N. Mascall: Diagnosis and Treatment of Gonorrhœa.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (University of Manchester.) *Section of Medicine.* Prof. R. E. Lane: Our Dilemma. (Presidential address.)

Notes and News

SENIOR REGISTRARS

THE Joint Consultants Committee has made fresh representations to the Ministry of Health on behalf of the senior registrars whose appointments are being terminated and for whom there are no suitable openings in hospitals or elsewhere. The Ministry is collecting figures from the regions with a view to ascertaining the exact extent of the problem, but the information received is not yet complete. The Joint Consultants Committee has protested at the delay and has received an assurance that the figures will be passed on to it as soon as they are available. It is hoped that the committee will be in a position to resume the discussion with the Ministry in the near future.

REACTION TO THE IRISH HEALTH BILL

THE Irish Medical Association on March 18 unanimously rejected the Health Bill now before the Dail, and set up a defence committee to devise means of defeating the government's proposals. The Irish News Agency reports that Dr. A. McCarthy, chairman of the central council, declared that the association would refuse to coöperate if the Bill became law; reports from branches and groups were unanimously against the measure. The association, he added, had a membership of 2200, representing 90% of the doctors in Eire, and whatever scheme was brought in would have to be worked by the doctors. They had the power in their hands, and what was needed was the determination and courage to use it.

Under the Bill[1] local health authorities would be given the power and duty to provide an extended health service outlined last year in a white paper.[2] The proposals call for the transfer to local authorities of responsibility to provide general health services for the lower income group, and a hospital service for both lower and middle income groups will be based on local authority hospitals. The association's objections to the Bill have been summarised as follows: (1) that it contains in essence State control of the medical profession; (2) that under it the State must enter unduly and very intimately into the lives of patients and of doctors; (3) that to implement it the whole community must be heavily taxed independently of the necessity or desire of the citizen to use the facilities that may be provided; (4) that its implementation by direct or indirect taxation would morally compel the citizens to avail themselves of the services; and (5) that under it the State must have recourse in great part to ministerial regulations as distinct from enactments of Parliament.

ANGLO-DANISH SANATORIUM SCHEME FOR BRITISH CHILDREN

UNDER a scheme inaugurated by the Anglo-Danish Society and the National Association for the Prevention of Tuberculosis, 50 British children were sent last year to a Danish sanatorium for several months' treatment. For 1953 sufficient funds have been raised by the societies concerned to send up to 100 children, and the first party left this country on March 19 for Vordingborg Sanatorium, South Zealand. Cases are selected by a committee of the N.A.P.T. from recommendations made by chest physicians and pædiatricians. Since the scheme started, the British Red Cross Society have provided a welfare officer to stay with the children and keep in touch with their parents, and now an English teacher is also being appointed.

BRITISH ASSOCIATION OF SPORT AND MEDICINE

FORTY-EIGHT members attended the first general meeting of this association, which was held at the Westminster Hospital Medical School on Feb. 27. Sir Adolphe Abrahams, the president, describing the aims of the association, said that he hoped that it would become the authoritative body on every medical aspect of athletics and exercise. It should in his view advise on the general principles of athletic training and the medical conditions which would and would not prohibit participation in sport. It would have to study the inevitable injuries of sport, the effect of violent exercise during the incubation period of poliomyelitis and other infections, and the dangers of boxing. The fitness of women and girls

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[1] See *J. Irish med. Ass.* March 1953, p. 72.

[2] Department of Health. Proposals for Improved and Extended Health Services. Dublin 1952. See *Lancet*, 1952, ii, 531.

Letters to the Editor

IMPROVED FLOUR

SIR,—Dr. Sheldon and Dr. Yorke last week claim to have demonstrated a syndrome attributable to chemically treated flour, but they have apparently failed to carry out control observations using strictly *untreated* flour. Their control material, called "chemically untreated flour," was subjected to an aeration process which the authors assume to have no modifying effect on the bread protein. This may not be the case, however, if the aeration process used involved mechanical agitation, since high-speed stirring and foaming techniques are known to denature proteins.

Another possible explanation of their findings would be that this patient was suffering from eczema due to sensitivity to wheat protein—a rare but fairly well recognised condition. If this was so, the characteristic properties of the allergen may have been damaged by the physical treatment but not by chemical treatment with agene or chlorine dioxide.

It may perhaps be emphasised that any proposed treatment of flour, or other foods, whether physical or chemical, and whether involving synthetic or natural materials, should be subjected to critical examination as a proper safeguard to the public health.

Department of Pharmacology,
University of Birmingham.

A. C. FRAZER.

VITAMIN E AND INTERMITTENT CLAUDICATION

SIR,—I have read with great interest the controversial correspondence in your columns on this subject. Dr. Hamilton and his colleagues appear to have fallen into the grave and age-old error of assuming that because they have never seen anything but white swans, therefore all swans are white. "All swans are white" is a null hypothesis, which can never be proved, as the first black swan seen disproves it. The statistical type of experiment can never prove the null hypothesis, but may disprove it.

The null hypothesis in the present controversy is: "Vitamin E is no more effective in relieving intermittent claudication than a control substance." If it can once be shown, as has been done in Professor Boyd's department, that a series of cases treated with vitamin E show a significantly greater improvement than a parallel series of controls, the null hypothesis is destroyed for ever. There is no justification whatever for Dr. Hamilton and his colleagues concluding that vitamin E is of no value in the treatment of intermittent claudication. No amount of experimentation can ever prove or justify such a statement. Professor Fisher has stressed the point I am trying to make:

> "It should be noted that the null hypothesis is never proved or established, but is possibly disproved, in the course of experimentation. Every experiment may be said to exist only in order to give the facts a chance of disproving the null hypothesis."

Insensitive experiments will always tend to confirm the null hypothesis; but science advances by the experimental disruption of null hypotheses, and their replacement by others which in their turn are disrupted by still more sensitive experiments. Nobody who has read the articles from Professor Boyd's department and those of Dr. Hamilton can doubt that the more sensitive experiments have been performed in Manchester.

Articles such as that of Dr. Hamilton and his colleagues with the backing of the Medical Research Council seem to be increasingly fashionable. It is therefore urgent that your readers should appreciate which questions can and which cannot be answered by this type of experimentation. The invalid conclusion that vitamin E is of no value in the treatment of intermittent claudication backed by the authority of the Medical Research Council is, to say the least of it, mischievous; and it may be responsible for practitioners denying a useful treatment to their patients. Let us hope it will not be a hindrance to true research; and that one day, through knowing how to treat some patients now, we may learn to help all.

Flimwell,
near Wadhurst,
Sussex.

GEOFFREY E. LOXTON.

CEREBRAL DISEASE DUE TO FUNCTIONING ISLET-CELL TUMOURS

SIR,—The report by Mr. Richardson and Professor Russell[1] is informative and challenging since the effects produced on the central nervous system by prolonged hypoglycæmia due to functioning islet-cell tumours are bizarre and not well understood and may go long unrecognised. The effects may be cerebral, cerebral and spinal, or spinal in location.

Lawrence et al.[2] have reviewed and collated the numerous reports of serious damage to the brain following severe and prolonged hypoglycæmia. Widespread damage both with and without hæmorrhage was found. Characteristic observations were diffuse degeneration and necrosis of nerve-cells with corresponding glial proliferation. In the six brains examined the cerebral cortex, the caudate nucleus, and the putamen were most affected, and the cerebellum less so; the lesions in the remaining centres of the brain-stem were slight. Moersch and Kernohan[3] have reported the occurrence of multiple petechial hæmorrhages or degeneration of some of the cells. In one patient sections from various levels of the spinal cord were normal except in a small part of the mid-lumbar enlargement. In these sections about two-thirds of the nerve-cells of one anterior horn had been destroyed and the cells replaced by proliferation of the glia, especially of the astrocytes.

In the six patients of Richardson and Russell the symptoms suggested widespread damage to the brain with particular reference to the hypothalamus. In four of the five cases that were analysed the accent on the vegetative disorders, such as sweating, pyrexia, tachycardia, flushing, and possible clouding of consciousness, suggested a lesion in the hypothalamus. In the advanced cases in this series, the levels of the glucose in the blood and the response to glucose were not consistent, thus leading to confusion.

Symptoms referable to damage of the cerebrum and the spinal cord have been reported in a patient with prolonged hypoglycæmia manifested by an unusual array of symptoms.[4] The patient had had repeated convulsions, periods of confusion and excitement, ataxia, muscular atrophy, intellectual impairment, and pseudologia fantastica. After the removal of the pancreatic adenoma, all of the abnormalities except the residual muscular atrophy disappeared.

Barris,[5] by his observations on functioning islet-cell tumours, may have cast some light upon the ætiology of progressive muscular atrophy. He points out that, in this group of muscle-wasting states, the anterior horn cells of the spinal cord are the site of demonstrable alteration. Progressive wasting of muscles, muscle fasciculations, increased myotatic irritability, electromyographic evidence of fibrillation, and progressive motor weakness involving chiefly the trunkal and appendicular muscles are seen. Barris has summarised the details of five patients—one previously discussed, three others from the literature, and one of his own.

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1. Richardson, J. E., Russell, D. S. *Lancet*, 1952, ii, 1054.
2. Lawrence, R. D., Meyer, A., Nevin, S. *Quart. J. Med.* 1942, 11, 181.
3. Moersch, F. P., Kernohan, J. W. *Arch. Neurol. Psychiat.* 1938, 39, 242.
4. Lidz, T., Miller, J. M., Padget, P., Stedem, A. F. A. *Ibid*, 1946, 62, 304.
5. Barris, R. W. *Ann. intern. Med.* 1953, 38, 124.

Whipps Cross Hospital Medical Society

At a meeting of this society to be held at 8 30 P M, on Friday April 10, at the hospital, London, E 11, Prof S P Bedson, F R S, will deliver a lecture on Recent Trends in Virus Research.

Committee on Disablement

The thirteen members of the committee which the Minister of Labour has set up to consider the problems of the disabled include Sir Claude Frankau, F R C S, and Dr C G Magee The chairman is Lord Piercy

World Health Day

On World Health Day, which is to be celebrated this year on April 7, a meeting is being held by the United Nations Association at the Caxton Hall, Westminster, S W 1 The speakers will include Mr Iain Macleod, the Minister of Health, and Dr H S Gear, assistant director general of the World Health Organisation

Central Council for the Care of Cripples

The annual general meeting of this council will be held at the Cowdray Hall, Henrietta Place, Cavendish Square, London W 1, on Friday, April 10, at 11 30 A M Miss Patricia Hornsby Smith, parliamentary secretary to the Ministry of Health, will address the meeting

International Congress of Gynæcology and Obstetrics

Prophylaxis in Gynæcology and Obstetrics has been chosen as the main theme of this congress which is to be held at Geneva from July 26 to 31 Further information may be had from the secretariat of the congress, Maternité, Geneva, Switzerland

Hertford Hospital, Paris

On March 18 it was announced that owing to financial difficulties this hospital, which has served the British colony in Paris for eighty years, will have to close A gift of £35,000, which was made last year for rebuilding and re equipment, has been reluctantly withdrawn by the donor, Sir Bernard Docker

Visits to Children in Hospital

At a meeting of the Leeds Regional Hospital Board, reported in the *Manchester Guardian* of March 13, Dr G W Black said that 10 hospitals in the region allowed daily visiting in children's wards, 8 allowed daily visiting in emergencies, 64 allowed regular visiting and 6 banned visiting He hoped that the 6 would reconsider this rule Prof P J Moir, consulting surgeon to the United Leeds Hospitals, did not share this view "I think there is a lot of sloppy sentiment talked about this," he said "If children are left alone for a day or two they forget their parents The hours in hospital after the visits of parents are chaotic The children all cry and shriek and will not go to sleep"

Problems of Virology

A symposium on this subject will be held on May 22 and 23 at the Institut d Hygiéne et de Bactèriologie, Lausanne, the speakers will include Professor Flückiger (Foot and-mouth disease), Professor L'Heritier (Hereditary Virus of Drosophila), Dr Cateigne (Influenza), Dr Kenneth Smith (Polyhedral Virus Diseases of Insects), Professor Verge (Virus Diseases of Animals), Dr Klieneberger Nobel (Organisms of the Pleuro-pneumonia group and the L Phases of Bacteria), Professor Hauduroy (the Sleeping Viruses), Professor Lepine (Polio myelitis), Professor Penso (Aggression and Demolition of the Bacterial Cell by the Phages) Further information may be had from Professor Hauduroy, 19, rue Cesar Roux, Lausanne, Switzerland

International Hospital Congress

Preventive Medicine as a Major Function of the Hospital and its Implication has been chosen as the central theme of this congress, which is being held in London this year at Church House, Westminster from May 25 to 30 The chairman of the congress is Dr Reno Sand, president of the International Hospital Federation and the speakers will include Prof H W C Vines, Prof G Sollazzo, medical director of the Nuovo Ospedale Maggiore, Milan, Dr E L Crosby, president of the American Hospital Association, and Prof G Portmann, dean of the faculty of medicine, Bordeaux Further particulars may be had from Captain J E Stone, hon secretary of the International Hospital Federation, 10, Old Jewry, London, E C 2

Auxiliary Royal Army Medical Corps Funds (1939)

The annual general meeting of the Funds will be held a 11, Chandos Street, London, W 1, on Monday, April 13, a 5 P M

British Standard for Patients' Trolleys

A new British standard (B S 1982 1953) has been is for patients' trolleys (fixed top) for indoor use in hospit Copies (2s 6d) may be obtained from the British Stand Institution, Sales Branch, 24, Victoria Street, London, S W 1

Wessex Rahere Club

The spring dinner of this club will be held at the C Hotel, Taunton, on Saturday, April 18 Membership of th club is open to all Barts men practising in the West Coun The hon secretary is Mr A Daunt Bateman, 3, The Circu Bath

Hæmatology Congress

The fourth congress of the European Society of Hæmato logy will be held in Amsterdam from Sept 8 to 12 Th subjects chosen for discussion are Immuno hæmatolog Erythropoiesis and Hæmoglobin Metabolism, Acute Leuk æmia, and Physiology and Pathology of Coagulatio Further particulars may be had from Dr S Verloop, secreta of the congress, Maliesingel 15, Utrecht, Netherlands

Association of Surgeons of Great Britain and Ireland

The annual meeting of this association will be held in London from April 30 to May 2 The programme w include discussions on the Management of Cancer of th Breast, the Treatment of Perforated Peptic Ulcer, Post operative Strictures of the Bile ducts, and Crohn s Disease Applications for tickets should be sent before April 18 to th office of the association, 45 Lincoln s Inn Fields, W C 2

Europe's Largest Hospital

A 298 bed geriatric ward has lately been added to th Stockholm Southern Hospital The hospital, which is th largest in Europe, can now accommodate 1559 inpatie and also has large outpatient clinics The staff of ab 1360 includes 100 doctors About £5 million has been spe on the buildings and their equipment since 1938, when th foundation stone was laid

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The Ministry of Food has produced a new edition of the *Ma of Nutrition* (H M Stationery Office Pp 59 2s) This man was first published in 1945 for the information of catering The new edition includes a list of relevant textbooks and speci journals

Appointments

BOOTHROYD L S A, M B Lond F R C S surgical regis Taunton and Somerset Hospital, Taunton

CRAIGHEAD, ISOBEL, M B Edin D P H asst M O, maternity a child welfare service, Edinburgh

CUMMINGS, I B, L R C P I appointed factory doctor Lanark

DAVIDSON I W, M B St And, D A senior registrar in anæsthetic Inverness hospitals

FERGUSON HAROLD, M B Edin, D M R D asst radiologist (who time) hospitals in the North Liverpool area

ISSERLIN BRUNO, M B Brist F R C S I consultant orthop surgeon, Tees side and Cleveland H M C groups

JACKSON, C R S M A B M Oxfd, F R C S E, D O M S ophthalm surgeon, Edinburgh Royal Infirmary

MCKECHNIE SAMUEL M B Glasg, D A asst anæsthetist (S H M O) Inverness hospitals

MOFFOOT A G M B Edin F R C S surgical registrar, Roy Cornwall Infirmary Truro

REID J A W M B Glasg D I H M O H, Jarrow, and the u districts of Hebburn and Felling

SEWELL E M, M B Edin D I H senior asst M O Linc regional blood transfusion service

WARD, J A, M R C S appointed factory doctor, Batley, York

The Hospital for Sick Children, London

ANDERSON, DAPHNE, M B Lond, D C H part time cli asst (radiotherapy)

BURNETT DOROTHY M B Lpool house physician

WILSON S G I M B Edin house physician

WINN PAULINE M B Edin house physician, neurological a neuro-surgical unit

WYLLIE, G G, M B Adelaide F R C S house surgeon

Welsh Regional Hospital Board

APTHOMAS IVAN, M B Edin D M R D F F R asst ra (consultant) Wrexham Powys and Mawddach H M C

MACKINNON, DONALD M B Lond consultant patho Merthyr and Aberdare H M C area

MEEK J C M B Glasg D M R consultant radiologist, New E Monmouthshire and N Monmouthshire H M C

OWEN, R H, M B Brist D M R D consultant rad Newport, E Monmouthshire and N Monmouth H M C.s.

Cooper et al.[2] also cast doubt on the reliability of skin-temperature measurements as an estimate of blood-flow, particularly as the skin-temperature approached 32°–34°C. My own investigations comparing the temperature of the skin over the pulp of the big toe with occlusion-plethysmograph estimations of blood-flow show that in normal people at room-temperatures of 20°–25°C a 340% increase in foot blood-flow produces an increase in skin-temperature of only 3°C when measured for 60 min. after warming.

I think most observers agree that except under the conditions described by Fetcher et al. skin-temperature measurements are of no value as an estimate of the degree of vasoconstriction occurring in the skin. Moreover, the temperature changes recorded by Dr. Martin after exposing the patient to room-temperature are in a number of cases he illustrates so small as to be insignificant. It would perhaps be better in any case if Dr. Martin produced reflex vasoconstriction by means of a *sudden* stimulus—e.g., ice on the forehead or pain.

Unless the vasomotor changes in diabetic neuropathy are investigated by means of a flow method it would seem necessary to preserve an open mind on Dr. Martin's conclusions, even though the changes he describes might be expected on a-priori grounds.

Physiology Department.
St. Mary's Hospital Medical School.
London, W.2.
ANGUS MCPHERSON.

HALLUX VALGUS

SIR,—Cathcart[3] and others asked: If footwear is alone to blame, why is it that the feet of peoples who are in the habit of going barefoot so commonly differ from what is regarded as the ideal? This question is still troubling students of hallux valgus. Your correspondent Dr. Booth[4] suggested that W.H.O. should investigate barefoot peoples, and your leading article of Feb. 14 suggests that such work might throw further light on this problem. May we refer to two important works on this subject?

The African expedition by Columbia University and the American Museum of Natural History[5] made the study of feet one of their main objectives. The great thickness of skin is noted: the "negroes sat for some time at a small outdoor fire with their feet resting on live coals." There is a peculiar wrinkling of the skin about the ankles in natives over 40 years of age. There is no hallux valgus, for "where we suffer from arch strains, they lose a toe or two" from injury, chiggers, or yaws! They are notably free from the ordinary types of static foot trouble with which we are familiar in our civilised centres of population.

James[6] in ten years' work in the Solomon Islands found "neither footgear nor flat foot"—only yaws, ulcers, infections, contractures, and loss of toes. He noticed a great difference between shod Europeans on the one hand and unshod Europeans and natives on the other, involving narrowing of the metatarsal region of the foot and lateral displacement of the toe in shod people. This change corresponds closely to Elmslie's[7] description of alteration in 80% of children on beginning to wear shoes.

One of us in the course of four years' work in an Egyptian anatomy school found not a single instance of hallux valgus. The material came entirely from the Fellahin, among whom the men work barefoot, though they may attend the mosque in shoes and leave them at the entrance, while the women seldom wear shoes at all. In the streets, on the contrary, typical valgus was commonly observed in the better-off women wearing shoes of European type whose open-work toes allowed careful observation: deviation of the great toe, bunion formation, and clawing of the other toes were common. In Egypt the distinction between the classes is sharp, and the distribution of valgus follows the class structure.

It seems, then, that footwear can still be blamed for the ordinary hallux valgus of the European adolescent. There are of course other causes, for there is certainly a congenital form, and hallux valgus may also appear rapidly with various forms of arthritis even though the patient is not wearing shoes. Probably these additional factors account for the odd cases of valgus found in unshod Annamites and Transvaal natives mentioned by Hardy and Clapham[8]; and causation by arthritis is consistent with Booth's statement (Feb. 21) that among the barefoot people hallux valgus is found only in adults.

Department of Anatomy,
University of Sheffield.
R. WHEELER HAINES.

Department of Orthopædics,
Glasgow Royal Infirmary.
A. MCDOUGALL.

MITRAL STENOSIS

SIR,—We have read with great interest your annotation of Jan. 10 and the subsequent letters from Dr. Wade (Jan. 24) and Dr. Gorlin (Jan. 31). We would like to comment on Mr. Brock's view that the mitral-valve orifice at operation is always the same size.

Walsh et al.[9] have described quite clearly the evolution of the murmur of pure mitral stenosis following rheumatic fever five or ten years before. The first sign is an early diastolic murmur, to which is added in later years a presystolic murmur. Taking into account Henderson's work on ventricular filling curves, it is reasonably certain that in the earliest stages of mitral stenosis adequate left ventricular filling can be achieved without an increase in left auricular systole. When the stenosis is more severe, the characteristic presystolic murmur appears and flow is maintained for a considerable period until diminished right ventricular competence leads to a fall in cardiac output. This usually occurs when the valve area is in the range 0·9–1·0 sq. cm. It is at this or a later stage that most patients nowadays see the surgeon. In nearly 100 cases of pure mitral stenosis treated surgically, Mr. F. H. Mills has found quite definite variations in the size of the valve orifice which agreed very well with the size predicted from the symptoms and the data obtained at cardiac catheterisation. Moreover, following a good valvotomy the presystolic murmur disappears, and only a diastolic murmur following the third heart sound remains.

In answer to your comment that resting pressures in the pulmonary artery may apparently be nearly normal in the presence of disabling symptoms, it should be pointed out that in the presence of auricular fibrillation, a narrow valve orifice, and a lowered cardiac output, the pulmonary-artery pressure is an unreliable index of the severity of the disease. For reasons which are not entirely clear the onset of auricular fibrillation causes a considerable fall in cardiac output; and as stenosis is almost invariably already severe, it follows from the laws governing mitral valve flow[10] that a fall in pulmonary-artery flow will be associated with a considerable fall in pulmonary-artery pressure. Calculation of the elasticity resistance of the pulmonary vessels in such cases will show that the vasculature is less tense than in the usual case of mitral stenosis, suggesting that it has previously been more distended. A similar state is occasionally found in patients with sinus rhythm, and it is reasonable to attribute it in both cases to diminished right ventricular competence, though congestive failure has not necessarily occurred. Support for this view is found when the patients are exercised, for pulmonary vascular

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[2] Cooper, K. E., Cross, K. W., Greenfield, A. D. M., Hamilton, D. McK., Scarborough, H. *Clin. Sci.* 1949, 8, 217.
[3] Cathcart, E. P. *Lancet*, 1938, ii, 1490.
[4] Booth, W. G. *Ibid*, 1952, i, 1258.
[5] Engle, E. T., Morton, D. J. *J. Bone Jt Surg* 1931, 13, 311.
[6] James, C. S. *Lancet*, 1939, ii, 1390.
[7] Elmslie, M. *Ibid*, p. 1260.
[8] Hardy, R. H., Clapham, J. C. R. *Ibid*, 1952, i, 1180.
[9] Walsh, B. J., Bland, E. J., Jones, T. D. *Arch. intern. Med.* 1940, 65, 321.
[10] Gorlin, R., Gorlin, S. G. *Amer. Heart J.* 1951, 41, 1.

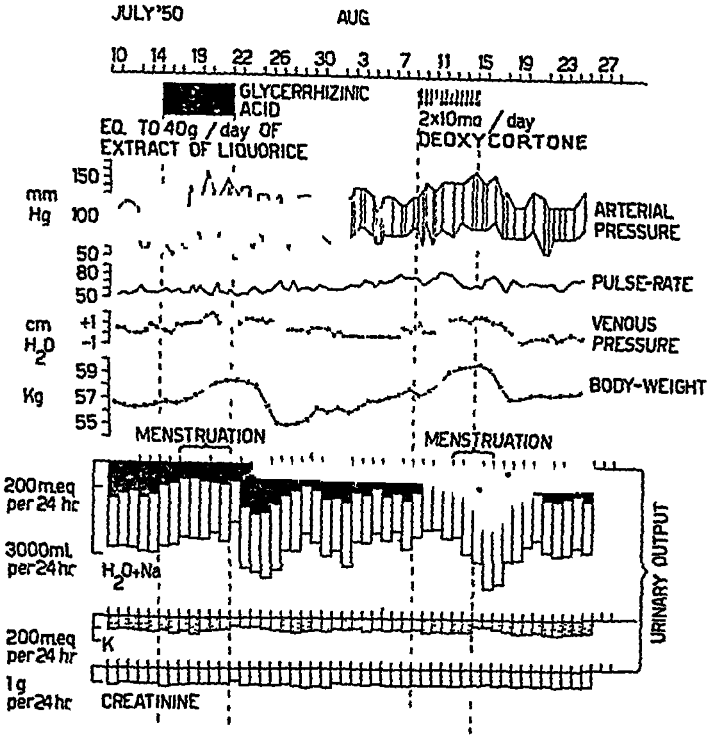

Fig 1—Wave-like alterations in excretion of water, sodium, and potassium following the sudden withdrawal of succus liquiritiæ or of deoxycortone in a normal person

potassium In a similar way an insufficient cardiac output, whether it is due to heart-failure or to an insufficient venous return, leads to a reduction in the excretion of water, sodium chloride, and potassium (Borst 1941, Borst and de Vries 1950, Borst 1952, Borst et al 1952) This mechanism is still active in the absence of adrenocortical tissue (ten Holt et al 1952) Probably there is also a homœostatic mechanism counteracting retention as well as depletion of potassium

Thus our data on water and electrolyte excretion do not reflect the pure effect of the liquorice but represent the net result of two opposing forces It is possible that "weak reactors" differ from "strong reactors" only in having a more vigorous homœostatic mechanism In "strong reactors" several litres of extracellular fluid must be retained before the stimulus for the counteraction is sufficient to establish a new balance Since the homœostatic reactions are slow to develop even part of the initially retained fluid is sometimes excreted at the end of the first week of treatment, in spite of continued therapy Where the extracellular fluid volume rises sufficiently, an increase in dosage of the drug, or the simultaneous administration of another potent agent, does not significantly reduce the output of water and sodium chloride

The changes in excretion rates which take place on withholding therapy show the effect of the homœostatic forces no longer held in check by the hormonal stimulus to the renal tubules *Owing to the* slowness of the homœostatic reactions to changing conditions, the rebound sometimes exceeds the response required to re-establish the normal state, and more sodium is excreted than was retained during the period of treatment Hence retention of sodium begins again a few days later, and a second rebound may follow There is also a wave-like change in the excretion of potassium, but in the opposite direction to the changes in sodium excretion Body-weight, hæmoglobin concentration, venous pressure and arterial pressure may also all show this undulating type of reaction An example is given in fig 1 It will be obvious that during such a period, which sometimes lasts more than 10 days, the in pretation of the effect of recommencing horm therapy can be very difficult A similar ph menon has been described by Conn and L (1950) They found on cessation of A C T H in tions a rebound to above the base line le followed by a temporary secondary depression the excretion of sodium and chloride in urine sweat Since corresponding fluctuations in t urinary output of ketosteroids uric acid, a glucose were found, Conn attributes all th changes during the recovery period to a tempor adrenal insufficiency followed by a reactive i creased production of endogenous A C T H Ag this hypothesis is the fact that the peaks electrolyte excretion in urine and sweat did coincide

If patients who have had complete bed res a long time are allowed up for several hours, t temporary reduction in venous return often ca a long-lasting retention of water and sod chloride and of some potassium In succe days a cumulative effect may be obtained W the patient is again kept in bed for the whole d a large volume of extracellular fluid and m potassium are excreted (ten Holt et al 1952) T great excretion of sodium and water by pati 1 on Aug 13 (fig 2) and by patient 2 on July (fig 3) is attributable to this With these exc tions, during our investigations we have onl kept the patients in bed the whole time, allowed them up for nearly the same period ea day

Finally fluctuations in mineral balance occurring women during the menses may complicate studies of th effects of adrenal cortical hormones When all precautio were taken, even a moderate retention of sodium accompanied by a decrease in excretion of potassium during the first 2 days of liquorice administration, and clear rebound in the 3 days after treatment wa discontinued were regarded as evidence that the liquorice was active To permit comparison of the potency of vario combinations of drugs in one subject, different form treatment were as far as possible begun when the patie had almost the same body-weight, hæmoglobin level, venous pressure, and arterial pressure

Observations in Addison's Disease

PATIENT 1

The observations made during a previous admission of this patient, a man of 47 suffering for 5 years from Addison's disease, have been presented by Molhuysen et al (1950) It was then shown that administration of large amounts of A C T H caused no fall in the eosinophil count and no change in the excretion of electrolytes Liquorice was ineffective and the patient was discharged with daily injections of 5 mg of deoxycortone

In the present investigation the diet was started 2 days after cessation of treatment with deoxycortone As may be seen from fig 2 the sodium balance during the two control days was slightly negative, presumably through the rebound Administration of 30 g of extract of liquorice daily was then begun To test the possibility that an active principle was liberated from the glycyrrhizinic acid by enzymes in the stomach and intestines the liquorice was administered in different ways for 2 days it was given together with the feeds and sodium bicarbonate, for a further 2 days it was given 1½ hours after the feeds, and then for 2 days it was combined with citric acid (pH of mixture, 5 2) In no period was any effect seen When the liquorice was stopped on July 5 there was, however, a slight indication of a rebound

TABLE IV—AVERAGE BIRTH WEIGHT, ACCORDING TO DATA OF HIRSZFELD AND ZBOROWSKI

Including the classes A infants of A mothers, &c.				Excluding the classes A infants of A mothers, &c.			
Group of mothers, and av. weight of infants (g.)		Group and av. weight of infants (g.)				Group of mothers, and av. weight of infants (g.)	
A	3230	A	3218	3206	B	3209	A
O	3204	O	3212	3191	AB	3205	B
B	3189	AB	3206	3182	O	3174	AB
AB	3189	B	3189	3180	A	3145	O

group as their mother with those of a different group from their mother. They showed that whilst the average birth weight was 3230 g. for the 371 infants in the four classes with the same ABO group as their mother, the average for the 348 infants whose group was different from their mothers' was only 3187 g. But it can be shown that the average for the 553 infants whose ABO group is the same as, or compatible with, their mothers' is only 3214, whereas for the 166 infants whose blood is not compatible with their mothers' it is 3195. Thus the average difference in birth weight between the ABO-compatible infants and the ABO-incompatible infants in the sample is less than that between the A infants and the B infants, as can be seen on the left-hand side of table IV, and is less still than the difference between the infants of A mothers and the infants of B mothers. The greater difference between the A and B infants remains when one excludes the classes A infants of A mothers (3250), O infants of O mothers (3236), AB infants of AB mothers (3234), and B infants of B mothers (3168), but now the descending order of weights is completely reversed; and this reversal also appears in the remaining infants of B and O mothers. If these differences in the birth weight of A and B infants, and of the infants of A and B mothers, should prove to be real, slight though they are, their explanation might have to be looked for not only in group but also in sex. The sex of the infants discussed was not given.

Aberdeen and North-East of Scotland
Blood Transfusion Service,
Bacteriology Department,
University of Aberdeen. T. M. ALLAN.

MODERN OUTLOOK ON EPILEPSY

SIR,—Your annotation last week neatly shows the confusion that results from failure to confine the term "petit mal" to attacks associated with 3 cycles per sec. spike and wave in the electro-encephalogram. You remark that troxidone occasionally aggravates petit mal. By this do you mean spike-and-wave attacks, or the much larger body of minor epileptic attacks which may originate from various cortical foci, but usually from those in frontal and temporal regions? Spike-and-wave attacks rarely fail to respond to troxidone, at any rate temporarily; other minor seizures rarely benefit, except myoclonic jerks which are closely related electrophysiologically. Surely such a condition as petit mal is worthy of a separate name, since it is distinct in ætiology, pathophysiology, treatment, prognosis, and (usually) clinical picture?

I should also welcome an authoritative opinion from blood-dyscrasia experts on the prognostic value of routine blood-counts for the detection of impending agranulocytosis from cytotoxic drugs. I have seen a neutrophil-count fall to 4% of a normal total white-cell count, and return two days later to a more usual figure without any change in the dose of troxidone. With other toxic drugs, agranulocytosis has been reported to occur within a few hours of apparently normal blood-counts. Warning the patient and his local doctor of possible serious symptoms such as sudden inexplicable fever, rash, malaise, or sore throat would seem safer than false reliance on a laboratory investigation, which is often inconvenient for the patient, who must attend hospital for it, and time-consuming for the clinical pathologist.

Department of Clinical Neurophysiology,
Institute of Psychiatry,
Maudsley Hospital, London, S.E.5. D. A. POND.

*** We are obliged to Dr. Pond for drawing attention to a mistake. We did not intend to state that troxidone may aggravate petit mal. Our comment that this and kindred drugs "may aggravate petit mal and even apparently produce grand mal" should have read "may aggravate and even apparently produce grand mal."—ED. L.

A DESIGN FOR FAMILY PRACTICE

SIR,—Extra fees are paid to general practitioners in the National Health Service who do obstetrical work. In his article last week Dr. Howard points out that other family doctors with special experience are also doing special work in their practices—pathological, E.N.T., &c.—and he hopes that in time they too may be rewarded. He suggests that the College of General Practitioners "tackles this anomaly."

This matter is one of many, involving terms and conditions of service, that are being investigated by the General Medical Services Committee of the B.M.A., and *not* by the College of General Practitioners, which will confine its activities to the academic field.

J. H. HUNT

14, Black Friars Lane,
Queen Victoria Street,
London, E.C.4.

Hon. Secretary, College of
General Practitioners.

POLIOMYELITIS

SIR,—In your leading article of Jan 10 you state that there are considerable differences of opinion on some aspects of poliomyelitis and you then go on to quote at length Dr. Ritchie Russell's views on the management of the acute phase.

Much discussion has ranged around the subject of "muscle spasm." In the past, British neurologists of distinction have denied the very existence of muscle spasm and yet have agreed that the signs of so-called "meningeal irritation" are a common feature of the disorder.

To one who believes that "muscle spasm" is an almost constant feature of acute poliomyelitis there is no difference between the muscle spasm that may occur in, say, a pectoral group of muscles and the tightness and spasm of the muscles of the neck, back, and hamstrings that make up the signs of so-called "meningeal irritation." In each case there is muscle tightness, and on stretch muscle spasm develops. In a recent small epidemic of forty-four cases in Dunedin, muscle tightness and spasm has again been an outstanding feature of the majority of cases.

It is refreshing to see that rigid splinting is at last banished. There is, however, still an important place for splintage without restraint, which is well achieved by nursing the patient on a firm mattress with the feet supported against a board which is placed six inches from the end of the mattress. Rotation of the tibial shaft, which is one of the most difficult of deformities to correct on account of the short iliotibial band, may be prevented by two movable boards which project back from the foot-board and prevent outward rotation of the feet.

In New Zealand most workers who have had experience with the last four epidemics of poliomyelitis favour the use of hot packs and hot baths, which relieve discomfort and pain, overcome muscle tightness and muscle spasm, and maintain the skin and muscles in good condition to prevent or correct deformities. Furthermore, in many instances pseudo-paralysis of tightened intercostals or other muscle-groups may at times be dramatically

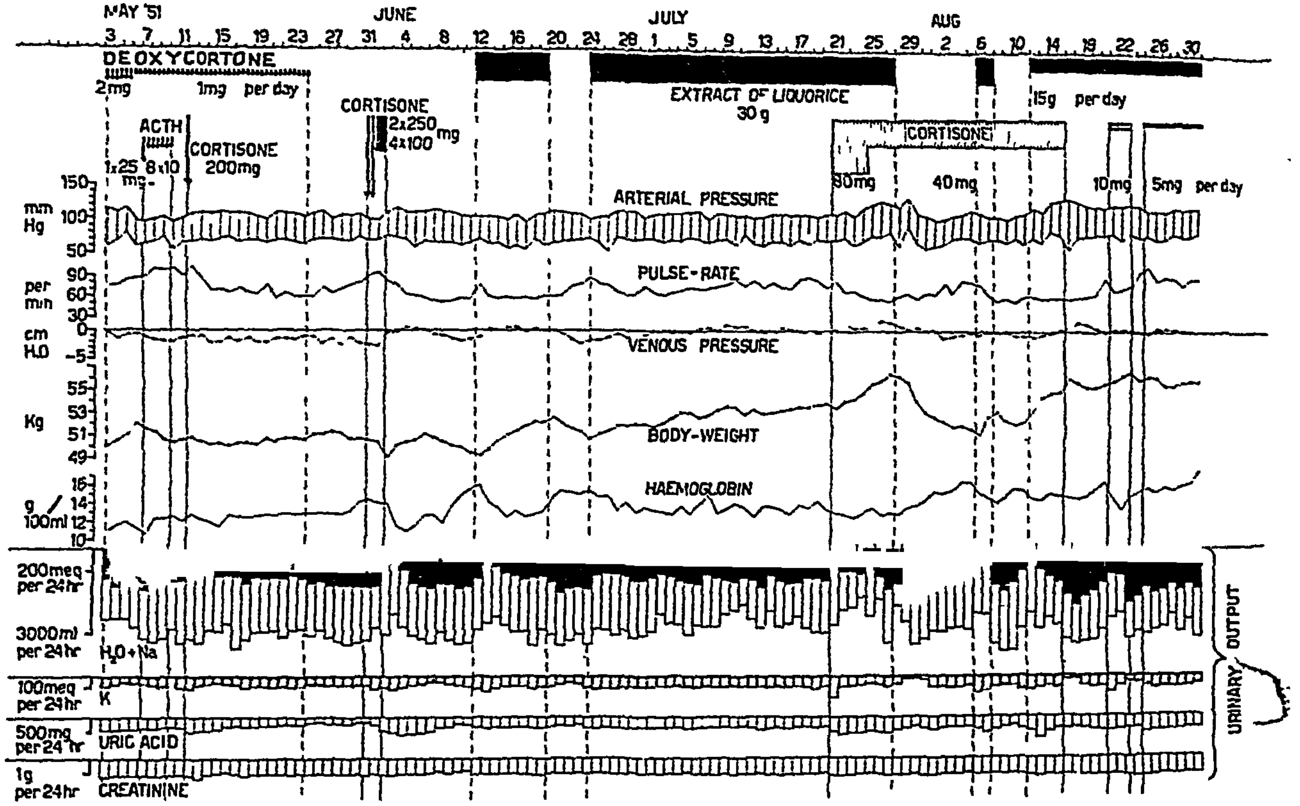

Fig 3 (patient 2)—Showing the powerful effect of a combination of liquorice and cortisone on the excretion of electrolytes in a 21 year-old patient with Addison s disease at a time when he still reacted to liquorice alone

in a patient with Addison's disease who was taking cortisone simultaneously

At the end of the period of investigation cortisone and liquorice were tried separately and in various combinations It was repeatedly seen that a combination of the two drugs had a very powerful effect, and it was striking to observe that 15 g of liquorice with 10 mg of cortisone had almost as great an effect as did 30 g of liquorice with 80 mg of cortisone

After discharge from hospital the patient continued to take 20 g of succus liquiritiæ daily and a daily supplement of 5 g sodium chloride above his normal intake At home he received no cortisone At first he managed fairly well, but his condition gradually deteriorated, and one morning his mother thought he was so ill that they came to the clinic by taxi

He was barely able to climb the stairs, and was obviously in a state of shock On admission his temperature was low (35 6°C) and the venous pressure had fallen to −5 cm of water His condition improved rapidly on the administration of 200 mg cortisone orally, together with deoxycortone injections

The diet was again standardised and the dose of cortisone gradually reduced to 10 mg A rise in hæmoglobin concentration and a fall in the venous pressure prompted early recommencement of liquorice therapy (fig 4) A combination of 20 g of liquorice and 10 mg of cortisone daily was found to be extremely effective The potassium excretion increased markedly at first and the retention of sodium and water caused a rise in body weight, hæmodilution, and a rise in venous and pulse pressures Equilibrium had not yet been reached when we stopped giving cortisone on Nov 5 There was a sharp rebound

On Nov 8 the investigation had to be interrupted because the patient developed pericarditis with a high pyrexia for some days He recovered completely from the pericarditis in 10 days

The investigation was resumed on Nov 20, at which time the patient was being treated with deoxycortone 4 mg daily From Nov 24 he received 20 g of liquorice daily in addition to the deoxycortone but with little effect The rebound which followed the discontinuance of deoxycortone was greater than we had expected, for he was still having liquorice The detrimental effect was most evident in the rise in hæmoglobin and the rise in the pulse rate

We were forced to conclude that liquorice was no longer active in this case, and we accordingly tried to ascertain whether any functioning suprarenal tissue was still present

Assuming that the action of endogenous glycocorticoids would also be potentiated by liquorice (as later appeared to be true in patient 4) we injected 25 mg ACTH and gave, from Dec 7 to 9, a further series of fourteen injections of 10 mg of ACTH 3 hourly without interruption in the administration of liquorice There was no fall in the eosinophils and no appreciable alteration in the mineral balance The fluctuations which were observed and which were accompanied by a slight fall in hæmoglobin concentration, were not greater than the spontaneous daily fluctuations Nor was there any rebound after the termination of the ACTH injections On the other hand during continuing treatment with liquorice, 2 5 mg cortisone daily was sufficient to bring about obvious changes in the mineral metabolism and the circulation Repetition of this part of the investigation with 10 mg of cortisone gave the same result, although to a greater degree

Thereafter, when extracts of liquorice was given alone, the patient showed signs of suprarenal insufficiency, whereas his general condition had been excellent during treatment with a combination of the drugs Discontinuance of liquorice did not accelerate the deterioration in his condition , there was a gradual downhill course and no clear rebound To forestall a crisis we had to commence treatment with deoxycortone three days later

We had already seen in the first period of observation of this patient that the effect of deoxycortone, unlike that of liquorice, was not increased by cortisone (fig 3 May 11) To confirm this we again gave 10 mg and later 20 mg cortisone daily during a period when the patient was receiving 4 mg deoxycortone every day No clear effect was observed (com

Since this experience an attempt has always been made at the end of an antecolic partial gastrectomy to anchor the afferent limb in its proper position with a few sutures so that rotation cannot take place.

Dartford, Kent. J. C. MORRIS.

ADVERTISEMENTS

SIR,—I have just received from a commercial firm a large and well-printed volume on an antibiotic: on it are to be found neither the name nor the qualifications of any editor or author. This prompts me to draw your attention to a pernicious trend in medical education.

Are medical practitioners to learn of recent advances in knowledge from the leaflets and advertisements of manufacturers selling their wares? The very success of treatment of bacterial and viral diseases, in which this country was a pioneer, has led to a neglect of the teaching of bacteriology. No-one denies the rôle that the manufacturers of antibiotics have played to the benefit of mankind—and no less to their own benefit—in placing these new drugs in the hands of medical practitioners, but I do feel that it would be fair and just if a greater part of their financial reward was turned into further medical research.

I most strongly urge that manufacturers spend at least part of their profits on financing research projects in universities and other suitable establishments—*not* in their own laboratories where a bias could be suspected. In the United States of America such support is producing [illegible] wealth of fresh and rewarding research, whereas in this country the main results appear to be tons of coloured paper.

Department of Bacteriology,
St. George's Hospital Medical School,
London, S.W.1. S. D. ELEK.

SIR,—The general practitioner of today comes under the influence of advertisements by the manufacturers of drugs. The quality of this influence is an important matter, for the present position in medical research is such that advances in drug therapy come mainly from the manufacturers, and contributions from the universities are usually indirect. The universities cannot compete financially, and this state of affairs need not be considered humiliating. But the attitude of the manufacturer towards the general practitioner deserves some criticism.

The advertiser often gives a fanciful name to his preparation and, in very small print, the organic formula. The fanciful name is repeated again and again throughout the advertisement. If I want to obtain some isonicotinic acid hydrazide, it is that substance, by that name, that I ask for at the chemist's. A preparation by any reputable firm will satisfy me, and I am not in the least impressed by the many odd names which have been given by manufacturers to the same substance. It is right that the formula should be given, but it should be remembered that most practitioners have no detailed knowledge of organic chemistry, and that a simple indication of the nature of the product would be helpful—for example, a statement that the preparation is the synthetic analogue of a drug whose nature is well known.

It is astonishing to see a full-page advertisement extolling the virtues of a preparation, without mentioning its ingredients. It is indeed humiliating if the medical profession is expected to use secret remedies.

Advertisements are now very important to the general practitioner, and it is to be hoped that in time they will become more helpful. Advertisers should remember that, while the practitioner is not an organic chemist, he is not impressed by high-sounding names, which confuse him, nor by formulæ which he does not understand, and that he is irritated by the oppressive repetition of a trade name without an adequate statement of the nature of the preparation.

Mombasa, Kenya. R. L. LANCASTER.

Obituary

JOSEPH BARNES BURT

M.D. Lond.

Dr. J. Barnes Burt, who died at his home in Bath on March 18 at the age of 72, was one of the last of the old order of balneologists, and he had made the rheumatic diseases his special study.

He was born at Kendal, the son of Dr. J. K. Burt, and was educated at Epsom College and University College Hospital, London, where he qualified in 1902. He held a research fellowship at Cambridge before going to Buxton, where he was physician to the Royal Devonshire Hospital for twenty years. In 1935 he moved to Bath and joined the staff of the Royal National Hospital for Rheumatic Diseases. Among his many appointments he was the first president of the section of physical medicine of the Royal Society of Medicine, when the sections of balneology and electrotherapy were amalgamated. For many years he was also chairman, and later vice-president, of the International Society of Medical Hydrology. Through these activities he was well known and held in great respect by hydrologists and rheumatologists on the Continent, where he travelled extensively. He wrote many papers, especially on balneotherapy, sciatica, and gout. He retired in 1948.

Outside medicine Dr. Burt had many interests; and he was a councillor of the city of Bath. He collected prints, water-colours, stamps, and etchings, and he was himself an etcher of considerable merit. Golf was his main outdoor recreation.

G. D. K. writes: "Barnes Burt was a great individualist and was always ready to fight for what he considered right, even when this did not coincide with his own interests. He was always open to conviction, ready to learn and to admit when he did not know. A kind, considerate man, he was much loved by his patients and colleagues. The young man who needed help and encouragement was one of his first thoughts at all times, but he had no use for slackers."

He leaves a widow, a daughter, and two sons, one of whom is Dr. Hugh Burt.

LIONEL GODFREY PEARSON

F.R.I.B.A.

Mr. Lionel Pearson, who died on March 19 at the age of 73, as a member of the architectural firm of Adams, Holden, and Pearson, was largely responsible for planning many of the hospitals built between the wars. They included the Westminster Hospital, the Royal Westminster Ophthalmic Hospital, the new Mineral Water Hospital, Bath, and the Southend Hospital.

"Though Lionel Pearson was not a doctor," writes E. R. C., "many in the medical profession will feel that they have lost a colleague. The staffs of half a dozen hospitals now in being, and of at least three in prospect, have been indebted to an architect who, though an artist to the finger-tips—or rather because he was first and foremost an artist—was intensely aware of the need for a functional approach to design. He never thought of a building as a monument to his own skill. What he set out to do was to throw an artist's glamour over a building that contained all the space, all the accessibility, all the convenient arrangements necessary for good professional work.

"No trouble was too much for him to take over a thorough understanding of what the doctors, the nurses, the technicians, the administrators wanted and why. It was the same with the different requirements for teaching and research. It was hard work sometimes for a man who loved beauty and form to curb his passion for material and colour within the limits of possible cost; and how he enjoyed himself when there was a chance to have his way! Witness the Chapel in the Westminster Hospital, so soon after completion to be the target of a bomb.

"But it was not only as an architect that his colleagues loved him. Shy, modest, generous-minded, he was a charming and stimulating companion: transparently a man of complete integrity: a friend whose passing leaves a gap that cannot be filled."

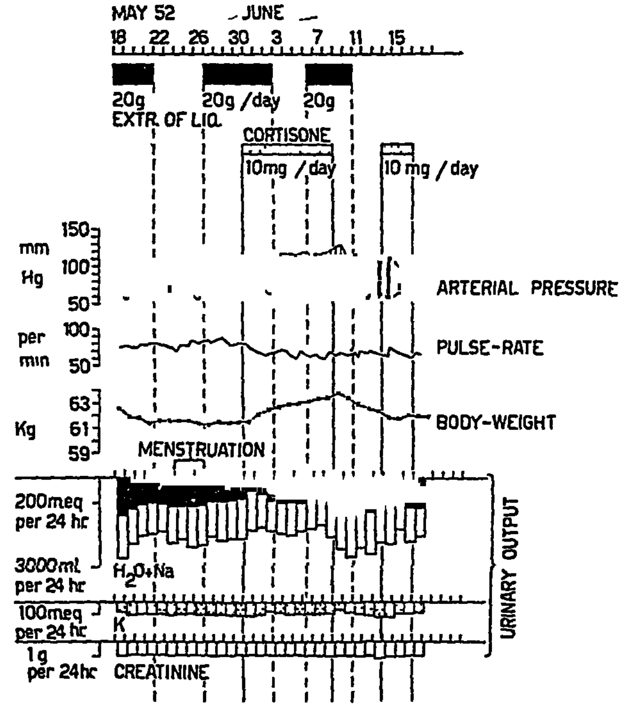

Fig. 5 (patient 3)—Addison's disease. Liquorice by itself is inactive or only slightly active. Cortisone and liquorice together are obviously active. (Note rebound on June 9.)

Thus this patient shows essentially the same reaction as the two preceding cases, but she is obviously a "weak reactor." Her condition at present is excellent and she is receiving 15 g of liquorice and 5 mg of cortisone daily. Her blood-pressure is tending to rise gradually and is now 160/100 mm Hg.

Observations in Simmonds-Sheehan Disease

PATIENT 4

The patient was a woman of 34 showing all the features characteristic of Simmonds's disease. These had developed 5 months before admission, following a hæmorrhage after the birth of twins, as described by Sheehan.

After a short control period, 10 mg cortisone was given daily for 2 days with but little effect (fig. 6). Liquorice, 15 g, caused marked retention of extracellular fluid, although the excretion of potassium scarcely changed. After equilibrium had been reached, 10 mg of cortisone was given in addition. In contrast with the previous occasion, this now had a conspicuous effect. Only the early part of the rebound following the withdrawal of the cortisone could be observed, for the patient went home for Christmas.

At home she continued to take liquorice, and she was readmitted to hospital in good general condition on Jan. 6. For the first few days she was given the standard diet. Apart from the influence of the diet the excretion of electrolytes showed the characteristic rebound expected after discontinuing liquorice administration on her readmission. By Jan. 12 equilibrium had been re-established. During the following three weeks the effects of liquorice and ACTH alone and in combination were investigated. From fig. 6 it may be seen that 15 g of liquorice was more active than 2 mg ACTH four times daily, and that 8 g of liquorice and 2 mg of ACTH four times daily, together had approximately the same effect as 4 mg of ACTH four times daily, the effect of which seemed to be equal to that of 15 g liquorice together with 10 mg cortisone.

Thus the endogenous glycosteroids were seen to potentiate the activity of liquorice as did the cortisone.

Discussion

For the absence of the deoxycortone-like action of liquorice in some patients with Addison's disease, and for the powerful effect of a combination of liquorice and cortisone in adrenal cortical insufficiency, the three most obvious explanations are:

(*a*) Liquorice has itself no influence on water and electrolyte balance but reduces the rate of breakdown of the glycocorticoids.

(*b*) Liquorice potentiates the effect of glycocorticoids on mineral metabolism.

(*c*) Liquorice is active only in the presence of glycocorticoids.

Were (*a*) the explanation, then liquorice should enhance in all respects the activity of the endogenous glycocorticoids in persons with intact suprarenal glands. It should reduce the eosinophil count in normal subjects, and improve the joint symptoms in rheumatic patients. We had previously found that it does neither of these things (Molhuysen et al. 1950). The second possibility (*b*) cannot be accepted unless we assume that as little as 10 mg of cortisone administered simultaneously with liquorice has an almost optimal effect. This could be largely due to the self-limiting character of deviations from water and electrolyte equilibrium. All the facts are in keeping with the hypothesis (*c*), that liquorice is active only when a minimum amount of glycocorticoids is present in the body. The administration of 10 mg, and probably 5 mg, of cortisone daily may suffice to obtain the full effect of liquorice. That patients 1 and 3 did not react to liquorice and that patient 2 did not

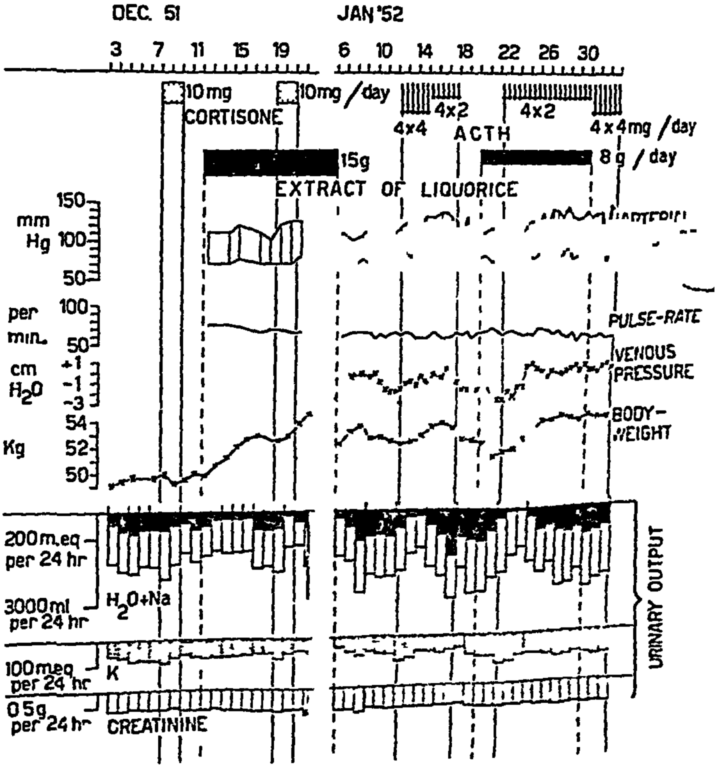

Fig. 6 (patient 4)—Simmonds-Sheehan disease. Cortisone alone is only slightly active, while extract of liquorice and A.C.T.H. have an obvious effect on mineral metabolism. There is a strong reaction to a combination of liquorice with A.C.T.H. or cortisone.

o take part in vigorous exercise also needed further investiga-ion. He suggested that the association might well sponsor research into such subjects as the biopsy of the muscles of athletes. Was the pre-eminence of the negro race in sprinting and jumping attributable to some special contractility or viscosity of their muscles? Much work had already been done on the biochemistry of the products of fatigue, but in his opinion something more searching was desirable, and he looked to the biochemist of the future to isolate some factor other than mere quantitative superiority.

The secretary of the association is Dr. W. S. Tegner, London Hospital, E.1.

THE SHIP THAT GOES

The pirate captain, Mary Lovell, sailed a ship called *Moonraker*. When Dr. E. A. Pye and his wife, Anne, bought the *Lily* for £25 they renamed her *Moonraker*, without changing her luck. "She was twenty-nine feet long by nearly ten feet beam and she drew six feet aft, when loaded down with gear." Dr. Pye had a duodenal ulcer, a love of sailing, and a practice; but the moment they had bought this boat only the second seemed important. So they sold up everything and sailed her away from Fowey to the West Indies and back; and in his book, *Red Mains'l*,[1] he takes us with him on the cruise. It was dangerous and exciting and boring and beautiful by turns, and those who love a seafaring life will find the book a siren song to lead them from their lives and homes out upon blue water. Dr. Pye's style is so economical and vivid that at first it seemed he might have Kipling's gift, displayed to advantage in *The Devil and the Deep Sea*, of drawing the outsider into another craftsman's mysteries, and making him burn with shared zeal and curiosity. He has not, in fact, quite this gift; but he tells his tale unaffectedly and well, and he looks about him in strange places and gives a brisk report.

SHIP'S SURGEON AT LARGE

Richard Gordon has followed up his story of life in a medical chool[2] with an account of life at sea,[3] and in the red-light areas of South American ports, from the viewpoint of a newly qualified doctor in the Merchant Service. It is life in the raw and in not too good a ship. The incidents are mostly characteristic of seamen and rarely incredible, and all are funny. Any newly qualified doctor thinking of a job on board ship should read this book first as a warning. But if the experience was not without its trials, the author has no doubt of its value:

> "I had found for the first time that the world isn't divided simply into two classes—doctors and patients. Three months at sea had taught me more than six years in a medical school. I had learned to give and take toleration, to grapple with grotesque predicaments, to appreciate there is some goodness behind everybody, that life isn't really so serious, and that doctors aren't such bloody important people after all."

CATALOGUE OF MEDICAL FILMS

The medical committee of the Scientific Film Association lans to publish a supplement to its catalogue of medical lms which was issued last May. The owners or distributors of films, not included in this catalogue, which are available for loan to medical audiences are asked to send details to Dr. Michael Essex-Lopresti, c/o the Association, 164, Shaftesbury Avenue, London, W.C.2.

University of Sheffield

Dr. A. H. Cameron has been appointed lecturer in pathology.

University of Leeds

Mr. Herbert Agar has been appointed honorary demonstrator in anatomy, Dr. F. G. W. Marson lecturer in the department of medicine, and Dr. R. L. Langley honorary lecturer in the department of pædiatrics and child health.

University of Birmingham

Sir Harold Himsworth, secretary of the Medical Research Council, will give the address at the inaugural meeting of the next session to be held on Oct. 5. Sir Harold will open the new block, now nearing completion, for clinical teaching and research.

University of Dublin

At a recent examination the following gained the diploma in gynæcology and obstetrics:

James Abraham, Indumati Balaram Adarker, Nilratan Adhya, Salar Akhtar Aziz, Harbans Bahry, Dinabandhu Bandyopadhyay, Satyendranath Basu, Ghulam Blieck. Ralph Anthony Boland, Gauripati Chattopadhyay, Praphullachandra Chaudhuri, Alaknath Dhol, Baidyanathbaran Ghosh, Din Hassan, Tehmi Dossabhoy Kapadia, Jayatissa Ediriwanna Mohotti, Madhu Somabhai Patel, Harrihar Jang Bahadoor Pershad, Asrukumar Ray, Prakaschandra Ray, Sachischandra Ray, Henry Carson Stevenson.

British Association of Physical Medicine

The annual meeting of this association will be held on April 17 and 18 at University College Hospital Medical School, London, W.C.1, under the presidency of Lord Horder. Further particulars may be had from the secretary of the association, 45, Lincoln's Inn Fields, W.C.2.

Faculty of Anæsthetists

At the anniversary dinner, held on March 18 at the Roya College of Surgeons of England, Dr. Bernard Johnson, th dean, announced that John Wyeth Brothers of New Yor had given the faculty £5000 to be used for scholarships for overseas students. Mr. Iain Macleod, the Minister of Health, proposed the toast of the Faculty. The health of the Guests was given by Dr. T. C. Gray, the vice-dean. Mr. A. A. Gemmell, F.R.C.O.G., and Mr. L. Farrer-Brown, secretary of the Nuffield Foundation, replied.

Royal Sanitary Institute

The health congress of this institute will be held at Hastings from April 28 to May 1, under the presidency of Lord Eustace Percy. Dr. B. E. Schlesinger is to be president of the section on maternal and child welfare; Prof. James McCunn, M.R.C.S., of the section of veterinary hygiene; Dr. Charles Wilcocks of the section of tropical hygiene; Dr. Andrew Meiklejohn of the section of occupational health. Further particulars may be had from the secretary of the institute, 90, Buckingham Palace Road, London, S.W.1.

Institute of Almoners

At the jubilee dinner on March 14, the health of the institute was proposed by Sir Russell Brain, F.R.C.P. Other guests included Dr. Hugh Clegg, editor of the *British Medical Journal*, Mr. L. Farrer-Brown, secretary of the Nuffield Foundation, and Prof. Andrew Topping, F.R.C.P., dean of the London School of Hygiene and Tropical Medicine. The company were received by Prof. Alan Moncrieff, F.R.C.P., chairman of the institute, and Miss E. C. Warren, vice-chairman.

Respiratory Diseases and Industry

Dr. Peter Edwards, superintendent of the Cheshire Joint Sanatorium, Market Drayton, will speak on this subject at a buffet-lunch meeting to be held by the Industrial Co-Partnership Association on Tuesday, March 31, at 12.30 p.m., in the hall of the Royal Empire Society, Northumberland Avenue, London, W.C.2. Applications for tickets (5s. 6d.) should reach the office of the association, 36, Victoria Street, S.W.1, not later than March 29.

Joint Tuberculosis Council

A report on the work of the council during 1952 refers to the forthcoming publication of a revised version of a report issued in 1948 on the protection of organised groups of children from the risk of infection by adults suffering from tuberculosis. The council's representatives on the British Student Tuberculosis Foundation have continued to take an active interest in the establishment and development of that body. The council also has continued its close association with the National Association for the Prevention of Tuberculosis on the Tuberculosis Educational Institute, and it i represented on the British Council for Rehabilitation, th Scientific Film Association, the Tuberculosis Rehabilitation Council, and the tuberculosis and pregnancy subcommittee of the National Birthday Trust Fund. Believing that the time is ripe for full consideration of the changing character of tuberculosis, the council has set up a committee to consider the best way in which this may be done. The officers of the council during the year were: chairman, Dr, Peter Edwards; vice-chairmen, Prof. F. R. G. Heaf and Dr. J. E. Geddes; hon. treasurer, Dr. Norman England; and hon. secretary, Dr. R. L. Midgley.

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[1] London: Herbert Jenkins. Pp. 199. 15s.
[2] Doctor in the House; see *Lancet*, 1952, i, 829.
[3] Doctor at Sea. London: Michael Joseph. 1953. Pp. 219.

Results

Effects on blood-pressure, venous hæmatocrit values, hæmoglobin, weight, urinary chloride and specific gravity, and "fluid balance" are illustrated in figs 1 and 2 Electrocardiograms showed no appreciable change in either subject while taking liquorice or after deoxycortone

A third subject (C) took 20 g liquorice daily, but without attempting to control sodium and potassium balance, and showed a maximum gain in weight of 4 lb in a four day test period

Discussion

Weight—The most striking effect of taking liquorice was a gain in weight This was accompanied by a more positive "fluid balance" and a fall in urinary chloride excretion In both subjects the "fluid balance" was more positive *in period* II *than in any period throughout* the trial Deoxycortone produced a positive "fluid balance" in W only, though not to the same extent as did liquorice During period III neither subject gained any more weight, though in S the dose of liquorice was almost doubled Withdrawal of liquorice was followed by a diuresis and loss of weight, as shown in period IV

The response to deoxycortone differed in the two subjects In W 5 mg deoxycortone in oil injected intramuscularly once daily produced a gain in weight and a positive "fluid balance" appreciably less than that due to liquorice in period II In S deoxycortone injections were accompanied by a loss of weight When the deoxycortone was stopped, the weight fell in both subjects, but this fall was accompanied by a diuresis in W only Judging by subsequent experience, it is probable that the period allowed for recovery from liquorice was too short for equilibrium to be regained

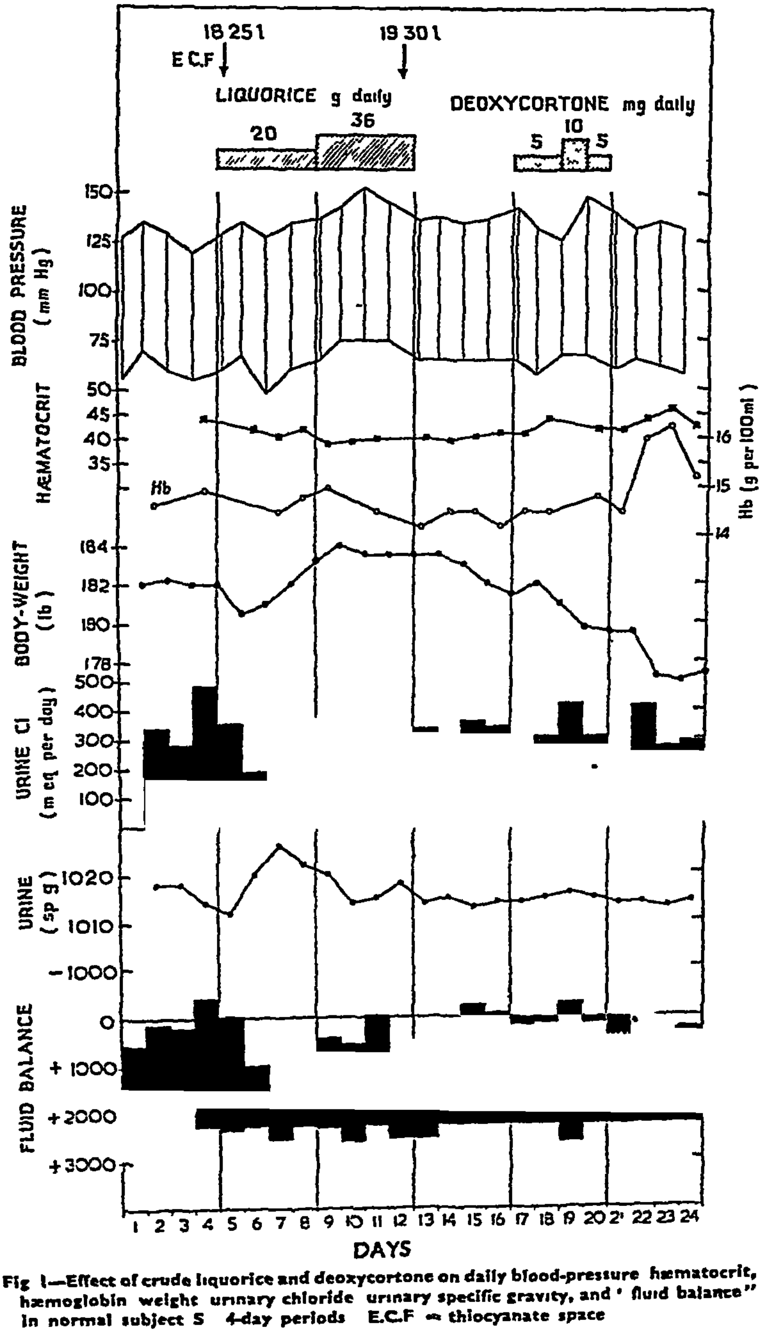

Fig 1—Effect of crude liquorice and deoxycortone on daily blood-pressure hæmatocrit, hæmoglobin weight urinary chloride urinary specific gravity, and ' fluid balance" in normal subject S 4-day periods E.C.F = thiocyanate space

Water distribution—The "thiocyanate space" (Crandall and Anderson 1934) was measured in both subjects on day 5, before starting liquorice, and on day 12, the last day of taking liquorice In both subjects two thirds of the gain in weight was accounted for by an *increase* of the "thiocyanate space"

Blood pressure—In both subjects there was a slight rise of systolic and diastolic pressures during the liquorice periods, and in W on deoxycortone

Sodium and potassium balances—These were not wholly satisfactory, but sodium balance approximately followed changes in urinary chloride, "fluid balance," and weight.

Sodium/potassium ratio—The ratio of urinary sodium to potassium was calculated for each period As a measure of deoxycortone-like activity this ratio is more sensitive than the change in the excretion of each ion taken by itself A fall in the sodium potassium ratio would then indicate deoxycortone like activity in liquorice In fact only a small fall was noted on liquorice, but even this was larger than was noted on deoxycortone

Conclusions—In general these findings confirm the claims of Molhuysen et al (1950), except that we failed to demonstrate any certain effect on potassium excretion

LIQUORICE FRACTIONS IN NORMAL SUBJECTS

Liquorice block juice was then fractionated by solvent and other treatment A screening test was devised by which we hoped to identify fractions rich in the substance responsible for the effects described The same three subjects were weighed daily Urine was collected in twenty four hour specimens and chloride output measured No attempt was made to control intake of salt or water, and it was hoped that, by taking the sum of four successive days together, the effect of variations in excretion due to changes in intake would be minimised Alternate periods of four days were taken as control and test periods The usual dose was the equivalent of 20 g of block juice daily

With the screening test described no definite evidence was found that any of these substances had had an effect Where one of them seemed to have an effect in one of the subjects, it was not always observed in the others This apparent inconsistency between subjects would not by itself invalidate the results, we have since satisfied ourselves that the subjects did show considerable variation in response, due apparently to differences in sensitivity

Conclusion

We do not feel that the method used was adequate to identify an active fraction

SYNERGISTIC ACTION OF LIQUORICE AND CORTISONE IN ADDISON'S AND SIMMONDS'S DISEASE

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ONE of the most characteristic properties of some of he adrenal cortical hormones is their action on the kidney, whereby sodium, chloride, and water (extracellular fluid) are retained while excretion of potassium is increased. When administration of these hormones is stopped, there is a "rebound": potassium is retained and extracellular fluid is excreted in excess. Deoxycortone (desoxycorticosterone) possesses this property to a greater degree than the glycocorticoids, 17-hydroxy-11-dehydroxycorticosterone (cortisone; Kendall's compound E) and 17-hydroxycorticosterone (Kendall's compound F) (Tait et al. 1952).

Molhuysen et al. (1950) demonstrated that oral administration of extract of liquorice, or of the glycyrrhizinic acid obtained from it, has the same effect as ministration of deoxycortone. As happens in long-tinued treatment with deoxycortone, the use of liquorice led to the retention of extracellular fluid, together with a fall in the hæmoglobin concentration, a rise in the venous pressure, and a rise in the systolic and pulse pressures, indicating an increased blood volume and a raised cardiac output. Probably as a result thereof, the excretion of water and sodium chloride increased again, and after several days a new equilibrium was reached between intake and output. If at this stage deoxycortone was given in addition to the liquorice it was practically without effect even in large amounts. Discontinuance of liquorice was followed by excretion of the retained extracellular fluid and by retention of potassium. The rebound appeared later, and lasted longer, than after discontinuance of deoxycortone; in particular there was sometimes a long delay before the blood-pressure fell.

bsence of Response to Liquorice in Some Patients with Addison's Disease

All persons treated with 20 grammes or more daily f the extract of liquorice showed the characteristic eactions, but both weak and strong reactors were seen. Only one person—a patient suffering from Addison's disease, showed no change whatever in his excretion of electrolytes when he was given liquorice, and no rebound when treatment was stopped.

Groen et. al. (1951) report a beneficial response to liquorice in Addison's disease. Not only was there retention of extracellular fluid, but there was also an improvement in the circulation and general condition of the patients, and it was possible to discharge them from hospital on maintenance doses of the succus liquiritiæ. No explanation could be found for the difference between their results and ours.

When cortisone became available we readmitted our patient with Addison's disease to hospital. It was again impossible to demonstrate any beneficial effect of liquorice, but an unexpected strong effect was obtained when we gave liquorice and cortisone simultaneously. We report here our observations on this patient and on two others with Addison's disease. We also report observations on a patient with Simmonds's disease designed to determine whether the natural glycocorticoids of the adrenal gland have the same effect as cortisone.

Methods of Study

The patients received the diet customarily given in this clinic for the study of the diurnal excretory rhythm—i.e., 3-hourly throughout the day and night constant amounts of milk, biscuits, and butter, and 100 ml. of water in which was dissolved fixed amounts of sodium chloride and sodium bicarbonate (Borst and de Vries 1950, Molhuysen et al. 1950). Therapeutic agents were similarly distributed throughout the 24 hours, one-eighth of the daily dose being given 3-hourly by mouth. Only deoxycortone and A.C.T.H. (adrenocorticotropic hormone) were given by injection, the deoxycortone twice a day (12-hourly) and the A.C.T.H. ('Cortrophine' Organon) eight times a day (3-hourly) or four times a day (6-hourly). Cortisone injections were given on only a few occasions: in the figures all injections are indicated by arrows. The liquorice used in our experiments since April, 1949, has all been from the same stock.

The patients micturated eight times a day at 3-hourly intervals. In connection with an investigation into the diurnal excretory rhythm all urine specimens were examined for sodium, potassium. and creatinine, and sometimes for uric acid. The graphs in this paper show only the amounts excreted during complete 24-hour periods. The fæces were not examined routinely. The loss of sodium in the fæces was found to be insignificant and approximately 15 m.eq. of potassium was excreted daily in the fæces. Throughout the period of observation, which sometimes lasted for several months, no change was made in the conduct of the investigations.

Since in patients without increased rate of blood-destruction large changes in the hæmoglobin concentration within a few days reflect changes in plasma volume in the opposite direction, the hæmoglobin was measured daily in two patients. The changes in arterial pressure were also followed, as were the venous pressure changes in patients with well-developed neck veins.

In patient 1, and during the first period of observation in patient 2, the uric-acid/creatinine ratio was determined. The excretion of creatinine per 24 hours is so constant under the test conditions that one must consider a breakdown in the collection of urine if there are fluctuations of more than 10%. The uric acid can fluctuate more widely, and consequently so may the uric acid/creatinine index. In patient 1 the fluctuations were strikingly small, and even the administration of large amounts of cortisone did not markedly increase the excretion of uric acid (fig. 2). In patient 2 the fluctuations were conspicuous (fig. 3). The excretion of uric acid did not, however, depend only on the administration of cortisone. Whenever there was an improvement in the circulation, the uric-acid/creatinine index increased, while deterioration of the circulation produced a fall in the index. We therefore gave up following the excretion of uric acid in the subsequent investigations, since the effect of glycocorticoids and of deoxycortone could not be distinguished on the basis of alterations in the index.

The method for the various determinations are described by Molhuysen et al. (1950), and Borst and Molhuysen (1952). Uric acid was determined by the method of Kern and Stransky (1937). In figs. 2–4 the values for the venous and arterial pressures and the pulse-rate are the averages of two or three determinations during the day.

Difficulties in Assessing Effect of Liquorice

When bed rest is complete and the standardised diet is taken, the excretion of the minerals shows only slight spontaneous fluctuations from day to day. Substantial changes in the excretion of sodium and potassium in opposite directions always indicate the influence of adrenal cortical hormones or related substances. It should be remembered, however, that retention of extracellular fluid in the presence of a normal serum-albumin level, a normal heart, and normal kidneys give rise to the following chain of events: increased plasma volume, rise in venous pressure, increase in cardiac output in excess of the demand, and increased renal excretion of water and sodium chloride and to a slight extent of

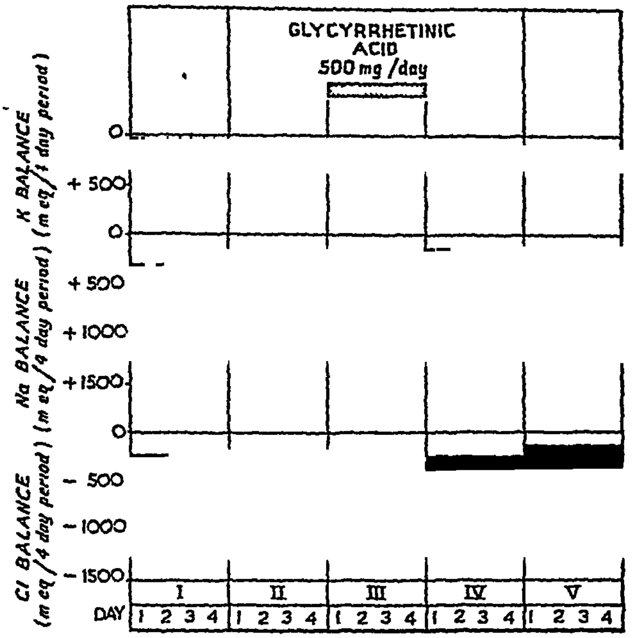

Fig 4—Effect of glycyrrhetinic acid on potassium, sodium, and chloride balances in subject C 4-day periods

pressure had fallen to 80/66 Accordingly it was decided that orthodox treatment should be instituted at once intramuscular cortisone and deoxycortone were given together and her clinical condition rapidly improved (figs 5 and 6) Besides subjective improvement, there was a gain in weight of 12 lb in two weeks The urine volume diminished, the hæmoglobin level fell from 90% (Haldane) to 62%, and the packed cell volume from 41 to 29% A metabolic balance study on this patient was thought inadvisable but the changes in the serum electrolytes are seen in fig 6

When the patient's condition was satisfactory, active treatment was discontinued and dummy therapy with arachis oil injections and oral lactose was substituted The body weight now fell and there was a fall in the serum sodium/potassium ratio though the general condition of the patient remained good Oral glycyrrhetinic acid was now substituted for the lactose, and was given in 50 mg capsules, one q i d for thirteen days The effects observed (figs 5 and 6) were similar to those seen with cortisone and deoxycortone therapy Weight was regained and the daily urinary volume again fell, with concomitant fall in hæmoglobin and packed cell volume The daily urinary chloride output also fell and the sodium/potassium ratio in the serum increased On stopping glycyrrhetinic acid there was prompt reversal of these changes

Apart from the above observations there was no alteration in the patient's clinical condition and she was judged well enough to be discharged without maintenance treatment under strict outpatient supervision That such treatment was in fact necessary was shown by her subsequent admission with a recurrence of symptoms and the characteristic deviation from normal of the serum electrolytes Conventional therapy was followed by a satisfactory remission

Conclusion —From this study it appears that glycyrrhetinic acid is capable of reversing certain features of Addison's disease, in a similar way to cortisone and deoxycortone

EFFECTS ON ANIMALS

These metabolic effects in man have so far not been reproduced in animals One of us (N R W T) made the following experiments in rats and guineapigs

1 Crude liquorice extract was administered by stomach tube to rats in dosage equivalent to that used in man In addition, they were given physiological saline solution to drink in order to load them with sodium chloride The weights of this series of animals were compared with those of an untreated control series, and with a group treated with a small daily dose of deoxycortone (25 μg per 100 g body weight) No increase in weight occurred in the animals treated with liquorice or deoxycortone Further massive dosage with crude liquorice (equivalent to 180 g per day for a man of 60 kg) caused no gain in weight

2 The same dose of deoxycortone was given to a series of rats which had been unilaterally adrenalectomised and nephrectomised This group showed no increase in weight as compared with an equal number of similar control rats

3 Crude liquorice extract was given by mouth to a group of adrenalectomised rats in dosage equivalent to that used in the human experiments This failed to prolong their survival time Likewise, one third and three times this dose had no effect

4 Glycyrrhetinic acid was next given to intact rats by mouth and by subcutaneous injection, as well as to adrenalectomised rats There was no increase in weight in the intact animals and survival time was not prolonged in the adrenalectomised series Ten times the equivalent dose used in man also failed in adrenalectomised animals

5 Glycyrrhetinic acid administered to intact guineapigs by subcutaneous injection caused no increase in weight either in dosage equivalent to that used in humans, or in doses of ten times this amount

Conclusion —From these experiments it would appear that crude liquorice extract and glycyrrhetinic acid have

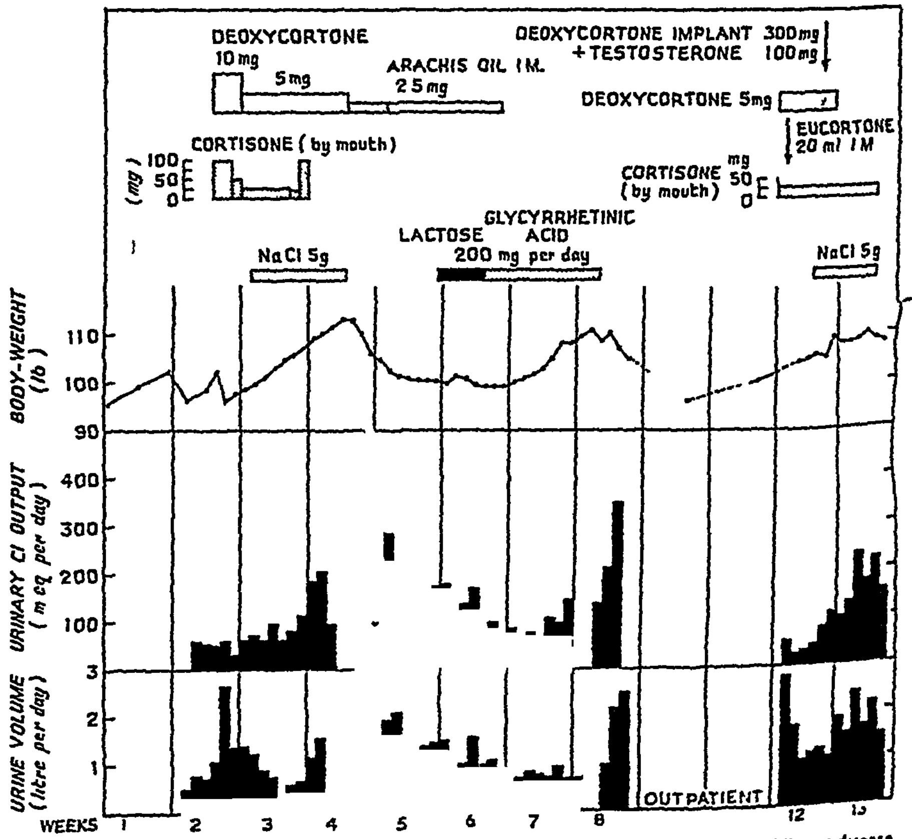

Fig 5—Daily body-weight urinary chloride output, and urinary volume in patient with Addison's disease Weekly periods

During these days the condition of the patient gradually eriorated. He became nauseated and managed to take meals only with increasing difficulty. Accordingly he was aporarily given a normal diet and 5 mg. of deoxycortone ly. The body-weight and venous pressure rose, and the moglobin fell. After stopping the deoxycortone injections standard diet was resumed. During the long control period sodium balance was negative.

Administration of glycyrrhetinic acid* on July 25 and , in an amount equivalent to 30 g. of liquorice, was thout effect. As the patient's condition again deterio-ted, while the hæmoglobin concentration rose and e venous pressure fell, we immediately commenced rtisone therapy, giving 40 mg. daily. A moderate tention of extracellular fluid was observed, and an creased excretion of potassium. In spite of the cortisone he body-weight fell; but the patient felt much better. he venous pressure rose and the hæmoglobin fell. ncrease in the amount of cortisone administered was ithout demonstrable effect.

Without stopping the administration of cortisone, we hen gave liquorice again, only 15 g. per day. The esult was completely different from that obtained on une 29 when liquorice alone had been given; this time he excretion of sodium was approximately halved and here was a retention of water, sharply contrasting with he increased excretion of potassium. Thus, not only id the patient now react to liquorice but the response as strong. Reduction in the amount of cortisone dministered was almost without effect, although the omplete withholding of cortisone led to a sharp rebound, in spite of the continued administration of liquorice. 5 mg. of cortisone daily sufficed to restore the full beneficial effect of the liquorice.

For the past 12 months the patient has continued to take, four times daily, 4 g. of liquorice and 2·5 mg. of cortisone, and has remained very well. For the first time he feels himself, which was never the case in the years when he was treated with regular deoxycortone injections. He is no longer unduly sensitive to cold, and his mental and physical stamina have returned. The blood sodium and potassium concentrations have remained normal, and the blood-pressure fluctuates around 120/80 mm. Hg.

PATIENT 2

This patient, aged 21, had been ill for only a short time before he was admitted to our clinic in severe shock, with all the signs of Addison's disease. After his condition had been improved with deoxycortone injections, he was given the standard diet. From May 7 to 9 A.C.T.H. was administered. This was without demonstrable effect, but he was still showing the rebound due to diminution of the dose of deoxycortone from 2 to 1 mg. per day on May 5 (fig. 3). The eosinophil-count did not fall. An intramuscular injection of 200 mg. of cortisone affected his mineral metabolism and circulation only slightly, though the excretion of uric acid increased markedly and the number of eosinophils in the blood fell to 25% of the initial figure. Cessation of the deoxycortone injections on May 25 brought about deterioration in his general condition, and a crisis was just averted by injecting a much larger amount of cortisone on May 31 and June 1 and 2. This had a clear effect most noticeable in the improvement in the circulation. 10 days later, when his condition was again deteriorating, extract of liquorice brought about complete reversal in the mineral balance, while at the same time the circulation improved. Thus this patient, unlike the previous one, reacted favourably to liquorice without the simultaneous administration of cortisone. Withholding of liquorice caused, a rebound, and its continued administration again had a beneficial effect.

On July 20 we began to give cortisone, while continuing to administer liquorice. The patient reacted to the cortisone with a negative potassium balance and positive sodium balance. The body-weight rose, as did the venous pressure. When liquorice was no longer administered there was a much greater “ rebound ” than on June 19, though the patient was still receiving cortisone.

During 2 days (Aug. 6 and 7) glycyrrhetinic acid was given in an amount equivalent to 30 g. of extract of liquorice daily. It was this same preparation which was without effect in patient 1 (fig. 2, Aug. 25 and 26). It here proved to be highly potent

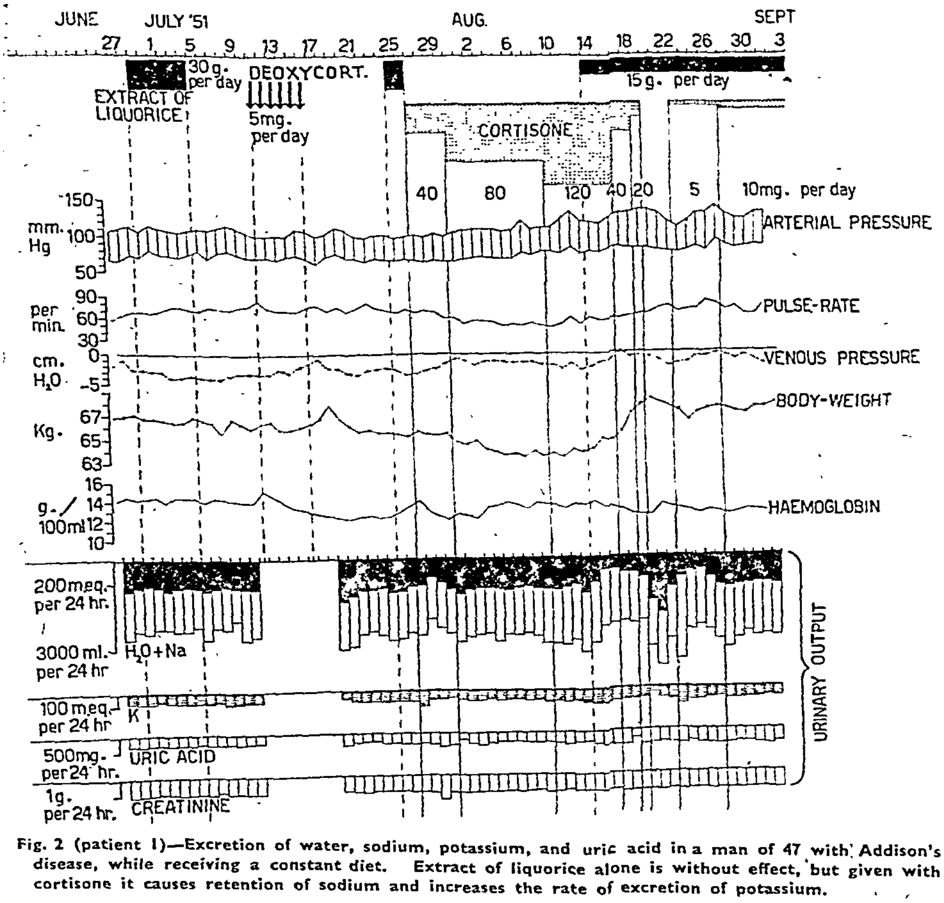

Fig. 2 (patient 1)—Excretion of water, sodium, potassium, and uric acid in a man of 47 with Addison's disease, while receiving a constant diet. Extract of liquorice alone is without effect, but given with cortisone it causes retention of sodium and increases the rate of excretion of potassium.

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* Glycyrrhetinic acid is a breakdown product of glycyrrhizinic acid, prepared by Willebrand and found by Groen et al. (1952) to be active.

TRICHOMONAS VAGINALIS IN THE MALE

THE EXPERIMENTAL INFECTION OF A FEW VOLUNTEERS

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Though much has been written on the subject, there is little general agreement about *Trichomonas vaginalis* infections in the male urogenital tract

In the female, trichomonas vaginitis is a well-recognised condition, and, although to many it may appear to be of little importance, gynæcologists and venereologists regard it as anything but trivial Writing recently on the organisation of a special clinic for patients with vaginal discharges, Donald (1952) said that the largest group attending were those with trichomonas vaginitis, which was the more troublesome because the incidence of relapses was so high (over 22%) More than a third of these patients were unmarried, and "a significant number contracted the infection as a result of their indiscretions"

In quite a large proportion of cases trichomoniasis must be regarded as a venereal disease, but there are others in which this mode of transfer can be ruled out Patients have developed trichomonas vaginitis while in hospital, or in similar circumstances, where some simple cross-infection was almost certainly responsible The way in which this rather delicate organism is transferred from patient to patient remains unsolved, though the investigations of Whittington (1951b) showed that the flagellates are more resistant to adverse conditions of temperature, &c, than had formerly been believed Indeed all doctors who make vaginal examinations, particularly in clinics, should carefully review their technique to make sure that they are not perhaps responsible for the transference of infection

Though care must be exercised in drawing any conclusions about human infections from analogous conditions in animals, such comparisons may occasionally be illuminating It is therefore interesting to consider the sequence of events in bovine infections due to the closely related organism *T fœtus*

An uninfected bull becomes infected as a result of coitus The infected bull may never show any symptoms, or it may develop a balanitis initially, which quite soon settles down The infection in the bull is essentially chronic An infected bull will usually infect any cow it serves and here the trichomonad gives rise not only to vaginitis but also to a uterine infection In the uterus conditions are produced which may prevent implantation of the fertilised ovum or subsequently cause abortion Thus, infected cows become virtually sterile

The economic consequences may be serious, for example, if the communal bull in a small rural area becomes infected, or when such infections occur in places where bulls of good stock are scarce, as in some of the Colonies Although artificial insemination has done much to prevent bovine trichomoniasis, constant vigilance must be maintained to keep the disease in check

Trichomoniasis in cattle has been thoroughly investigated and is still the subject of considerable research By comparison human infections with *T vaginalis* appear to arouse very little interest It is perhaps unlikely that trichomoniasis has any effect on human fertility, but the possibility should not be dismissed without some thought The observations of Schnitzer et al (1950) that mice can be infected with *T vaginalis* by intramuscular injection, giving rise to a localised abscess, throw further doubt on the general conception of *T vaginalis* as a parasite of little more than nuisance value

If trichomoniasis in the female is important, the occurrence of the same parasite in the male must also be important, whether its presence gives rise to symptoms or not, for, whatever the mode of infection in the female, there seems little doubt that in the male the infection is almost always venereal

THE LITERATURE

One of the first accounts is that of Miura (1894)

The patient had no signs or symptoms of urethral infection other than the presence of numerous threads, similar to those of gonococcal *origin, in the first glass of a two glass test* Noting that the urine contained *T vaginalis* and that the second glass in the above test was clear, Miura concluded that the protozoa were derived from the urethra The patient's wife was found to have a trichomonas vaginitis

Dock (1896) described a chronic urinary infection in a man aged 27, whose urine contained large flakes, which were found on microscopy to consist of pus cells, epithelial cells, and trichomonads The source of infection was not discovered

Katsunuma (1924) published details of the finding of *T vaginalis* in the preputial sac of a boy, aged 3 years, who had a fairly severe balanitis

The first definite account of a *T vaginalis* urethritis in a male is probably that given by Capek (cited by Riba 1931), it was in a man of 40 whose wife had trichomonas vaginitis In subsequent years many more papers appeared reporting not only urethritis but prostatitis and epididymitis caused by *T vaginalis* Extreme claims were made the incidence and severity of the infection were perhaps overemphasised by some workers though minimised by others, but slowly it was becoming clear that trichomoniasis in the male was a definite clinical condition

Examinations of the husbands of infected women, such as those reported by Allen et al (1935) and Drummond (1936), strengthened the case for male infections Although most of the infected husbands in these investigations were found to be symptom-free, they were none the less a potential source of reinfection in wives successfully treated

While investigating the cause of recurrences of trichomonas vaginitis Karnaky (1938) found trichomonads in 38 of 150 husbands of infected women The protozoa were found in the prostate, urethra, or preputial sac, any one of which, Karnaky claimed, might be the sole site of infection Karnaky concluded that the infection was self limiting and, in the absence of reinfection, tended to die out in two or three months

Liston and Lees (1940), investigating 400 men attending a venereal diseases clinic, searched for trichomonads not only by the usual method of examining wet preparations but also by the examination of Leishman stained films, in the latter it was claimed that the protozoa were characteristic and easily distinguished from pus cells Of the 400 patients 16 (4%) harboured trichomonads Only 1 of these positive cases was found in 264 patients with gonorrhœa, whereas the remaining 15 were found in patients who were classed on clinical grounds as having "non specific urethritis"

Since 1940 there have been many reports about male trichomoniasis These show more agreement than some of the earlier ones on the clinical features of the infection but there is still the widest discrepancy regarding the incidence

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pare with that of the combination of liquorice and cortisone on Dec. 16–22). In August, 1952, the patient left the hospital in excellent condition, taking 15 g. of liquorice and 5 mg. cortisone daily. In the preceding month this good progress had, however, been interrupted several times, for at intervals of a month he developed six recurrences of the pericarditis (presumably due to a virus infection), which on Nov. 8, 1951, had necessitated administration of large doses of deoxycortone and cortisone. The pericarditis, which healed without sequelæ, was probably of the same type as that described by Tomlin et al. (1952) and was not related to the disease of the adrenals.

Figs. 3 and 4 show that the patient's general condition during the second period of observation was constantly less satisfactory than during the first. Nevertheless, apart from the period Nov. 7–24, his temperature, sedimentation-rate, and white-cell count were normal throughout the period represented in fig. 4. The venous pressure, which during the summer had only fallen below −3 cm. of water on May 31, 1951, when he was in a state of shock, latterly did not rise above this figure except when liquorice and cortisone were being given simultaneously. The disease thus appears to have been definitely progressive.

He remained in good general condition during June and July, 1951, taking 30 g. of liquorice daily, and during the period from Aug. 15–19 when he was taking 15 g. of liquorice daily, equilibrium was rapidly established following the rebound caused by the withdrawal of cortisone (fig. 3). On the other hand, during the winter, while he was receiving 20 g. of liquorice daily, there were two episodes indicating progressive suprarenal insufficiency. *Thus with the progress of the disease the ability was lost to react to liquorice by retention of extracellular fluid and by increased excretion of potassium.*

PATIENT 3

A woman of 34 had been treated in a sanatorium for pleurisy, and, while there, had developed all the signs of Addison's disease. She was treated with deoxycortone, two daily injections of 5 mg., and all signs of the disease disappeared.

On admission to hospital she felt very well, but had a hypokalæmia and a high serum-sodium concentration. We stopped the injections of deoxycortone and she remained fairly well; but she could not tolerate the standardised diet without vomiting unless at the same time she received deoxycortone. Only after she had become accustomed to the diet did we replace the deoxycortone by inert oil, and this change caused a "rebound." In the following weeks we gave 15 g. of extract of liquorice daily for several days at a time, sometimes with 20 mg. of cortisone and sometimes without. In no period could we demonstrate any clear effect. It is possible that the effect of the liquorice and the cortisone were masked by the menstrual period and the fluctuating excretion caused by the "rebound" after withdrawal of the deoxycortone. The injection of large amounts of A.C.T.H. while the patient still received liquorice was also without effect either on the excretion of electrolytes or on the eosinophil-count.

The patient was then given a normal diet with 5 g. of liquorice four times daily and 5 mg. of cortisone twice daily. To our amazement her general condition improved dramatically; her weight increased by 5 kg. and even the blood-pressure rose from *110/70 to 165/96 mm. Hg. The blood-*pressure and the body-weight fell again when the cortisone was withheld. She again received the standardised diet, this time without vomiting. Further observations are shown in fig. 5. It is seen that discontinuance of liquorice therapy caused at the most only a slight increase in the excretion of sodium, while its resumption led to a slight retention of sodium. There was no demonstrable effect on potassium excretion. The administration of 10 mg. of cortisone daily and its withdrawal clearly affected mineral metabolism more strongly during periods when the patient was taking liquorice than when the cortisone was given alone. The stopping and starting of liquorice during a period when cortisone was being administered had little effect. That this effect was definitely present, however, could be seen more clearly from the individual urine specimens than from the 24-hour outputs as given in fig. 5.

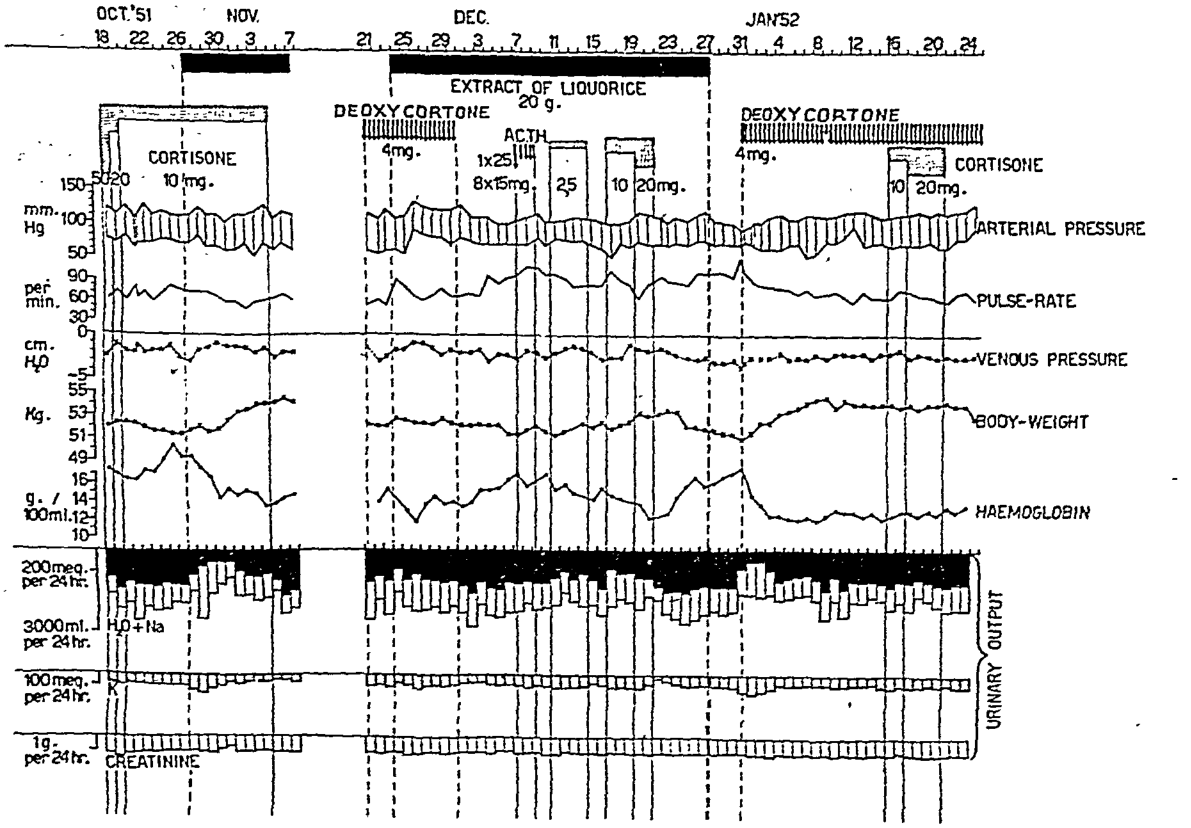

Fig. 4—Patient 2 in a later stage of the disease. The liquorice has become inactive when given without simultaneous administration of cortisone.

light thread was found in the first specimen of urine Microscopically this consisted of pus and epithelial cells with a few coliforms and diphtheroids On the 2nd and 3rd days no signs of infection were found, but on the mornings of the 4th, 5th, and 6th days a mucoid "dampness" was present at the meatus This consisted of pus and epithelial cells The urine contained a few light threads No trichomonads were found in any of the specimens examined Thereafter, no further evidence of infection was found, and at no time was it possible to demonstrate *T vaginalis*, although the patient was kept under observation for 3 months

Case 2—A man, aged 55, under treatment for latent syphilis, uncircumcised On the morning after inoculation there was a slight mucoid discharge and the urine contained a few light threads Microscopically the discharge and threads consisted of pus, epithelial cells, and a moderate number of coliform and diphtheroid bacilli, no trichomonads were found Subsequent examination revealed no signs of infection, and on no occasion was *T vaginalis* demonstrable This patient was observed for 6 weeks

Case 3—A man, aged 49, under treatment for minor manifestations of tabes dorsalis, circumcised On the morning after inoculation he had a mucoid discharge similar to that recorded in the preceding case His urine was clear but contained a few heavy threads Both the urethral discharge and the urine threads contained pus, epithelial cells, and non specific organisms No trichomonads were found This condition persisted until the 6th day, when the urethral discharge became more pronounced and the urine developed a slight haze and contained many fine light threads Next day the mucoid discharge was unchanged, but the urine was more hazy The prostatic secretion was notable because of the presence of several bodies of uniform shape and size which appeared to be degenerated forms of *T vaginalis* On the 9th day the urethral discharge had become far more copious and was milky in colour and consistence This contained many actively motile trichomonads, pus, epithelial cells, and non specific bacteria The prostatic secretion was normal and contained neither active nor degenerative trichomonads The patient complained of slight urethral irritation, this was the only occasion in the series when such a complaint was made For the next 3 days the condition remained generally unchanged, but the urethral discharge showed signs of ceasing and the trichomonads became somewhat fewer and less active During this period the urine developed an appearance which was later recognised as being characteristic and almost pathognomonic of heavy *T vaginalis* urethral infections This was a hazy urine containing large numbers of minute light threads From the 13th day onwards no trichomonads were discovered, and a mild symptomless urethritis, as shown by a morning gleet and threads in the urine persisted for a further 3 weeks After cessation of this urethral discharge the patient was observed for a further 3 months without abnormal findings

Case 4—A man, aged 27, under treatment for advanced syphilitic aortitis, uncircumcised On the day after inoculation a mild symptomless urethritis developed No trichomonads were demonstrable, and the discharge consisted of pus, epithelial cells and a few non specific organisms On the 6th day the urethral discharge became more pronounced, it was whitish and mucoid The urine had become hazy and contained many fine light threads, as in case 3 No trichomonads were found in either the urethral discharge or the urine but they were present in considerable numbers in the prostatic fluid, which also contained a moderate number of pus cells The condition remained unchanged until the 9th day, when a distinct increase in the urethral discharge heralded the presence of the trichomonad in urethral specimens From this time until the 34th day a urethral discharge of varying amount and character was present Although usually mucoid and whitish, on some occasions it became thick and purulent and could have been mistaken clinically for an acute gonococcal exudate Often no trichomonads could be found in the discharge, but meatal scrapings always contained the organism During this period it was always possible to find trichomonads in the prostatic fluid

After the 34th day no urethral discharge was present, but the urine continued to exhibit a slight haze, and the trichomonads persisted in urethral scrapings and in the prostatic fluid up to the 50th day No further observations were made

Case 5—A man, aged 25 under treatment for latent syphilis uncircumcised On the day following inoculation a mild urethritis was present This persisted until the 6th day, but no trichomonads could be demonstrated in the urethral and prostatic secretions The urethral discharge contained pus, epithelial cells and non specific organisms On the 6th day the urethral discharge was increased and a urine of the type previously described as typical was passed Although no trichomonads were found in the urethral discharge, the prostatic fluid contained large numbers of active flagellates The condition remained unchanged for the next few days Trichomonads were first discovered in the urethral discharge on the 10th day Thereafter a mucoid urethral discharge persisted until the 80th day and during this time the trichomonads could always be found in urethral scrapings and in the prostatic fluid About the 80th day the urethral discharge ceased, but the trichomonads were recovered from the urethra and prostate until the 100th day By the 110th day no abnormality could be detected, and frequent examinations during the succeeding 3 months were likewise negative

SEROLOGY

Samples of serum were obtained from the test group of volunteers on the 3rd, 7th, 14th, 21st, 28th, and 48th days after inoculation These were examined by the hæmagglutination method for the presence of antibody to *T vaginalis* None of the samples gave a significant titre of agglutination, irrespective of the clinical condition of the patient The negative serological results were not unexpected in view of the findings in *T fœtus* infections of bulls, where a serological response is elicited only in unusually severe cases

DISCUSSION

Three out of five volunteers inoculated intra-urethrally with a pure culture of *T vaginalis* developed a urethritis from which the protozoa were recovered for different periods The remaining two patients developed a mild transient urethritis, but no trichomonads were recovered from them at any time The controls, who received a similar inoculum of sterile medium, showed no abnormality

The experiment has proved of considerable value in subsequent clinical work and especially in diagnosis In particular it was noted that the urine of volunteers who showed a well-developed trichomonas urethritis had a very charactersitic appearance, similar to that described by Lydon (1945) in naturally occurring infections Examination of carefully taken urethral scrapings often revealed trichomonads when they could not be demonstrated by any other method The importance of this technique both as a test of cure and in the investigation of suspected cases is evident, for it is almost certain that, so long as active protozoa persist, the patient can transmit the infection An unexpected finding was that in three of the successfully infected volunteers careful daily examination failed to reveal the presence of *T vaginalis* before the 6th–9th day after inoculation despite the early development of mild symptomless urethritis This suggests that patients with non specific urethritis should be investigated for *T vaginalis* on several occasions over a period of 7–10 days after the probable date of infection

Although the number of cases recorded is very small, there is nevertheless considerable variation in the clinical findings, as, for example, in the nature of the discharge or the duration of the infection Only one patient complained of symptoms, and these were trivial The infection appeared to be self limiting in the cases which were fully observed, and the period during which the protozoa could be found varied from 4 to 94 days In one case the urethral discharge persisted for 3 weeks after the disappearance of the protozoa, an observation which gives rise to speculation about the possible role of this organism in the production of non specific urethral discharges where no obvious cause can be detected Two of the patients who were heavily infected developed a mild prostatitis, and trichomonads were demonstrable react in the second period of observation, was presumably due to the almost complete absence of functioning suprarenal tissue. According to this hypothesis patient 2 must have had some functioning tissue initially.

We still have no direct evidence that the patient with Addison's disease who reacts favourably to liquorice still has a remnant of functioning suprarenal tissue. It remains to be demonstrated that the injection of A.C.T.H. during treatment with liquorice causes such patients to retain sodium and excrete increased amounts of potassium.

Our observations throw no light on why the effect of liquorice in normal subjects varies so much. It is evident that the intensity of the response is not determined by the amount of glycocorticoids produced by the suprarenal glands—unless this falls below a certain level. At the moment the most attractive hypothesis is that the "weak reaction" of certain subjects is merely the consequence of a very active counteracting homœostatic mechanism.

Conclusions

(1) The deoxycortone-like effect of liquorice, always seen in people with intact suprarenal glands, was found to be absent in three patients with Addison's disease. One of the three had suffered from suprarenal insufficiency for only a short time and had at first reacted well to liquorice.

(2) In these three patients administration of 2·5 mg. of cortisone daily, divided into eight doses, partially restored the effect of liquorice on the mineral metabolism. 10 mg. of cortisone restored the effect fully.

(3) A patient with Simmonds-Sheehan disease reacted favourably to liquorice. A good response followed treatment either with liquorice and cortisone or with liquorice and A.C.T.H. Two of the patients with Addison's disease who were treated with liquorice and A.C.T.H. simultaneously failed to respond.

(4) It is probable that those patients with Addison's disease who respond favourably to liquorice still have remnants of functioning suprarenal tissue.

(5) The effect of suprarenal cortical hormones, or related substances, on water and electrolyte metabolism is counteracted by homœostatic reactions. The significance of this factor in the assessment of the activity of liquorice is discussed.

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EFFECTS OF LIQUORICE AND ITS DERIVATIVES ON SALT AND WATER METABOLISM

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RECENT reports have suggested that some samples of liquorice and their extracts may possess previously unsuspected pharmacological activity.

Revers (1946, 1948, 1951) noticed that about 20% of patients taking liquorice developed œdema. Molhuysen et al. (1950) described retention of water, sodium, and chloride, with increased output of potassium, following the use of a dried aqueous extract of liquorice. This action they defined as deoxycortone-like, and we shall use the term in this sense throughout this paper. They treated one case of Addison's disease with this preparation, without apparent effect. Groen et al. (1951) claim to have controlled one case of Addison's disease with liquorice, and a further case with salts of glycyrrhizinic acid, a component of liquorice (1952). The effects described in these two patients resembled those of deoxycortone.

We decided to investigate these effects, and in addition we examined certain components of liquorice for deoxycortone-like activity.

CRUDE LIQUORICE IN NORMAL SUBJECTS

Methods

Two healthy male adult subjects (S. and W.) were investigated. The trial extended to six periods, each of four days. An initial control period was followed by two on liquorice, then a second control period. During the fifth period deoxycortone in oil was injected intramuscularly once daily, after which a final control period was included to compare the recovery from liquorice administration and from deoxycortone. Sodium and potassium were measured in the diet. This provided an intake of approximately 3200 calories daily, which was enough to prevent the subjects going into negative nitrogen balance, and thus losing water, potassium, and nitrogen from protein katabolism. Gelatin capsules of salt were taken as supplements to provide approximately 9 grammes of sodium daily in all. The analytical methods used were those described by King (1951).

Fluid intake, urinary output, and chloride content were measured for twenty-four-hour periods. Sodium and potassium were determined in an aliquot of the bulked urine for each period. Stools were collected and their electrolyte content measured separately. The "fluid balance" shown in figs. 1 and 2 takes account only of measured fluid intake and urinary output, without allowing for water of metabolism, food water, and water lost in the expired air and through the skin. The weight was taken daily before breakfast.

The liquorice used was part of a bulk sample of Turkish "block juice" set aside for clinical trial. "Block juice" is the commercial name for the dried aqueous extract of liquorice prepared by primitive methods. The roots of the plant are boiled in water and the solution is evaporated to dryness. As supplied to us, it consisted of small black granules with the characteristically sweet taste; it was made up in rice-paper packages containing 4 g. each, and in this way was readily swallowed.

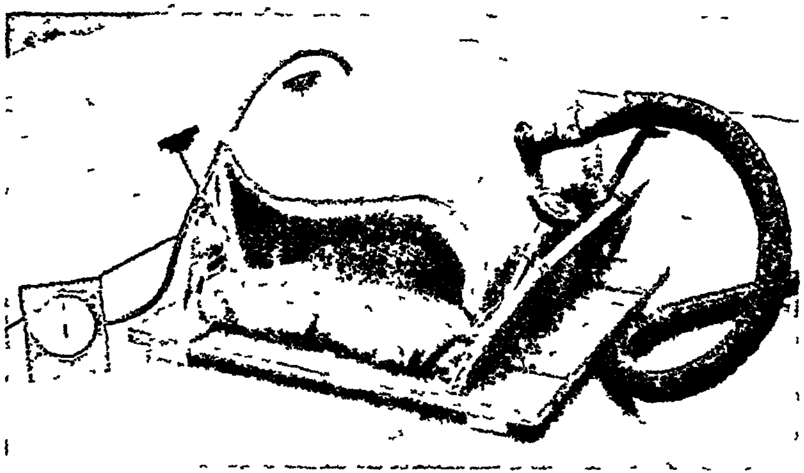

Fig 2—Type-2 cuirass with base-plate and airtight rubber mattress

The L C C cuirass consists of a chest piece resembling a suit of armour divided across the shoulders and down the axillary lines The neck seal consists of a rubber diaphragm fitting over the neck and round the rim of the chest piece The arm and trunk seals are effected in the same way

The Chestspirator resembles a miniature tank respirator with the head emerging through the upper opening Most of the body is enclosed in the apparatus A spirally closing or iris diaphragm collar is used to form the neck seal, and the other seals are obtained by tubes of rubber sheeting round the arms and over the lower abdomen

The most serious disadvantage of these patterns is that the rubber seal sucks in and blows out with the alternating pressures in a disturbing manner, and, owing to the wide difference between the areas of the neck and trunk openings, the patient is moved up and down the respirator for a distance of 1 or 2 cm with each pressure cycle Also, if the patient tries to sit up, the cuirass slides down and rests on the shoulders Otherwise respirators of this type—e g , Chestspirator—may be as efficient, as regards ventilation, as a tank respirator

TYPE 1 NEW MODEL

Rather than use a standardised pattern we tried to construct a cuirass with the same efficiency but individually moulded for each patient A hinged cuirass in two halves was impracticable, because of the difficulty of fitting it on a severely paralysed patient In consequence our apparatus consisted of anterior and posterior 'Polythene' shells sealed together along the two sides of the body (fig 1) The posterior shell was made on a positive plaster cast of the individual patient The taking of the negative cast in a paralysed patient presented considerable difficulties, and a perfect fit was lost if further wasting of muscles took place Pressure sores over bony prominences were always a problem The two halves were sealed along the axillary line by bolting two metal strips together over an intervening rubber washer The neck seal was made from sponge rubber cut into a truncated cone and covered with chamois leather, and on the whole it was satisfactory The arm seals were made with short sleeves, again with sponge rubber as far as possible At the lower end the seal was more difficult, to avoid alternating pressure on the bladder the seal was placed between the cuirass and the thighs and took the form of airtight pants These, however, tended to suck into the cuirass and also presented nursing difficulties

After a period of experiment this type of cuirass did not seem to be a practical proposition

TYPES 2 AND 3 EXISTING PATTERNS

Preliminary considerations on the other two types must be based on their efficiency and comfort

Of the commercial patterns the Stille (Sahlin) type is as efficient as any we have tested It consists of a rigid dome placed over the thorax and abdomen and fixed to a special table on which the patient lies The suction pressure is exerted round almost the whole lower chest and upper abdomen, and the chest piece does not move or distort appreciably with the pressure cycle

Some of the commercial models of anterior shell pattern are open to the objection that, if the patient lies on an ordinary bed, the negative pressure draws the shell down on to the mattress with the total force at working pressures of nearly one hundredweight This prevents the sternum from moving forwards and it also presses on the abdominal content The Kifa (Freiberger-Rudbach) and Fairchild-Huxley respirators have adjustable legs to reduce this downward movement

Many respirators are made with some flexibility of the dome or shell to facilitate fitting on to the patient, but if the posterior edge is too flexible it will be sucked inwards on to the lower ribs Radiographs taken in both phases of respiration have suggested that the Monaghan or Kifa patterns may produce paradoxical movement of either diaphragm or lower ribs In the Fairchild-Huxley an adjustable metal bar passing over the top of the cuirass appears to abolish this effect

TYPE 2 NEW MODEL

An experimental cuirass (fig 2) was designed in which the patient was placed on a 4-in foam-rubber mattress and a polythene shell was designed to fit over the body and rest on the mattress The seals were of foam rubber covered with an airtight skin, and the line of the seal extended from the manubrium sterni round under the armpits to the posterior axillary line, where it touched the mattress In the lower part of the body

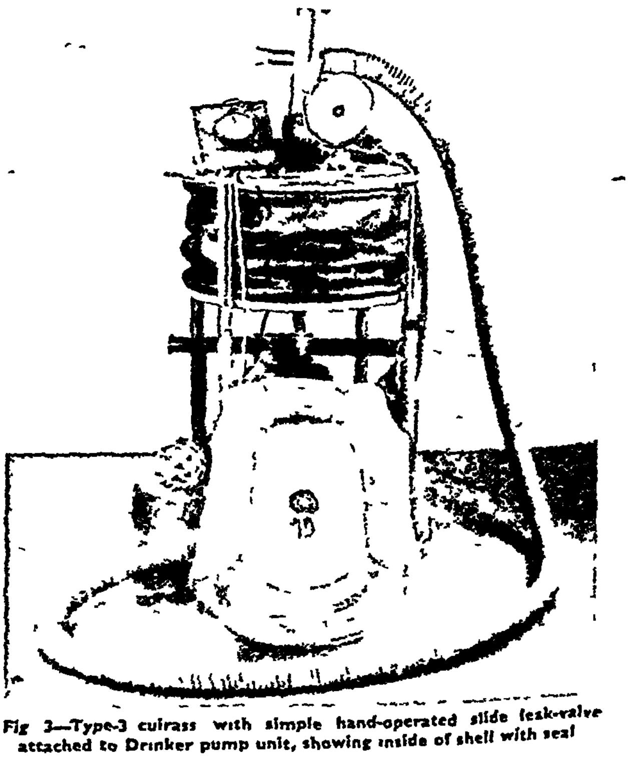

Fig 3—Type-3 cuirass with simple hand-operated slide leak-valve attached to Drinker pump unit, showing inside of shell with seal

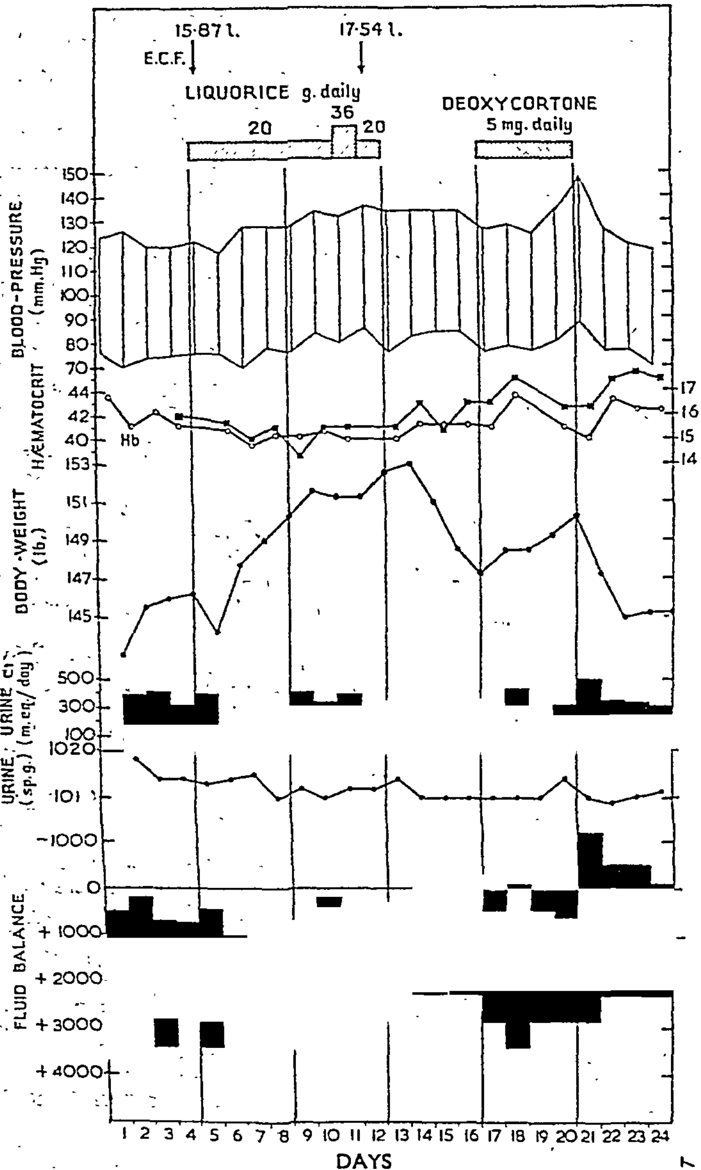

Fig. 2—Effect of crude liquorice and deoxycortone on normal subject W. 4-day periods.

GLYCYRRHETINIC ACID IN NORMAL SUBJECTS

Groen et al. (1952) suggested that the water-and-salt-active substance in crude liquorice might be glycyrrhetinic acid, which when conjugated with glucuronic acid forms glycyrrhizinic acid. This in turn forms 2–7% of different samples of crude liquorice, as its potassium and calcium salts (*B.P.C. 1949*). (The *U.S. Dispensatory 1947* quotes 5–10% glycyrrhizin in raw liquorice.) A sodium, potassium, and chloride balance was carried out to test this suggestion.

Method

The same three subjects took a diet of constant composition over five four-day periods. After two control periods, glycyrrhetinic acid was taken orally for the next period in doses respectively of 0·2, 0·25, and 0·5 g. daily. Two further control periods followed. Daily measurements were made of body-weight, urinary volume, and chloride output. Daily aliquots of the urine in each period were mixed, and sodium and potassium content determined. Daily blood-pressure was also recorded in two subjects, but no notable changes were observed.

Results

The findings in subject C. are shown in figs. 3 and 4. It will be seen that body-weight rose on glycyrrhetinic acid (0·5 g. daily), with a corresponding diminution of urinary volume and chloride output. The balance shows retention of sodium and chloride, but no alteration in potassium exchange. (The apparently positive sodium and chloride balances during the control periods can be explained as unmeasured losses of these ions in the fæces and sweat.) The findings in subjects W. and S. showed similar though less marked changes.

Conclusions

In the three subjects tested glycyrrhetinic acid had a retaining effect on water, sodium, and chloride, but its influence on potassium exchange was equivocal.

GLYCYRRHETINIC ACID IN ADDISON'S DISEASE

An opportunity arose to test the effect of glycyrrhetinic acid on a patient with Addison's disease.

The patient, a woman of 45, complained of periodic blackouts and dizziness for seven years. For three months she had noted weakness and nausea, but no vomiting. There was no past or family history of tuberculosis.

She was thin (95 lb.); her face, neck, and hands were deeply pigmented, including the palmar skin folds; and there was also pigmentation of the buccal mucosa. The blood-pressure was 108/70 mm. Hg on first examination, falling to a minimum of 80/40 in hospital.

Investigations.—Robinson-Kepler-Power test: A=8. (Normal: A more than 25.) Thorn test: 30 mg. adrenocorticotropic hormone failed to depress the eosinophil-count appreciably after four hours. Urinary 17-ketosteroid excretion: 1·3 mg. per day (average of two days). Chest radiography: some calcified foci, otherwise no abnormality. Blood chemistry on admission: serum-sodium 137 m.eq., serum-potassium 5·5 m.eq., serum-chloride 92 m.eq., and plasma-bicarbonate 21·4 m.eq. per litre. Blood-urea nitrogen 18 mg. per 100 ml.

Treatment.—On her admission to hospital the patient complained increasingly of a feeling of faintness and she began to vomit. Her blood-

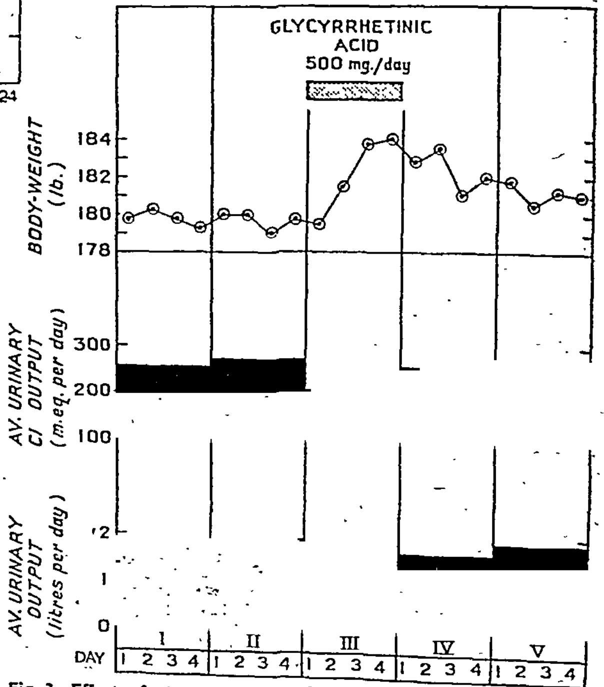

Fig. 3—Effect of glycyrrhetinic acid on daily body-weight, urinary chloride output, and urinary volume in subject C. 4-day periods. Urinary volumes and urinary chloride are expressed as an average for each period.

Pressure Recordings and Tracings

Pressure changes within the cuirass were measured with an aneroid-type manometer (adjusted to critical damping) attached by a small length of narrow-bore pressure tubing Tracings of the pressure-wave forms and the curves of tidal-volume negative pressure have been made When they are compared with those produced by various types of available respirators, it is seen that the simple shell cuirass gives as satisfactory a curve as that produced by more expensive apparatus The curve given in fig 5a shows the effect of varying negative pressures on the tidal volume These curves are obtained from the same poliomyelitis patient with complete paralysis of diaphragm and intercostals by using a recording spirometer and recording pressure gauge (Bourdillon et al 1950) Their technique consisted in altering the negative pressure in the respirator for each respiration so that the whole pressure range is covered in about half a minute This avoids the physiological adjustments which tend to return the size of the tidal volume to nearer the body's requirements

It will be seen that the Drinker tank respirator gives the largest tidal volume for a given negative pressure The type-3 cuirass fits the patient very well, and the sides go well down on to the bed and so are partially fixed Thus the tidal volume approximates to that of the type-2 cuirass If the sides do not catch on the mattress, the tidal volume obtainable is much more like that given by the Kifa If the supporting legs of the Kifa shell are removed, the tidal volume with this machine is reduced still further The tidal volume produced by the type-3 cuirass is reduced nearly to that of the Kifa if the tube is reduced to $1^1/_4$-in bore The wave form depends largely on the characteristics of the pumps and their valves Fig 5b shows that with a Drinker pump and leak-valve the curve resembles that of the Drinker tank respirator The spring-loaded valve produces a more abrupt change of negative pressure (fig 5c)

CONCLUSION

It is not claimed that the problems connected with the use and design of the cuirass respirator have been finally solved This experimental work is put forward to stimulate interest in these problems and to illustrate some of the difficulties that have been encountered during the two and a half years' work The advantage of the apparatus described is that it is not difficult to construct, given access to the moulding of plastic material It does not require the construction of a special pump unit existing ones can be used, and there is no doubt that in this way with a minimum of expenditure many patients with temporary or permanent respiratory paralysis can have their lives made more bearable by the extra mobility and freedom that the cuirass gives compared with the tank type of respirator

Our special thanks are due to a number of our colleagues and commercial firms who helped in many ways Dr W H Kelleher, of the Western Hospital, Dr Ritchie Russell, and Dr R B Bourdillon gave us the benefit of their great experience, and there are many others whose suggestions have been adopted but not necessarily acknowledged To Imperial Chemical Industries Ltd , who gave us considerable quantities of material, J G Franklin & Sons, Ltd , Dunlop Rubber Co, Ltd , Hairlok Co, Ltd , Jovtex Fabrics Ltd , and William Warne & Co, Ltd, we are particularly indebted, and without the help of these organisations the work would have been impossible Our thanks are due for a grant from the Breathing Machines Group of the Medical Supplies Working Party of the Ministry of Health One of us, A B K W, was in receipt of a Medical Research Council grant during the course of this work

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MODIFIED BOTH RESPIRATOR

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In November, 1938, Lord Nuffield announced his intention to manufacture Both respirators and to present them free of charge to institutions in Great Britain and the Empire which had a genuine need of them At the end of March, 1939, there were in the British Isles, including the Services, 43 Bragg-Paul machines, 30 Drinker machines, and 965 Both machines , and judging by a survey of the hospitals of the Birmingham Regional Hospital Board, the same proportions probably obtain nowadays The Birmingham board has 6 Bragg Paul machines, 2 Drinker machines, and 48 Both machines

A committee comprising Dr S J Scurlock, senior administrative medical officer (Chairman), Dr J Macdonald Holmes, Dr F L Ker, Dr R E Smith, Captain G T Smith-Clarke, Dr J O Terry, and Dr. G L O Williams was appointed in April, 1952, by the Birmingham Regional Hospital Board This committee decided that the only practical way of meeting the needs that might arise in a sudden epidemic was to improve their 47 Both respirators Recognising that without expert engineering skill this would be impossible, they asked the help of Captain G T Smith Clarke, recently director and chief engineer of Alvis Ltd , and chairman of the No 20 Group Hospital Management Committee The improvements described in this paper incorporate the requests from the physicians on the committee and ideas from the working party for the improvement of respirators The engineering work was done at the Coventry and Warwickshire Hospital under the guidance of Captain

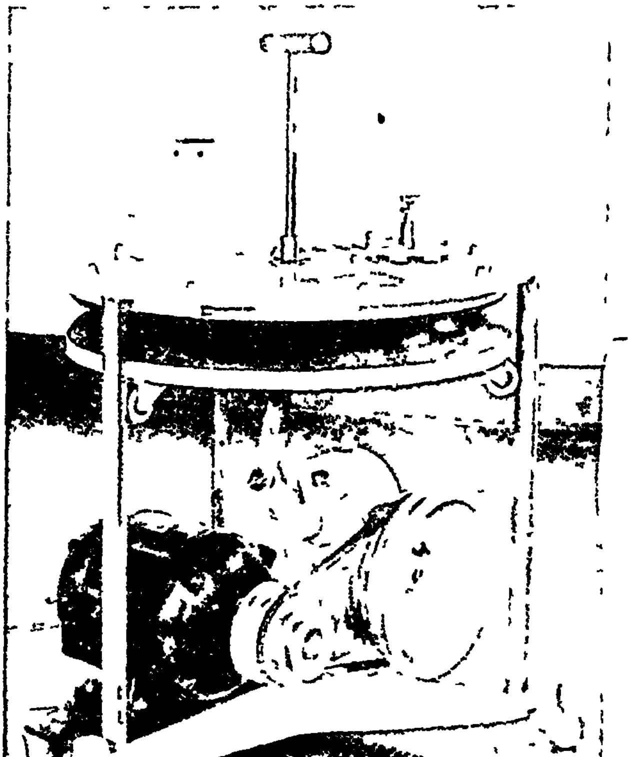

Fig 1—The pump showing arrangement of five speed pulleys and reduction gear box, improved bellows-guiding mechanism and bellows, and positive-pressure control valve above bellows

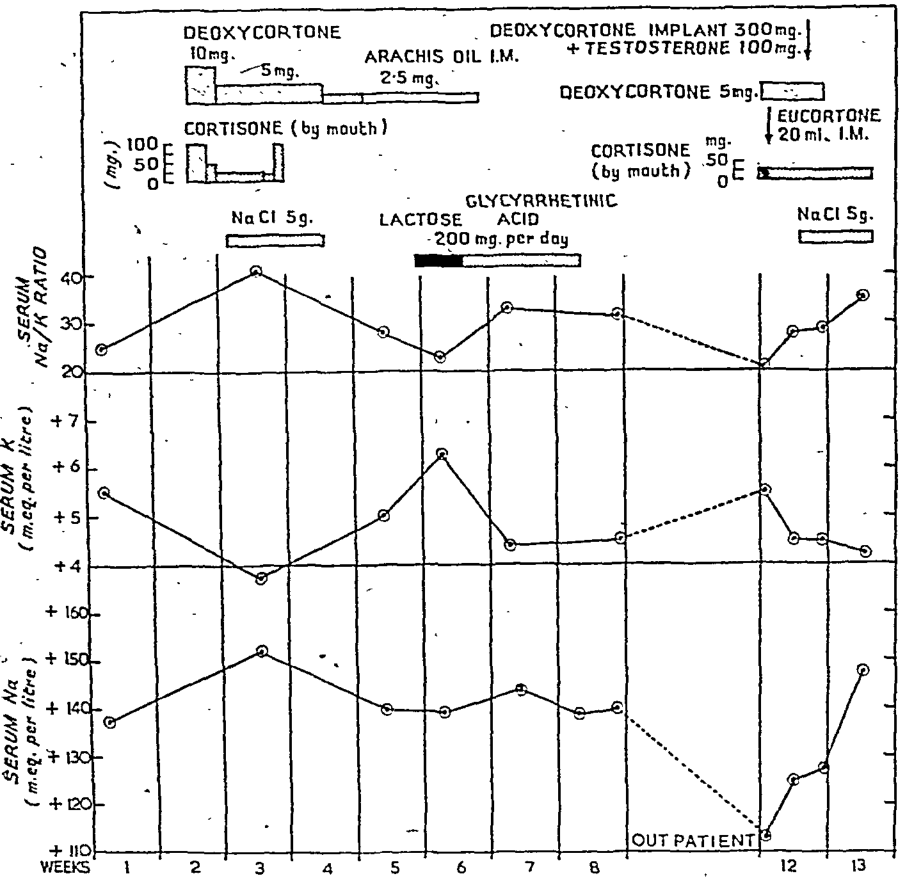

Fig. 6—Serum sodium, potassium, and sodium/potassium ratio in patient with Addison's disease.

no deoxycortone-like action in adrenalectomised rats as judged by survival-time.

DISCUSSION

Previous workers have claimed for liquorice a deoxycortone-like action, with sodium, chloride, and water retention and potassium diuresis. Thus, Molhuysen et al. (1950) present a balance study in a patient with gastric ulcer on succus liquiritiæ demonstrating these findings. In our work we confirm the weight gain and sodium and chloride retention on taking liquorice block juice, but we have not observed any striking change in potassium metabolism in normal subjects.

Any attempt to assess the pharmacological activity of liquorice, extracts of liquorice, or purified components will meet several major difficulties. In the first place, the composition of commercial liquorice is very variable. For example, glycyrrhizin content of the raw root is variously stated to lie between 2% and 10%, depending on the country of origin. Secondly, the crude extracts usually imported in this country, such as block juice, are prepared by rough and ready methods, which may well produce considerable variety in the composition of different batches. The “ succus liquiritiae ” used by Molhuysen et al. (1950) and Groen et al. (1951) is prepared by similar methods. It would therefore be possible to get different effects from “ liquorice ” as used in different countries.

In addition the variation in individual response to these preparations is considerable. The difficulty in predicting the effect of deoxycortone on water and electrolyte excretion is well recognised (Gaunt et al. 1949). One of our subjects on deoxycortone gained weight, while the other lost weight on a similar dose. Revers (1948) noted that only 20% of his liquorice-treated patients developed œdema and Molhuysen et al. (1950) remarked that none of ten patients treated in hospital with liquorice developed œdema, though it was observed in outpatients.

As previously mentioned, glycyrrhetinic acid was tried on the assumption that it represented the active constituent of liquorice. We are satisfied that this acid reproduced the effects of crude liquorice, and it forms about 50% of glycyrrhizin. The glycyrrhizin content of block juice is variable, but in the specimen we used was probably in the neighbourhood of 10%, that is 20 g. of block juice must have contained about 2 g. of glycyrrhizin. It would therefore seem that glycyrrhetinic acid is perhaps more active than the equivalent weight of liquorice in which it is combined as glucuronide.

If liquorice and its components possess deoxycortone-like activity, one would expect their effects to be most clearly demonstrated in patients with Addison's disease, when the variations in the output of adrenal cortical hormones must be very slight. Molhuysen et al. (1950) used crude liquorice in one patient with Addison's disease without apparent effect, while Groen et al. (1951, 1952) were satisfied that crude liquorice, and ammonium and potassium glycyrrhizinate, were effective in replacing deoxycortone in the control of two patients with Addison's disease. We were able to treat one patient with Addison's disease, and in her the effects of previous and subsequent treatment with deoxycortone and cortisone were reproduced by glycyrrhetinic acid.

We are unable to say how the drug exerts its effect on salt and water metabolism. These effects, however, are most readily explained on the assumption that its action on the kidney is similar to that of adrenal cortical hormones. The excretion of “ corticosterone-like ” substances (Tompsett 1953) was examined in two subjects during the experiments with block juice. No evidence of increased excretion was noted.

SUMMARY

1. Block juice, a preparation of crude liquorice, is capable of producing water, sodium, and chloride retention in normal individuals.

2. Glycyrrhetinic acid which occurs in liquorice in the form of its glucuronide (glycyrrhizinic acid), reproduced the effects of crude liquorice in normal subjects.

3. Glycyrrhetinic acid, when given to one patient with Addison's disease, had effects on weight and electrolytes similar to those found after the administration of deoxycortone and cortisone.

4. In contrast to deoxycortone, crude liquorice and glycyrrhetinic acid did not prolong the survival of adrenalectomised rats.

We wish to thank Miss A. H. Halley, dietitian at the Western General Hospital, for much help with the preparation of the diets. Messrs. Stafford Allen & Sons (through one of us, W. M.) kindly provided all the preparations of liquorice used in this investigation.

References overleaf

Mobility of the respirator is secured by fitting two 9-in rubber-tyred *wheels* on the foot end of the stand This obviates the use of brakes because when the respirator is not being moved it is standing firmly on the pads which have been fitted on to the feet of the stand at the head end

An adjustable *footboard* is provided for fitting to the stretcher

The *end supports* of the stretcher-bearing roller have been raised a little and moved closer in to provide more positive guiding and location of the stretcher when the cabinet is being closed

On one of the cabinets so far modified the *headboard* has been split horizontally through the centre of the neck aperture, the top half being hinged at the end of the head-rest supports (fig 4) The top section can be swung up and over the patient's head to rest back against the stretcher support legs Fittings have been provided on the headboard to allow for the use of a split collar, which is a great improvement from the nursing standpoint and very much more comfortable for the patient For patients with tracheotomy a special top half collar has been developed which provides an airtight seal low down on the patient's neck, so that it does not interfere with the tracheotomy tube

Two *drawers* have now been made which fit in the stand below the cabinet, one of which contains the extra collars, &c , and one of which contains the instruction book, &c

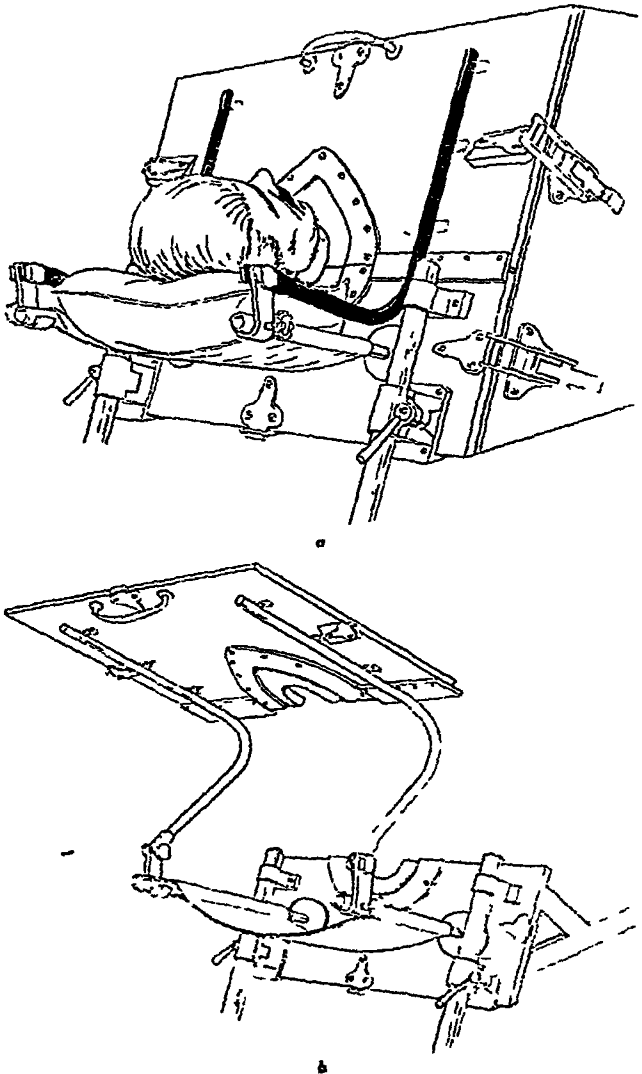

Fig 4—Split front of cabinet (a) top half of front is hinged from two pivot arms to allow upper half to be brought upwards and backwards (b)

ADMINISTRATION

It is obvious that improvements like these done on a few machines are expensive It is understood that the Ministry of Health are considering the conversion of the existing Both machines on a national scale, and this will considerably reduce the cost per machine

The primary object of these improvements is to make the patient more comfortable and nursing easier The alarm system will reduce the anxiety of the nurses and doctors as well as that of the patient Many of the improvements speak for themselves The split front will have the great advantage that the patient can have artificial respiration restarted within a matter of seconds, and this will greatly assist patients taken out of the respirator for the first time The pump can be left working, and, instead of saying that the patient can be out for ten minutes, one can say he can be out for as long as his respiration is not embarrassed, but he can go back immediately he is in difficulty

P–Q VARIATION IN INFLUENZA VIRUSES

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van der Veen and Mulder (1950) described strains of influenza virus which were similar to one another antigenically but which differed in their avidity for antibody They called strains of virus with high avidity for antibody P strains and those with low avidity Q strains These observations were confirmed in this laboratory by Isaacs and Andrewes (1951), who also recorded that it was possible to change a P virus to a Q virus in the laboratory by growing it in the presence of homologous antiserum, and to change a Q virus to a P virus by one or two passages in mice We suggested that the change might be a biphasic variation Clearly the survival of Q virus with its low power of combining with antibody, might be favoured in a partially immune population, and the P–Q variation would therefore represent an adaptive response of the virus to unfavourable conditions When conditions were more favourable to the virus the reverse change might take place, and it was most interesting to observe that the strains of virus isolated from Scandinavia early in the 1950–51 influenza outbreak were all in the Q phase whereas those isolated later were serologically similar but mainly in the P phase

In addition to the Scandinavian viruses, 47 strains of influenza virus of a slightly different serological subtype were recovered from the 1950–51 epidemic and studied in the World Influenza Centre They were all very closely related to one another and to the strains of virus recovered from the severe outbreak in Liverpool , they were called Liverpool subtype, and all were found in the P phase One of these strains (A/Johannesburg/7/50) was selected for intensive study, and it was found that, by growing pure clones of this strain in the presence of homologous antiserum, one could readily isolate Q variants (Isaacs et al 1952) with distinctive serological properties which made them readily identifiable In October, 1952, two strains of influenza virus were isolated from an outbreak in Bahrein in the Persian Gulf by Dr B E Andrews, of the Central Public Health Laboratory, from garglings sent by Dr D A Kerfoot , it was of great interest to discover that these strains displayed the same unusual properties as those found in the laboratory-produced variants The change of Liverpool virus from the P to the Q phase seems to have occurred under natural conditions about a year after the variation had been

Whittington (1951a) found trichomonads in the semen of 7 of 26 men whose wives either had, or had recently recovered from, trichomonas vaginitis. She used cultural methods in addition to the usual direct examination of moist preparations. The medium used was a modification of that described by Dobell and Laidlaw (1926). Six of the specimens examined were positive culturally, but only two of these were positive also by direct examination. (One microscopical positive was not cultured.) It is of interest to note that these patients were attending a subfertility clinic.

A remarkable claim was made by Kolesoff (1950) in an account of the action of *T. vaginalis* on spermatozoa in vitro. He stated that the spermatozoa first lost their motility and then were ingested by the protozoa; even those that escaped this fate were lysed within about three hours. These observations have not, we believe, been substantiated, but if they were there might be even further reason to emphasise the importance of male infection with *T. vaginalis*.

MATERIALS AND METHODS

In view of the somewhat conflicting published reports, particularly about the incidence of *T. vaginalis* infection in males, we made an attempt to determine the occurrence of such infections in men attending the venereal-diseases clinic at the Liverpool Royal Infirmary. At the same time we hoped to assess the value in male cases of a hæmagglutination technique which appeared to be successful in demonstrating serum antibody to *T. vaginalis* in the female (McEntegart 1952). Thus we were primarily seeking male patients who, from the clinical point of view, might be expected to have such antibody. As neither clinical nor serological evidence of male trichomoniasis seemed to be forthcoming, it was decided to try to produce typical infections experimentally in volunteers with a pure culture of *T. vaginalis*. By this method we hoped not only to gain information about the ability of the protozoa to produce infection but also, if successful, to study the process from the outset, and to determine conclusively whether or not such infections give rise to the formation of antibody detectable by the hæmagglutination technique.

Ten male volunteers were obtained from hospital inpatients, and the exact nature of the proposed investigation was explained to them; no attempt was made to minimise our relative ignorance about the possible consequences. The volunteers, aged 25–55, all had late syphilis; there was no evidence of genito-urinary disease, nor was there any history of gonorrhœa or of urethritis. These patients were considered most suitable for the experiment because the nature of their illnesses made their confinement to hospital essential and thus obviated the possibility of sexual exposure during the somewhat long period of observation which would be necessary.

Three days before the proposed start of the experiment a sample of serum was obtained from each man and tested for antibody to *T. vaginalis* by the technique previously described. None gave a positive result. On each of these 3 days early morning examination of the urethra was made before the patient passed urine. Specimens of urine and prostatic fluid were then obtained. All the specimens were examined microscopically and bacteriologically, and in particular for *T. vaginalis*. Volunteers were not included in the series unless these investigations were negative on all 3 days.

A strain of *T. vaginalis* isolated from a patient with vaginitis was being maintained in bacteria-free culture in a modification of the C.P.L.M. medium (Johnson and Trussell 1943, McEntegart 1952). This strain had been isolated 4 months previously, and it was hoped that it would not have lost virulence in that time. In the medium used growths of about 2 million protozoa per ml. were consistently obtained after 24 hours' incubation, and this count was confirmed for the culture which was used to infect the volunteers. The bacteriological sterility of the culture was confirmed both aerobically and anaerobically.

To exclude non-specific reactions due to the culture medium, five of the volunteers were used as controls and received sterile culture medium. The other five were inoculated with a culture prepared in the same batch of medium. Both the culture and the control sample of medium were taken directly from the incubator and were still warm when used to inoculate the patients. The volunteers were requested to urinate, and immediately afterwards 2 ml. of the appropriate inoculum (either culture or control) was introduced through a warm pipette inserted about $1^1/_2$ in. into the urethra. No unpleasant sensations were complained of by any of the volunteers either immediately or throughout the remainder of the day. After removal of the pipette voiding was prevented by digital compression of the urethra for about 3 minutes, and the patients were then requested to abstain for an hour from passing urine.

The patients were examined at 7 A.M. and 11 A.M. each day for the first 10 days, and thereafter at longer intervals. All the patients were requested not to pass urine after midnight until the 7 A.M. examination had been made. At this examination search was made for the presence of any urethral discharge both before and after urethral stripping. Specimens of urine were then examined for the presence of threads, and subsequently centrifuged and the deposits examined for trichomonads. If any discharge was present it was examined directly for *T. vaginalis*, and by means of stained films for bacteria and pus cells. At 11 A.M. examination was made of material obtained by gently scraping just inside the urethra with a small blunt curette, particular care being taken not to injure the tissues. This procedure was found to be most effective, and indeed essential, because on many occasions, even when there was a urethral discharge, the scrapings provided the only evidence of the presence of *T. vaginalis*. Prostatic fluids were also examined. The patients were examined at longer intervals after the 10th day, but the same routine was used.

RESULTS

Controls.—The controls were examined daily for 3 weeks and on no occasion was any urethral irritation or infection found, nor was it possible to demonstrate *T. vaginalis* in urethral scrapings, urine, or prostatic fluid.

Cases.—Although it was impossible to demonstrate trichomonads in any of the patients before the 6th day, all showed evidence of a mild urethritis in the first 24 hours (see table). With one exception none of the volunteers complained of any symptoms during the experiment.

Case 1.—A single man, aged 54, under treatment for specific aortitis; uncircumcised. On the 1st day after inoculation there was no urethral discharge, but a large

SUMMARY OF CLINICAL FINDINGS

Case no.	Age (yr.)	Married or single	Clinical findings	Complications	*T. vaginalis* first observed	Period during which *T. vaginalis* could be demonstrated (days)
1	54	Single	Transient urethritis	..	..	..
2	55	Married	Transient urethritis	..	..	..
3	49	Single	Moderately severe urethritis	..	9th day	4
4	27	Married	Severe urethritis	Prostatitis	6th day	44*
5	25	Single	Severe urethritis	Prostatitis	6th day	94

* Patient not observed beyond this period.

strains were isolated in the Central Public Health Laboratory, Colindale, which did not have our laboratory variants, and were studied serologically in this laboratory before being passaged in eggs Furthermore, slight serological differences were found in cross-tests between the natural and laboratory-induced Q variants The presence of P and Q variants in the same "strains" suggests that the variation was occurring at the time the strains were isolated, and it is tempting to speculate which direction it was taking It may be suggested that Liverpool viruses in the P phase were present in the Persian Gulf, possibly in latent infections, as a residue of the epidemic two years earlier, that they met with some resistance to their unimpeded multiplication in the form of a rapid development of antibody to a well-remembered antigen, and that, as a result, the P to Q variation was favoured Alternatively, the Q phase may be the common form which the virus assumes between epidemics, and these strains may have been caught in the act of emerging from the interepidemic form

Further evidence for the occurrence of the P–Q variation under natural conditions was given earlier (Isaacs et al 1952) In addition to the P–Q differences found in Scandinavian strains isolated early and late in the 1950–51 epidemics, we have previously noted evidence of heterogeneity of three strains in regard to the P and Q characters The additional evidence presented here strongly suggests that the P–Q variation should be considered as having been raised in status from a laboratory curiosity to an epidemiologically significant entity Its precise significance to the survival of influenza virus between epidemics cannot however, be assessed at present

It is interesting to consider the possibility of predicting future epidemic strains If a Q strain is recovered in the summer six months before an influenza-A epidemic is anticipated, as happened in 1950–51, one might be able to predict its future antigenic behaviour by making one or two passages in mice Similarly, a P strain from an epidemic could be passaged in homologous immune serum in attempts to predict Q variants which might later occur naturally However, the P–Q changes probably represent a less important type of variation epidemiologically, than antigenic variations, and there have not yet been any predictions of the latter It is interesting to note that no Liverpool Q variants were recovered naturally until two years after the first isolation of the Liverpool viruses In line with the above arguments it may be suggested that the presence of a new antigen would give the Liverpool viruses sufficient survival advantage to make the P–Q variation unnecessary until the immunity of the population had increased

SUMMARY

Two strains of influenza virus A recovered from the Persian Gulf were found to resemble closely a variant strain which had been prepared one year earlier in the laboratory

Evidence is presented that variation in the combining power of influenza virus with antibody (P–Q variation) occurs under natural conditions and is of epidemiological significance

I should like to thank Dr C H Andrewes F R S, for his most valuable advice and criticism Dr A W Gledhill for preparing the ferret antisera Dr B E Andrews and Dr D A Kerfoot for the Persian Gulf viruses, and Mr E Owen for his careful technical assistance

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DISORDERS OF MOTILITY OF THE SMALL BOWEL

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Gill and Falle (1952) found disorders of motility of the small intestine in 0 53% of 1500 patients sent for radiography of the digestive system Such studies are helping to draw attention to this much neglected field of small bowel function For too long we have tended to ignore the appearances of small bowel radiographs because of the great difficulty experienced in interpreting them and in correlating them with clinical symptoms

My interest in this work developed from observations on patterns of small-bowel motility in the post gastrectomy syndrome Subtotal gastrectomy, by shortening the period of gastric digestion, throws into prominence the inherent weakness of the small bowel in some people Glazebrook (1952) has described some of the disorders of small-bowel rhythm which can be detected after subtotal gastrectomy Such patients, of course, form a small proportion of those who suffer from post gastrectomy syndromes

My purpose here is to draw attention to one disorder of small-bowel motility which, though uncommon, is particularly hard to interpret and to treat I found it in 4 out of more than 400 cases of subtotal gastrectomy—an incidence of about 1%

RADIOLOGICAL FEATURES

The specific radiological appearance of this condition is segmentation of the small bowel contents Fig 1*a* illustrates the normal small bowel pattern, and fig 1*b* typical segmentation Segmentation can be made prominent in milder cases by giving a dextrose barium meal before radiography (Glazebrook 1952) When segmentation is present, the normal "feathery" appearance (fig 1*a*) of the jejunum and ileum is lost, and the barium collects into distinct aggregations separated by areas of spasm (fig 1*b*) The special feature of this condition is that the segmentation persists for an hour or more, indicating continued segmental spasm of the gut (fig 2) In addition, the passage of the meal, especially the dextrose barium meal, is slowed in the small intestine This is curious because the symptoms suggest small bowel hurry Indeed, at an earlier stage we confused this picture with that of small bowel hypermotility Glazebrook and Welbourn (1952) have reported a case of intestinal hurry following subtotal gastrectomy where the dextrose-barium meal had reached the cæcum at the end of five minutes (fig 3) Though the radiological features are quite different, the patients often experience similar sensations in the two conditions

CLINICAL FEATURES

My experience is confined to those cases precipitated by subtotal gastrectomy The condition can best be illustrated by the following case

A man aged 31, began to have symptoms of duodenal ulcer in 1944 On March 10 1950, he underwent subtotal Polya type valved gastrectomy for chronic duodenal ulcer After this he complained of general debility abdominal pain after meals, and diarrhœa On Oct 12, 1950, his hæmoglobin was 101% On Oct 24 1950 the total amount of fat in his stools was 6 9% by weight of the dried fæces, 59 6% of the fat being split, and 40 4% not split Fat balance study showed that 86% was absorbed The patient had angular stomatitis and cheilosis Hexamethonium bromide 250 mg t d s p c produced no improvement On March 6, 1951 his symptoms persisted, and there was no improvement on various vitamin B factors On Nov 12, 1951, he was admitted with œdema of ankles and legs, anæmia, abdominal in the prostatic fluid, but the number of pus cells present was less than in a corresponding bacterial infection.

SUMMARY

A controlled experiment was made to establish the pathogenicity of a pure culture of *T. vaginalis* for the male urogenital tract and, if possible, to study the clinical course of such infections as might be produced.

Ten hospital inpatients volunteered. Five of these were inoculated into the urethra with a pure culture of *T. vaginalis*, and five with a control sample of sterile culture medium.

No abnormality developed in the controls, whereas at least three of the patients who received the protozoan culture developed signs of urethritis.

The clinical signs and course of these infections are recorded and discussed.

Examination of the sera of the volunteers failed to demonstrate antibody to the protozoa.

We wish to thank Dr. A. O. Ross, for his advice and encouragement, Mr. D. Carter for valuable technical assistance, and the volunteers for making this study possible.

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CUIRASS RESPIRATORS

THEIR DESIGN AND CONSTRUCTION

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EPIDEMICS of poliomyelitis bring with them cases of respiratory paralysis of various degrees of severity. Some of these patients have to be treated in tank-type respirators or iron lungs, of which the Both and Drinker are commonly found in this country. But, though it may save life, the use of any type of tank respirator imposes many limitations. The problems encountered include difficulty in changing the patient's posture, awkwardness in nursing, and mental discomfort and distress. It is generally accepted that in the treatment of the severe or acute case this type of respirator must play an important part; but if during the recovery period the patient has some capacity for spontaneous respiration the use of a cuirass or dome respirator has many advantages—not least the patient's greater freedom in posture and the ability to move the limbs (Kelleher et al. 1952).

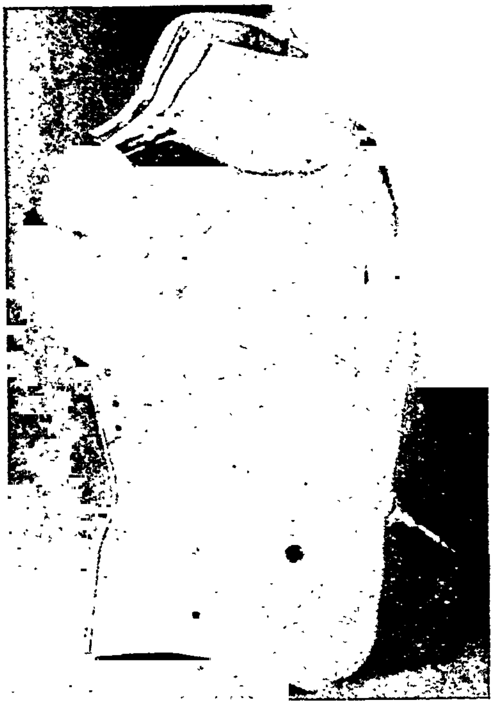

Fig. 1—Type-1 cuirass.

The idea of the cuirass is not new, and many forms have been designed; but none of them is entirely satisfactory. Our attention has therefore turned to providing a fairly simple apparatus which can be used in conjunction with one of the standard respirator pumps available in most hospitals or hospital groups.

Any cuirass has to include as much of the trunk as possible and it must be constructed of a shell rigid enough to resist suction or negative pressure. Three types are in use:

Type 1 consists of a shell which envelops the trunk with seals round the neck and arms at the upper end and at the waist or thighs below (fig. 1).

Type 2 consists of a shell or dome lying over the front of the body and sealing on to a mattress or special frame. The upper seal runs under the arms, and the lower across the hips (fig. 2).

Type 3 consists of an anterior shell or dome which is sealed over the chest and down the sides but may derive mechanical support from the mattress. Negative pressure is applied to the front and sides of the trunk and not all round as in types 1 and 2 (fig. 3).

Efficient respiration is possible only if the abdomen is included as well as the thorax; a cuirass that ends at the waist level exerts too little suction over the abdomen, and most of the effective movement of the diaphragm and lower ribs is lost.

TYPE 1: EXISTING PATTERNS

Several respirators of this type have been manufactured including the London County Council cuirass respirator and the Chestspirator.

WHALE FINGER AND SEAL FINGER
THEIR RELATION TO ERYSIPELOID

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DURING two and a half years spent in South Georgia, in Antarctic waters, and in the Falkland Islands, I have found that erysipeloid (Baker-Rosenbach) is a common infection of the hands of men engaged in whaling and sealing

During the Antarctic winter no whaling takes place, but maintenance and repair work is done at the land stations on the sub-Antarctic island of South Georgia In handling the whaling gear, and particularly in replacing the steel ropes ("wires"), the men often receive superficial injuries of the fingers and hand In the summer season these wires are employed in hauling the harpooned carcases ashore and for pulling them across the *flensing plan* (a wooden platform on which the whales are cut up), and after they have been used in this way for six months or so their surface is covered with short sharp bristles bearing remnants of whalemeat

In pelagic whaling the "floating factory" uses highly mechanised methods of catching and processing The men work in two shifts of twelve hours each on a piece-work and bonus system Their flensing knives—sharp as razors, shaped like hockey-sticks, and fastened to handles about 4 ft long—must be handled with care, especially on a crowded ship But at sea as on land it is the wire ropes that bring about most of the superficial injuries to the fingers and hand which subsequently become infected The wear and tear on the wires is such that often they have to be replaced monthly

Sealing is nowadays carried out far less extensively in the Southern Hemisphere than in the North Commercial sealing for seal oil was however, done until quite recently on a small scale in the West Falkland, and only one sealing station is being operated in South Georgia As in whaling, wire ropes are used for hauling the gutted carcases on and across the *flensing plan*, and are liable to injure the fingers Other injuries are caused by the flensing knife commonly used by sealers—a Swedish sheath-knife about 6$^1/_2$ in long and, at the base, 1$^3/_4$ in broad

CLINICAL OBSERVATIONS

At a South Georgia land station in the winter period of 1950 (April to September) I treated 16 cases of finger infection in men who were preparing gear for the next season The diagnoses were

Subcutaneous abscess	4
Subcuticular abscess following cellulitis	1
Cellulitis	7
Erysipeloid	1

At the same station during a few weeks in the summer (November and December, 1950) I saw a further 10 cases

Cellulitis	7
Paronychia	1
Erysipeloid	2

At sea, on a floating factory between December, 1950, and March, 1951, I dealt with 34 hand infections, almost all of them digital Here the diagnoses were

Subcutaneous abscess	1
Subcuticular abscess following cellulitis	6
Pulp abscess	1
Paronychia	3
Cellulitis	20
Erysipeloid	3

Most frequently affected were the index and middle fingers, and the infection was nearly always volar, as would be expected in men gripping infected wire ropes In 3 cases the injury had been definitely caused by instruments—a harpoon, a bone saw, and a meat-hook In the floating factory there were more cases among men dealing with entrails and bones than in those solely engaged in the initial stages of flensing (i e, cutting up whalebone and blubber) During the same period at sea I treated 3 men for deep cuts and severed tendons, but healing was uneventful in all 3, though presumabl they were exposed to infection I mention them t illustrate the important fact that in whalers finge infection is common after superficial scratches but n after deep cuts

In sealers conditions seem to be rather differen Though superficial injuries leading to infection hav been observed in Northern sealers (Olds, Candolin 194 I have not myself seen any infected fingers attributabl to handling wire ropes On the other hand I have seen such infections in men who had cut themselves whil dealing with seal carcases, and in 2 of these the infectio was erysipeloid (preceded in 1 case by subcutaneou abscess)

The relation between the two main types of infectio seen—i e, cellulitis (about $^2/_3$ of my 66 cases) an erysipeloid (about $^1/_6$)—was apparent from the con currence of both in 3 cases In the same patients, but o different fingers and at intervals ranging from six day to over a month, cellulitis was followed by erysipeloi once, and preceded by it twice The incubation period of erysipeloid could be ascertained only on 4 occasions, being three days in 1 and two days in 3

The well-known tendency of erysipeloid to spread from the original site to other fingers was not observed Spreading, however, took place in 8 cases of cellulitis, 1 of them following erysipeloid Neither generalised nor intestinal forms of erysipeloid were seen In 1 case of erysipeloid a long persisting cubital lymphadenitis was observed In 3 erysipeloid cases there was a relapse Septic arthritis in a finger complicated erysipeloid in 1 case this condition is characterised by rarefaction and later atrophy of the bone, followed by permanent stiffness of the joint It has been reported in sealers in Northern regions, where it is dreaded because it entails a long period of disablement which may be permanent (Olds, Candolin 1949)

Suppuration is not a feature of erysipeloid, but it occurs in cases of mixed infection (Sonntag 1947) It will be noted that in my series 7 cases of cellulitis were complicated by subcuticular abscesses In 1 case of cellulitis a subcutaneous abscess developed which required incision two days later an erysipeloid appeared around the site of the incision

When I saw my first case of clinical erysipeloid two days after my arrival in South Georgia, I recalled the local outbreak of erysipeloid I had observed in 1943 on the south coast of the Baltic There, in a small country town, a load of fish was distributed, and shortly afterwards about 40 people came for treatment, nearly all of them housewives Except in 1, the lesion was on the volar side of the left middle finger the right handed patients had held the fish with their left hand in order to scale it, and the 1 left handed housewife had the lesion on her right middle finger Slight scratches, but never any deeper cuts, had been caused by the sharp protruding backfin of the fish These rather trivial injuries were followed two to four days later by the characteristic shiny erythematous discoloration on the site and in the neighbourhood of the scratch, and this was accompanied by itching, pins-and-needles, and in some cases stiffness, but no pain Cubital lymphadenitis ensued in a few patients, lymphangitis in none One of the fishmongers who had distributed the fish also developed erysipeloid

I feel sure that in many of my cases in whalers cellulitis would have developed into erysipeloid had there been any delay in medical attention The piecework and bonus system led the men to seek early treatment so as to cut down any loss of working hours Also the development of erysipeloid may have been delayed or prevented by the exceptional thickness of the cutis usual in whalers and sealers

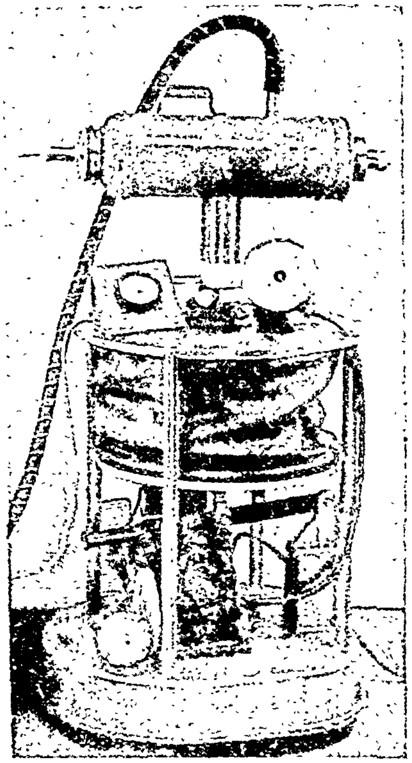

Fig. 4—Container fitted with spring-loaded inspiratory and expiratory valves.

the seal passed from the greater trochanter forwards over the pubis. The shell was clamped to the baseboard on which the mattress lay, and this clamping prevented any excursion of the edges of the cuirass. The shell, being made of polythene, was somewhat flexible, and on the application of strong negative pressure the centre of the shell was pulled towards the patient and the sides tended to bulge outwards. This abolished pressure on the lateral aspect of the ribs and allowed the suction to be applied almost all round the trunk. Conversely, on positive pressure, the movement of the shell helped recoil of the ribs.

This type of cuirass, with which further experiments are being made, is efficient but clumsy. The cuirass is most suitable if it is long, but this means that a patient cannot flex the hips or be raised into the sitting posture.

TYPE 3: NEW MODEL

A shell rather shorter than in type 2 and without a base-plate was the next pattern to be constructed (fig. 3), and this seems to be the model with the most immediate application. The shell extends from the manubrium to just above the symphysis pubis, with the seal running from the posterior axillary line round the flank to just inside the anterior superior spine. This allows the patient to sit up. The side pieces extend far enough posteriorly to reach the bed when the patient is lying down. This prevents excessive pressure on the manubrium and abdomen and avoids constriction of the lower ribs.

Shells

The shells were made from $^3/_{16}$-in. polythene reinforced by the same material where required. Moulding was made over a positive cast built up to allow a 3-in. space anteriorly. The edges of the mouldings of type-2 and type-3 shells were slightly everted to avoid linear pressure. Polythene was chosen as a suitable material because of its ease of manipulation, light weight, and flexibility. It does not shatter. The material for a shell moulding costs less than £4.

Seals

Inflatable tubes used as seals have not proved satisfactory. They have to be made from specially moulded tubing and have the disadvantages of perishing with age and being liable to puncture. Moreover they do not allow a uniform pressure over the surface. Bony prominences which sink further into the inflated cuff are subjected to greater pressure.

The most satisfactory material is cellular continuous air phase foam-rubber, such as 'Dunlopillo' or 'Texfoam,' which because of its structure allows the bony prominences to sink into it. *It should be not less than* 3 in. deep, with the width of contact over the skin about 2 in., and should be attached to the shell to form a continuous margin. The outer surface of the foam-rubber and that in contact with the patient are covered with a thin sheet of impermeable rubber to prevent air leaks. The inner surface is left unsealed. The seal is partially evacuated owing to the continuous air-phase when suction is applied. This results in the seal being readily moulded over bony prominences, but the design must be such that it is not sucked inwards. The flexibility of the polythene shell and the softness of the rubber make it easy to apply the cuirass to the patient.

Pump Unit and Valves

It was considered important to have an apparatus that could be used with one of the existing pump units that are part of a tank-respirator system. The Drinker unit, with which the experiments were made, has a simple positive-pressure leak-valve, and it is therefore only necessary to have some means of controlling the suction or negative phase. A container was interposed between the pump and the cuirass in an attempt to reduce any sudden changes in pressure, and this container was fitted with spring-loaded inspiratory and expiratory valves (fig. 4). The advantage of the spring-loaded valve is that the full negative phase of the pump is allowed to act until the desired upper limit is reached. This results in a rapid intake of air into the lungs, excessive suction being reduced by the opening of the valve, though the effective pressure is still maintained. In practice, with this particular type of spring-loaded valve the patient found that the pressure effects were unduly abrupt or irregular.

More recently a simple hand-operated slide leak-valve has been used; this acts during negative and positive phases with excess of positive pressure being lost through the leak-valve (fig. 3).

Connections

The tubing that connects the pump to the respirator must be of such a form as to prevent gross alterations in response to pressure changes; it must be light and flexible and at the same time must not concertina or collapse. The diameter of such tubing should be at least 2 in.

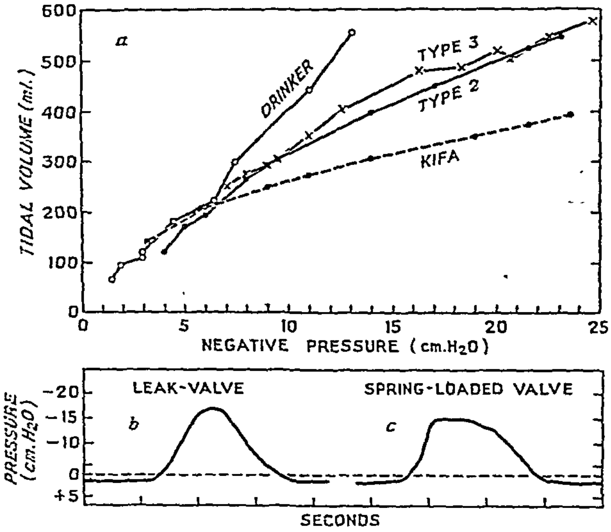

Fig. 5—Effect of varying negative pressure on tidal volume (a); and changes produced in pressure curves by leak-valve (b) and spring-loaded valve (c).

Reviews of Books

Die zerebrale Angiographie

H Krayenbuhl, professor of neurosurgery, and Hs R Richter, assistant neurosurgeon, University Clinic, Zürich Stuttgart Thieme 1952 Pp 213 DM 59 70

A radiological textbook must always be to some extent inadequate in that no words or diagrams can inform the reader of the many variations which may be encountered in the normal or abnormal X-ray film A collection of radiographs, described too often as a ' radiological atlas " may similarly mislead its students for no author can include in such a work the variety of illustrations, even of one particular condition which would be fully informative The authors of this book have successfully combined the text, drawings, and radiographs in an admirably balanced work A good account of the technique of angiography, the normal anatomy of the cerebral vessels, and its alteration in various pathological conditions, is the prelude to a collection of radiographic prints illustrating the pathological appearances revealed by cerebral angiography Each radiograph is accompanied by a brief case-history of the patient and explanatory line-drawings The reproductions are of the highest quality, and the drawings first-rate and the book as nearly as possible closes the gap between learning from a textbook and learning from personal observation of a large number of cases

Acute Renal Failure Including the Use of the Artificial Kidney

John T MacLean, MD, FRCS(C) FACS, assistant urologist, Royal Victoria Hospital, director of urology, Queen Mary s Veterans Hospital, Montreal, Canada Springfield Ill Charles C Thomas Oxford Blackwell Scientific Publications 1952 Pp 114 47*s* 6*d*

This monograph gives an account of the causes, pathology, and treatment of cases of acute renal failure with anuria or severe oliguria Many illustrative case-records are included, but no attempt is made at a general survey of Dr MacLean's very considerable experience of the condition Prognosis is inadequately discussed, and the statement that ' if recovery does not occur, death occurs on the 10th or 11th day, but may be earlier " seems unduly pessimistic in view of the results obtained by modern methods The important condition of renal cortical necrosis is not described, and no mention is made of the use of cation exchange resins to reduce the extracellular concentration of potassium Methods of treatment by peritoneal irrigation, continuous intestinal perfusion, and dialysis using the artificial kidney, are admirably discussed, but the author admits that the necessity for their use has been reduced by the success of a conservative regime of a high-calorie but protein-free and electrolyte-free diet given by intragastric drip The high price of this comparatively small monograph is no doubt partly due to the inclusion of five coloured plates, all of them reproductions from other publications

New Concepts of Hypnosis

Bernard C Gindes, MD London Allen & Unwin 1953 Pp 272 15*s*

Interest in hypnosis is often regarded as a normal phase in the development of a mature psychiatrist Relatively few however, remain fixated at this stage and it is later usually given a reasonable place among the techniques available in psychotherapy to be used when the presenting symptoms of neurosis must be removed quickly, or where the patient responds best to a dominant rôle on the part of the physician Hypnosis, with its brevity and directness is attractive to the patient who wishes to recover but is not prepared to take a very active part in his readjustment The writing of a book partially aimed at the layman is a common accompaniment of an enthusiasm for hypnosis, and these works may be divided into those which never use the word "cure" and those which use it in care-free fashion—plain in italics or in capitals followed by an exclamation mark It is unfortunate that in its opening chapter this book falls into the second group, for this is out of keeping with the thoughtful and readable treatment of the subject in some of the later chapters

Dr Gindes points out that superstition precedes knowledge and as an illustration of this truism one might quote the fact that Mesmer explained the effects he could produce in terms of "animal magnetism" when magnetism was as much a mystery as hypnosis Dr Gindes, in his generation explains hypnosis in terms of orthodox psycho analysis and finds in his use of it daily confirmation of the Freudian doctrines He assumes throughout that all manifestations of psycho neurosis will eventually respond to full psycho analysis if only the patient will persevere—a view which is very difficult to disprove But he admits that this sometimes takes a long time and that it may be difficult to hold the patient, and this, he says is one of the indications for hypnosis The reader, provided he does not expect Dr Gindes to be without bias, or over modest in his claims, will find him a therapeutic enthusiast who has consulted original sources for his material and who is able to convey a clinical situation vividly His account of the precautions to be taken, the techniques for the induction of hypnosis, and the causes of failure, is likely to be of value to the psychiatrist who already has some experience of the method But in a field in which there is so much competition it is difficult to recommend an account which is good in parts only, and which, despite the title, contains no new concepts

Standard Values in Blood

Being the first fascicle of a Handbook of Biological Data Edited by Errett C Albritton, AB, MD, professor of physiology, George Washington University Philadelphia and London W B Saunders 1952 Pp x + 199 22*s* 6*d*

Prepared under the direction of the Committee on the Handbook of Biological Data, whose publication herewith begins under the ægis of the American Institute of Biological Sciences (which in turn is a unit of the division of biology and agriculture of the National Research Council), all kinds of hæmatological data are here presented in tabular form, having previously been issued as Air Force Technical Report no 6039 The tables appear to be as complete as possible and besides a representative normal value the normal range is given The items covered include physical properties, blood groups, blood-cells of man and many animals hæmoglobin, water carbohydrate, lipids, proteins, amino acids, non-protein nitrogen, phosphorus, sulphur, vitamins, hormones enzymes, electrolytes minerals, gases effects of radiation and of storage not only on blood but also on hæmopoietic tissues, and the effective blood levels of therapeutic agents The volume closes with 17 pages of bibliography and 5 pages of index

Introduction to Physiological Optics

Armin von Tschermak Seysenegg, University of Munich Translated by Paul Boeder, PH D director, Bureau of Visual Science, American Optical Company Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1952 Pp 299 75*s*

Tschermak-Seysenegg has devoted a lifetime to some aspects of ocular physiology, particularly those dealing with space sense and ocular movements His publications are not well known to English-speaking ophthalmologists partly because they have appeared in highly specialised journals and partly because they are somewhat heavily presented The American Committee of Optics and Visual Physiology have marked the appearance of a second edition of Tschermak-Seysenegg s *Einführung in die physiologische Optik* by bringing out an English version This work is not a systematic survey of physiological optics, but a highly personal commentary on such aspects as the optical image, the light sense, the colour sense, and the space sense, and rather much is expected of the reader There are no references to individual publications, and seldom any full account of experiments on which conclusions advanced are based—either the author's or those of other workers The book should help to make Tschermak-Seysenegg s work better known here but is unlikely to give it wider acceptance

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The illustrations in *A Modern Practice of Obstetrics* reviewed in our issue of Feb 28 (p 424), were drawn by Miss Susan M Robinson

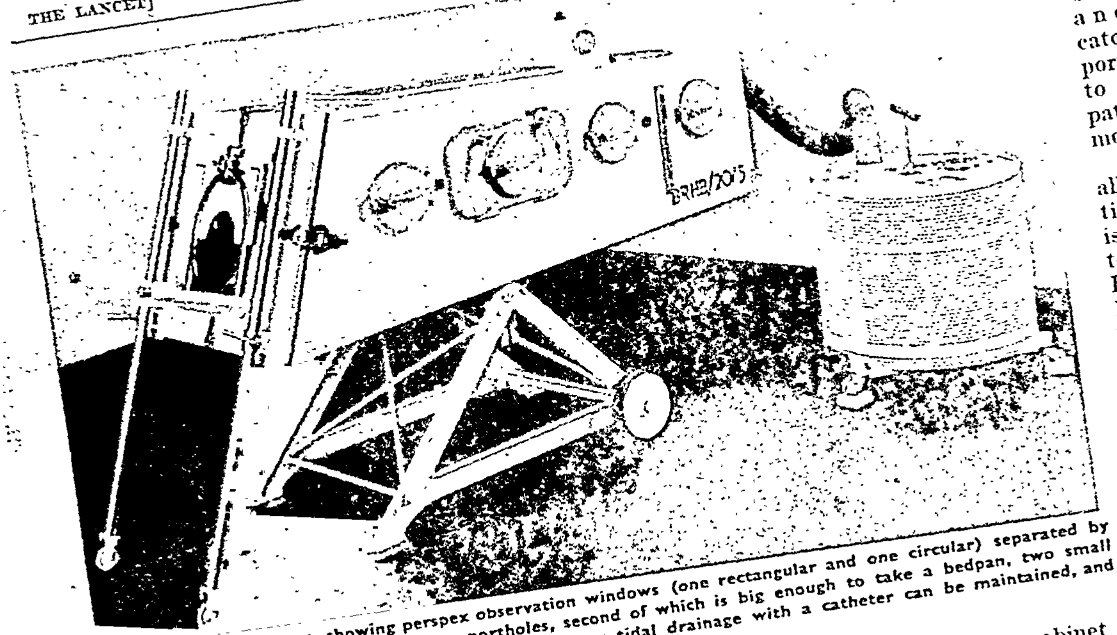

Fig. 2—Pump and cabinet, showing perspex observation windows (one rectangular and one circular) separated by alarm system on top of cabinet; four portholes, second of which is big enough to take a bedpan, two small holes for corks through which intravenous therapy or tidal drainage with a catheter can be maintained, and pressure gauge between third and fourth portholes on side of cabinet.

Smith-Clarke, and the costs were defrayed from free monies of the Coventry group of hospitals.

The improvements have been to the pump unit and to the cabinet.

PUMP UNIT

The respiration-rates of the original Both pump unit were 20·5, 26, and 32·8 per minute. The pump unit as modified (fig. 1) provides five rates of respiration at 13, 16, 19, 22, and 25 per minute, and it has been made more efficient and robust by fitting the following items:

(1) A stronger motor platform.

(2) Five speed pulleys on the motor and the reduction gear-box.

(3) Improved bellows-guiding mechanism and leather bellows.

(4) Improved positive-pressure control valve.

The improved *motor platform* provides means for 'iding the motor to allow f the belt being placed n the required pulley groove. It also has means for adjusting the tension of the belt and for locking the motor platform when the desired tension has been reached.

A *positive-pressure valve* has been placed directly on to the pump unit and is now a disc valve controlled by a screw with a knurled head and knurled locking-nut. This arrangement ensures smooth adjustment of the operating pressure with a positive lock to prevent accidental alteration.

CABINET (FIGS. 2 AND 3)

The improvements to the cabinet include four *arm ports* on each side of the cabinet, one being included in a large bedpan opening. They are complete with rubber sealing discs and positive catches. These arm ports provide access to all parts of the patient by one or more nurses.

A large *window* allowing for inspection of the patient is provided in the top of the cabinet. It consists of two 12 × 12 in. apertures covered with a sheet of 3/8-in. 'Perspex' carried by a 'Duralumin' frame. The original circular window is moved to a position near the foot end of the cabinet.

The *alarm system*, self-contained in a small box, is mounted on top of the cabinet and gives audible and visual warning if the negative pressure falls below 10 cm. H_2O for more than about 15 seconds. No switch is provided, but the alarm can be put out of action, when not required, by opening the lid of the battery-box. This method was used in preference to a switch because when the lid of the battery-box is open it is clearly visible and is unlikely to be overlooked.

A negative-pressure *control valve* provides fine adjustment with positive locking.

The *cabinet-tilting gear* is a commercially available component which, after slight modification, can easily be fitted to the exterior of the cabinet. It provides tilting from 10° head up to 25° head down. An angle-of-tilt indicator is provided, and the tilting mechanism is very easily operated.

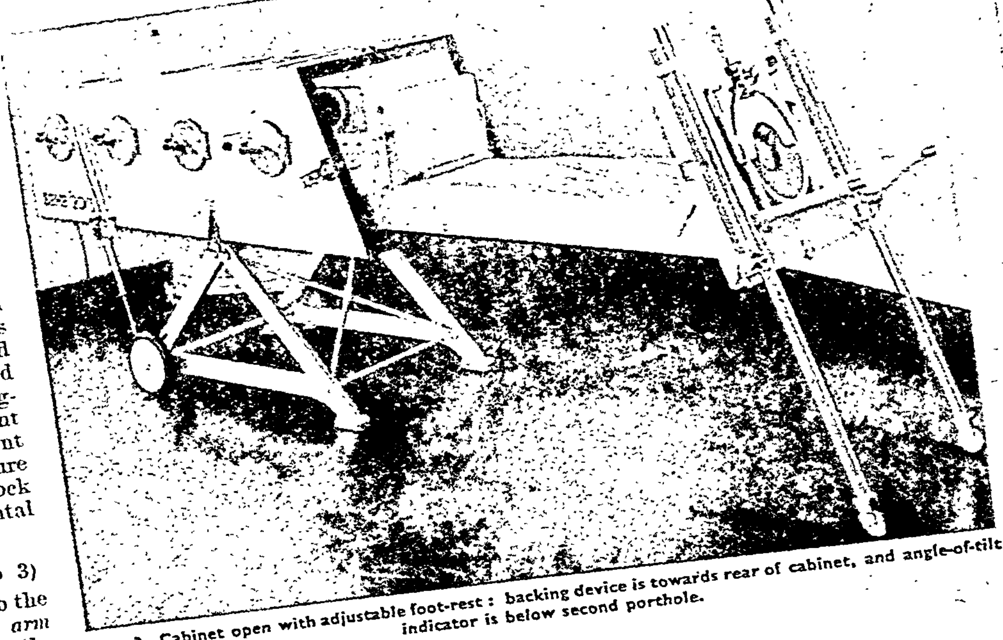

Fig. 3—Cabinet open with adjustable foot-rest: backing device is towards rear of cabinet, and angle-of-tilt indicator is below second porthole.

general question of hospital staffing. Should hospital work be done largely by nurses in training, or should it be done by trained nurses, as suggested by the advisory panel to the Nuffield job-analysis team? In the fever hospital of the future a fully trained staff, with a training-school for post-certificate nurses seeking a higher qualification, could ensure skilled nursing for every patient with an infectious disease. This plan, however, cannot be put into operation immediately, because the fever hospitals are heavily handicapped in the competition for trained staff. At one time they were able to offer inducements in the form of higher pay; but these were abolished by the Rushcliffe Committee. Moreover, a general-trained nurse who seeks a further qualification in infectious diseases now drops £20 per annum on her salary. It is not realistic to argue that, because she is taking a course of training, she should get less money, or to compare her situation with that of a doctor seeking a higher qualification. Let us look full at the fact that State-registered nurses in hospitals are a valuable commodity, which is scarce; and then let us take the elementary economic step of paying what they are worth to us, instead of what we think they ought to be content with.

If it again became possible to attract nurses for post-certificate training in fevers we could hope to find the necessary senior staff for the isolation wards which it is proposed to set up in general hospitals. But let us not, in the meantime, saw through the branch on which our ladder is leaning. The only effect of suppressing the infectious-diseases register at this juncture would be to hasten a decay of standards in the fever service, thus bringing it into disrepute with both postgraduates and prospective students. And the cost of this experiment would be paid by the patients.

Trichomonas Vaginitis

HUMAN trichomoniasis is one of those unspectacular conditions which, although troublesome and often intractable, causes neither death nor acute illness; and, by producing its major effects on those long-suffering members of the community, the women of child-bearing age, it has escaped the attention it really deserves. The causative organism was described as long ago as 1836, but any considerable interest in the problem has been limited to the last twenty years and, even then, investigations have been sporadic and inconclusive. All who have studied the subject agree that trichomonal infestation is extremely common in women, but, as TRUSSELL[1] pointed out in his detailed review, it is hard to estimate the exact prevalence because of the many factors involved in the demonstration of the parasite and because most of the patients examined for trichomonads are either pregnant or have some gynæcological complaint. He collected the reports that had been published on 48 groups of patients studied by different investigators in several countries. The reports described a variety of techniques in diagnosis and included pregnant and non-pregnant women. But many of them did not indicate the number of women who presented with symptoms of vaginal disease—an omission which seemed likely to introduce another source of error. The numbers of patients in different groups varied from 32 to 5712, and the incidence from 100% (in an investigation[2] of 61 women thought to be suffering from gonorrhœa) to nil (in an examination[3] of 55 presumed virgins). The average prevalence for all 48 groups was approximately 32%. TRUSSELL himself estimated that 1 out of every 4 or 5 women in the United States harboured the parasite, giving an approximate total of 10 million cases among American women. Mr MCCULLAGH, in his letter on p. 698, states that he sees 200 new trichomonal infections each year among his gynæcological cases, and he estimates that 13% of hospital gynæcological patients and 11% of private gynæcological patients are suffering from this condition.

Opinions have been divided on the question of how vaginal infection occurs. The evidence that transmission results from coitus is overwhelmingly strong, but it is by no means accepted that this is the only or even the commonest method of infection. It is difficult to estimate the frequency of non-sexual transmission, for it seems that few data have been collected to support or to throw doubt on the view that women are commonly infected from lavatory seats, towels, or douche nozzles, or in swimming baths. On comparing the evidence, such as it is, with the positive views that have been expressed, it is difficult not to suspect that some of these ideas are based very largely on an unwillingness to regard so common a condition as a venereal disease. In an article in this issue, Dr LANCELEY and Dr MCENTEGART say that trichomoniasis must be regarded as a venereal disease in quite a large proportion of cases; but they believe that there is evidence to support the view that some infections are in fact accidental, and they give a warning that all doctors who make vaginal examinations, particularly in clinics, should carefully review their technique to make sure that they do not transfer infection in this way. MCCULLAGH, however, states categorically that the main cause of transmission of infection with *Trichomonas vaginalis* is the ordinary lavatory seat, although the evidence which he gives seems insufficient to support so positive a conclusion. He believes that the condition is acquired by sexual intercourse in only 15% of cases. To his way of thinking, the remedy lies in the immediate general adoption of the "gap" type of lavatory seat in all lavatories used by large numbers of women and girls. TRUSSELL mentioned unpublished data collected by WILSON indicating that *T. vaginalis* could be demonstrated, though infrequently, in specimens from lavatory seats used successively by a number of women, of whom about 25% were known to be carriers of the parasite. The seats examined were of the U type and it was thought possible that circular seats would have yielded more parasites. No one with experience of trichomonal infection in women will question the truth of MCCULLAGH's assertion that it is a major cause of ill health and unhappiness; but more evidence is required before we can accept his conclusion that mass adoption of the gap seat would reduce new cases by 80%. What is required is a careful investigation into methods of transmission of human trichomoniasis. Much evidence should be readily available from case induced in the laboratory, and evidence in support of this contention is brought forward here.

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[1] Trussell, R. F. Trichomonas Vaginalis and Trichomoniasis. Oxford, 1948.

[2] Assinder, E. W. *Brit. med. J.* 1936, i, 582.

[3] von Jirovec, O., Breindl, V., Kucera, K., Sebek, V. *Zbl. Bakt.* 1942, 148, 338.

MATERIALS AND METHODS

The strains were identified serologically by the agglutination-inhibition technique. The materials and methods used have been described in detail by Isaacs et al. (1952). The only change in technique was that, instead of *Vibrio choleræ* enzyme (R.D.E.), trypsin was used to remove non-specific inhibitors of agglutination from the ferret sera (Sampaio and Isaacs 1953).

RESULTS

A Q variant had been prepared in the laboratory by growing A/Johannesburg/7/50 virus in homologous immune serum and had been passaged in eggs thereafter in the absence of serum; it was very poorly neutralised by antiserum to the parent virus but nevertheless induced the production of antibody to the parent virus (table Ia). It was concluded from this that the variant contained "Liverpool" antigen, possibly in a site in which it combined poorly with antibody but could still stimulate formation of antibody. When cross-hæmagglutination inhibition tests were made with the same A/Johannesburg/7/50 and the naturally occurring A/Persian Gulf/1/52 and A/Persian Gulf/2/52 viruses, very similar results were obtained (table Ib). The tentative conclusion was drawn that these might be Liverpool strains in the Q phase.

TABLE I(A)—CROSS-HÆMAGGLUTINATION INHIBITION TESTS WITH A/JOHANNESBURG/7/50 AND ITS LABORATORY-INDUCED VARIANT

Virus	Serum: A/Johannesburg/7/50	Serum: A/Johannesburg/7/50 variant
A/Johannesburg/7/50	1920	960
A/Johannesburg/7/50 variant ..	80	800

TABLE I(B)—CROSS-HÆMAGGLUTINATION INHIBITION TESTS WITH A/JOHANNESBURG/7/50 AND THE NATURALLY OCCURRING A/PERSIAN GULF/2/52 VIRUS

Virus	Serum: A/Johannesburg/7/50	Serum: A/Persian Gulf/2/52
A/Johannesburg/7/50	1920	960
A/Persian Gulf/2/52	80	320

The figures in these and the other tables show the reciprocal of the serum dilution present at the end-point. In all the tests eight agglutinating doses of virus were used.

The Persian Gulf strains were therefore investigated further. They were grown in eggs at limiting infective dilution as a test for homogeneity, and it was found that both strains were heterogeneous. In the case of both strains it was found that the two components present were essentially similar to one another serologically except for their behaviour with antisera to Liverpool viruses. Table II shows a representative experiment in which two of these components, labelled P and Q to describe their reactions with Liverpool antisera, were tested with antisera representative of all the A-prime subtypes known in this laboratory.

It will be seen from table II that only Liverpool sera differentiate these two components.

The P and Q components of this strain A/Persian Gulf/2/52 were used to prepare further antisera. Cross-tests showed that the P component was indistinguishable from A/Johannesburg/7/50 virus and was therefore a Liverpool subtype virus in the P phase. The relation between the P and Q components of the Persian Gulf strains (table III) is again very similar to those shown above in tables Ia and Ib. This is evidence, therefore, that the Q strain is a naturally occurring Q variant of the Liverpool virus, and presumably that the P–Q change was taking place at the time when the strain was recovered. Inoculation of eggs with the Q variant at limiting infective dilution has shown no evidence of gross heterogeneity, a result which had also been found with the laboratory-induced variant. The other strain, A/Persian Gulf/1/52, has been less completely investigated, but again two components showing P–Q differences in regard to the Liverpool antigen only have been found.

TABLE II—HÆMAGGLUTINATION INHIBITION TESTS WITH Q AND P COMPONENTS OF A/PERSIAN GULF/2/52 VIRUS AND A-PRIME ANTISERA

Virus	Component	Serum: F.M.1. (1947)	Serum: A/Sweden/3/50 (Scandinavian)	Serum: A/Japan/5/51 (Japanese)	Serum: A/England/1/51 (Liverpool)	Serum: A/Belfast/1/51 (Liverpool)	Serum: A/Persian Gulf/2/52
A/Persian Gulf/2/52	Q	240	240	120	480	320	240
A/Persian Gulf/2/52	P	240	240	160	1920	960	1280

DISCUSSION

Hirst (1943) described preparations of a single strain of virus which differed in their avidity for antibody, probably owing to different states of aggregation of the virus present. For several reasons it seems unlikely that the P–Q variations discussed here and elsewhere (van der Veen and Mulder 1950) have the same cause:

1. The order of differences in avidity found is sometimes much greater than that found by Hirst (1943).
2. Attempts to demonstrate aggregation sufficiently great to explain our more striking results were unsuccessful.
3. Two strains which show profound differences in their avidity for specific antibody may show no differences in their combining power with normal inhibitors of agglutination—a result which would be unexpected if aggregation were the cause.
4. One could not easily invoke aggregation to explain differences in avidity of antiserum for only one particular antigen.

For these reasons it is suggested as a working hypothesis that a strain may contain an antigen in a site in which it is unable to combine efficiently with antibody but may nevertheless stimulate production of antibody. It is hoped that studies of absorption of antibody may clarify this point further. It should be emphasised that these results were obtained with ferret sera; Sampaio (1952) has shown that post-infection ferret and hamster sera allowed of much finer differentiation between A-prime strains than did rabbit and fowl sera obtained after immunisation.

The occurrence of Liverpool-Q viruses under natural conditions a year after the preparation of similar variants in the laboratory was of great interest. The possibility that these could have resulted from laboratory contamination can be effectively excluded, since the

TABLE III—CROSS-HÆMAGGLUTINATION INHIBITION TESTS WITH P AND Q COMPONENTS OF A/PERSIAN GULF/2/52

Virus	Component	Serum: A/Persian Gulf/2/52 P	Serum: A/Persian Gulf/2/52 Q
A/Persian Gulf/2/52	P	2560	960
A/Persian Gulf/2/52	Q	180	1440

special frame For the patient who is recovering from respiratory paralysis and who is able to get out of the tank respirator for twenty minutes or half an hour at a time an efficient cuirass is invaluable He can lie or sit as he chooses, his limbs are free and accessible when physiotherapy is required, and the bedpan offers no fears, the psychological benefit may be imagined Though the cuirass cannot be expected to replace the tank respirator in acute or severe phases of paralysis, it can nevertheless do much to mitigate distress and aid patients on the road to recovery if this is to be their lot

The perfect respirator is still far from being attained, and it is perhaps only those doctors, nurses, and engineers who are working on the problem that appreciate the enormous difficulties encountered For their part in the evolution of apparatus the names of **Drinker**, **Both**, **Nuffield**, and **Bowers** will long be held in esteem

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Annotations

QUEEN MARY

Queen Mary, unlike the consorts of any of our Kings since Tudor times, was born and brought up in this country, and in her long years of public life she became almost a national possession Her childhood was spent in one era and her old age in another, but through all vicissitudes she appeared consistent, unshaken, and still interested In the strengthening of the Monarchy during the reign of George V her part was perhaps as great as her husband's, and their example of duty and virtue was effective because the King and Queen were liked as well as respected That liking and respect are reflected in the impression made by her death To most of us Queen Mary had been Queen Mary since the days of our childhood, and the longer our knowledge of her the more we must feel that our world has lost something solid and enduring

THE AERATION PROCESS

On March 21 we mentioned the aeration of dough as a possible alternative to the use of nitrogen trichloride (agene) or other chemical improvers used in the preparation of flour We are now informed that for the past eighteen months Beatties Bakeries of Glasgow, the largest bakers in Scotland, have been making a substantial proportion of their bread by an "aeration process," and that in their new factory at Dundee they have dispensed entirely with chemical improvers or bleachers In both Glasgow and Dundee bread made by this method is being sold to the public

In the new process half the flour used in the final dough is whipped with water at very high speeds for about five minutes During that period the whipped dough, or batter, absorbs from the atmosphere so much oxygen that it becomes an oxidising agent, and when it is removed from the mixer and placed in a normal dough-kneading machine it bleaches and improves the other half of the flour which has not been subjected to aeration Violent agitation of the batter at very high speeds is needed to procure oxygenation, and this agitation is achieved by two statically balanced blades

The high speed mixing machine built by the Morton Machine Company Ltd, of Wishaw, Scotland, is employed with a process patented by Joseph Rank Ltd, using untreated and unbleached flour The one sack (280 lb of flour) machine is not designed for doughing, but is capable of feeding a number of the orthodox types of dough kneaders Small bakeries have been catered for with an extra heavy vertical mixer incorporating special features Besides beaters necessary for the aeration process standard equipment can be supplied, and this machine, handling up to a quarter sack at a time, will complete the doughing without removing the batter from the pan

Before chemical improvers came into use, some forty years ago, flour was stored or "aged" for a period so as to improve its baking qualities Those who have devised the aeration process claim that in a few minutes, under full control, this reproduces the alteration of the flour which formerly took place during the period of storage In our last issue, however, Prof A C Frazer suggested that the proteins of wheat may perhaps be denatured as much by this vigorous physical treatment as they are by treatment with chemical improvers such as agene

RESISTANCE TO TUBERCULOSIS

Vaccination with B C G and other attenuated strains of tubercle bacilli induces a limited immunity in experimental animals With small groups of vaccinated and unvaccinated mice the difference in survival time after infection is too slight to be an accurate measure of immunity But estimates of the numbers of tubercle bacilli in the lungs and spleen under standard experimental conditions show much greater differences Dubos and his colleagues[1 2] found that the average survival time of a group of vaccinated mice was 27 days, compared with 19 days for the unvaccinated animals, but the number of bacilli in the lungs two weeks after infection was 200 times as great in the unvaccinated as the vaccinated With this more delicate test they showed that immunity was directly related to the extent to which the attenuated strain multiplied before the challenge infection Avirulent strains do not multiply in the tissues, nor, in the relatively small doses used, did they produce any detectable immunity Small doses of vaccine required longer to produce immunity than large doses, and the more highly attenuated strains, multiplying more slowly in the tissues, were least effective If multiplication was impeded by treating the mice with isoniazid after vaccination the development of immunity could be retarded or completely prevented

As far as is known, tubercle bacilli do not produce any substance essential for the production of immunity during their multiplication It seems likely, therefore, that immunity is a response merely to the presence of sufficient numbers of bacilli in the tissues It might, then, be possible to immunise an animal by the injection of larger numbers of dead bacilli and there have been many contradictory reports on this point Dubos and his colleagues[3] have now reinvestigated the problem They found that vaccination with 0 2 to 1 0 mg of phenol-killed bacilli did produce immunity in mice—an immunity shown both by increased survival time and decreased bacterial content of the spleen and lungs There was no evidence that the level of immunity was related to the virulence of the strain, and vaccines produced from avirulent bacilli appeared as effective as those from virulent or attenuated strains The immunity was of the same order as that resulting from vaccination with smaller doses of a living attenuated strain It seems that the immunising factor is not related to the constituent of the bacilli responsible for virulence The differences in immunising properties of living bacilli of different virulence appear to depend only on the rapidity with which they multiply in the body The factor was destroyed by heat but persisted after the cells had been disintegrated and rendered non-acid fast by grinding with concentrated phenol Dubos et al suggest that it may be possible to separate it from other constituents of the bacilli especially from "cord factor," which is

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[1] Pierce C H, Dubos R J Schaefer, W B *J exp Med* 1953 97 189

[2] Dubos R J Pierce C H Schaefer W B *Ibid* p 207

[3] Dubos R J, Schaefer, W B, Pierce C H *Ibid*, p 221

Fig. 2—Segmentation persisting at 30 minutes.

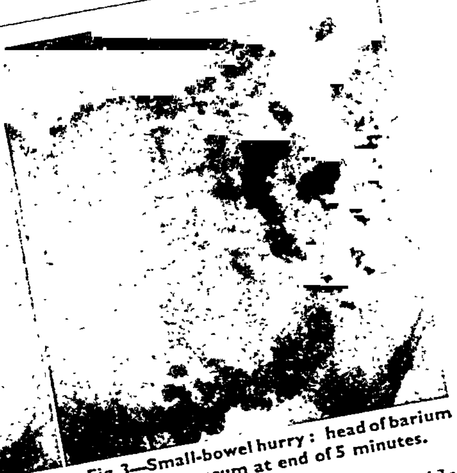

Fig. 3—Small-bowel hurry: head of barium meal in cæcum at end of 5 minutes.

pain after meals, severe deficiency of riboflavine, and dyspnœa.

Investigations.—On Nov. 26, 1951, examination of the blood showed Hb 82%, reticulocytes 8%, and plasma-proteins 5·15 g. per 100 ml. (albumin 2·60 g., globulin 2·55 g.). Sternal-marrow puncture showed no evidence of megaloblastic anæmia. Examination of fæces showed undigested meat fibres and fat. On Dec. 14, 1951, the total fæcal fat was 27·2% (split fat 88·4%. unsplit fat 11·6%).

Treatment and Progress.—In spite of massive parenteral vitamin-B therapy the evidence of riboflavine deficiency persisted, and the hypochromic anæmia did not respond to oral and intravenous iron. The symptoms were not relieved by treatment with folic acid, hexamethonium bromide, or belladonna during the following three months. After a meal the patient had to rest for an hour, and during this time the abdominal pain persisted. Glucose-tolerance curves did not show evidence of hypoglycæmia.

TREATMENT

These patients have proved resistant to medical treatment. In cases of small-bowel hurry we have obtained very satisfactory results with hexamethonium bromide. No benefit, however, was obtained with hexamethonium bromide in these cases of segmental spasm. Belladonna and its derivatives also proved unsuccessful. Some slight measure of relief was obtained by reducing the carbohydrate content of the meal. Milk and milk puddings were particularly prone to increase the bowel spasm.

DISCUSSION

From the clinical features it will be observed that, as a result of the rapid emptying of the stomach after subtotal gastrectomy, these patients experience considerable abdominal pain. The pain starts almost immediately after a meal, is visceral in character but unlike typical colicky pain, and is often continuous for up to an hour. It is experienced across the umbilical region and is associated with severe nausea but not with vomiting. Prostration is often quite considerable, sometimes accompanied by perspiration. These symptoms coming on immediately after a meal I interpret as visceral reflex symptoms. When the pain and exhaustion subside, the patients feel quite well.

I am aware that abdominal pain after meals, associated with flatulent distension and deficient fat-absorption, may result from stasis in the afferent loop of the Polya-type gastrectomy. But, though spasm in the afferent loop may contribute to the condition described here, the clinical and radiological features are quite distinct from afferent-loop stasis.

In all four cases which I have detected and investigated the patients complain of " diarrhœa." The motion is not usually fluid, and the bowels rarely move more than three or four times daily. The fæces are always light in colour, sometimes even clay-coloured, and contain a high proportion of fat, split and unsplit. Fat-balance studies show that about 70–85% absorption takes place. This seems curious considering that the passage of food through the small bowel is not rapid. As other evidence of deficient absorption, however, there is severe hypochromic anæmia in three of the four cases, and a severe riboflavine deficiency in two cases.

These features, both clinical and radiological, are in many respects similar to those of idiopathic steatorrhœa. No response has, however, been observed after treatment with folic acid. There is no evidence that the condition had been present before operation. Subtotal gastrectomy seems to unmask an inherent bowel defect of deficient absorption associated with an abnormal motility pattern.

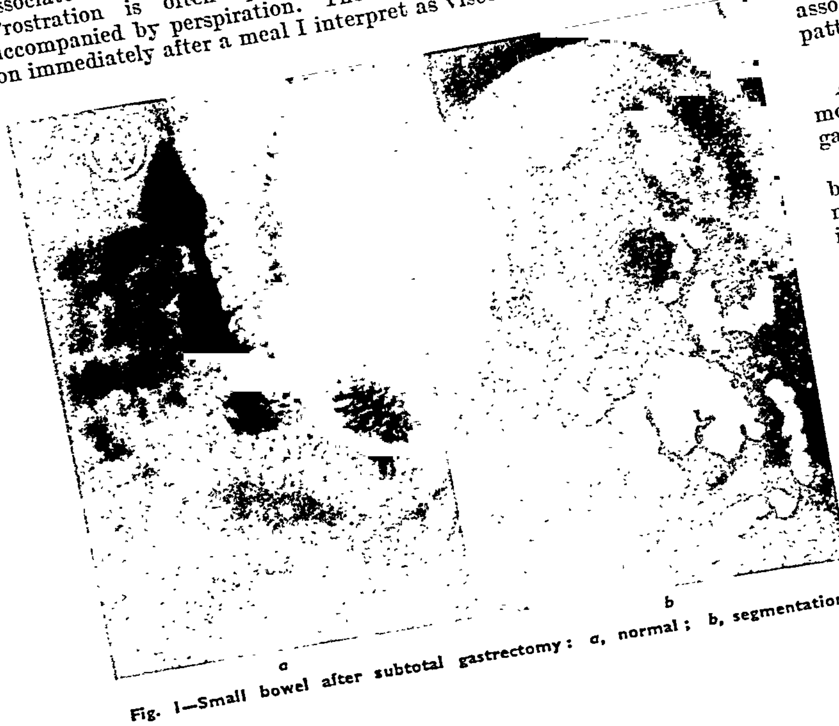

Fig. 1—Small bowel after subtotal gastrectomy: *a*, normal; *b*, segmentation.

SUMMARY

A peculiar disorder of small-bowel motility sometimes develops after subtotal gastrectomy.

A similar disorder has been observed by other workers in patients who have not had an operation on the gastro-intestinal tract.

After gastrectomy a distinct syndrome develops which is particularly difficult to treat.

The condition is, in some respects, similar to that of idiopathic steatorrhœa.

I am indebted to Colonel J. W. Bowden, of the Ministry of Pensions Hospital, Liverpool, for permission to publish details of three of these cases, and to Prof. Charles Wells for details of the fourth case.

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foreseeable future the professional staff could be expanded to nearly five times its present size. The offer of help by practitioners, willing either to treat school children in their practices or to work on a sessional basis in the school clinics, should be welcomed, but it will never be sufficient to transform the present wholly inadequate school service. If full advantage were taken of all the help offered under the British Dental Association plan, perhaps 200,000 or 300,000 more children could be given satisfactory treatment each year; but the majority of the 5½–6 million school children in the country would still only be able to get emergency treatment for the relief of pain.

It seems to us beyond question that a satisfactory school dental service will have to employ dental ancillaries. In opposing the Dentists Bill, which proposes a three-year experiment in the training and employment of such ancillaries in the public health services, the dental profession is surely being remarkably short-sighted. It is in the eventual interest of the profession as of the public that an adequate school service should be established as early as possible. The British Dental Association should ponder the testimony of dentists in New Zealand, who praise the work of the school dental nurse and set a high value on the habits of regular attention which this work induces.

INHERITANCE AND MANIC-DEPRESSIVE PSYCHOSIS

THE idea that genetic factors may be important in the causation of psychiatric disorder meets with much resistance from those who treat this type of illness; and Slater[1] remarks that the growth of this idea has made it necessary to duplicate much of the work on the inheritance of mental disorder. The resistance is based on two false premises—that a condition is either genetically or environmentally determined, and that if it is genetically determined it is untreatable. There is no reason why a disease which is in part genetically determined should be untreatable; and success in preventing mental disorder may come only when it is possible to discover those who are genetically predisposed to react in this way, and then to protect them from factors likely to precipitate the illness.

Both twin and family studies give good evidence that the inherited constitution is concerned in the development of both main types of psychosis—schizophrenia and manic-depressive psychosis. The twin studies also show that even identical twins brought up together are not always both affected, and thus that the genetic predisposition is not always realised. But the greater resemblance between monozygous than dizygous twins leaves little doubt that the concentration of manic-depressive psychosis within families represents genetic as well as social inheritance. The family studies have also proved that, despite occasional difficulties in classifying the illness of an individual patient, the two main types of psychosis are genetically independent. The near relations of a patient with one of these types have an increased risk of developing psychosis of the same type, but probably only a random risk of developing psychosis of the other type.

Stenstedt[2] has confirmed these points in an excellent family study in Sweden, where the parish registers are unusually complete and the people are ready to coöperate. Stenstedt studied the families of 261 patients with manic-depressive psychosis; he examined personally 469 of the relations and got reliable information about many more. Among these relations there was no noteworthy excess of any psychiatric disorder other than manic-depressive psychosis; but the increase of this form was definite. In the general population of Sweden the risk of developing manic-depressive psychosis is estimated at about 1%. The risk for the first-degree relations of the patients (that is, the parents, children, and siblings) was about 10–15%; and the risk was roughly the same for each relation, when allowance had been made for age. This agrees closely with the findings in earlier studies. There was no obvious tendency for the disease to take the same form and intensity within families; which strongly supports the clinical view that the types of manic-depressive psychosis are variants of the same disease. The proportion of relations affected did not vary with the form taken by the psychosis in the index cases. The prevalence was as high in relations of those with purely depressive attacks as in relations of those with manic as well as depressive attacks; and it was as high in the relations of those with few as in those with many attacks. The proportion of brothers and sisters affected was not altered when one parent was also affected; but the proportion of brothers and sisters affected was increased when the patient (and therefore his brothers and sisters) came from a broken home. This strongly suggests that a broken home is one environmental factor that favours the development of manic-depressive psychosis in those who are genetically predisposed.

These findings do not indicate clearly any particular type of inheritance. The simplest hypothesis is that a dominant gene is concerned, but that only about one in five of those who inherit this gene ever becomes psychotic. If this is so we should, with the intense research that this subject warrants, discover the predisposing factors in the 20% in whom the genetic predisposition *takes effect*.

PULMONARY COMPLICATIONS OF DYSPHAGIA

ANY condition which interferes with swallowing may cause food and secretions to enter the trachea and set up inflammation in the lung.[1] Patients with pharyngeal pouches, tracheo-œsophageal fistula, or bulbar paralysis, as well as those with organic œsophageal obstruction by a fibrous structure or a carcinoma, are all liable to this risk; and true aspiration pneumonia is commonly the immediate cause of death. The most extensive lung changes, however, are likely to develop in those who are longest at risk; and thus the widest variety and most florid examples are found in patients with cardiospasm.

Anderson et al.,[2] at the Mayo Clinic, have examined the records of 600 patients with cardiospasm who were observed and treated between 1935 and 1946. They find that just over 10% had pulmonary changes. The commonest change was "aspiration pneumonitis, unilateral or bilateral, usually situated in the mid zone on the right." Though occasionally acute and transient the illness was more commonly chronic and insidious, with a distinct tendency to progress to diffuse fibrosis. Only one patient developed an acute abscess. A small group of four patients showed a diffuse nodulation in the lungs "resembling miliary tuberculosis, pulmonary tuberculosis with bronchogenic spread, silicosis or metastatic malignant disease." Four other patients developed asthma after cardiospasm had appeared, and two of these noted an improvement when the cardiospasm had been relieved. Over 10% had a cough without detectable lung disease, confirming Grey Turner's[3] observation that achalasia occasionally presents as a chronic cough.

The Mayo Clinic workers draw attention to the occasional coincidence of pulmonary tuberculosis and cardiospasm, but wisely point out that no case should be diagnosed as tuberculosis until virulence tests have proved the bacillus to be the true *Mycobacterium tuberculosis*

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Special Articles

SITTING DOWN TO SURGERY

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M.B Dubl, F R C S

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THE practice of surgery is dominated by the patient—his care, his comfort, and his survival No-one bothers overmuch to consider the care, comfort, or survival of the surgeon Statistics deal with the fate of the patient, and if occasionally the occupational hazards of the surgeon crop up for discussion they pass as reasonable risks of a career abounding in Lord Birkenhead's "glittering prizes"

Many operations today are long fatiguing procedures in which the stamina of the surgeon may be taxed almost as much as the patient Part of the trouble arises from the tradition of the one-man show The days when Sir William Double-Barrel arrived in stately fashion to be met by a retinue of deferential white-coated underlings, and a ripple of excitement preceded him from the porters' lodge, along the corridors, into the wards and the operating-theatre, are vanishing When Moynihan talked of himself as a physician "doomed to the practice of surgery" he may or may not have had his tongue in his cheek, for in his heyday the surgical maestro was as temperamental and spoilt as a prima donna Today surgery is a job of work which becomes less glamorous and more humdrum as operations become safer and more standardised

So, unpalatable though the fact may be to some, it does not require a lifetime of experience to do most of the standard operations in surgery well This we owe largely to modern anæsthesia There was a time, not so long ago, when even a cholecystectomy was a major adventure with the abdomen heaving like a stage sea and the surgeon making frantic dabs between heaves It was a time which, on the Continent particularly made local anæsthesia universally popular There is little to be said in its favour nowadays, even if some surgeons still piously infiltrate cœliac ganglia and do paravertebral blocks on the doubtful assumption that shock is diminished thereby

In spite of the growing ease of operations and the multiplicity of surgeons a tendency persists for the young surgeon who is a registrar or assistant to spend years doing minor major surgery while his "chief" goes bald, loses his teeth, develops peptic ulcers and high blood-pressure, hogging enormous lists on his operating day Finally, when in his turn the junior becomes a senior he grabs from *his* juniors So you have the paradox of the fit young man eating his heart out because the "big noise" does all the gastrectomies, œsophagectomies, and thyroidectomies in sight at just the time when he ought to be conserving his energies, thinking about his work, and spending a modicum of thought on research and the sorting out of his ideas Indeed (wild thought) he might even be reading outside his own professional subject, learning something of art and general science, so that when he sits down to write a paper he may achieve literacy and readability

All of which leads me to put forward some suggestions designed to lengthen the surgeon's days, to lighten the burden of nurses and secretaries, to sweeten the atmosphere in operating-theatres, and perhaps to add to the comfort of that much-pampered person the patient

THE OPERATING-LIST

From what has already been said it follows that the operating-list should not consist of a whole row of formidable operations The man who boasts of having performed an œsophagectomy, three gastrectomies, and a couple of thyroidectomies in one day may achieve the reputation of a virtuoso but he may well wreck the orchestra At the end of such a day he leaves behind him a mountain of bloody swabs and the aching backs of tired, hungry, and thirsty nurses house-surgeons, registrars, and porters fit for nothing but dull leaden slumber True, over most of the world there is a shortage of operating theatres, and this may be held to justify long lists On the Continent it is not unusual to have more than one table in one theatre In 1935 I saw five in full swing in one Moscow operating-room But this is a barbaric practice It should not be impossible to spread work out more evenly, and certainly it is high time that senior surgeons came to realise that operating is only a part of their work They have a responsibility to their students, to surgery in general, and to themselves

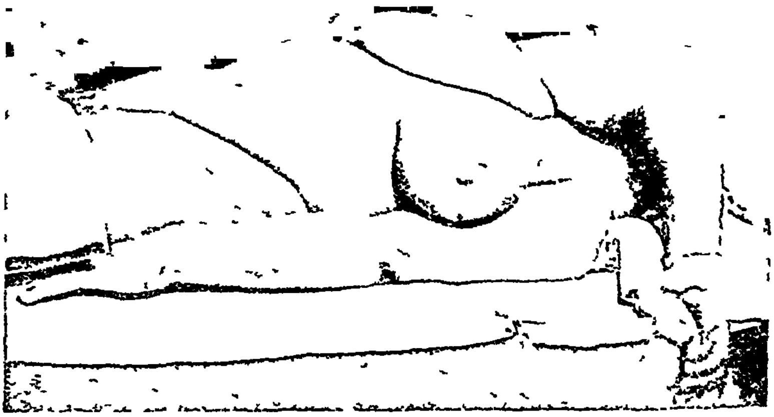

Fig 2—Patient s position for upper abdominal operation right arm is brought across to hang over left shoulder, and face is turned to left. Patient lies as close to left side of table as possible, and surgeon sits at left side of patient.

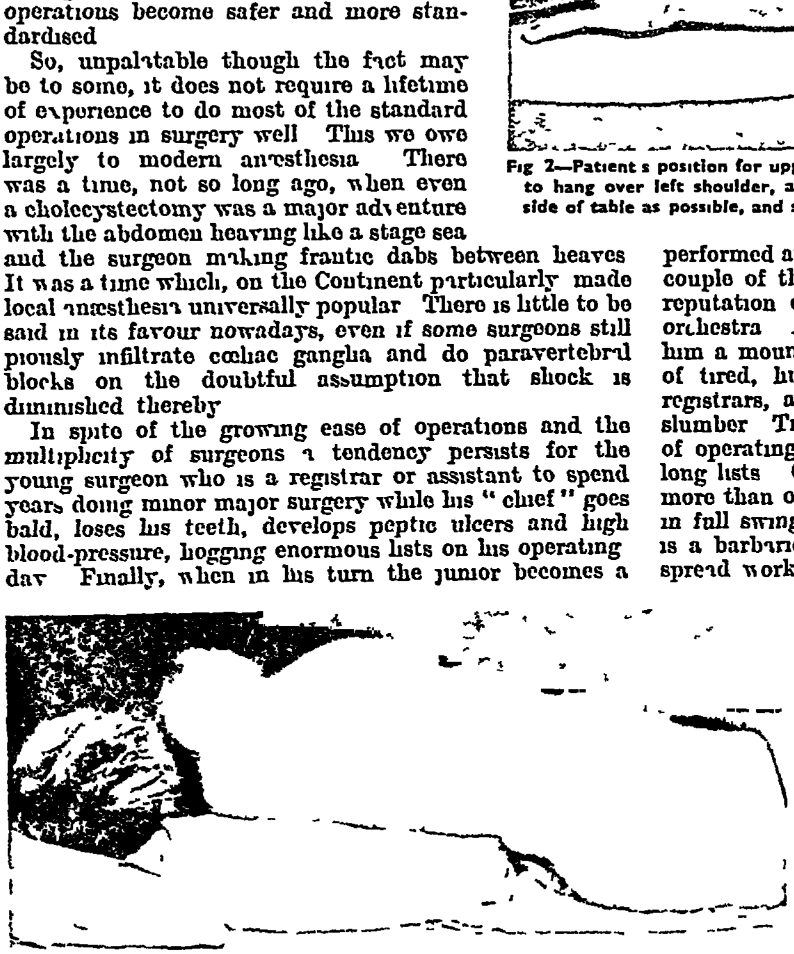

Fig 1—Patient s position for upper abdominal operation sand-bag under right thorax tilts torso to left while leaving pelvis flat on table.

Two major operations and three minor majors are enough for one day This leaves time for adequate meals (instead of stewed tannin, sandwiches, and cigarettes), for rest, and for the exercise of judgment It gives anæsthetists time to look after their patients

THE THEATRE ATMOSPHERE

Inside the theatre the atmosphere should be quiet and restful I do not go so far as my friend Professor Penn, of

THE LANCET
LONDON: SATURDAY, APRIL 4, 1953

The Fever Nurse

THE rivets in *The Ship that Found Herself* took some time to realise that they were holding the whole thing together; and it is doubtful whether the other parts of the ship ever fully grasped this fundamental fact. The ship, however, when she finally knew herself and delivered judgment on her previous behaviour, was aware of the purposes of all her members.

Our National Health Service is held together by our nurses; and if their quality fails the service will founder. The people most concerned with maintaining the quality of the nurse are the members of the General Nursing Council, whose business it is to see that she is properly trained. The council have taken the line that the general-trained State-registered nurse should be qualified to meet every nursing demand that may be made on her, and they have never been fond of supplementary registers attainable by nurses who have not had a general training. In principle the council are no doubt right, and they may be right also in practice some day when nursing attracts all the best school-leavers, and when young women are thicker on the ground than they look like being for the next forty years. But meanwhile a large proportion of the girls entering nursing are quite ordinary girls; great mbers of patients have to be cared for; and the gent question is not so much how to turn any andidate into a first-class single-pattern all-purposes urse, but how to make the best use of the candidates we have. This question is brought again to the forefront by the plight of the fever hospitals, described in our correspondence columns during the past few weeks. Anyone who has coached a football team or an amateur dramatic society knows that even mediocre performers can achieve wonders when they are familiar with each other and with the tasks required of them, and this has been the experience of the fever hospitals with their nurses. Till recently they could be sure of offering a two-year training for the infectious-diseases register; and they found that girls trained directly for this specialty acquired a reliable barrier technique, and could later be given appointments as staff nurses and sisters in the fever service. The offer of training also helped recruitment, and this was further favoured by the fact that many of these hospitals accepted girls of 17. Two things, however, have now combined to make recruitment to the fever service difficult: first, the age of entry to any type of nursing training has been raised to 18, and secondly, the G.N.C. have announced their intention of asking the Minister of Health to close the infectious-diseases register—at some date not so far specified. Dr. JAMES GRANT[1] and other contributors[2] unanimously protest against this second decision, and some even protest against the first.

The suggestion that the age of entry should again be lowered is one that we cannot support. The average 17-year-old girl is not physically fit for any form of nursing, least of all for a branch which regularly exposes her to chances of infection. Moreover there is evidence that the setback to recruitment occasioned by the rise in the age of entry is already beginning to adjust itself, at any rate in some places. But the second blow is more serious, for closure of the infectious-diseases nursing register will put the fever hospitals in a situation which the G.N.C. are powerless to alleviate. Some of our correspondents suggest that the council, being concerned only with training, care for none of these things; but this can scarcely be the attitude of a body whose regulations have a profound effect on the distribution of the country's nurses. In this respect the G.N.C. are far more powerful than the General Medical Council, who deal with whole-time medical students in a few university centres, and have no influence whatever on the distribution of medical man-power—except perhaps in relation to the pre-registration year that now follows qualification. Whereas medical students have no official responsibilities in hospital, nurses throughout their training are doing responsible work. Indeed, as the Nuffield job-analysis team[3] have shown, three-quarters of the nursing in the wards of training hospitals is done by student nurses. In fever hospitals, likewise, important work is done by the nurses in training (where there are any), and it is essential both that the work should be done and that the training should continue. Barrier technique is precise, and cannot be picked up in a moment by transient staff, or taught by seniors who have not themselves been rigorously trained in it: in the general training of nurses it is not so emphasised as to become second nature with all. Some of our correspondents foretell the loss of skills which have taken half a century to reach their present high level.

It is widely supposed that the fever service is in any case dying; but several correspondents insist that this is not so: as the old familiar exanthems sink to a relative obscurity, mysterious strangers turn up and fill the beds afresh. There is always the risk, too, of a severe poliomyelitis epidemic, in which the lives of patients often depend on skilled and experienced nursing. Even in the everyday emergencies of the fever service lack of skilled help may have grave results, and even the best of doctors cannot do their work properly without a competent nurse.

Naturally there are other sides to the question. Many small fever hospitals have been closed down, and the filling of the bigger ones represents a concentration of patients in fewer sites rather than a rising incidence of infectious diseases. The G.N.C. hope that, with the closing of the infectious-diseases register, general hospitals will be moved to second student nurses for a brief experience of fever nursing. Yet even if this were likely to become a popular practice with the general hospitals—and a good many groups are trying it—the fever hospitals would not think it solved their problems. They do not want birds of passage. unhandy, bewildered, waiting to be taught: they want young women settling into their professional life in a particular and highly specialised branch of nursing. And here, of course, we come again to the

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[1] *Lancet*, Feb. 14, 1953, p. 344.

[2] *Ibid*, Feb. 21, 1953, p. 393; Feb. 28, 1953, pp. 439–441; March 7, 1953, p. 497; March 21, 1953, p. 596.

[3] The Work of Nurses in Hospital Wards. London, 1953. Sc
Lancet, Feb. 21, 1953, p. 379.

ENVOI

Sitting down to surgery literally becomes sitting down metaphorically as well Less tension and more relaxation spread from surgeon to the rest of the staff in the theatre Peace and quiet reign

The surgeon's responsibilities do not end with the establishment of a record for the number of stomachs, rectums, and pancreases he can claim as trophies If he can show that his assistants are able to take his place without harm to his patients he will have served surgery better, and he will probably live longer

REFERENCE

Rons M C (1947) *Clin Proc* 6, 88

HEALTH AND SOCIAL POLICY

FOUNDED in 1951, the British Sociological Association held an annual conference in London last weekend, when it discussed Social Policy and the Social Sciences After a plenary meeting at which Prof GUNNAR MYRDAL (executive secretary, Economic Commission for Europe) gave an address on the Relation between Social Theory and Social Policy, the conference split into three groups, of which the first, meeting under the chairmanship of Prof J M MACKINTOSH, F.R.C.P., was concerned with Health The following is a summary of the six introductory papers contributed to this group

Changing Needs

Dr J N MORRIS (director of the M R C's social medicine research unit) suggested that the problems of health we face today are more difficult than those of yesterday, for instead of the acute infections of early life we have to deal with the chronic diseases of the middle-aged and elderly Thus we have exchanged diseases of well-understood ætiology and satisfactory treatment for those of largely unknown ætiology and unsatisfactory treatment, and interest has shifted from mortality to morbidity In dealing with the diseases of yesterday we had reason to believe that they would respond to a rise in the standard of living But there is no suggestion that coronary disease, the psychoneuroses, or duodenal ulcer are due to poverty some are probably the consequence, direct or indirect, of the rising standard of living Dr Morris believes that we cannot grapple with these problems until we enlarge our notions of the relationship of man with his environment, and to do this we need the help of the social scientist For instance, one of the unanswered questions facing the National Health Service today is the assessment of need

> "What do we know about the expectations of people today as regards health, what is their tolerance, their threshold of pain and disability ? How much of these mental health problems for instance, are the proper concern of medicine, or social work or of anyone but the sufferers themselves ?
> I have a hunch myself that a more meaningful assessment of needs will show how increasingly tenuous is the distinction between physical problems, mental, and *social*, *and how the* general practitioner of the future will increasingly and consciously be dealing with all three His place in the scheme of *things in my phantasy*, will include a rôle as captain and coördinator of social medical services at the 'grass roots level of people in trouble and it is with such public servants that I think the social worker of the future will be mainly associated '

We are spending hundreds of millions on health services, but we have little information on how well the different parts are working Here, again, Dr Morris sees an opportunity for the social scientist, and he would like *to* see the Central Health Services Council, "a body of immense promise but doubtful achievement," strengthened by a research secretariat to act as its intelligence service, offering critical and constructive analyses of the workings of various parts of the N H S, and observing the success of experimental ventures

Social Reorientation of Psychiatric Treatment

Perhaps no specialty has had to cope with greater changes than psychiatry, and Dr T FERGUSON RODGER (professor of psychological medicine in the University of Glasgow) argued that in meeting these changes we are handicapped by the institutional tradition of the service

> "Our thoughts have traditionally been fixed on patients suffering from major mental illness, and although they constitute only a small fraction of the total, half of all the hospital beds in the country are devoted to their care '

In the past thirty years more effective methods *of* treatment have increased the turnover of the hospitals, the task of the staff is now therapeutic activity rather than custodial care The provision of beds in mental hospitals is no longer, he thinks, the best way to deal with most psychiatric problems It is possible, for instance, that more patients could be kept at home if there was an adequate domiciliary and nursing consultative service Is there any reason why electroconvulsive therapy should not be given at home? He would also like to see the provision of day hospitals economical in staff and space, which patients would attend only from 9 A M to 4 30 P M, thus remaining in daily realistic contact with the home and avoiding the regressive escape into hospital For other patients who are able to work but are not stable enough to manage their own affairs he suggested a hostel service staffed by understanding but not necessarily highly trained people

But even with these aids, he admitted, to deal by formal psychotherapy with more than a tiny fraction of the patients suffering from psychoneurosis is well nigh impossible As these disorders are traceable to the disorganisation of society due to industrialisation and the breakdown of the family unit, he suggested that one hopeful and as yet neglected approach is the education of key members of the community in skills in dealing with human relationships A course of this kind on Mental Health in Modern Society, held in Glasgow this winter, has proved a success Another example of this *social movement is the work of the marriage guidance* councils

Health Service Organisation as a Task in Applied Science

Dr MILTON ROEMER described public health work as the intelligent application of known techniques to social situations As such it calls for social rather than biological wisdom, yet advanced training in public health is still 90–95% biological, and the public health worker must turn to the social scientist for help in the clarification of the structure and function of society The pattern of each new form of organised health activity is defined by the social setting of the community and the technical knowledge available As the situation and knowledge change the pattern must be adjusted if the organisation is to remain fully effective But in making changes the public health administrator is likely to meet resistance, and here he needs the help of the social scientist who can interpret for him the nature of the resistance and how much the social structure may be budged Dr Roemer discerned a tendency among anthropologists to underestimate the rate of dynamism of society He invited his listeners to consider

> " *the adjustment of this land of deeply rooted tradition* to the National Health Service which, overnight, placed centuries old voluntary hospitals under government control eliminated the cash nexus from nearly all doctor patient relationships, and recast the structure of the nation's *entire* public health system '

Turning again to the international level, Dr Roemer said that when the ideas of one culture are being transferred to another the help of the social scientist is most urgently needed Dr Roemer was often asked what can be exported from one culture He held that innovations based on truth and science and dedicated to the ries and from examination of lavatory seats and suspected sources of infection, although it is that identification of the organism in male acts of infected patients often presents difficulties. Human trichomoniasis is an important and neglected oject which has received less systematic study than e related disease of cattle, due to *T. fœtus*. Many its aspects are difficult and complicated, but a ontrolled investigation should answer with reasonable ssurance the question of methods of transmission, and decide whether the simple solution which McCULLAGH advocates is, in fact, likely to be helpful.

Respirators

POLIOMYELITIS now comes so frequently and so suddenly that we ought to be fully prepared in advance. Each epidemic seems to have its own features, and in Denmark last autumn the high incidence of bulbar and bulbospinal paralysis put a great strain on the resources of the hospitals and the medical profession. Of 866 patients admitted to Blegdam Hospital in Copenhagen no fewer than 316 had severe respiratory paralysis, and in face of this situation great enterprise was shown in maintaining respiration by positive-pressure methods. After tracheotomy the lungs were ventilated through a cuffed anæsthetic tube by continuous relays of doctors, nurses, and medical students squeezing a rubber bag—with results that speak worlds for the conscientiousness and skill of those who did it.[1] Intubation and active inflation by one means or another has also found favour in the United States, and may obviously be of great value; but when required for weeks and months it also has serious drawbacks of the kind indicated by KELLEHER and SELLICK.[2] In this country respiratory paralysis is commonly treated on the suction or negative-pressure principle, as applied in the tank or cabinet type of respirator. But if the mechanical efficiency of many such machines is undisputed, so also are the discomforts and disadvantages. Once placed in an iron lung, the patient is almost immobile and inaccessible; moreover the apparatus is expensive, and in spite of Lord NUFFIELD's generous gift of Both-type respirators to a great many hospitals, we certainly have not enough machines to treat anything like the number of cases of respiratory paralysis that would se if this country were afflicted as Denmark has en.

Two articles published on other pages aim at lving some of the problems of negative-pressure espiration. The disadvantages of the original tank-ype respirator have already been partly overcome in new designs, but these are not being produced on a large scale and they are also expensive. Means of modifying existing machines have therefore been sought, and the Birmingham Regional Hospital Board, by encouraging the mechanical genius of Captain SMITH-CLARKE, has produced a scheme by which existing Nuffield-Both respirators can be modernised to remedy many of their deficiencies. A split collar for the neck seal, with a divided front, is a considerable improvement because it allows patients to be put in and out of the cabinet much more quickly; and also there is less movement of the collar, because the two moulded pieces of rubber that form the neck seal are strengthened by a plate of thin metal. Enlarged ports in the side of the tank will be welcomed by nurses, and an improved alarm system is a further advantage. In addition, a method of gearing down the motors to work at suitable speeds has been put forward; for one of the faults of the original pattern was that the motor could not be made to work slowly enough for most cases. It is to be hoped that regional boards and those responsible for the maintenance of the existing machines will consider the relatively economical modernisation that is suggested, and that a central register will be kept so that if machines are suddenly needed in any locality they can be transported there quickly.

Possibly the biggest disadvantage of most tank respirators is that the patient has to lie flat on his back, because the sloping front does not allow of his being placed in the face-down position. Any patient who remains stationary in the supine position is liable to accumulate secretions in the base of the lung, and there have been many deaths from collapse of lung followed by infection. This danger is greatest in the case of bulbar paralysis, where life depends on removal of secretions by postural drainage or endobronchial suction; and in such cases more harm than good will be done if loose secretions or fluid in the bronchi are sucked further into the lungs during the negative phase of mechanical respiration. The bad reputation of the "iron lung," which has sometimes been called an iron coffin, will be maintained so long as it is used for unsuitable cases, particularly those with bulbar paralysis. To this part of the problem the solution seems to be a cabinet with a straight front or angled neck-opening which will allow the patient to be placed, at any rate for some time each day, in the face-down position. The design of one or two of the newer machines incorporates this principle.

For the patient who can be removed, even for a short time, from a tank respirator, we need some method of aided respiration allowing greater physical and mental freedom. Intermittent mask inflation, such as can be given with the Oxford respirators or the McKesson apparatus, is valuable when a patient with complete respiratory paralysis is removed from the tank, but it cannot be used for more than a limited period. Positive-pressure apparatus working directly on the chest wall and abdomen (e.g., the Bragg-Paul) also has a restricted range of utility; for, though it enhances expiratory efforts, it has no effect on inspiration. Attention has largely been focused, therefore, on some form of suction apparatus less cumbrous than the tank. In principle the so-called cuirass respirator seems to meet the need, but unfortunately its practical efficiency has left much to be desired. KELLEHER et al.[3] have reported on the merits of two forms, the Monaghan and Kifa, and have expressed a hope that further improved designs would be forthcoming. This week Dr. SCALES, Dr. KINNIER WILSON, Mr. HOLMES SELLORS, and their colleagues describe plastic cuirasses that can be made quite simply for use with existing pump units. One type, which was made like an enclosing jacket, was found not to work well, but more satisfaction was obtained with an anterior shell or dome which fits the patient direct or rests over the patient on to the mattress or in 1938 Professor Titmuss doubted whether those who suggested cuts in the social services give sufficient weight to these considerations

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[1] Lassen, H. C. A. *Lancet*, Jan. 3, 1953, p. 37.

[2] Kelleher, W. H., Sellick, B. A. *Ibid*, Feb. 28, 1953, p. 439.

[3] Kelleher, W. H., Wilson, A. B. K., Russell, W. R. *Brit. med. J.* 1952, ii, 413.

> "Considerations of morality are thus intertwined with considerations of social health as such, they cannot be subordinate to and separated from considerations of economic efficiency Ways of living in marriage, as members of families in old age, in the work group and in the wider society are as relevant to the performance of the economic system as they are to the performance of the social services This implies the annihilation of concepts of 'separateness', of a view of these services as a beneficent appendix to the economic order, of a stereotype of the Welfare State which is steadily acquiring the characteristics of a national illusion"

The conference closed with another plenary session at which Prof T H **Marshall**, who presided, summed up the work of the groups The address of the association is 13, Endsleigh Street, London, W C 1

Occasional Survey

EFFECTS OF HORMONES ON SILICOTIC NODULES

A **silicotic** nodule consists of whorled reticular and collagenous fibres formed as the result of irritation of the lung tissue by particles of free silica one form of which is quartz There have been several experimental studies to determine whether the formation of such nodules is affected by the administration of cortisone or A C T H

EXPERIMENTAL OBSERVATIONS

Magarey and Gough[1] found that cortisone suppressed the fibrotic reaction to quartz in the peritoneal cavities of mice, in rabbits and to a less extent in rats the reaction was retarded, whereas in guineapigs it was not appreciably affected Probably, however, these differences were *partly due to differences in dosage by body-weight* As Curran[2] points out, high dosages of cortisone may produce atrophy of the adrenal cortex, and Magarey and Gough state that mice which received cortisone acetate in a daily dosage equivalent to 125 mg per kg body-weight died within 17 days, whereas controls showed no evidence of illness By the 11th day in the controls there was an obvious macroscopic connective tissue reaction round the clumps of quartz, which were adherent to the peritoneal surface, but in the cortisone-treated animals the quartz was lying free in the peritoneal cavity At the 17th day in these animals a few small clumps had become adherent to the peritoneum but there was no reaction round them, whereas in the controls there were discrete nodules with fibrous capsules

Rabbits appeared to tolerate quite well cortisone in a daily dosage of 8 mg per kg body weight, and on the 15th day there were qualitative and quantitative differences in the peritoneal reaction to quartz in the cortisone treated and control animals In the former most of the aggregates were adherent to the peritoneum, while in the controls all were firmly adherent In the treated rabbits there was a moderate number of fibroblasts, but these were plump and polygonal, and there was only little formation of reticulin and collagen The control animals showed elongated fibroblasts with many connective tissue fibres After 30 days an unexpected change was found in the cortisone treated rabbits The abdomen was filled with pink gelatinous polypi in which were entangled aggregates of quartz, histologically this polypoid growth consisted mainly of thin walled blood vessels in a structureless ground substance Later this vascular overgrowth was replaced by widespread and disorderly fibrous tissue apparently unrelated to the few quartz aggregates which it contained The control animals did not show these diffuse changes, but in them were found nodular deposits of quartz surrounded by capsules of dense white fibrous tissue Magarey and Gough think that further investigation is needed to determine whether the redundant fibrosis seen in the rabbit is really a cortisone effect

The lesions in cortisone treated *rats*, compared with those of the controls, showed some diminution and retardation of the formation of fibrous tissue, but the differences were less distinct than those seen in the rabbit and mouse

In both treated and control *guineapigs* the quartz powder *formed clumps which adhered to the* peritoneal surfaces and became covered by a firm white fibrous capsule The cortisone in the dosage given (16 5 mg per kg body weight) *therefore failed to* prevent the typical silicotic tissue reaction The relative resistance of the guineapig to cortisone and A C T H has previously been noted by Upton and Coon[3]

Curran[2] in his experiments injected a suspension of 20 mg of quartz into the peritoneal cavities of four groups of mice, one of which was used as a control

The reaction to quartz in the control group was first a viscous peritoneal exudate, the cells of which were first polymorphonuclear and later mononuclear The dust particles aggregated into nodules with early formation of reticulin in them, associated with cells like macrophages which were fibroblastic in type and which ultimately replaced the whole nodule Collagen fibres were seen by the 10th day and increased in number until typical silicotic nodules were formed

One group of animals was given subcutaneous injections of 0 4 mg cortisone acetate for 14 days, and the quartz suspension was injected intraperitoneally 4 hours after the second cortisone injection Another group was treated similarly, but in addition received 0 1 mg cortisone daily for 76 days A third group, after the initial intraperitoneal injection of quartz, received no treatment for 90 days, when a 14 day course of cortisone (0 4 mg daily) was given

In the first two of the cortisone treated groups the peritoneal exudate was *much less pronounced and much free* dust persisted up to 21 days There were no prominent nodules but from the 8th day a thin pearly fibrous membrane covered the peritoneum of the abdominal wall and was more evident after some months, occasionally fine nodules were seen The aggregations of dust on the omentum, mesentery and viscera were like those in the controls In the third group in which the cortisone treatment was begun after the silicotic nodules had formed, *no significant effect was seen up to 2 months after the cortisone injections*

In general Curran found that, with the dosage of cortisone used, the ultimate response of the animals to quartz was unaltered and cortisone had no effect on mature silicotic nodules

Schiller[4] also used mice in his experiments, but in view of the fact that high doses of cortisone can produce atrophy of the adrenal cortex, he decided to stimulate it to produce its own cortisone by administering œstrogens insulin, and thyroxine

Albino mice varying in weight from 18 to 24 g were given a single intraperitoneal injection of 10 mg of quartz suspended in saline solution and were then *divided into* seven groups one of which was used as a control

In the control group well defined silicotic nodules *formed within a month, and both reticular and collagenous* fibres were present The largest granulomata had necrotic centres surrounded by a zone of fibroblasts histiocytes, lymphocytes and leucocytes The second group of animals was given a daily dose of 20 µg *of cortisone from the* 21st day of the experiment, by which time the silica had become adherent to the peritoneum Cortisone caused the lymphocytes to disintegrate and inhibited the formation of fibrous tissue *The third group,* which received diethyl stilbœstrol dipropionate from the 2nd day of the experiment, showed effects similar to those seen in the second group Insulin, given *to the fourth group,* retarded the formation of connective *tissue* to such a degree that there was only a very fine network of reticulin on the 60th day Thyroxine in the 5th group inhibited the formation of fibrosis in the same way as cortisone The 6th and 7th groups were given deoxycortone acetate and testosterone propionate respectively and in both there was proliferation of fibroblasts and of collagenous fibres

In contrast with these observations on peritoneal silicosis, the experiments of Harrison et al[5] were con ght to be intimately connected with virulence. The that small numbers of dead bacilli appear to have e immunising power is interesting in connection with known variation in the proportions of dead and living cilli in different batches of B.C.G. vaccine. Although a oderate proportion of dead bacilli in the vaccine will ake little difference to the tuberculin sensitivity,[4] it ay make a much greater difference to the level of immunity attained. In man, the addition of a small amount of living B.C.G. to a dead vaccine produces a degree of sensitivity greater than would be expected from a simple summation of the separate effects.[4] The effect of this apparent interaction of dead and living bacilli on immunising power has not yet been investigated.

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[1] Magarey F R Gough J *Brit J exp Path* 1952 33, 76

[2] Curran R C *Ibid* p 82

[3] Upton A C Coon W W *Proc Soc exp Biol, N Y* 1951 77 153

[4] Schiller, F *Brit J industr Med* 1953, 10, 1

[5] Harrison C V King E J, Dale J F Sichel, R *Ibid*, 195 9 165

Dubos and his colleagues have already obtained much information from their investigation of immunity by quantitative bacteriological studies of whole organs. Suter,[5] on the other hand, has observed the reaction of the cells themselves. Using the technique of in-vitro cultivation of monocytes,[6 7] he has shown that the multiplication of attenuated and virulent tubercle bacilli is greatly retarded or inhibited within mononuclear phagocytes from B.C.G.-vaccinated animals. This inhibition appeared to be independent of the presence of humoral factors in the culture medium, for the result was the same whether serum from normal or from vaccinated animals was used in the tissue-culture medium. Nor did serum from vaccinated animals inhibit multiplication of bacilli within the cells derived from normal animals. Both these experimental systems seem to be valuable tools for investigating the complicated factors concerned in the interactions between tubercle bacilli and the body.

PREGNANCY AND THE MENSTRUAL CYCLE

ANY method that helped to determine more accurately the expected date of confinement would be welcome. The normal interval between the onset of the last menstrual period and the onset of labour is usually taken to be 280 days; but, even excluding abnormal pregnancies, there is a standard deviation of about 10 days on each side of this figure.

From time to time it has been suggested that the duration of pregnancy depends on the length of the menstrual cycle. Ovulation normally occurs about 14 days before the onset of menstruation, and a woman with a long cycle may seem to have a long pregnancy if he duration is calculated from the date of the last period; but, apart from this, there has been little support for the opinion that the duration of the pregnancy is influenced by the length of the menstrual cycle.

Seager,[8] who has studied 303 pregnancies in patients with known menstrual cycles, revives the view that labour starts at the end of a certain number of cycles, but emphasises that this number may not be the same from case to case or even in different pregnancies in the same patient. He shows by simple multiplication that for each of the cycles ranging from 21 to 35 days, except that of 33 days, menstruation is due to occur within ±10 days of 280. By relating the durations of pregnancy in his patients to the appropriate cyclical date instead of to 280 days, he reduces the standard deviation from 10·5 to 3·5 days. Seager would suggest that in the case of a woman with a regular 30-day cycle who did not go into labour at about the 270th day (9 cycles), labour will not start until the end of the next menstrual month—i.e., about the 300th day.

Seager's figures are open to two main criticisms. First, not all his patients had kept menstrual diaries. Arey[9] and others have clearly shown that even women who state that their cycles are regular do in fact show considerable variation from month to month when the periods are carefully recorded. Arey says that "not the slightest evidence pointing to perfect regularity has so far been produced for even a single exceptional individual." The second criticism is that Seager's reduction of standard deviation from 10·5 to 3·5 days gives an over-optimistic impression of the validity of his thesis: clearly the standard deviation would be very considerably reduced if the durations of pregnancies were grouped round several arbitrarily chosen numbers of days rather than all grouped round 280 days.

No information regarding excretion of gonadotropin, œstrogen, or pregnanediol gives the slightest indication that an ovarian cycle continues during pregnancy, nor do basal temperature charts show any cyclical variation. We must therefore await the results of Seager's continuing studies before assuring patients that if labour has not started by a given date the pregnancy is likely to continue for another menstrual month.

THE DENTAL SERVICES

MANY dentists practising under the National Health Service are passing through a period of financial difficulty. In many parts of the country, especially in industrial areas, the demand for treatment has declined so greatly that practitioners are no longer fully occupied, and their income has suffered seriously. Indeed, the average income earned by dentists in the National Health Service is now much lower than the figure recommended by the Spens Committee as a necessary minimum to attract sufficient new recruits to the profession. Of late years the number of students leaving the dental schools has never sufficed to expand the profession, and there is now some danger that even its present inadequate strength will not be maintained.

The profession attributes the decline in demand to the charges made to patients for dental treatment, which were imposed by the Ministry of Health in an effort to reduce the cost of the service to the Exchequer. There must, however, be a more fundamental, "long-term" cause for the public reluctance to seek treatment: for the maximum cost to the patient for treatment other than the provision of dentures is never more than £1. That so many people prefer to forgo regular dental care rather than make this relatively small contribution to its cost demonstrates an extraordinary public indifference to dental health, which must be ascribed to a serious failure in health education and a failure to form the habit of regular treatment early in life. By contrast, the people of the United States support, at a considerably higher standard of living, nearly four times as many dentists in proportion to population as we do in Britain, because they have been brought up to appreciate the importance of regular care of their teeth.

The difficulties of the dental profession are likely to persist until a more enlightened attitude has been created; and the most effective way to create it would be to bring into being as quickly as possible a really efficient and fully staffed school dental service, able to inspect and treat regularly the nation's children. Then the rising generation might develop habits of regular treatment which would persist throughout life; for instruction in dental health during this formative period, coupled with regular visits to the school clinics, could hardly fail to produce an adult population taking care of its teeth and regarding as a matter of course frequent visits to the dentist.

A really satisfactory school service could hardly be brought into being with a staff of less than 4000 dentists, unless a smaller staff of dentists were supplemented by ancillaries, trained to work under professional supervision and perform the simpler routine operations which make up so much of children's dentistry. The present strength of the school service is less than 850 full-time dentists, and it is quite inconceivable that within the

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4. Palmer, C. E. *Lancet*, 1952, i, 935.
5. Suter, E. *J. exp. Med.* 1953, 97, 235.
6. Suter, E. *Ibid*, 1952, 96, 137.
7. Mackaness, G. B. *J. Path. Bact.* 1952, 64, 429.
8. Seager, K. G. *J. Obstet. Gynæc.* 1953, 60, 92.
9. Arey, L. B. *Amer. J. Obstet. Gynec.* 1939, 37, 12.

I had to go This is all many years ago and it is high time I looked him up again He will be expecting me, I know I'll send him a card next Christmas to warn him of my coming, addressed to "Oldmeadow Gill, Eſquire ſurgeon to the Pariſh of —"

* * *

All along our road the cherry trees have punctually kept their appointment with spring On Saturday not a flower caught the eye, on Sunday splashes of pink agreeably tinctured the prevailing sepia of the suburb Walking to church with my son, I found myself expatiating on Nature's major miracle of timing and pointing out that this was a key problem in biology What are the conditions that determine simultaneous flowering throughout a large tree and equally in all the members of a species over a sizeable area ? "Come to think of it," I said, "the only book I can recall which you might look at would be D'Arcy Thompson's *Growth and Form* which, though written some thirty years ago, is far from out of date In my fairly wide reading of late years I have not seen much about biological timing mechanisms There is an American physicist who is doing exciting work on minute divisions of time, and he has the theory that time may not be a continuous function, but is quantised as light is Some day you might be looking for a research problem and there is a wide open field for you" But as we approached our destination my hafflin seemed occupied with another thought "That reminds me, Dad," he said, "I think I need a new pair of flannels and a couple of decent shirts" Spring

* * *

A few weeks ago I started to hear voices They usually came over the telephone with words of instruction or command, and, as they bore no relation to anything happening in my environment, I assumed that they were just hallucinations—merely the early symptoms of schizophrenia But when I was told to move into lodgings I decided to make a complete differential diagnosis, before, like Bunyan's pilgrim, forsaking my family for the solitary life It was then that I discovered that a psychiatrist with the same name as mine had moved here, already a city of duplicated and quadruplicated medical names The occasional psychiatric case that had arrived in my outpatients by mistake had been hardly noticed, as so many belong to that category anyway It was only when a man with unusual sexual inclinations appeared, together with a request from his doctor to cure him, that I definitely felt out of my depth So this weekend I am perusing the novels of P G Wodehouse in the hope of finding a satisfactory double barrelled name—once and for all unchallengeable by any newcomers

There are so few means of advertising left to a doctor in this country (cf the chance of taking up a full page in the daily newspapers of Los Angeles) that a carefully chosen surname may prove to be an invaluable way of increasing my private practice I hope to back it up by my newly designed young consultant's car This has a body (removable at weekends) of immense length, even as long as the cars of the G P s who call me in to see a case, yet inside is a small 10 H P engine, in order to save petrol and to ensure travel at a slow sedate pace

* * *

"Are *you* a Superman, Daddy ?"

"Well, I have been during the last few weeks I have also Packed Punch, Paying No More and Getting the Best My Pistons have been given a Good Hearty Shove instead of a Wallop, I have Tried it and Seen I have sampled the Six Extras, and that inseparable trio, Sparkling Performance, Smooth Running and Extra Mileage have made their bow I have Got Off to a Flying Start I have also Banished Pinking"

"What is Pinking, Daddy ?"

'No one knows what Pinking is, sonny, but it is caused by cheap and bad kinds of petrol'

"What kinds of petrol are cheap and bad Daddy ?"

"There are no cheap and bad kinds of petrol, sonny There are only Guaranteed, and Superb Value, and Good All Round But it is better to use a Brand You Can Be Sure Of"

"What brand can you be sure of Daddy ?"

"I am not sure sonny boy But I have just Filled Up and am waiting to Feel the Difference"

Letters to the Editor

THE PROBLEM OF PEPTIC ULCERATION

SIR,—Sir Heneage Ogilvie's annual lecture on Peptic Ulcer (March 21) was as entertaining as usual, and it may seem churlish and impertinent to cavil at any of his well chosen phrases However, I hope he will not mind being asked one or two questions from the back of the class

The ætiology of ulcer is unknown and "stress" is just as likely to be responsible as anything else, but it is becoming such a catch-word that it is in danger of being accepted as an axiom Does Sir Heneage seriously believe that the struggle for existence amongst common men and between nations is a "new factor" since 1914–18 ? Surely it is the Theory of Adaptation and not the struggle for existence which is new Ranting against the Welfare State is good clean fun, but it will not find the cause of ulcer I dare say that most of Sir Heneage's ulcer patients are both "intelligent" and "ambitious", on the other hand, most of mine are just ordinary chaps How on earth does one find out if a bus driver is ambitious ? It might not be a bad thing if these meaningless phrases disappeared from the literature on peptic ulcer

Certainly one should think very carefully before advising operation, and the most grateful patients are those who have been near to death, or have suffered for so long that their caps are in their hands, but it may be misleading to draw too close a parallel between ulcer, which can be satisfactorily treated by operation, and osteo arthritis of the hip, for which no really satisfactory operation has been found It is easy to forget that medical treatment has its economic hazards I have an acquaintance—a German van driver—who, at the age of 27, had suffered from duodenal ulcer for two years He was sent to bed for a month on the advice of a physician at a London teaching hospital, and that month cost him his job, his lodgings, his life savings, and his cherished motor bicycle on which he had paid only four instalments Needless to say, it did not cure his ulcer I feel—and I hope Sir Heneage will agree—that in the treatment of peptic ulcer there must be one law for the rich and another for the poor Does a man's age, as opposed to the severity and duration of the symptoms, matter ? Has the magic figure "40" got anything to do with this discussion at all, and if so what ? How should we treat the occasional intractable duodenal ulcer in adolescence or early manhood ? If we should not operate on it, why not ?

Although Sir Heneage finds gastrectomy for gastric ulcer remarkably easy, there are many, including myself, who would be grateful for his advice on the treatment of very high gastric ulcers Should they be left alone ? Is gastrectomy below the ulcer of any use, and what are his views on total gastrectomy for a simple condition ? Mr Norman Tanner is one of the few gastric surgeons to commit himself to print on this subject, and it would be interesting to hear the views of others

Barnet General Hospital,
Herts

V J DOWNIE

JUNIOR HOSPITAL STAFF

SIR,—I should like to draw attention to the urgency and magnitude of the general problems of junior hospital staff—which surely now require consideration on a national basis

It seems to me that there are three main groups concerning which the complete absence of long term policy, unless remedied, will inevitably ruin the National Health Service

(1) *Casualty Officers*

The problem here has resulted from an almost total disregard of the skill versatility and high degree of "occu

Many harmless saprophytes living in the mouth and œsophagus are acid-fast; but tests will show that these are not alcohol-fast and are avirulent. Neglect of these tests may lead to cases of cardiospasm in which the lung symptoms predominate being treated unsuccessfully for years in a sanatorium. Even where tuberculosis really complicates the picture proof may be very hard to obtain, and occasionally it may be obtained only years later when the patient dies in a sanatorium. In this the lesions resemble those of silicosis where positive proof of an added tuberculous lesion is often unobtainable except at necropsy. Furthermore, the chronic fibrotic pneumonia associated with cardiospasm may continue to develop even after treatment has relieved the difficulty in swallowing, in much the same way as a silicotic lesion may progress although exposure to dust has ceased

Cardiospasm can result in overflow changes in the lung long before the œsophagus itself can be seen projecting beyond the mediastinum: and even those aware of this may mistake the fluid level seen in the postero-anterior view for an intervertebral space. Occasionally, the pulmonary symptoms predominate, and the underlying cause may only be recognised by a diagnostic tour-de-force. Every patient with an unexplained patch or patches of mid-zone consolidation, or repeated attacks of pneumonia, should be examined with a barium swallow to exclude an œsophageal abnormality.

COLOUR-VISION

THE latest number of the *British Medical Bulletin*[1] deals with the physiology of vision; and the fact that at least half the papers have some bearing on colour-vision suggests that we should now consider how our theories must be modified in the light of recent work. The present generation of physiologists, like many before them, have, by and large, been brought up on Thomas Young's trichromatic theory, as modified by Helmholtz. This theory has been under attack from one side or another almost continually since 1859, when Helmholtz first accepted Young's suggestion that human colour-vision could be explained by three retinal mechanisms, showing maximum sensitivity to the red, green, and blue parts of the spectrum respectively. Young thought that these mechanisms were nerves, while Helmholtz supposed that they were three types of cone. The trichromatic theory was based on the facts of colour mixing and on what was then known of defective colour-vision. It did not explain the phenomenon of simultaneous contrast, nor does it cover the types of colour blindness more recently discovered, known as anomalous trichromatism and cone monochromatism. Moreover, the blue insensitivity of the fovea and some of the characteristics of peripheral colour-vision are not easily fitted into the framework of the theory.

In spite of these difficulties, the main facts which the Young-Helmholtz theory was originally formulated to explain have, for the most part, been confirmed, and much work in recent years has been directed towards discovering the spectral sensitivity curves of the three retinal mechanisms—the fundamental sensation response curves. This is by no means an easy task, for each curve overlaps at least one of the others—in other words, each mechanism involves sensitivity to a larger part of the spectrum than is suggested by "red," "green," and "blue." A possible way of disentangling these curves is to reduce the sensitivity of one mechanism by adapting or fatiguing it, by prolonged exposure to a suitable colour, before measuring the total spectral sensitivity of the eye. In this volume of the *Bulletin* Stiles describes two investigations based on this idea. The two methods used, one due to Wright and the other to Stiles himself, gave similar but not identical results; both suggested that under most conditions three mechanisms, with maximal sensitivities in the red, green, and blue, are in fact the foundation of human foveal colour-vision. A similar conclusion is reached by Thomson, in his paper on small-field experiments, as a result of his own work, and that of Stiles and Crawford, on the spectral sensitivity of the fovea when very small test-fields are used. In addition Weale, discussing colour-vision in the peripheral retina, gives evidence for three such mechanisms at the periphery. This paper is also important for Weale's demonstration that, so long as the peripheral retina is light-adapted, it is not so colour blind as many people think, although hue discrimination is not as good as in the fovea.

On another page of the *Bulletin*, Wright sets out the modern ideas on defective colour-vision. Helmholtz believed that the three types of dichromatic defect known as protanopia, deuteranopia, and tritanopia were the results of failure of the red, green, and blue mechanisms respectively; and, on the whole, recent work confirms this view. Protanopia seems to be due to inactivity of the red mechanism, deuteranopia to linking of the red and green mechanisms so that they act as one, and tritanopia to inactivity of the blue mechanism or to its linkage with the green one.

Simultaneous contrast is the phenomenon whereby a coloured surface affects the appearance of a neutral surround so that it becomes tinged with the complementary colour. This has always been difficult to explain on any theory of colour-vision based solely on different spectral sensitivities of visual end-organs. A clue has, however, been provided by recent work on the nervous reactions of the retina, measured by studying changes of electrical potential in single optic nerve-fibres in animals; and Rushton gives a short survey of some of these results. It has been found that, while stimulation of a small area of the retina produces excitation in an optic nerve-fibre coming from it, simultaneous stimulation of the surrounding area inhibits the discharge from the centre. Such experiments have so far only been made with white light, but if, for example, a red light were to inhibit the response of neighbouring retinal areas to red, we might expect the simultaneous stimulation of these areas by white light to produce a preferential response to the complementary colour—in other words, a green sensation would be produced.

The present position of colour-vision theory seems, then, to confirm the broad outline of the Young-Helmholtz theory to a remarkable extent, although, of course, many new results have been reported. It would be quite wrong to look on all recent research as simply revolving round a theory formulated nearly a hundred years ago. Many of the findings discussed in these papers were undreamed of in Helmholtz's day. Some, such as the nervous interaction within the retina, can probably explain phenomena which have always been impossible to fit into the classical theory. Others, such as anomalous trichromatism are still entirely unexplained. The Young-Helmholtz theory is incomplete, but so far as it goes it remains satisfactory.

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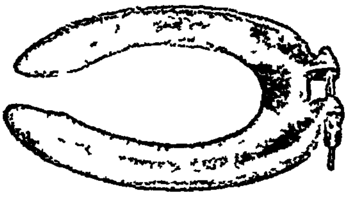
[1] *Brit. med. Bull.* 1953, 9, no. 1.

THE GAP SEAT

SIR,—What proportion of women in this country, what proportion of general practitioners, and what proportion of gynæcologists realise that 13% of hospital gynæcological patients and 11% of private gynæcological patients in the London area are afflicted with *Trichomonas vaginalis*? These figures are exceeded by those for cities in other countries, especially in the U S A where, according to Trussell[1] there are 10,000,000 women affected

In 1936 I first saw the small organism with its single cell, the size of a pus cell, and its four flagella, and since then—except for the war years—I have seen 200 new infections each year amongst my gynæcological cases By 1946 my interest in this complaint had been increased by the unhappiness of infected women in the Forces who had to attend venereal disease clinics for the treatment of this infection Those who now know this infection realise how often it can cause chronic ill health and unhappiness in women, how often the husband is condemned by his wife as the cause of the infection, and how often the disease proves extremely difficult to cure

The main cause of *T vaginalis* infection is the ordinary lavatory seat The trichomonas can live on a wet swab for days, if kept warm and moist On the inner front lip of a lavatory seat, it need not live so long to infect subsequent users The medical officer of health of a Central London Borough has investigated the frequency with which lavatory seats in public conveniences for women are used He found that in peak hours a toilet seat was used by 30 women an hour in one area and by 60 women an hour in another area The watery leucorrhœa and the slightly increased frequency of micturition will readily allow infected discharge to be deposited on the inner front lip of the ordinary lavatory seat, with risk of infection to several subsequent users



Many cases first report for treatment shortly after their return from a summer seaside resort where they stayed in crowded boarding-houses

Prevention, therefore, lies in the mass adoption, and even the exclusive use, of the gap seat, particularly in girls' schools, railway stations, women's institutions, and where infection is most likely to be present, as in the lavatories for female hospital patients, both inpatients and outpatients

The infection is not derived from *T hominis* infection of the bowel *It is only venereal in possibly 15%* of cases It can be acquired in the lavatories of swimming-pools, but not in the pools or in baths themselves

A rapid reduction of 80% in the prevalence of this depressing disease awaits the general supply of the gap seat This will save several thousands of women in this country from weeks, months, or years of illness, and it will in time benefit the health and happiness of the nation In England and Wales in 1952 there were 314,843 new gynæcological outpatients If the London figure of 13% of trichomonas infections in outpatients is an average for the country, then there were 41,000 new cases last year

Your readers may agree with what I have said, and they may admit that the conclusions are obvious, and readily put into practice But let them visit any sanitary engineers' showrooms, and they will have great difficulty in finding one gap seat for every forty on display

My question as to what proportion of the female public know of this complaint is possibly answered by the sophisticated women of the Central London area I mentioned, for over half of them do not use the lid seat, they wisely raise the seat and squat over the toilet without touching it

Active interest on the part of the general practitioners and specialists in women's diseases would greatly aid medical officers of health in forcing through this much needed reform to introduce the non-infecting lavatory seat London will be crowded with visitors this summer, and action is needed now

London, W 1 W McKIM H McCULLAGH

COMPLICATION OF CAUDAL BLOCK

SIR,—The following case is of interest as it illustrates (1) the development of high spinal analgesia from a caudal block despite precautions to prevent it, (2) unconsciousness with complete arrest of spontaneous respiration for $1^1/_4$ hours without circulatory failure, and (3) the efficacy of Sylvester's method of artificial respiration, by which such good pulmonary ventilation was obtained that semiconsciousness was restored before the resumption of normal respiration

An African woman, aged about 26 years, admitted for dilatation and curettage on Feb 18, 1953, was anæsthetised with a caudal block Cerebrospinal fluid escaped on introducing the needle, this was withdrawn until no fluid could be aspirated, and 5 ml of 1% xylocaine with adrenaline was slowly injected After a lapse of 10 minutes the patient could flex both knees and move her toes A further 55 ml was then slowly injected with repeated aspirations to ensure that the needle had not re-entered the theca vertebralis The patient's condition remained apparently satisfactory, but a few minutes later she became unconscious and stopped breathing

The patient was placed on the floor and artificial respiration was performed by Schäfer's method Oxygen, nikethamide, and strychnine were administered The colour of the tongue was fair, but the volume of the pulse remained poor After 65 minutes the pulse became more feeble and could no longer be counted The patient was then turned over and artificial respiration applied by Sylvester's method The improvement in pulmonary circulation was striking, both from the sound produced by the air entering and leaving the lungs and from the improvement in the colour of the tongue

After 10 minutes the patient began to struggle but did not start breathing for a further 30 seconds or more Subsequent recovery was rapid Analgesia of the legs was still present when consciousness had become fully restored, though she could move her legs There were no after effects

C.A S T Hospital, Akwatia,
Gold Coast S V HUMPHRIES

FREQUENT ATTACKS OF CARDIAC ASTHMA

SIR,—The occurrence of as many as 67 attacks of cardiac asthma in one patient with hypertensive left-ventricular failure has not so far been recorded An account of this case may therefore be of interest

Mrs A, aged 75, was first seen in November, 1949, complaining of pain in her right knee Considerable hypertension was found—260/160 mm Hg The apex beat was displaced downwards and outwards The rhythm was normal, and there was no evidence of incipient heart failure The patient's activity was limited by old monarticular rheumatoid arthritis of the right knee, which was indeed the only other abnormal finding

In March, 1950 she complained of pain down both arms, not related to exercise, of dyspnœa on exertion, and of feeling weak and tired Her blood pressure was 240/140 Bed rest was ordered, and she was given digitalis and phenobarbitone (gr $^1/_2$ t d s) By the end of March it was clear that her left ventricle was failing and by April 19 her blood pressure was 190/120

She had her first attack of cardiac asthma in April, and subsequent attacks were distributed as follows

1950	*April*	*May*	*June*	*July*	*Aug*	*Sept*	*Oct*	*Nov*	*Dec*
No of attacks	1	10	5	7	1	3	3	10	5

1951	*Jan*	*Feb*	*March*	*April*	*May*
No of attacks	2	5	6	4	5

The patient died suddenly in the 67th attack The attacks themselves were typical, but in the first 24 white frothy sputum was expectorated in the latter part of the attack, while in the remaining 43 the pink frothy sputum of acute pulmonary œdema was produced

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[1] Trussell R E Trichomonas Vaginalis and Trichomoniasis Oxford 1948 p 154

Johannesburg, who has soft music playing while he does his plastic operations. But I find it amazing that surgeons who are quite content to work in private nursing-homes with a sister and a couple of runners have to put up in their hospital work with about eight nervous houris fluttering round the theatre. Matrons tell us that it is essential for nurses to have theatre training. Since only a few nurses are likely to gravitate to theatre duty, it should be possible to organise their training without disorganising theatres.

SITTING DOWN

But the greatest need is for the surgeon to be relaxed whilst operating. It was in Rome while watching Professor Valdoni that I first realised the importance of sitting down to operate. He told me he could never persuade his London friends to see that if they sat down they could add five years to their lives. They merely laughed. And yet there is scarcely an operation I can think of which cannot be done better with the surgeon sitting down. The ordinary theatre stool does not readily lend itself to a seated position for the surgeon. One day, perhaps, surgical manufacturers will get round to improving them. The one Valdoni uses has a powerful spring for the pedestal portion, so that it accommodates itself somewhat to movement. It is an interesting comment that I had to pay heavy customs duty on two stools from Italy, though no duties are levied on surgical goods in South Africa. The customs authorities took the view that if I had brought in an operating-table I should not have had to pay, because it was for the use of the patient, but a stool only served the purpose of the surgeon.

ABDOMINAL OPERATIONS

In abdominal operations certain adjustments must be made if the surgeon is to operate in comfort and with ease in the sitting position. But, having made them, he will never go back to a stance calculated to bring on metatarsalgia, varicose veins, and an aching back. And if his colleagues seeing him seated become facetious and ask solicitously whether he is cracking up, the correct reply is dignified silence. In no time at all they will be imitating him.

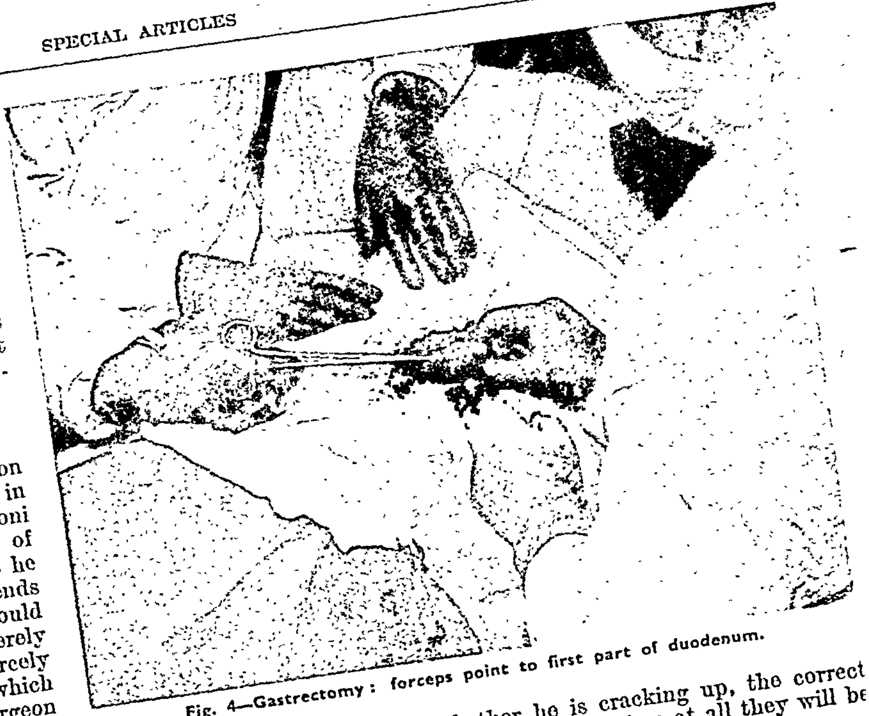

Fig. 4—Gastrectomy: forceps point to first part of duodenum.

I owe to my anæsthetist colleague, Dr. N. C. Smiedt the various suggestions which have made abdomin operations so much less stressful for me. He has adapte the Cole-Rous position (Rous 1947) in the followi manner for upper abdominal operations. With t patient lying on her back, a sandbag 18 in. long and about 6 in. wide and deep is placed under the right side of the thorax so that the torso is tilted to the left, while leaving the pelvis flat on the table (fig. 1). The right arm is brought over so that it hangs over the left shoulder, and the face is turned to the left (fig. 2). The patient lies as close to the left side of the table as possible, and the table is tilted slightly laterally. The surgeon sits on the left side. A cholecystectomy or a gastrectomy performed in this position becomes vastly simplified. In cholecystectomy the gall-bladder, even in difficult circumstances, is comfortably handled, and (more important) the common bile-duct is nicely accessible (fig. 3). If the dissection of the gall-bladder from its bed is begun at the fundus and the plane of cleavage is decently established, the surgeon, holding the gall-bladder in his hand, can advance towards cystic duct and artery in perfect ease and safety. I am aware that a tradition exists which condemns the method of proceeding from above as being almost as unsporting as tickling trout. Nevertheless by this method nothing is cut which does not go towards the gall-bladder, and so there can be no injured ducts.

In gastrectomy the duodenum comes forward admirably (fig. 4), and the surgeon sits with his hands in the correct position to close its cut end. The most difficult case becomes easy. Tying the left gastric artery is enormously simplified. Scarcely ever are retractors called for in either operation.

In operations on the descending colon and rectum the surgeon sits on the left and the patient is laterally tilted this time without the use of sand-bags.

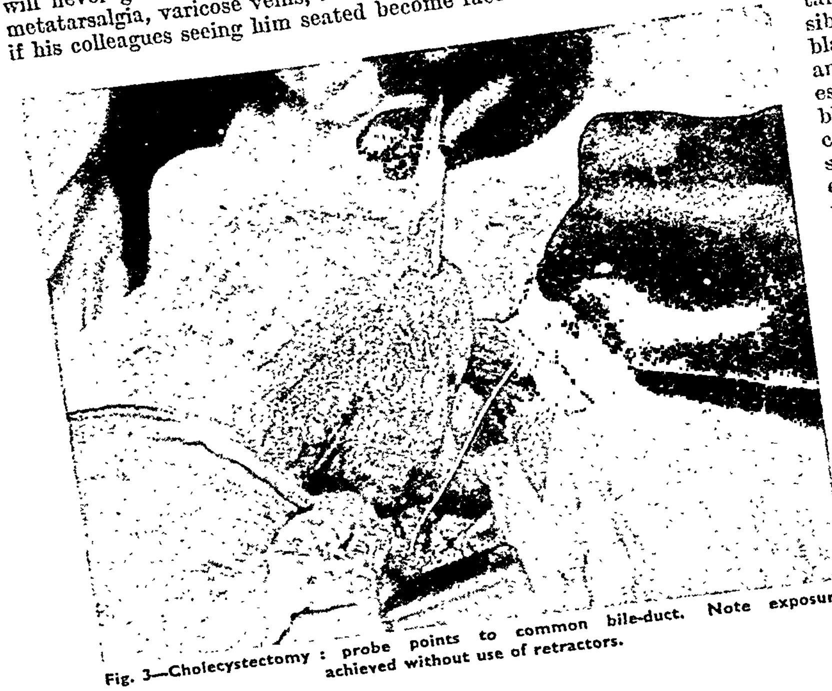

Fig. 3—Cholecystectomy: probe points to common bile-duct. Note exposure achieved without use of retractors.

in the left axilla and left and right supraclavicular regions. There was radiographic evidence of metastases in the greater trochanter of the right femur and in the sacrum.

Drill biopsy showed spheroidal cell carcinoma involving the breast, left axilla, and supraclavicular nodes.

CASE 2.—A woman, aged 44, with carcinoma of the cervix, had 6 months previously undergone Wertheim's hysterectomy after preliminary radium therapy. At operation bilateral iliac lymph-node involvement was found. This was followed by X-ray treatment to the pelvis. When selected for A.C.T.H. treatment the patient was complaining of pain in the right loin and back and had a hard irregular liver edge palpable 6 cm. below the right costal margin.

Microscopic examination of the operation specimen showed epidermoid carcinoma of the cervix, Broder's grade III.

CASE 3.—A woman, aged 56, with bilateral ovarian carcinoma, had 6 months previously undergone subtotal hysterectomy and bilateral salpingo-oöphorectomy. Extensive involvement of the peritoneum and omentum had been found with metastatic nodules in the liver. When selected for A.C.T.H. treatment the patient had a mass in the vaginal vault and diffuse involvement of the abdominal wall in the region of the operation scar. Palpable nodes were present in the left supraclavicular region and both groins. The liver was enlarged, the edge coming down to the umbilicus.

Microscopic examination of the operation specimen showed ovarian cystadenocarcinoma.

In these cases A.C.T.H., although it caused the usual eosinophil response and gave rise to no toxic effects, had no significant action on the malignant disease.

In case 1 the patient showed pronounced euphoria, and early in treatment she had far less pain in her leg; after the intravenous therapy was discontinued she could walk about the ward in contrast to her bedridden state on admission. The other 2 patients showed no such objective improvement. Case 2 continued a rapid and miserable decline, and the patient died deeply jaundiced 10 days after the intravenous A.C.T.H. was discontinued.

These 3 cases were far advanced and no general conclusions can be drawn with certainty from this very limited experience. We feel, however, that further clinical trial on similar lines is not at present justifiable.

Bristol. W. G. MACGREGOR.
Oxford. CHARLES L. LEWIS.

CHLORIDE DEPLETION IN INFLUENZA

SIR,—In the current influenza epidemic, one of the most constant findings in our patients has been prolonged and severe sweating, irrespective of the height of the initial pyrexia. Some patients described rivulets of sweat trickling down the skin.

The resultant loss of fluid and chlorides was, in one case, probably the cause of cramp of the abdominal muscles, simulating an "acute abdomen."

I was called to a man, aged 45, late one evening. He had agonising abdominal pain, causing him to writhe about his bed. He had been unwell for two days, but had tried to carry on with his work. His main complaints had been excessive sweating and general malaise. His daughter was recovering from influenza.

He was pale with sunken eyes, and he was in a cold sweat. His temperature and pulse-rate were subnormal. The blood-pressure was 110/75 mm. Hg. His tongue was dry and furred. The abdominal muscles were rigid, and there was slight tenderness in the epigastrium. The heart and lungs were normal. While I was with him, he had an attack of abdominal pain which doubled him up, lasting about three or four minutes and ending in vomiting.

Approximately 4 g. of salt in orange juice was given slowly by mouth and retained. A specimen of urine showed specific gravity 1028 and chlorides 1·6 g. per litre, indicating salt depletion.

He subsequently had no further attacks of pain, and made an uneventful recovery.

Although one cannot categorically assign the cause of the pain to the salt depletion alone, it is likely, on probabilities, that it was the rapidity of the fall in the plasma-chloride level coupled with the evident dehydration that precipitated the crisis. I consider the case worth recording in view of the uncommon complication in a common ailment.

It is interesting to speculate on the clinical similarity between postinfluenzal depression and moderate salt depletion. One recalls the loss of appetite, mental apathy, and muscular weakness of servicemen suffering from heat exhaustion in the tropics, and the response to the administration of salt.

The poor appetite which occurs regularly after a bad attack of influenza is what might be termed epicurean. The "choosiness" is a desire for savouries rather than sweets, the inference being that the salt content of the former is temporarily more in demand by the body fluids.

The routine administration of Dover's powder with aspirin to get a "good sweat" is, on this hypothesis, sound treatment only if the chlorides lost in this way are subsequently replaced by the oral administration of salt.

Shap, Westmorland. L. E. WEAR.

SEDATIVES IN THE PREPARALYTIC STAGE OF POLIOMYELITIS

SIR,—In a large epidemic of poliomyelitis in the Brunswick area (500 cases, of which 115 were admitted to our hospital) we administered sedatives to all children in the preparalytic stage in order to intensify the physical rest which is so important then. An initial dose of 0·4–1 ml. of 'Somnifaine' (Roche), according to age, was given intramuscularly, and oral administration was continued for some days to ensure continuous sleep, though the children could be roused. Of 39 children thus treated 4 developed paralysis, while of 26 untreated children 5 developed paralysis—i.e., about 1 in 10 of the treated, but 1 in 5 of the untreated. In a further 23 cases with paralysis on admission which were treated in the same way the paralysis did not develop to such an extent as in an equal control group.

The suggestion is that sedative therapy (*Schlaftherapie*) will probably prove successful, though the present figures are too small for a decision. The following clinical and experimental facts indicate the rationale of sedative treatment in poliomyelitis.

1. Russell[1] and Horstmann, who compared two large groups, showed that the risk of paralysis is some 140% greater if the patient does not rest completely after the onset of preparalytic symptoms.

2. According to Bodian[2] a "hovering state" exists (Sabin calls it an "armed truce") in the relationship between the virus and the cell, and in our opinion it is still possible during this time to stop the chromatolytic destruction of the anterior horn cell.

3. Under normal conditions every muscular action uses up a certain amount of cytoplasm in the anterior horn cell (proteins and ribosenucleotides). Growing like a parasite the virus also uses up the same substances in the cells. Thus it is evident that an anterior horn cell invaded by a virus and also functioning through muscular action is likely to be destroyed quickly and irreparably.

4. Trauma, vaccinations, painful peripheral contractions and selective action of groups of muscles modify the physiological condition of the spinal cord and locally increase the vulnerability of the nerve cells connected with the "traumatised" area.[1 3-5]

5. Each anterior horn cell is connected with a variable number of muscle fibres—a few only in the case of small muscles (5 to 6 in the external rectus), but many in the case of large muscles (120–160 in the gluteus), and therefore the intracellular metabolism is higher in those cells which supply

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1. Russell, W. R. *Brit. med. J.* 1947, ii, 1023; *Ibid*, 1949, i, 465; Second International Poliomyelitis Conference, Copenhagen, 1951; *Edinb. med. J.* 1952, 59, 530.
2. Bodian, D. Second International Poliomyelitis Conference, Copenhagen, 1951.
3. Fanconi, G., Zellweger, H., Botsztejn, A. Die Poliomyelitis und ihre Grenzgebiete. Basle, 1945.
4. Pette, H. Die akut-entzündlichen Erkrankungen des Nervensystems. Leipzig, 1942.
5. Bradford Hill, A. Second International Poliomyelitis Conference, Copenhagen, 1951.

greater good of the health of the people can and should be exported. But the social scientist can advise on the rate and the form in which these ideas can be most effectively introduced.

Place of the Social Scientist in Medical Training

"Medicine is an aspect of social policy," said Dr. J. H. F. **Brotherston** (lecturer in public health, London School of Hygiene and Tropical Medicine); and he too regretted that science has almost captured medical training. He thought the time has come to strike a fresh balance, but he was anxious not to suggest that the doctor's training is poorly organised or planned. Indeed he believed the quality of medical education and the professional stamina of doctors to be good. But he suggested that the organisation of medical practice has fallen behind the development of the medical sciences. The black-bag era of medicine ended long ago and now the care of the patient is isolated into compartments with a poor system of inter-communication. He was sure that a long overdue reform is to bring those looking after the patient closer together. But his most important criticism of the general practitioner's training was that it does not prepare him for conditions of practice outside hospital.

Clinical science is so complex that the bulk of medical training must remain in the laboratory and at the hospital bedside, but Dr. Brotherston sees the solution of this dilemma in the fact that the hospital is a community institution

> ". . . in no way separated from the outside world or from the rest of the system of medical care. If the sense of community interest permeates the hospital teaching of the student, and if the place of the hospital can be kept in perspective for him while in hospital, the importance of the function of providing medical care outside the hospital will be much more apparent to him that it sometimes is at present."

One way of achieving this, Dr. Brotherston suggested, is to lay more importance on the teaching of social medicine. Such teaching techniques as the case conference, he thinks, are useful in diverting the student's attention from the hospital to real life, but they are not the whole answer. At present, though the student is trained to think scientifically about his clinical problems, no effort is made to teach him to look with scientific detachment at the social situation in which he must practise. Communication between doctor and patient is another skill which in Dr. Brotherston's opinion is neglected in the curriculum. More emphasis should be put on the empirical art of dealing with the patient as a person as opposed to the science of studying his disease processes.

The student should also be taught the history of medicine in such a way as to make him appreciate the changing rôle of the doctor. A knowledge of the terms of service of his profession in the past would help him to look objectively at the developments of the future. Indeed, Dr. Brotherston found that the medical profession is haunted by lingering loyalties to arrangements developed to deal with situations that no longer exist. For instance we have barely managed to re-equip and reorganise our hospitals as diagnostic and treatment centres, though it is more than two generations since they ceased to be mere refuges for the pauper infirm. In this process of centralising expensive equipment and skill the hospital has acquired a life of its own, and now we fail to recognise that it is after all only a convenient means of centralising certain resources of the community. As a result, we have failed to expedite the possibilities which improved housing offers of delegating back to the home some of the residential functions of the hospital. But medical sociology can only be diffused through the doctor's training with the guidance of the sociologists, and Dr. Brotherston asked their help in collecting a body of knowledge of the social sciences and in translating it into terms appropriate for the medical student.

Hospital Organisation under N.H.S.

Mr. T. E. **Chester**, dr. jur. (acting director, Acton Society Trust) thought this part of the service improved both in quantity and quality, especially in neglected provincial areas. Some of the problems of today, such as the lack of accommodation for the mentally sick, are legacies from the past, but others have arisen during the change-over to the N.H.S. Apart from transient growing pains they fall into two groups. The first group are due to environmental factors which though not inherent in the organisation have shaped its development. Thus the under-budgeting of the first year led to a hasty tightening of central control, and continuous economic difficulties to the imposition of an arbitrary ceiling. Again shortage of staff is general in industry and is due to full employment rather than to the N.H.S. Into the second group Dr. Chester gathered the real problems inherent in the service itself. Some centres on institutional framework—such as the best size for the different administrative units, the hospital, the hospital management committee, and the region. Some problems, centred on the relation between the different levels of the organisations, raise such points as centralisation versus decentralisation, specialisation versus coördination, and flexibility versus uniformity. Other important problems centre on staffing—especially on the quality of the paid administrator and of the 10,000 voluntary committee members on whose joint ability the success of the N.H.S. ultimately depends.

Social Needs and Costs

Mr. R. M. **Titmuss** (professor of social administration, University of London) recalled that the economic attack on the social services on grounds of lavishness and undue rapidity has grown during the last few years, and successive governments have limited expenditure. Critics seem generally agreed that the main cuts should fall on the N.H.S., and, within the N.H.S., in the hospital sector. Beneath the debate on the cost of the social services seems to be the assumption that they are concessions extracted from one class for the benefit of another, but this point of view takes little account of the social changes of the past century.

> "We find ourselves still heavily weighed down by thoughts of benefactions and beneficiaries: still dependent on outworn notions of what constitutes a social service 'need'; still regarding these services as ends rather than means; still attaching to them a supernumerary and separate rôle in the social system . . . we have not yet developed an adequate theoretical framework within which the dynamic rôle of the social services can find a balanced appraisal as an integral part of the total performance of the social system."

It is not easy to think clearly about social services, Professor Titmuss pointed out, when we are not even sure what a social service is. It seems almost accidental whether a particular need when met is regarded as a social service. Juvenile crime, for instance, is met by a social service, but not adult crime; family allowances are a social service but not child allowances as remission of tax. In the midst of this confusion attempts to compare the costs of the social services today with those before the late war are unrealistic.

In a modern community the needs of the poorer sections of the population are met by the "redistributive" social services, while similar provision in the sense of transfer payments in favour of dependent groups among the better-off sections are not always so classified, though they may cost the public dear. There is thus confusion of thought and practice over the social costs arising from the needs of childhood, old age, and ill health. The social services also meet the concealed "disservices" of our modern world, caused by such things as premature retirement from work, reduced earning-power, and deterioration in skill. Despite these growing if hidden burdens, the total of hospital beds, for instance, in relation to the population was smaller than accommodation in doctors' premises under the National Health Service, how many had been inspected by executive councils, and how many had been declared unsuitable —Miss HORNSBY SMITH replied The relevant regulation is paragraph 7 (4) and (5) of part I of the first schedule to Statutory Instruments 1948, no 506 The Minister has no details of inspections by executive councils, he is, however, hoping shortly to discuss the best way of securing an improvement, where necessary, in the condition and equipment of general practitioners' surgeries and waiting rooms with representatives of the medical profession

Mr ARTHUR BLENKINSOP Will the Minister agree that the attention of the executive councils might well be drawn *to this matter, especially in view of the considerable sums of* back pay recently awarded to the medical profession, and that this may be one of the most desirable ways of utilising at least some of that money ? Miss HORNSBY SMITH I think that we should await the outcome of the discussions which are pending

Capital Allocations to Hospitals

Mr KENNETH ROBINSON asked the Minister what special capital allocation he was making for the coming financial year to meet the needs of the mental hospitals —Mr MACLEOD replied It is for regional hospital boards to decide what particular projects shall be included in their capital programmes, but I have again asked them to devote at least 20% of their allocations to mental health projects In addition, two major mental health schemes are being financed from a special central reserve Of course this is probably the most serious problem facing the National Health Service, and it is precisely for that reason that I insisted upon the minimum figure I have given The position would have been a great deal easier if, in the first year or two of the health service, a larger proportion of resources had been devoted to the mental field

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Public Health

Smallpox

BY March 27 the number of confirmed cases of smallpox in the outbreak in Lancashire and the West Riding had risen to 16 including 11 at Todmorden, 2 at Bacup, and 2 at Bury There have been no more deaths since the second one on March 20 In Todmorden 2 general practitioners and a number of their patients have been placed in quarantine Dr J Lyons, medical officer of health for Todmorden, said that it was too early to say that they had beaten the outbreak, but they had localised it[1]

Replying to a question in the House of Commons, Mr Iain Macleod, the Minister of Health, said that the outbreak started among workers at a spinning mill at Todmorden who handle imported raw cotton It seemed possible that the cotton was the source of infection There was no evidence from previous experience that the disease could be spread by cotton except in its raw state, or as cotton waste None of the recent cases had occurred outside the range of known contacts with the original cases The Minister added that he had asked the Medical Research Council to investigate the highly technical and difficult question of the transmission of smallpox by raw cotton Replying to supplementary questions, he said that there had been some delay in diagnosing the first case, but this was not surprising, because, happily, doctors in this country saw virtually *no smallpox* There was not the slightest danger of infection being spread by cotton yarn or clothing, or by any finished materials made from that particular cotton All possible steps had been taken to isolate the suspected bales of raw cotton

Influenza

In the week ended March 14 there were 139 deaths from influenza in the 160 great towns of England and Wales In the three preceding weeks deaths numbered 321, 314 and 193 So far this year there have been 2710 deaths from influenza in the great towns, compared with 393 in 1952 and 7247 in 1951 The number of claims for sickness benefit received by the Ministry of National Insurance (including Scotland) is still in excess of last year's figure, but the weekly total has been falling steadily since the week ended Feb 17

Diphtheria Prophylaxis

In a circular to local authorities and medical officers of health, the Ministry of Health says that an intensive effort must be made to achieve the level of immunisation necessary to secure the full benefit of the campaign against diphtheria The object of the campaign remains the same to secure the immunisation of not less than 75% of babies before their first birthday During the first half of 1952, however, only 31% of the estimated number of children reaching the age of one year were immunised, and though this is 3% higher than the figure calculated for 1951, it is "disturbingly low" In an illustrated brochure accompanying the circular, Sir John Charles, chief medical officer of the Ministry emphasises the importance of these figures, and calls for "a sustained effort of persuasion directed to each generation of new mothers" The brochure includes a newly designed health visitor's card and general leaflet, which will supplement the campaign conducted by press advertisements, posters, and cinema slides

Scotland in 1952

In a preliminary return for 1952 the Registrar General for Scotland[1] reports that the provisional figures for tuberculosis show a further decline in the death rates from both pulmonary and non-pulmonary disease The death-rate from all forms of tuberculosis was 0 32 per 1000 population, compared with 0 37 in 1951 and 0 66 in 1948 The birth-rate was 17 7 per 1000 population—the same figure as in 1951 The stillbirth rate —26 per 1000 total births—was 1 less than in the preceding year The infant-mortality rate of 35 per 1000 live births was 2 less than in 1951 and 9 less than the average for the previous five years This was the lowest infant-mortality rate yet recorded in Scotland.

The Delicate Child

Writing in the report of the county medical officer for the West Riding of Yorkshire, Dr C C Harvey pædiatrician to the West Riding County Council dismisses the "delicate child" as an "iatrogenic artefact"

"By the hesitancy and caution of our pronouncements, by our emphasising the wrong aspect of a situation, or by the failure of inadequate treatment, we easily confirm parents' worst fears Behind our backs they are also subjected to morbid grandparental gossip and the cryptic hints of the lady in the bus queue At our best we wage a defensive struggle against the scorn of dogmatic parents, loth to lose the glamour of abnormality and disease which they have cast over their children Symptoms grow up round a supposed defect discovered casually, such as the 'breathlessness on effort since infancy, with lips going blue on exercise' pinned upon a normal child with innocent heart murmur and full effort tolerance There was also the twelve year old boy with postural (not rheumatic) pains due to crouching permanently over a television set procured to keep his (innocent) heart murmur away from football fields My records of innocent heart murmurs still out number the rheumatic hearts If we consider the wastage of school time between 7 and 11, which is educationally irremediable, we need to review the fallacy that 'health is more important than success' Scores of children are kept off school months at a stretch, instead of half days, with 'bronchitis' I assume it is because we cannot trust ourselves to ascertain that it is non tuberculous In nearly all such cases, lengthy absence contributes nothing to health while precluding scholastic success Such children adequately handled, could usually enjoy both health and success We need to establish that normal people are entitled to certain normal pains, among which stomach ache can be a respectable diagnosis, once organic causes are fairly eliminated One Grammar School girl lost five weeks with a sick dizzy sinking feeling on rising which amounted to healthy hunger contractions "

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[1] *Times* March 27, 1953

[1] Quarterly Return of the Registrar General Scotland for the Quarter ended Dec 31, 1952 H M Stationery Office Pp 36 2s 6d

HUMAN FACTORS IN INDUSTRY

THE Department of Scientific and Industrial Research and the Medical Research Council have jointly set up two committees to work on human problems in industry One will study individual efficiency , the chairman of this committee is Sir Frederic Bartlett, F R S , its medical members are Prof Esther Killick and Prof W E Le Gros Clark, F R S , and the joint secretaries are Dr Brandon Lush and Mr Winston Rodgers The second committee, which will deal with human relations, has Mr A B Waring as chairman and Prof T Ferguson, Prof A J Lewis, and Dr A T M Wilson as medical members , the joint secretaries are Mr J R Gass and Dr Lush

BUYING FOREIGN BOOKS

LAST month a peripatetic correspondent described the formalities that had to be completed before he could pay for a book published in a foreign country[1] UNESCO, we learn, has an international scheme by which the purchaser obtains with his own currency dollar coupons which are cashed with UNESCO by publishers or booksellers in any of the countries participating in the scheme These coupons are intended to enable institutions and individuals to obtain publications in the fields of education, science, and culture , and they may be used not only for books but also for subscriptions to periodicals for copies and for membership subscriptions to learned societies provided that the subscription is mainly a means of obtaining the society's publications In the United Kingdom applications for coupons should be sent to Unesco Book Coupons, c/o Book Tokens Ltd , 14, Buckingham Palace Gardens, London, S W 1

NEW GENETICS JOURNAL

THE *Journal de Génétique Humaine*, the first journal in French on this subject, began publication about six months ago, edited by Prof A Franceschetti, of Geneva, Prof L Van Bogaert, of Antwerp and Prof Maurice Lamy, of Paris It is to be issued four times a year There are English and German summaries An unfortunate system of pagination mars the production of at least the first two numbers each of which has individual pagination, with an indication of the volume pagination on a gummed strip at the head of each strip The publishers are Médecine et Hygiène, 15, Boulevard des Philosophes, Geneva

PROVINCIAL CONVALESCENT HOMES

THE British Hospitals Contributory Schemes Association have published a directory of convalescent homes in the provinces The first issue lists 20 independent homes with details such as almoners may require given in the form used by the King's Fund convalescent homes directory The two directories are thus complementary The association have set a high standard, for although they know of ten times the number of homes they have only published details of those which have been inspected and approved by a responsible almoner A further 28 homes belonging to contributory schemes are listed but without details Copies of the directory may be had (1*s* 6*d* , post free) from the association, Royal London House, Queen Charlotte Street, Bristol, 1

University of Manchester

At recent examinations the following were successful

D P M Part II —K J R Ford, O J Slowik.

International College of Surgeons

This college will hold meetings at the University of Amsterdam on April 8 9 and 10 , at the University of Rome on June 5, 6 and 7 and at the University of Vienna on June 11, 12, and 13 Further information can be had from Dr J F Brailsford, the secretary of the British Chapter of the college, 20, Highfield Road, Edgbaston, Birmingham, 15

Board of Control

Mr H R Green, at present a commissioner of the board, has been appointed a senior commissioner in succession to Mr C I Penton, who is retiring

Manson Medal

This year the council of the Royal Society of Tropical Medicine and Hygiene have awarded the Manson medal to Prof Jerôme Rodhain director of the Institute of Tropical Medicine, Antwerp and the Chalmers medal to Mr David J Lewis entomologist in the Sudan government service

Carlisle 24960

The Carlisle Medical Bureau, which is to open on Wednesday, April 1, will enable a doctor who has to leave his house or surgery unattended to inform the operator on duty of the arrangements for the time he will be away When a patient receives no reply from his doctor's telephone he may then ring Carlisle 24960 for information and help The bureau will be staffed by operators of the fire and ambulance control

CORRIGENDUM *Smoking and Lung Cancer* —In the debate on this subject, reported in our parliamentary columns last week (p 645), Miss Patricia Hornsby Smith said that research into exhaust gases of petrol and diesel engines had not been abandoned as a possible source contributing to cancer of the lung

Dr Albert Sharman as a vice president of the International Fertility Association, representing the United Kingdom is attending the first World Fertility Congress which is to be held in New York from May 26 to 31

Births, Marriages, and Deaths

BIRTHS

MATTHEWS —On March 16, at St Helier Hospital, Carshalton, to Diana, wife of Dr H W Matthews—a daughter (Flora Elizabeth Marguerite)

Appointments

KNOWLES R R , M B Sydney registrar in psychiatry, Bristol mental hospitals

LUDLOW, JOYCE M B E , M B Lond , F R C S asst county M O in the North East Kent area

Diary of the Week

APRIL 5 TO 11

Wednesday, 8th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
3 45 P M Prof Lambert Rogers Tumours of Central Nervous System (

ROYAL SOCIETY OF Street, W 1
4 30 P M *Section* Group Captain C J S O'Malley, Kininmonth Present State of Physical Medicine in Countries of Europe

ROYAL EYE HOSPITAL St George's Circus Southwark S E 1
5 30 P M Dr A A Guild Mechanism and Appearances of Papilloedema

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place W 1
3 30 P M Dr G W J Bousfield Case for Combined Diphtheria Pertussis Prophylaxis in Young Infants

MIDLAND MEDICAL SOCIETY
8 15 P M (Dudley Road Hospital Birmingham, 18) Clinical meeting

Thursday, 9th

ROYAL SOCIETY OF MEDICINE
6 P M *Sections of Neurology and Comparative Medicine* Some Neurological Diseases of Man and Animals Dr E Weston-Hurst Dr J W Trevan Mr H B Parry Demyelinating Disorders Dr A M G Campbell Mr T W F Fay Toxoplasmosis

ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P M Brigadier J S K Boyd F R S Some Aspects of Chemotherapy in Tropical Medicine

ALFRED ADLER MEDICAL SOCIETY
8 P M (11, Chandos Street W 1) Dr Walter Schindler Group Psychology

Friday, 10th

ROYAL SOCIETY OF MEDICINE
5 30 P M *Section of Anaesthetics* Dr W W Mushin Dr J Rendell Baker Are Anaesthetic Records Worth Keeping ?

ROYAL EYE HOSPITAL
1 30 P M Mr A J Cameron Ophthalmic Aspects of Hypertension and its Treatment

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY, Whipps Cross Hospital E 11
8 30 P M Prof S P Bedson, F R S Recent Trends in Virus Research

Saturday, 11th

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
10 30 A M (Benenden Sanatorium Benenden Kent) Clinical meeting

SOUTH WEST LARYNGOLOGICAL ASSOCIATION
2 30 P M (Portsmouth Eye and Ear Hospital Grove Road North Southsea Hants) Mr Seymour Jones Mr Robert Morley Clinical demonstration

BIOCHEMICAL SOCIETY
9 A M (Faculty of Medicine University of Brussels) Scientific papers

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[1] *Lancet*, March 14, 1953, p 544

pational risk" involved in this perennial professional cul-de-sac. Reading the newspapers, we can see for ourselves that *this job nowadays* carries with it a high degree of legal responsibility. Assuming that some recent judgments have *created* legal precedent, it is a matter for small wonder that applicants for these posts are much too scarce. Absence of prospects plus a risk of *litigation* are hardly inducements. Hence the casualty-officer situation approaches a *crisis*; indeed the crisis has already been reached in some hospitals.

(2) *Registrars*

Now, by official confirmation, the registrar's is another "dead-end" job. A management committee recently protested that the quality of applicants for these posts would inevitably decline because of the denial of advancement to senior-registrar grade save to teaching-hospital registrars. The regional board replied, in effect, that it was not true that only teaching-hospital men would get senior registrarships—it was simply that preference would be given to these men. One may permissibly make the analogy: "coloured applicants are not barred, but it is preferable to be white-skinned." Now, in the midst of our senior-registrar troubles, an advertisement for a senior thoracic registrar specifically invites overseas applicants. One wonders if this is not a novel approach to mitigating the shortage of consultant establishments.

(3) *House-officers*

The chief problem here is surely the disparity between the "attractive" posts where applications are adequate, and the "Cinderella" posts where applications are too few and the hospitals involved are in consequence chronically understaffed. At the one extreme we have the teaching-hospital houseman (commonly with only 12 beds plus "odd-job" duties), and at the other the overworked houseman in the ex-municipal hospital who is too busy to learn, even were modest teaching facilities available. It is surely high time to face the fact that many housemen are getting little but general debility out of their appointments.

We cannot afford to wait for a major crisis *to force* on us a solution to problems which would long have been settled by a modicum of foresight and simple respect and humane consideration for the people involved. One has only to witness the pathetic insecurity of our senior registrars to realise that no-one in power has even bothered to notice that they have homes, wives, and children—let alone that they are *good* specialists with higher degrees, hard-earned for nothing.

London, N.W.3. A. GEE.

OSTEOPATHY

SIR,—I am afraid that Dr. Cyriax misquoted me in his letter (March 21). I know that manipulation is being taught by him, but I still maintain that specific, controlled, and accurate manipulation of vertebral joints is adequately taught only in osteopathic schools. I am fully aware that Dr. Cyriax is making a determined effort to teach manipulation to physiotherapists; but he states in his book *Rheumatism and Soft Tissue Injuries* (p. 392) that in his experience it takes only an hour a week for six of the thirty months of a student's training to impart a good grounding in remedial manual methods. It is my opinion that this is quite *inadequate training.* The properly qualified osteopath spends two years at anatomy, physiology, and basic sciences, then *two further years* in full-time training in the art of manipulation—not just a few hours. Even then he is but at the beginning of acquiring an accurate tissue sense, which is essential to successful manipulation.

When the physiotherapists are prepared to spend two extra years at this work, and when the teaching is on standard osteopathic lines, then I shall be willing to support Dr. Cyriax in his aim at replacing the lay manipulator by the physiotherapist. I consider that until then the physiotherapist-manipulator is as dangerous as the unqualified osteopath.

London, W.1. ALAN STODDARD.

SIR,—One wonders why the word osteopathy is used in connection with the discussion between Dr. Stoddard and Dr. Cyriax since it bears no relationship to the osteopathic theory of health and disease. Dr. Stoddard's point that osteopathic manipulative technique is useful in manipulative surgery is purely incidental to osteopathy, and Dr. Cyriax's physiotherapy students will be taught minor manipulative surgery and not osteopathy.

OSTEOPATH.

CHILD-WELFARE CLINICS

SIR,—I would like to reply to some of the criticisms of the suggestions I made in your issue of Jan. 24.

I agree that the service described by Dr. Lawson (Feb. 7) and provided by Dr. Charlotte Naish (Feb. 7) is an ideal to be striven for, but even such an ideal service would be greatly enhanced by close *integration* between the general practitioner and the health visitor. Far from wishing to "throw it overboard" the aim of my proposals was to assist a greater proportion of G.P.s to give a comprehensive child-health service—a useful start to the process of returning the responsibility for child health to the family doctor.

The present division of services between G.P.s and clinics is generally agreed to be unsatisfactory, but Dr. Gordon (Feb. 21) is prepared to envisage its continuation "until such time as most family doctors are interested in health education and have suitable premises for this work (such as may be provided in health centres)." One possible result of the continuation of this policy would be the discontinuation of centres by local authorities who are seeking to curb their expenditure, as suggested by Dr. Barrow (Jan. 31). Such action is rightly deplored by Dr. Gordon, and it was with a view to bridging the gap until the emergence of health centres that my proposals were made. Admittedly, many child-welfare centres today are in unsatisfactory premises, *but surely the essential need is for the close integration of preventive and curative services.* The buildings will follow.

Dr. Barrow suggests that I have overlooked the time factor. The additional capitation fee for children would be some compensation for the reduction that a G.P. would have to make in his list in order to find the necessary time to *give the children the attention* they deserve. If he is overworked and has not the time to spare, it is unreasonable to expect a doctor to be able to give adequate midwifery and child-health services. There seems to me to be no fundamental reason why general practitioners should not be encouraged to develop their interest in one particular branch of medicine in addition to their general services—they would still be family doctors, responsible for the health of their *patients. In any group of 4–8 practitioners one* could usefully be a G.P. and a pædiatrician and/or obstetrician; but I cannot agree with Dr. Naish that this would not be feasible except in small market towns. I believe that a multiplication of the specialties is undesirable but some degree of specialisation among groups of G.P.s would improve the standards of practice and relieve some of the pressure on *outpatient departments.*

Dr. Gordon says that it would be inappropriate to select 15 of the 70 practitioners in Ilford to look after the children. I agree, of course, but I suggest that the probability would be that he would have some difficulty in getting as many as 15 of the doctors to undertake a comprehensive preventive and curative service. Where group practices exist it would be simply a matter for the group to select one of their members to act as G.P.-pædiatrician for the group; but unless and until group practices become more generalised, these appointments would be sought by G.P.s with special interest in the health of mothers and children and willing to give the necessary time to their proper care.

Oldbury.

H. TABBUSH,
Area Medical Officer.

leading one in the health service—its freedoms or privileges relate both to the individual member of the profession and to the profession as a whole The individual doctor claims, and to a very large degree is granted, personal independence in his care of his patients, acting according to his own informed judgment and being answerable only to his own conscience Apart from a high social status and a power of influence of a degree one sometimes suspects not fully appreciated even by the profession, the privilege of the profession, as distinct from its individual members, is a very large measure of self-government Entry to the profession is controlled by the profession itself and it has power to expel or suspend a doctor from membership At the present time the profession exercises this latter power only in cases of conviction in a criminal court or of infamous professional conduct It could, if thought fit, exercise authority over its members in other respects , but, like most other professions, though perhaps to a somewhat greater extent, it has been reluctant to do so The assumption of greater responsibility for the conduct of its weaker members, when that conduct is detrimental to patients, seems to me to demand serious attention by the profession, not only in the interests of the public but as the profession's surest defence of the freedoms which it prizes

It is not an immutable law of Nature that the profession of medicine, any more than any other profession, should have the privileges it now enjoys These privileges exist by consent of the public, being grounded on the public's respect and confidence, and in its belief, born of experience, that its needs are better met by allowing these freedoms As with academic freedom so with the professional freedoms, they exist because the public is prepared that they should, and they will continue so long as the public—if only tacitly—consents If they are not to be lost or impaired, the profession must give continuing evidence, by the way it fulfils its responsibilities, that, because it has freedom, the public good is better served

Freedom for the Incompetent ?

There is not likely to be much dispute about the general principle , where differences of opinion arise is over its application In his Croonian lectures for 1951 Dr T F Fox, in stating the case for the individual practitioner's freedom, said

> “ we need freedom to serve , we need it because it is indispensable if we are to do our work as it should be done On a short view there are often advantages in interfering with the doctor's freedom, but the public will buy these advantages very dear if it discourages any member of our profession from bringing his own judgment to his patients' problems ”

This is fair and well stated Experience has shown that for the doctor responsibly doing his best the largest possible measure of professional independence is in the best interests of his patients But what of the doctor who is not good ? The man who presumes to a competence he does not, and knows he does not, possess , the man who persistently is negligent , or the man who regularly—and regardless of the fact that he could change the conditions, if he wished—practises under conditions which render good doctoring impossible Without disputing that the numbers in these categories constitute a small proportion of the profession, the public is surely not unreasonable in looking to the profession, as a self-governing body to deal more effectively with these, its weaker members for the better protection of the public It is not a question of the occasional mistake, everyone, whether professional or not, no matter how good he may be, makes mistakes from time to time It is consistent incompetence and persistent neglect that is in question It would be wrong to think that professional action is never taken it is For instance, professional opinion has slowly led to the exclusion of doctors who have not had a long special training in surgery from the performance of all but very minor surgery, except in emergencies But it is true that like other professions, the medical profession has shown great reluctance to accept responsibility for the technical competency and efficiency of its members once they have qualified for membership

The desire to guard against heresy-hunting is sometimes put forward in justification This desire is good , but are we to understand that the profession of medicine is incapable of devising means which would distinguish between those who are incompetent and negligent and those who are honestly unorthodox ? To think so is to doubt unjustifiably its integrity and capacity for self government It is also contended that good doctors might fail to give of their best, might become timid and routine minded rather than constructive, if their standards and conduct of practice were subject to review and judgment even by their *peers*—their professional colleagues This contention is hard to accept That there should be an element of playing for safety—the safety of his patient—in every doctor's decision seems to me desirable And I have not yet been able to convince myself, despite authoritative contentions to the contrary, that medicine differs significantly from other professions in which constructive judgments also have to be made

No matter what sphere he may be in, the competent man is not deterred from doing his best by fear of criticism by his professional colleagues It is the incompetent, or the fellow who has ceased to try, who usually objects, and he is not worthy to have his objections heard Does a judge become timid and fail to do his best because his work is subject to review by higher court and his errors of judgment may be corrected in public by his senior colleagues ? Does the efficient farmer farm less efficiently because he knows that a farmer adjudged by a committee of his farming colleagues to be inefficient may be removed from his farm ? Does the pilot of a jet air-liner or the captain of a ship fail to make the best constructive judgments and to act in the most positive and effective way in face of an emergency which may threaten the lives of those in his care, because his decisions and actions may be subject to expert investigation later ? I cannot resist the feeling that the suggestion which has been made—not only by members of the profession—that medicine is exceptional from the nature of the allegedly constructive decisions which have to be made by medical practitioners, has a flaw in it, and that the medical profession in the essentials of its work is not so unique

Requirements for Entry

The reluctance of the professions to exercise more supervision over their members contrasts interestingly with their great activity in the prescribing and testing of the qualifications of new entrants Let us look at the problem of entrance requirements On training and examinations, there has been and still is a spate of reports, conferences, and “ reforms,” invariably with the result of making the training fuller and longer and the requirements more difficult It is natural and right that a profession should strive to attain the highest reasonable standard of new entrants and a course of pre-entry training that will give them the best preparation for their careers But the over drilling of the innocents should not be a substitute for a proper disciplining of the hardened troops To the public, the quality, ability, and standards of a professional man or woman *five, ten,* twenty, thirty years after qualification are more important than the knowledge and largely unproved skills of the new recruit

Entry requirements to any profession must have a reasonable regard to the actual job which the profession

leading one in the health service—its freedoms or privileges relate both to the individual member of the profession and to the profession as a whole The individual doctor claims, and to a very large degree is granted, personal independence in his care of his patients, acting according to his own informed judgment and being answerable only to his own conscience Apart from a high social status and a power of influence of a degree one sometimes suspects not fully appreciated even by the profession, the privilege of the profession, as distinct from its individual members, is a very large measure of self-government Entry to the profession is controlled by the profession itself and it has power to expel or suspend a doctor from membership At the present time the profession exercises this latter power only in cases of conviction in a criminal court or of infamous professional conduct It could, if thought fit, exercise authority over its members in other respects, but, like most other professions, though perhaps to a somewhat greater extent, it has been reluctant to do so The assumption of greater responsibility for the conduct of its weaker members, when that conduct is detrimental to patients, seems to me to demand serious attention by the profession, not only in the interests of the public but as the profession's surest defence of the freedoms which it prizes

It is not an immutable law of Nature that the profession of medicine, any more than any other profession, should have the privileges it now enjoys These privileges exist by consent of the public, being grounded on the public's respect and confidence, and in its belief, born of experience, that its needs are better met by allowing these freedoms As with academic freedom so with the professional freedoms, they exist because the public is prepared that they should, and they will continue so long as the public—if only tacitly—consents If they are not to be lost or impaired, the profession must give continuing evidence, by the way it fulfils its responsibilities, that, because it has freedom, the public good is better served

Freedom for the Incompetent ?

There is not likely to be much dispute about the general principle, where differences of opinion arise is over its application In his Croonian lectures for 1951 Dr T F Fox, in stating the case for the individual practitioner's freedom, said

> " we need freedom to serve, we need it because it is indispensable if we are to do our work as it should be done On a short view there are often advantages in interfering with the doctor's freedom, but the public will buy these advantages very dear if it discourages any member of our profession from bringing his own judgment to his patients' problems "

This is fair and well stated Experience has shown that for the doctor responsibly doing his best the largest possible measure of professional independence is in the best interests of his patients But what of the doctor who is not good ? The man who presumes to a competence he does not, and knows he does not, possess, the man who persistently is negligent, or the man who regularly—and regardless of the fact that he could change the conditions, if he wished—practises under conditions which render good doctoring impossible Without disputing that the numbers in these categories constitute a small proportion of the profession, the public is surely not unreasonable in looking to the profession as a self-governing body, to deal more effectively with these, its weaker members for the better protection of the public It is not a question of the occasional mistake, everyone, whether professional or not, no matter how good he may be, makes mistakes from time to time It is consistent incompetence and persistent neglect that is in question It would be wrong to think that professional action is never taken it is For instance, professional opinion has slowly led to the exclusion of doctors who have not had a long special training in surgery from the performance of all but very minor surgery, except in emergencies But it is true th like other professions, the medical profession has sho great reluctance to accept responsibility for the techni competency and efficiency of its members once they ha qualified for membership

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Before these promising fields can be cultivated better, the professions concerned with medical-social work, in cooperation with the authorities need to clear up the developing chaos of types and different qualifications of medical social workers Much has already been spoken on this topic and I need not add to the spate of words but will wait expectantly for the introduction of the all-purposes medical social worker

Opportunity—or Frustration ?

There is a prima facie case that broadly the provision for the medical care of the population is better than it was, and that it could be better still, even within the present framework and under the present "ceiling" of financial resources, if the professions responsible for its operation and their members so determine

Some professional members of the service have been unhappy in adjusting themselves to the new conditions , but on the other hand there are those—people who are first-class at their job—who are fully convinced that they are now able to give better service to their patients than before I cannot myself see cause why any doctor or nurse or member of any of the other associated professions should feel that the National Health Service prevents the rendering of at least as good a standard of medical care as he or she previously gave But there are complaints to this effect There are complaints of frustration needed buildings cannot be obtained , approval for the appointment of additional staff may be refused arbitrarily and without understanding of the need , local initiative is being stifled by excessive, unnecessary, and undesirable centralisation , the hospitals are regimented by the Ministry and they in turn regiment the workers , proper attention and care cannot be given because the number of patients to be dealt with is too large , people have no incentive to do their best and many are becoming time-watchers

Inevitable Limitations

These and like complaints can be classified under two heads those which relate to conditions outside the control of the professions and those which can be dealt with by the professions themselves Let us begin by looking at the first class

Obviously, limiting and irksome conditions exist—for example, insufficient financial resources, the inability to replace bad, inefficient buildings, or to obtain additional staff But there have always been and always will be boundaries to professional activity, boundaries imposed from without by what the public wants or thinks it wants, boundaries which the professions may rightly at times regard as contrary to the public good, but boundaries which nevertheless the professions have to accept until they can persuade the community to change them Such boundaries confined the activities of the medical and its associated professions before the coming of the National Health Service, and the situation is much the same now The total sum made available for the health service and the relatively low priority given to its capital projects are arbitrarily decided it is true, because there is no other way , but they are the guess made by the public's elected representatives—men and women whose political survival depends mainly upon their ability to guess the public's wishes correctly—of how much of the nation s capital and recurrent resources the public is prepared to have devoted to hospitals and the health service generally There are many competing claims on these resources It may be regrettable that the amount spent on the health service is little over one third of the amount spent on tobacco and drink, and is over £100 million less than the estimated amount spent on gambling , but, until the clients change their opinions and habits, the professions have to accept these limitations imposed upon the scope of their professional work *Clearly they have the right to make their views* heard and to use their intimate and special knowledge and all their professional influence in attempts to persuade the public to remove hampering obstacles *But it is* equally clear that in the meantime, if they are to be worthy of professional status and privileges, they must do the best they can within the existing boundaries and with the resources available It is equally clear that they must resist the temptation to make these limitations or any other difficulties coming from outside an excuse for their failure to live up to the professional ideal The greater the difficulties, the greater the need to be on guard Some at least of the grumblings which are heard about the effect of the Welfare State and of the National Health Service on standards of professional work are to be deplored as excuses for professional shortcomings and the yielding to commercialism

Civil Servants and other administrators are often regarded by the professions as a sore trial, and sometimes with good reason , but this in fairness must be said The Civil Servants and the officials concerned with the health service have had a very difficult task placed upon them Much of their resistance to decentralisation and many of their regulations restrictions, and attempts at standardisation are not the outcome of their desire to build little empires but are forced upon them by the Legislature's insistence on continuous Parliamentary oversight not only of the policy but of the details and daily operation of the health service What would be said if the directors of a company had to meet the shareholders in almost continuous session throughout the greater part of the year and satisfy them on all the details of the company's activities ? The arrangement would be regarded as unworkable and intolerable and yet the position is not very different with the health service So let us, *at least occasionally*, spare a silent tear for the officials , they have their problems too

Conditions under Professional Control

Professor Toynbee in his recent Reith lectures on the B B C compelled his listeners to consider how *other peoples viewed the past actions of our own nation and of other nations of the West* It is painful but salutary to realise that civilising missions undertaken from high motives may be regarded by those to be civilised as acts of aggression If only to ensure their continuance in the

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to the view that the existence of private practice is the only safeguard against a lowering of professional standards While accepting that the professions number among their members people of the highest ability and finest quality, the professions do not, so it seems to me, have a monopoly of the ablest and most admirable personalities Far from thinking that the right course for the professions is to parade themselves before the world as the best people, I believe that the wiser course will be for them to give daily evidence from the way they conduct themselves that theirs is an element worth perpetuating and strengthening

Wilfred Trotter in his *Instincts of the Herd in Peace and War* wrote

> " prodigies of genius have been expended in obscuring the simple truth that there is no responsibility for man's destiny anywhere at all outside his own responsibility, and that there is no remedy for his ills outside his own efforts "

Is not a like simple truth applicable to the professions in the health service ? They have no cause to be depressed, fearful, or of poor morale, there is more exciting and satisfying work waiting to be done by them than they can exhaust They have a great opportunity to demonstrate that the professional way of life is not defeated by changes in the public will, because the ideals towards which they strive will always serve the public good, no matter what the form or circumstances of the State may be

IMMEDIATE PRIMARY REPAIR OF SKIN DEFECTS WITH LOCAL FLAPS

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PLASTIC SURGEON, QUEEN VICTORIA HOSPITAL,
EAST GRINSTEAD, SUSSEX

In many branches of surgery the repair of skin defects constitutes a frequent and urgent problem These defects are often the immediate outcome of a planned operation, and follow an adequate excision of diseased or damaged tissue

The duty of closing raw areas as a primary procedure falls not only on the plastic surgeon but also on those working in other branches of surgery No-one, on any later occasion, has such a good opportunity of providing skin cover as the original operator at the time of operation Sherren once wrote " Anyone who opens the abdomen should be capable of dealing with any condition he may find there " Similarly, any surgeon who finds or establishes a skin defect at operation should be capable of dealing with it

In this paper emphasis is laid on immediate *primary* repair, and the advantages of repair with local skin flaps are indicated

DISADVANTAGES OF FREE GRAFTS

The use of free grafts is today so widely practised that this method of repair is now unlikely to be overlooked In the early treatment of burns, and in many other circumstances, it is invaluable Nevertheless, in ordinary instances of skin loss, whether surgical, traumatic, or pathological, the surgeon's thoughts should first turn not to free grafts but to local repair with pedicled and therefore living skin flaps The disadvantages of free grafts are as follows

(1) In functional areas they often lead to a disability, particularly where they lie in contact with tendons or with bone

(2) Their cosmetic appearance is seldom perfect

(3) It is impossible to use free grafts to cover grafts of other materials whether bone, cartilage, or fascia

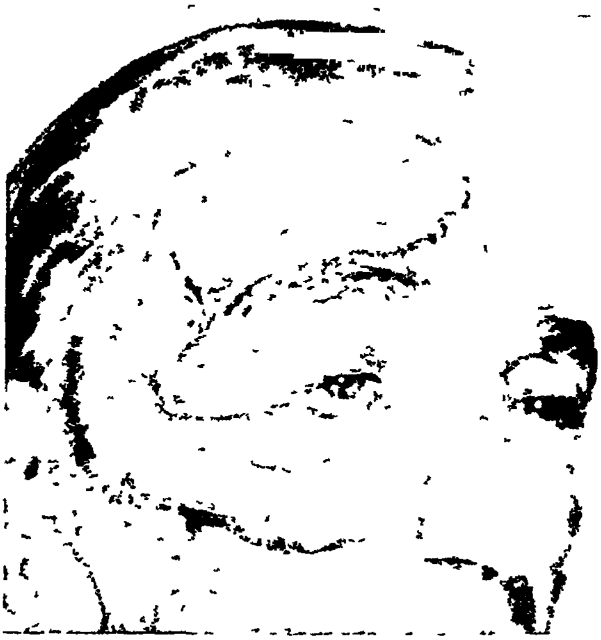

Fig 1—An Esser arterial flap used for immediate repair of lower li and cheek. This patient had multiple rodent ulceration involvin the malar bone The second stage is yet to be completed Goo function with relief of ectropion here outweighed cosmeti considerations

SKIN FLAPS FROM A DISTANCE

Flaps which have to be transported from a distance go by various names but are mainly of three kinds *direct abdominal flaps, cross leg* (and cross arm) *flaps*, and *tubed pedicles* Although the reasons for preferring local skin may appear obvious, it is necessary to consider some points relating to the use of flaps from a distance

Provided proper skin cover is afforded at the primary operation, there are certain indications for these distant manœuvres They find their best use in limb defects, where the use of local flaps is often unwise, but they are much less suited to facial defects It should be remembered that direct flaps, and especially tubed pedicles,

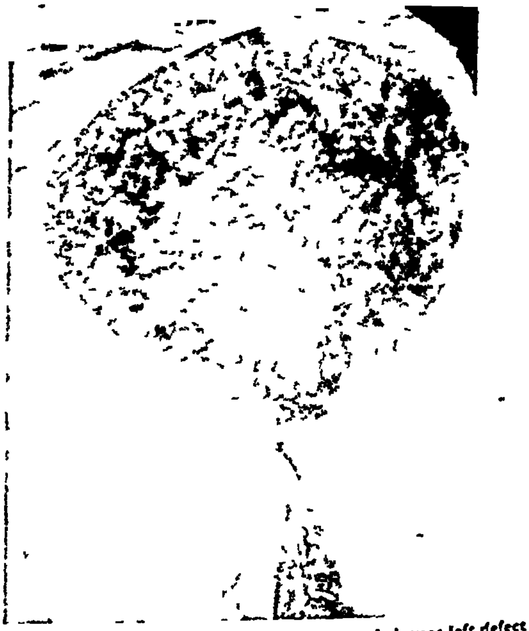

Fig 2—Adequate excision of multiple sacrococcygeal sinuses left defect 6 in in width This type of lesion is best closed by lateral sliding flaps, using Oldham s method of suturing Patient fully healed in 14 days

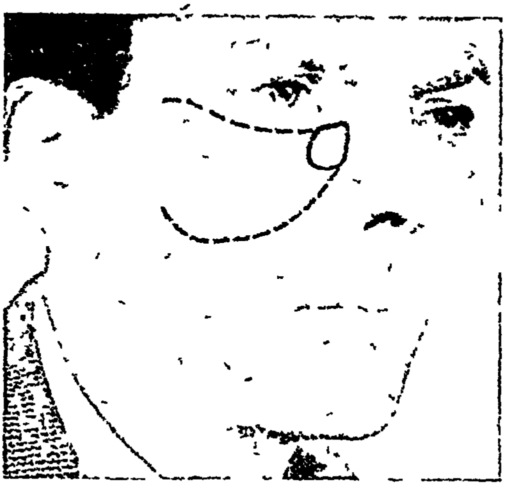

Fig 5—Repair of recurrent rodent ulcer after unsuccessful irradiation, base unsuited to free graft. Imre advancement flap must be generously designed in relation to defect. Note complete absence of ectropion after operation

1 5 to 1, but there are many exceptions, particularly on the face

The last but least defined factor is the blood supply There are no exact rules or mathematical criteria to guide the surgeon in assessing this vital issue Though it may ultimately be a matter of experience and even common sense, certain points should be appreciated

(1) The venous outflow through the base of the flap is just as important as the arterial inflow

(2) The normal vascularity of certain areas is notoriously poor—e g, the ankle, and in other sites the vascular pattern may be unfavourable, as in crossing the midline of the abdomen

(3) Very thin tissues like the eyelids, though highly vascular, are extremely susceptible to injury by careless handling

It should be pointed out that, whereas thick flaps may carry much fat, which in terms of blood supply is parasitic, very thin flaps are easily bruised and may suffer marginal thrombosis The important subdermal plexus lies in immediate contact with the under surface of the dermis, but clumsy or excessive thinning of a flap can nevertheless do unseen damage with dire results

The safest design is the arterial (or Esser) flap (fig 1) These flaps are based on a known artery—e g, the superficial temporal—and in selected cases they may be designed with a length/breadth ratio of 6 to 1 Unfortunately they cannot often be used thus, but they emphasise the principle of making the best use of the precise anatomical pattern of the adjacent vessels

Technique

The first rule of skin flap surgery is "avoid tension" It is tension which causes ischaemia, kinks the base and retards the venous return, makes sutures cut out, and results in permanent distortion The whole aim of the operator should be towards so disposing the tissues that the flap lies naturally, without either causing or suffering distortion

Flap operations do not create new skin, they simply shift it to suit the exigencies of the situation If there is no skin "reservoir" at hand, there may be a secondary defect which must always be grafted

The handling of vulnerable skin flaps demands not so much special methods as special standards Surgeons do not generally treat the abdominal skin edges with the same meticulous care that they reserve for a gastric anastomosis But any surgeon who attempts reconstruc tion with skin flaps must exercise a degree of gentlene usually associated with eye surgery Fine skin hooks, sharp needles silk sutures of minimal calibre, and the avoidance of all crushing and pulling of the skin margins—these are the simple but imperative requirements of plastic surgery

TYPES OF FLAP

The standard classification comprises sliding, advanc ment, rotation, and transplantation flaps Many surgeo will also be familiar with the double transplantatio flap, or Z-plasty, this, however, should seldom, if eve be used to close skin defects, though it remains the ide method for releasing the linear pull of a webbed an contracted scar These five varieties should be regarde merely as convenient labels and not as rigid division In any case certain designs, such as the Imre flap, d not fit exactly into any one category

The *sliding flap* is the simplest of all designs and wa described (though probably not invented) by Celsu in A D 30 It has the widest sphere of use, but depend on careful and *generous* undermining of the adjacen skin Its basic function is to convert an ellipse, wit sides of equal length, into a linear scar (fig 2) It is no intended as a euphemism for the common practic of dragging skin edges together under tension

Advancement flaps are rarely used in their pure form The case illustrated (fig 3) is a reasonably true example

Rotation flaps are particularly useful in the repair o scalp defects, in the closure of decubitus ulcers, and in a great variety of lesions of the face and trunk (fig 4) A scalp rotation flap may also be used, often on a generous scale, to close a raw area after a radical excision in the region of the ear

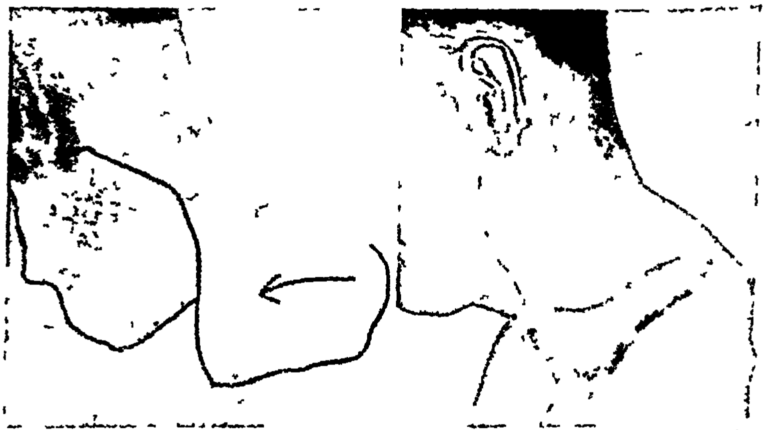

Fig 6—Epithelioma of neck extending down to carotid sheath A large transposition flap from the shoulder was used for immediate repair

Imre (1928), of Budapest, developed a flap which embodies elements of advancement as well as rotation It achieves its best results in the region of the lower eye lid, acting as a wedge which increases the amount of skin (measured vertically) and thus preventing ectropion (fig 5)

Transposition flaps are taken in most instances from the forehead or the neck, they are transposed over intervening normal tissue to reach the defect They are the basis of the forehead (Indian) rhinoplasty, though here a second stage is nearly always needed to return the base of the pedicle to its original site In the case of repairs to the lower half of the face, the neck offers the best "reservoir" of skin (fig 6) This latter type of flap has been greatly developed in recent years, and the scope of its many variations is now considerable

SPECIAL AREAS

The problems of scalp closure were concisely reviewed in 1944 by Sir Harold Gillies He laid stress on the s called upon to perform now and so far as can be foreseen in the generation ahead. Otherwise there is an abuse of the privilege of professional self-government. Admittedly on any issue there may be a difference of opinion about what is reasonable, but the obligation s on each profession honestly to look at its requirements rom the standpoint of the public as well as that of the profession, to consider confidently and without fear well-substantiated criticisms, and to justify its decisions by results. The insistence by a profession on entrance requirements markedly out of touch with the qualities and qualifications demanded by the work to be done by members of the profession entitles the community to take steps to have its needs met in other ways. If these steps lead to the substitution of other groups of workers for those of the profession, the profession has no real cause for complaint about infringement of its privileges or about dilution. The profession and its privileges exist solely to serve the public need. Any profession which has established itself securely in the public's respect will not quickly lose that respect; but it may sink in the public's estimation if it should ever appear, pigheadedly, to be setting professional advancement or administrative convenience before the public interest.

Although the cost to the State in training grants may be unnecessarily greater, little objection to the enforcement by a profession of severer entrance requirements is likely to be heard if the profession has plenty of candidates and the number admitted maintains a total supply of practitioners adequate to the work which can be undertaken with the resources the community makes available. But if the opposite is the case, what then? A clear-cut answer is difficult. Consider, for example, the serious shortage of dentists. Despite the quite high level of remuneration, dentistry does not appeal to enough young people or their parents. The profession, nevertheless, has been striving to raise the standard of qualification. The quality of the training in the dental schools has improved and a larger number and proportion of students are taking a university degree. In defence of the raising of entrance qualifications it is claimed, with some force, that this step is necessary if the prestige of the profession is to be increased sufficiently to attract more candidates. The profession seems right in this contention; but two corollaries follow.

The first is that while the profession pursues its aim, it must be careful not capriciously to oppose means of increasing the effectiveness of its existing membership. The proposal at present before the profession for the training of dental nurses to assist dentists as other nurses assist doctors is a case in point. Is there really any substance in the argument which has been voiced that such a development would lower the status of the profession? Has the skilled assistance of nurses in technical procedures lowered the status of doctors?

Simplification of Training?

The second corollary concerns the length of the training. A profession, in my submission, is in duty bound to seek ways of bringing students to the desired standard of efficiency and maturity in the shortest possible time —as was done, for instance, during the war in the training of men and women for the fighting forces and for war production. Little seems to have been published about the methods which were introduced at that time, but some of the apparently striking results give ground for thinking that a like process in the simplication and speeding up of training might with benefit be applied to some aspects of professional training in peace-time. The dental profession might well call in some of those who studied these problems during the war and give them the chance to experiment.

Some of the other professions might well do likewise. Over five years ago the Working Party on the Training and Recruitment of Nurses came to the conclusion that the basic training for nurses could without any lowering of standards be given in two years. The length of the prescribed course still remains at not less than three years. Recent evidence adds weight to the view that nurse training has got badly out of touch with the demands of the job. If it be correct that the end-result of nurse training, under present conditions, is administration and not nursing, and that in the main the rôle of nursing is being filled by people who have not yet qualified for admission to the profession, a radical overhaul is overdue. May we hope that some unfettered educational experiments, accompanied by experimental changes in the organisation of nursing, will be tried? The nursing profession will yet further strengthen its hold on the public's affection and goodwill if it tackles this difficult problem with determination and promptitude.

Duty to the Public

Man's powers being limited, it is perhaps fortunate for him that many of his problems break down into the consideration of whether he should do a little more or a little less, whether he should go a little faster or a little slower in a given direction. Implicit in what I have already said and in what I have yet to say is the plea not for something completely and radically new, but for a little more of some good things. With a sense of public duty the professions assume some responsibilities for the professional conduct of their members; my plea is that they should extend their responsibilities in this respect. They have all striven to achieve entrance requirements which will ensure recruits of the best quality; my plea is that, in their own interests and those of the public, they should be still more self-critical. And so with my last plea, which is that the professions in the health service should assume more corporate responsibility in the exercise of their self-governing powers, for the effectiveness, economy, and humanity of the medical care which coöperatively they provide.

Situation of Professions in the N.H.S.

Generally speaking the professions engaged in the health service have been well treated. For the professional freedoms of the older-established professions there has been the tenderest of regard. Whatever dangers, present or future, there may be of restrictions on these freedoms —freedom can never be free from such dangers—up to now there has been no impairment of them by the health service. On the contrary, in so far as the influence of the professions is if anything stronger than it was, the defences of the professional freedoms may also be stronger.

As regards remuneration and conditions of service, most of the professions do not seem to have much cause for complaint. For the great body of the members the financial rewards are higher than before the National Health Service, and no evidence appears to have been published establishing convincingly that the load of work falling on them individually is heavier; in some professions it seems to be less. It is no doubt true—indeed it would be surprising if it were not so—that in "real" as opposed to money terms professional members of the health service are not better off than before the war. But if this be their state, they are suffering from ills which afflict no less the other professions and the vast majority of the population. The general medical practitioners are relatively better off than the members of other professions in so far as in no other profession have earnings been increased to offset the rise in the cost of living since 1939—as has been done for them under the Danckwerts award.

The almoners have not fared as well as the rest either in pay or conditions of work. Be it said in their honour that their professional code has led them, despite official neglect, to do their utmost even at the cost of gross

POLYCYTHÆMIA AND ERYTHRÆMIA TREATED WITH PARA-HYDROXYPROPIOPHENONE*

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THAT overactivity of the pituitary-hypothalamic system can be demonstrated in symptomatic polycythæmia and erythræmia was shown by Haynal and Gráf (1950), who tried to reduce the pituitary function by giving sex hormones, vitamin B_1, and radiotherapy without, however, obtaining decisive results

Lacassagne et al (1951) and Desclaux et al (1952) reported the pituitary-depressant property of *p*-hydroxypropiophenone, which produced histological changes in the ovaries, testes, seminal vesicles, and prostate, and they attributed these changes to decreased secretion of the luteinising hormone They also showed that the secretion of thyrotropin and somatotropin was decreased

Perrault and Vignalou (Perrault and Vignalou 1949, Perrault 1950, 1951) used *p*-hydroxypropiophenone with satisfactory results in all those forms of hyperthyroidism in which the excessive production of thyrotropin plays an important part They got the same good results in hyperfolliculinæmia due to overaction of the follicle-stimulating hormone They could not establish any depressant action on the secretion of the adrenocorticotropic hormone (A C T H) Guillemin (1951) and Hertz and Tullner (1951) could not confirm these findings, nor could Netter et al (1952) find any depressant action on the secretion of the pituitary gonadotropic hormone None of these workers observed any effect on the erythropoietic system or on the blood

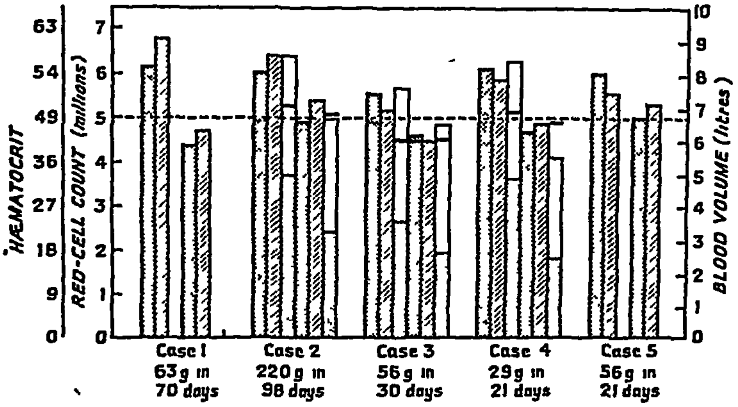

Fig 1—Findings before and after treatment in symptomatic pituitary polycythæmia

▯ Red cell count (millions) ▨ Hæmatocrit

▯ Plasma
▯ Red cells
— Normal blood volume calculated from body-weight

Key to figures

For these reasons we tried this new pituitary-depressant, *p* hydroxypropiophenone, in four cases of symptomatic polycythæmia and nine cases of erythræmia The treatment of five of the cases of erythræmia had unfortunately to be stopped because of temporary lack of *p* hydroxypropiophenone We studied the clinical signs and symptoms, the blood-pressure, and the hæmatology, including the bone marrow picture, and we made the usual laboratory tests of the function of the pituitary, thyroid, adrenals, liver, and kidneys

The clinical and laboratory findings are summarised in the accompanying table and figs 1–3 The table contains some clinical and laboratory findings before and after treatment Fig 1 shows the red cell counts, hæmatocrit values, and blood volume of the patients with symptomatic pituitary polycythæmia, fig 2 those of patients with erythræmia who received full treatment, and fig 3 those of patients with erythræmia whose treatment had to be stopped because of temporary lack of *p*-hydroxypropiophenone

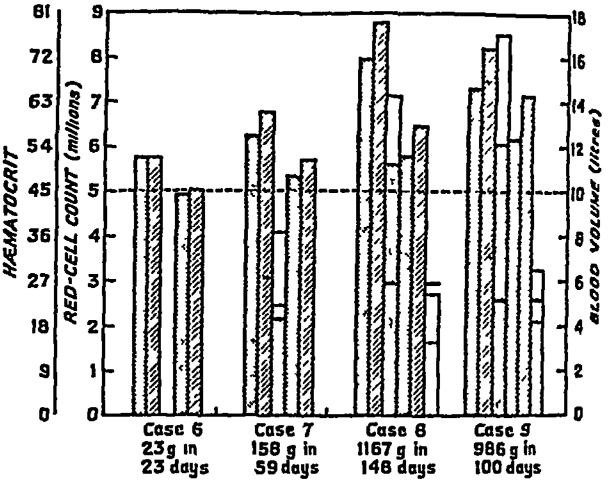

Fig 2—Findings before and after treatment in erythræmia

MATERIAL

Cases 1 and 2 had hyperpituitary obesity (principally on the face, neck, and trunk, the extremities being less affected) with high blood pressure but without changes in the sella turcica, striæ, osteoporosis, ocular manifestations, or enlargement of the spleen They may have had Gaisbock's disease (polycythæmia hypertonica) Case 3 was an obese young girl with diabetes mellitus and symptomatic polycythæmia Cases 4 and 5 were two treatments in one and the same acromegalic giant without hypertension or enlargement of the spleen Case 10 probably had Gaisbock's disease and was slightly acromegalic, with a normal sella, no ocular changes, a normal spleen, and moderate hypertension All the other patients had erythræmia

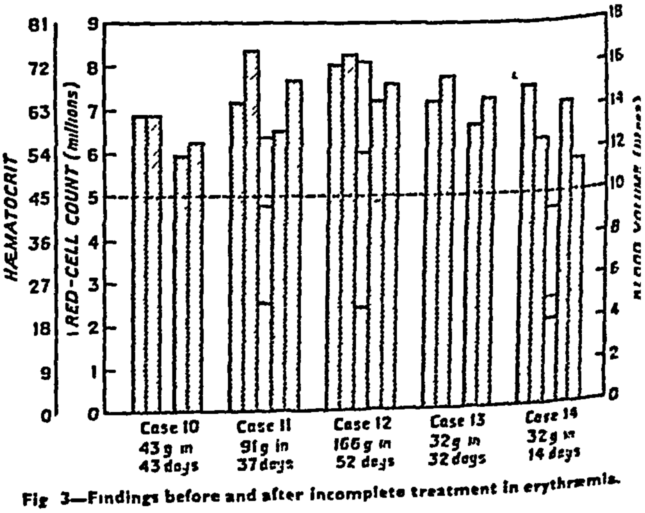

Fig 3—Findings before and after incomplete treatment in erythræmia

public's good graces and thus to safeguard their freedoms, the professions in the health service might be well advised to try more frequently and openly to put themselves in the place of the client and attempt to understand what he feels about their ethics and practices. In moments of idle speculation I have toyed with the notion that the professional members of the health service might be assisted in such an attempt if they adopted the convention that any medical treatment or care they needed for themselves or their relations should be received only as ordinary patients of the health service under the same conditions as the ordinary patients.

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*Based on a paper read at a meeting of the medical section of the Hungarian Academy of Sciences in Budapest on June 30, 1952

A few weeks ago the Central Health Services Council issued a memorandum on the Reception and Welfare of Inpatients in Hospitals. No-one is likely to contend that any of the recommendations in that memorandum was unreasonable or unnecessary. The conditions and practices which, in the mildest language, the council seeks to change are not the product of misguided decisions of Ministers of the Crown or of unfeeling Civil Servants. They are the product of the past practices and attitudes of hospital staffs—of members of honoured professions. The Central Health Services Council cannot be described as an ignorant or unsympathetic or revolutionary body. That it has considered the publication of this memorandum to be necessary reflects upon the professions which run the health service and should give cause for heart-searching. In a service staffed by professional people should it be necessary to include among the main recommendations statements such as these ?:

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The hospital of today is a complex and highly technical organisation, but its chain of responsibility is too often anarchic. It might be compared to a medieval army which unlike the army of today was not an integrated organism but an aggregate of independent knights each with his squire (or registrar) and his followers. Though bound together vaguely by a common purpose, each knight was independent and free to do much as he pleased. Such analogies must not be pressed too far, and there is much that is right in the doctor's insistence that he must be allowed to do his work in his own way. But I suggest that some collective responsibility should be accepted by the clinicians in association with the other professional workers in each specialty for the service that is given to the population, and that they should consider it their duty so to arrange their work as to make the best possible use not only of their own skill but of the facilities of the hospital. There is some evidence for suggesting that they could do much to improve the arrangements for outpatients and also that by operating a more flexible allocation of beds to different specialties they could greatly reduce waiting-lists without any increase in the total number of beds.

Medical Leadership or Medical Domination ?

This question is not one solely for the medical profession. As the profession with the duty of leadership, it has the heavier responsibility, but all the professions are involved. Given true leadership, in place of domination, by the medical profession I feel little doubt that the other professions would increasingly make their contributions; and valuable contributions they could be.

At this stage it is necessary to refer to the relations between the various professions. Here I find myself at variance with a view which is sincerely held, I believe, by quite a number of admirable doctors and which seems to have been the view of those who signed the majority reports of the Cope Committee on Medical Auxiliaries—namely, that members of the non-medical professions are the servants of doctors, their inferiors and subordinates, in whose occupational organisations and affairs medical opinion should predominate. It is not disputed that upon the medical profession and upon the individual doctor falls the duty of leadership. In the care of an individual patient, the doctor is and must be the leader of the team, and those working with him must loyally comply with his decisions and instructions ; but if he is a real leader he will, in reaching his decisions, have distilled his own and his colleagues' knowledge and experience. And so it should be in the relations of the medical profession and the other professions in the health service. The clue is in the word "colleague," and here I turn again to Dr. Fox's Croonian lectures. In considering the problems arising between members of the medical profession engaged in group practice or in team-work in hospital he said :

> ". . . all are colleagues, not inferiors or superiors. If we want freedom *for* the profession, we must cherish freedom *within* the profession. The colleague is a responsible person, whereas the subordinate is not ; and responsibility is the best known means of evoking effort."

You will note the last words. Believing that experience shows them to be true, I should respectfully add to Dr. Fox's statement that if the medical profession desires freedom for itself and the fullest and best help from the other professions—without whose devoted and loyal assistance it cannot give proper medical care to its patients—it should cherish freedom not only within its own profession but *for* and *within* those other professions, regarding those other professions as its valued colleagues.

Old Attitudes or New ?

The recommendations of the Central Health Services Council touch also upon the question of those attitudes and practices of members of the professional staffs of hospitals, to which there is reason to think objection is taken by an increasing number of patients. These are practices which by the wildest stretch of the imagination cannot be regarded as an essential of medical care. Those which evoke the strongest adverse comment are by no means general. In many cases, I am quite sure, those guilty of them are not so by deliberate intent —indeed are not conscious that they are acting in an objectionable manner unbecoming to a professional man or woman. The trouble is that the professions grew accustomed to these attitudes and practices in the days before hospitals became national institutions serving all sections of the population ; they have become accepted or tolerated without protest by the professions with the result that they are thoughtlessly adopted by some as normal conduct. Stories of discourtesy are too persistent and widespread to be ignored and are damaging to the good name of the professions. Sometimes it is little more than a thoughtless attempt to make the patient fit the rule.

Within all professions there are strong herd feelings. It is to be hoped that the professions will look at their unwritten codes of what is and what is not done and use herd opinion to encourage improvements in conventional habits and attitudes of their members.

It will, I hope, have become clear that, while agreeing with much that they have written, I take a somewhat different view of the professions from that of Lewis and Maude in their recent book *Professional People.* While I believe that the professions at the present time are a most valuable element in social life, I cannot subscribe

DOSAGE

At first we used the "higher" doses of the French workers—i e, 0 5–1 0 g daily Later we increased the dosage to 3 or 4 g daily and in our last patients to 8–12 g daily This increased dosage was necessary because it proved to be in some cases the only efficient one We dared to increase it because the lower dosage was smaller than that usual in experiments on animals The dosage for a man weighing 60 kg would be 36 g per day calculated from the dosage used in animals (40 mg daily in mice and 120 mg in rats—i e, 0 6 g per kg body-weight)

RESULTS

In two cases there were undesirable effects nausea and vomiting in case 14, and toxicoderma in case 13 Since we had to stop the treatment in both cases owing to lack of *p* hydroxypropiophenone, these effects disappeared rapidly

The *red cell count* and the *hæmatocrit* value decreased in most of the cases of symptomatic polycythæmia in response to a small total dosage of 23–63 g (cases 1, 3, and 4) and in one case of erythræmia (case 6) Most of the cases of erythræmia (cases 7, 8, and 9) and one of symptomatic polycythæmia (case 2) needed a much higher dosage (158–1167 g) Four of the cases which could not be completely treated through lack of *p*-hydroxypropiophenone reacted well to a small dosage, and the fifth (case 12) only to a larger one

The treatment lasted 21–148 days A quick result could not be expected, because the decrease of the red cells due to the depressant action of *p* hydroxypropiophenone on the pituitary must be a slow process and cannot be expected until some time has elapsed The blood volume of those fully treated patients who were checked in this respect (cases 2, 3, 4, 8, and 9) decreased to normal, principally owing to the decrease of the red cells and, to a lesser degree, to that of the plasma (figs 1 and 2) The characteristic external appearance of the patients disappeared more or less pari passu with the hæmatological improvement

The *body-weight* of five patients diminished during treatment the pituitary obese (case 1) lost 12–13 kg, and the pituitary giant (case 4) lost 6 kg The patients with erythræmia generally maintained their weights, except two, one of whom lost 3 kg (case 8), the other 1 kg (case 14) The decrease of the body weight was not due to increased excretion of water One patient with erythræmia (case 9) gained 2 kg during treatment

The *spleen* in three patients (cases 6, 8, and 9) diminished considerably The *blood-pressure* of four patients (cases 1, 2, 7, and 10) fell during treatment

The *bone-marrow* picture was generally hypoplastic with preponderance of the erythropoietic system over the granulopoietic one (1 1 instead of $^{1}/_{3}$–$^{1}/_{4}$ 1) The bone-marrow picture did not alter essentially during treatment, there was no conspicuous morphological change in the maturation or proliferation of the cells, and signs of intoxication of the erythropoietic system (toxic granulation, vacuolisation, pyknosis) were absent There was probably a slight alteration in the ratio of the erythropoietic and granulopoietic systems at the expense of the former

Nothing that could have pointed to increased hæmolysis during treatment could be established, the serum-bilirubin and urine-urobilinogen levels did not increase, nor did the osmotic resistance of the red cells diminish There was no change in the reticulocyte-count, which was rather low (4–5%) and pointed also generally against the possibility of increased hæmolysis

Liver-function tests (thymol turbidity and goldsol reaction) and examinations of *urine* did not show any change either

The *B M R* of four patients (cases 7, 8, 9, and 11) decreased slightly, that of one patient (case 1) increased moderately, and that of six patients did not alter The *serum cholesterol* levels were raised, thus indicating the same change of thyroid action From these findings we dare not form any opinion on the change of thyroid function, further investigations of the serum protein bound iodine will have to decide the question

The changes in the *serum-potassium* and *serum sodium* levels and urinary excretion of *17 ketosteroids* were not great enough to allow any definite conclusions to be drawn The serum sodium level seemed to fall, if that were true, it would point to a diminution in the secretion of the mineralo corticoids of the adrenals The changes in urinary excretion of the 17-ketosteroids are also uncertain, but perhaps they point also to a decreasing function Further investigations are necessary to decide whether the adrenal cortical function diminishes during the treatment

No changes were found in the *sexual organs*, nor was there any change in the potency or in the libido of our patients The spermatogenesis of one patient (case 9) was impaired the sperm count was diminished (about 2,000,000 per ml), the motility was $^{4}/_{10}$–$^{5}/_{10}$, but more than half the spermatozoa were of normal structure

The *glucose tolerance* curves became flatter in only four patients (cases 1, 9, 10, and 13), one of these was the pituitary obese patient (case 1) Very probably the reason for the lack of this change in the other patients is that *p-hydroxypropiophenone depresses the secretion of only* one of the pituitary hormones acting on the carbohydrate metabolism—i e, the pituitary growth hormone —and does not depress the production of A C T H

There was no conspicuous change in the *white cell* picture

The therapeutic results were not permanent The return of the blood of the pituitary giant (case 4) to normal lasted only two months after treatment was stopped, then the red cells increased again to 6,000 000 per c mm and the hæmatocrit value to 50 5, and the patient had to undergo a second treatment, consisting of 56 g of *p* hydroxypropiophenone in twenty one days, until his values became again normal (case 5) His blood has remained normal since then with a maintenance dosage of 1 g daily Two patients (cases 2 and 6) had a relapse after two months and four and a half months respectively, their red cells increased to 5 500 000 per c mm and their hæmatocrit values to 52 and 53 respectively One patient (case 1) died meanwhile elsewhere of a perforated appendix Unfortunately we learnt too late of his death to make a post mortem examination The blood of the diabetic girl (case 3) was still normal six months after the end of the treatment, probably she will need a maintenance dosage

DISCUSSION

We introduced the treatment of erythræmia and symptomatic hyperpituitary polycythæmia with *p* hydroxypropiophenone as a result of our previous investigations (which suggested that overactivity of the pituitary hypothalamic system plays a part in the pathogenesis of these diseases) and of the discovery of French pathologists and clinicians of the depressant action of *p* hydroxypropiophenone on the pituitary So far our therapeutic results indicate the possibility of improving or bringing back to normal the blood in these diseases by diminishing the pituitary secretion without hæmolysis of the red cells or toxic effect on the bone marrow The different ways in which the two types of polycythæmias—i e, symptomatic pituitary polycythæmia and erythræmia—react point also to this pathogenesis

The depression of the pituitary activity could have influenced the blood formation either directly or through the target glands, the thyroid, the adrenal cortex, and the gonads All of them play, as experimental and public's good graces and thus to safeguard their freedoms, the professions in the health service might be well advised to try more frequently and openly to put themselves in the place of the client and attempt to understand what he feels about their ethics and practices. In moments of idle speculation I have toyed with the notion that the professional members of the health service might be assisted in such an attempt if they adopted the convention that any medical treatment or care they needed for themselves or their relations should be received only as ordinary patients of the health service under the same conditions as the ordinary patients.

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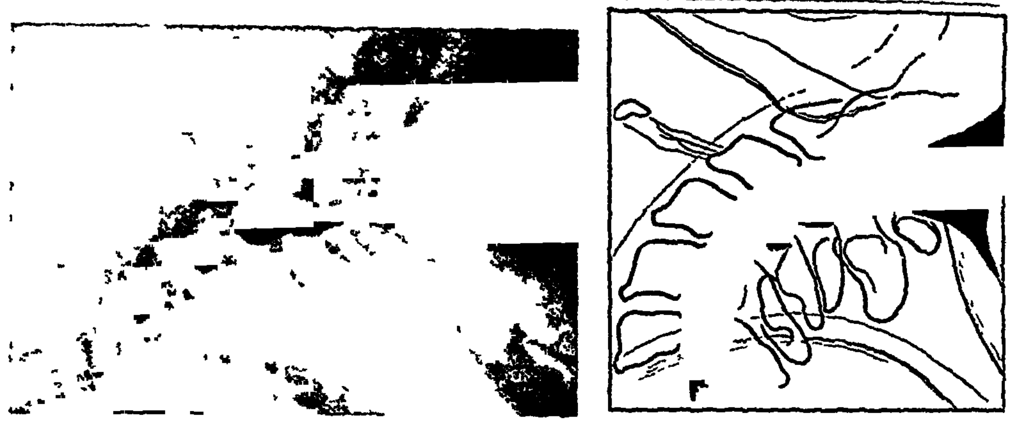

Fig 2—Myelogram of cervical spine in hyperextension in cadaver

pyramidal tracts are involved earliest and most severely, the spinothalamic tracts are implicated next, often with an ill-defined upper level, and the posterior columns either escape or show minor signs of dysfunction such as depression of vibration sense or of joint position sense at the periphery Signs of cervical root compression and symptoms referable to the neck may be absent This last and rather odd fact causes difficulty in localisation of the responsible lesion and is the reason for the frequent initial diagnosis of degenerative or demyelinating disease of the spinal cord

MECHANISM OF COMPRESSION

Kahn (1947) suggests that the ligamenta denticulata and the short transversely disposed nerve roots fix the cord forward against the disc protrusions He has charted the lines of stress thus occasioned, and shows that the main burden falls on the pyramidal, spinothalamic, and lateral spinocerebellar tracts This accords with the common clinical picture Allen (1952) has observed at operation that adhesions round the protrusions and the nerve roots fix the cord, preventing the gliding which normally takes place during cervical movement. Kinking of the cord and vessels, with resultant ischæmia, is thought to occur mainly during flexion Brain et al (1952) emphasise the formation of extradural adhesions which limit movement of the spinal cord and they mention the greater deformity occurring in extension We have observed at operation not only the extradural vascular adhesions, surrounding the nerve roots in thick sleeves, but also, in many cases, spidery intradural adhesions running from the posterior part of the cord to the dura mater at the site of the disc protrusions It has further been observed that the extradural fat on the posterior part of the dura is often scanty or absent, and that adhesions form between the dura ligamenta flava, and laminæ This is thought to furnish evidence for the posterior compressing agent to be described Bedford *et al* (1952) follow Kahn in their emphasis on the fixation of the cord by thickened ligamenta denticulata, and suggest that it is thereby rendered vulnerable to normal neck movements Bucy et al (1948) emphasise the up and down movement of the cord over the protrusion at each respiratory movement and cardiovascular pulsation Mair and Druckman (1953) have shown, in sections of spinal cord, that demyelination takes place mainly in areas supplied by the terminal branches of the anterior spinal artery They imply that diminution in the arteriolar blood-flow secondary to compression of the main vessel causes this demyelination

POSTERIOR COMPRESSING AGENT

Hitherto attention has been focused on the anteriorly placed protrusions and on the adhesions forming round them secondarily to the venous congestion and serous exudation which they are presumed to cause Evidence is presented here for the important intervention of structures lying posterior to the cord—the ligamenta flava

It has previously been shown (Taylor 1951) that, when the neck is hyperextended, the ligamenta flava are compressed between the adjacent laminæ to form bulges which project forward into the spinal canal Figs 1 and 2 show tracings of a column of oil in the cervical canal with the neck in the neutral position (fig 1) and after forced hyperextension (fig 2) It can be seen that in hyperextension the ligament projects about a third of the way across the canal In a normal person this is of no importance, because the spinal cord can move forward towards the anterior wall of the canal and escape damage If there is a protrusion on the anterior wall, the cord will be compressed between the two projections when the neck is extended Fig 3 shows a column of oil in the cervical canal compressed in this way in a cadaver and fig 4 shows complete interruption of the column in a living person whose symptoms were later relieved by operation

From previous writings a considerable volume of evidence can be obtained in support of this conception Morton (1936) described a case of spondylitis deformans, with compression of the spinal cord, in which the symptoms were more pronounced on extension of the neck This movement also

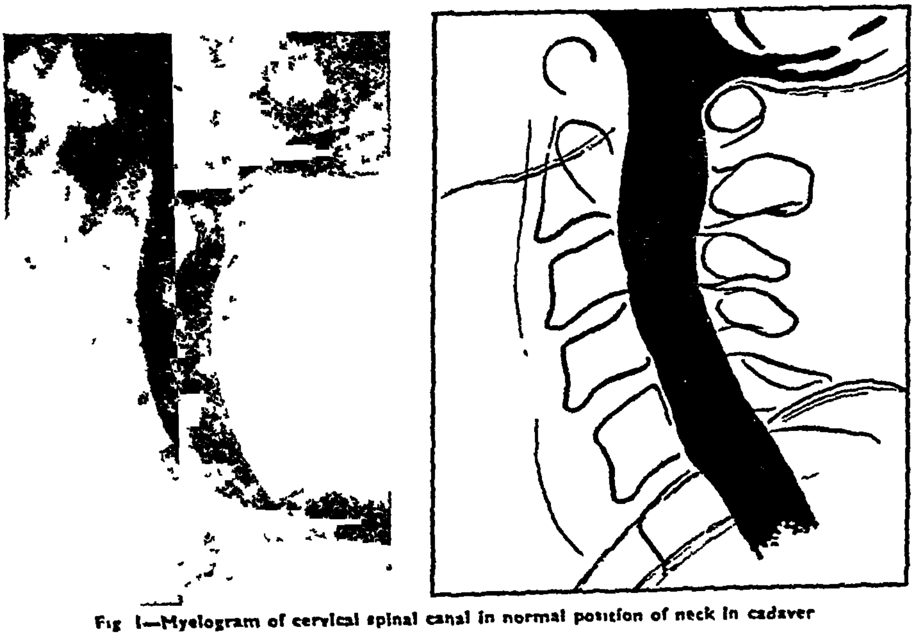

Fig 1—Myelogram of cervical spinal canal in normal position of neck in cadaver

are peculiarly vulnerable to infection if applied to granulating wounds. Also the usefulness of cross-leg flaps in operations for primary wound closure is governed by the necessity, in most circumstances, for a preliminary "delaying" operation.

As regards the tubed pedicle, it must be frankly admitted that ever since its invention in 1917 it has exercised an undue fascination. Its novelty, its vitality, and its astonishing migrations have lured some unsuspecting surgeons into grave trouble. There is, of course, no difficulty whatsoever in raising an impressive tubed pedicle; but to complete the necessary four or six stages is often risky, tedious, complex, and disappointing. Elaborate tests designed to expedite these stages and to ensure safety do not remove the inherent hazards of the method. In any case the perfectly designed tubed pedicle is never available to the surgeon who, often through no lack of foresight, is confronted with a large defect in urgent need of immediate repair.

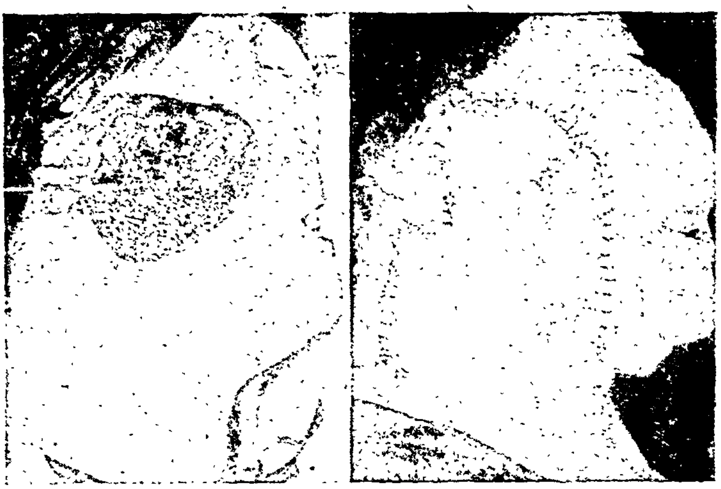
Fig. 3—Excision of fungating rodent ulcer involving parotid in patient aged 80. This might be repaired by a split skin graft, but a neck flap gives a more satisfactory and certain result.

These arguments, however, in no way apply to the proper use of tubed pedicles in extensive and necessarily elaborate reconstructions. Criticism is here only directed against their injudicious use for repairs that can be made much more safely by simpler means.

ADVANTAGES OF LOCAL FLAPS

The primary advantage of local skin in the repair of an adjacent defect is its similarity of texture and colour. The skin of the cheek is sure to look better on the cheek than skin from the abdomen or even postauricular skin.

A second advantage arises from its accessibility; it saves a great deal of time to operate wholly in one area and not to be concerned with remote donor areas. This mainly applies to cases where local flaps leave no secondary defect; but it is not unfair to suggest that with increasing skill and experience such secondary raw areas in need of grafting are surprisingly infrequent.

Many defects produced by major excisions for malignant disease require primary skin cover with some type of local flap. The essence of the method is to achieve primary cover; and this object is fulfilled even in those patients who subsequently need a later surgical trim to tidy up an ugly redundance or to replace the base of a transposed flap.

LIMITATIONS OF LOCAL FLAPS

It should be clearly recognised that in certain parts of the body local flaps are either inadvisable or entirely wrong. Their use is slightly limited on the upper limb and distinctly hazardous on the leg. The palm, the ankle, and the sole of the foot should in most cases be prohibited areas. If local flaps are used to repair extensive lesions of the limbs, very stringent precautions are necessary.

Elsewhere difficulties are apt to arise in certain awkward and restricted sites. For example, in rodent ulceration at the inner canthus involving a portion of both upper and lower lids it is quite possible to carry out a repair using one or more local flaps of the types described by Imre (1928) and others. But it may be better surgery to use a free graft (provided there is no exposed bone), since in this site it often provides better function with a less distorted contour and allows earlier recognition of any recurrence.

Another problem arises from the presence of radiodermatitis round a previously irradiated lesion which is often the result of ill-advised treatment. This tiresome complication may restrict the use of adjacent skin flaps.

A warning must also be added on the danger of attempting to use contused, lacerated, or ischæmic skin to repair recent traumatic injuries. The necessary undermining and the inevitable postoperative œdema and tension will often suffice to kill skin which would otherwise survive. In such injuries the use of provisional free grafts is fully justified.

PRINCIPLES OF LOCAL FLAPS

The skin over most of the body is elastic, though in varying degree. Apart from its intrinsic capacity to stretch, it is also mobile and can thus be moved within limits in relation to deeper structures. Both these characteristics depend on many factors, but mainly on site and age. The scalp is inelastic and relatively immobile; by contrast the skin of the neck, especially in the aged, is remarkably adaptable.

Though a large flap tends to be less vulnerable than a very small one, the question of shape is much more significant. The important point is the ratio of length (base to apex) compared with breadth. It is usually taught that this ratio should in general not exceed

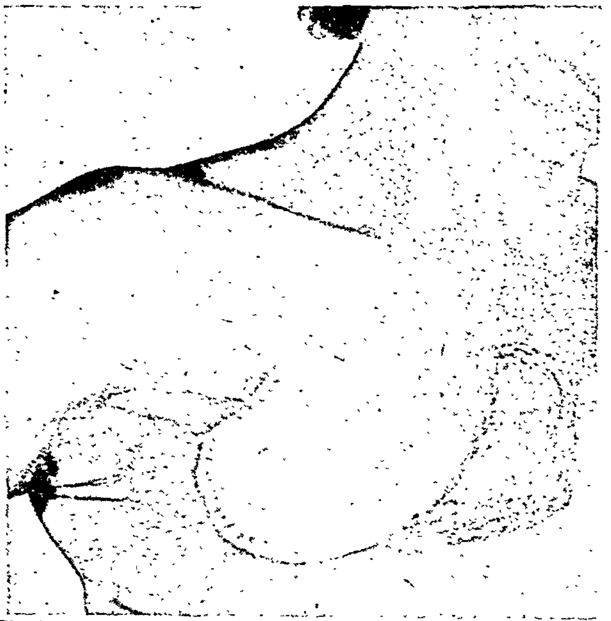
Fig. 4—Ten years after a radical excision for carcinoma of breast this patient had a recurrence involving two ribs. Excision down to pleura left a defect best closed with a rotation flap. Patient free from trouble 21 months later.

It is suggested therefore that this form of treatment should be reserved for patients who are physically unfit for operation A trial period of conservative treatment is illogical Some improvement may take place but it does not warrant the postponement of surgical relief

Posterior spinal fusion may bring permanent relief by immobilising the ligamenta flava, but as a mechanical solution of the problem it has less to commend it

Surgical measures so far described are laminectomy, removal of periradicular adhesions, division of ligamenta denticulata, and removal of disc protrusions Opinions differ about the advisability of removing hard bony ridges from in front of an adhering theca and spinal cord Allen (1952) describes his own technique for their eradication Brain et al (1952) advance considered reasons for holding removal to be dangerous and unjustified If removal can be safely accomplished it would clearly be a considerable mechanical gain for the spinal cord, but it must be a matter for each surgeon to decide in the light of his own experience The author's present and tentative opinion is that where the compressing agent is a nuclear protrusion—15% of a recent series in Edinburgh—it should be removed Where a bony ridge composed of ossified annulus and osteophytes is found it should be left undisturbed The following measures are available to ensure that it no longer fixes or causes compression to the spinal cord

Approach is by laminectomy and removal of ligamenta flava *It is not enough to make a window in the adjacent laminæ, leaving the ligaments and their attachments relatively undisturbed It should, however, be sufficient* to remove one lamina with its two attached ligaments for each anterior protrusion There is an advantage in conserving laminæ, for spinal stability, and it does not seem necessary to remove two routinely, as is usually suggested An exception might be made where the anterior bar is unusually high, requiring a greater degree of posterior decompression

Vascular extradural tissue surrounding roots and dura is systematically coagulated and removed thereby mobilising the theca

If the roots are raised and compressed against the articular facets the borders of these are trimmed to widen the *intervertebral canals* The least traumatic method of doing this is to grind down the bony shelves with a dental burr until there remains only a thin layer of cortical bone which can be picked off with fine rongeurs or a blunt hook Any cutting instrument inserted below the bone readily injures the roots How much of the articular facets may be removed without danger of later subluxation is a matter of opinion Certainly the less removed consistent with root decompression the better

The dura is opened in the midline Adhesions between the cord and the dura are systematically divided Ligamenta denticulata above *and below the protrusion* or protrusions are cut It will then be found that the spinal cord is freely movable within the range determined by the intradural course of the nerve-roots

ILLUSTRATIVE CASE RECORD

A railway foreman, aged 55, came for examination in January, 1952, complaining of stiffness in the right leg for two years *The stiffness had affected the ankle first and the* hip and knee later In the last four months the left leg had become similarly affected to a lesser degree Walking was becoming very difficult and he had had to stop working He reported no previous illnesses of importance and no injuries There were no disturbances of sphincters no stiffness or clumsiness of the upper limbs and no pain in the neck or shoulders

On examination he was intellectually well preserved No abnormality was found in the cranial nerves, in particular no nystagmus or increase in the jaw jerk There was no atrophy or fibrillation of muscles *There was loss of power* in both legs greatest in ankle movement, and more in the right leg than in the left There was no loss of power in the arms or trunk *Tone was increased in both lower limbs*, in the right more than in the left Some incoördination in rapid movements of both toes and ankles was found worse on the right The gait was typically spastic, with circumduction and scuffling of the right foot Examination of reflexes showed depression of the right biceps jerk and inversion of the right supinator jerk, with associated finger flexion, increased right finger jerk, with positive Trömner and *Hoffmann* signs, bilateral increase of knee and ankle jerks without clonus bilateral absence of abdominal reflexes, and extensor plantar responses The only sensory abnormality was some loss of *appreciation of vibration over the right foot and shin*

Lumbar puncture produced clear C S F Response to jugular compression was normal in flexion and extension, and the protein content was 50 mg per 100 ml

Radiography showed narrowing of the C5–C6 interspace with pronounced formation of posterior osteophytes Myelography confirmed the presence of a ridge at C5–C6 indenting the oil column anteriorly When the neck was hyperextended the usual ligamentum flavum indentations appeared, producing a complete break in the oil column opposite the disc protrusion.

Operation was on the lines suggested above The appropriate lamina and ligamenta flava having been removed, a bony ridge was found at the point of emergency of the C6 roots, and the spinal cord and dura were freed from it

Postoperative Course—Two days later there was subjective improvement in the stiffness of the legs In fourteen days the patient could walk better, and in twenty one days he walked almost normally, with a trace of right foot drop Power in the individual muscle groups was greatly improved The reflex changes in the limbs were unchanged In five weeks he returned to work Six months later it was found that he still had some weakness of the right ankle, with a tendency for the foot to invert after walking about fifty yards Knee and ankle jerks were no longer exaggerated, *but the plantar* responses remained extensor Abdominal responses had returned on the left side but were still absent on the right There was still loss of vibration sense in the toes of the right foot only

If the patient comes to surgery before irreversible changes have taken place in the spinal cord, recovery may be fairly complete and surprisingly rapid. If he comes too late for recovery, removal of the compression will halt the onward progress of the condition

SUMMARY

The association of spinal cord disorders with cervical spondylosis is briefly reviewed The difficulty of explaining a cervical cord compression syndrome in the apparent absence of true compression is stated.

It is suggested that the ligamenta flava, bulging anteriorly in cervical extension, cause recurring trauma to the cervical cord raised upon a disc protrusion or an osteophytic bar Experimental and clinical evidence in favour of this hypothesis is advanced

Proposals for treatment are made, and an illustrative case is *described*

I wish to thank Prof Norman Dott, in whose department the work was done, for helpful criticism, Dr Robert Saffley and Mr R White, of Bangour Hospital, for the radiological studies, Mr G A Smith, of the Royal Victoria Hospital, Belfast for the illustrations, and the *Journal of Bone and Joint Surgery* for permission to reproduce the radiographs in figs 1–3

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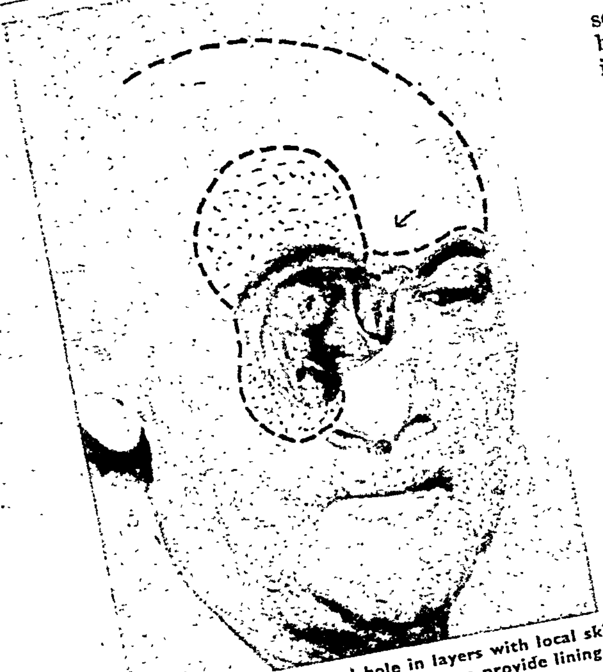

ig. 7—Repair of large compound hole in layers with local skin flaps. The shaded portions were turned in to provide lining.

importance of properly designed flaps and the fact that, since the scalp lacks elasticity, suturing under tension may lead to serious delay in healing. The surgeon's object should be to give safe cover by relieving tension at the point of danger, and free grafts should be reserved for areas of no importance. To achieve this the incision outlining a rotation flap must be generously planned, and the area of the flap must greatly exceed the area of the original defect. It is wise to remember that the scalp covers a convex surface, and the laws of spherical geometry involve unexpected difficulties in obtaining the necessary gain. It has been estimated that to advance the apex of a scalp rotation flap by 1 in. demands a curved incision 8 in. long; otherwise the secondary defect will not be self-closing.

A complex problem arises in relation to skin defects associated with loss of mucosa. Such compound defects are met in carcinoma or lupus of the face involving the nasal or the paranasal cavities, in full-thickness losses of lip or cheek, and in pharyngeal fistulæ following radical surgery for cancer of the larynx. In each case it is imperative to establish a lining that carries an adequate blood-supply, and that is therefore a living flap of either mucosa or inverted skin. On the face it is usual to turn in a flap of adjacent skin, which then lies inside out; this generally involves a turn of 180°, and special care is therefore necessary to prevent kinking of the "hinge" (fig. 7). These operations are commonly carried out as a secondary procedure, but in selected cases they should be completed as a primary repair. A similar problem is the closure of a large pharyngostome, which may be a troublesome operation for the laryngologist, especially if it is complicated by the effects of adjacent irradiation. Again two layers are usually essential, but the necessary skin cover can in most cases be given in a single operation, without recourse to many stages and multiple migrations.

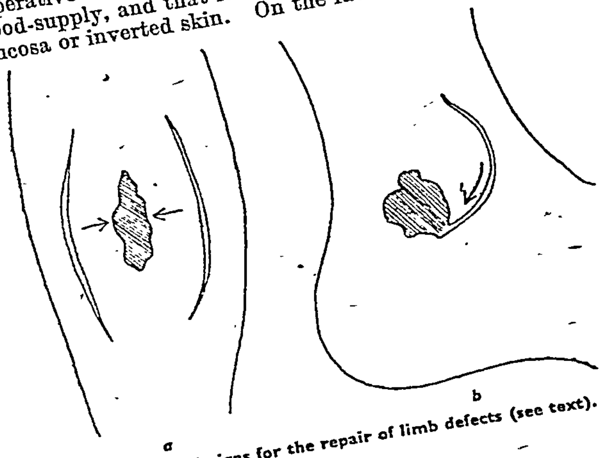

Fig. 8—Inferior designs for the repair of limb defects (see text).

A different principle lies behind the Abbe and Estlander flaps in lip repairs; these flaps include all layers—skin, muscle, and mucosa—and are nourished by a narrow *arterial* pedicle. The same principle is involved in the "fan" flap of Gillies. This also includes the full thickness of the cheek, and (unlike most other flaps) may be designed with a broad apex. It is based on a narrow pedicle near the corner of the mouth and is rotated to reconstitute the upper or the lower lip. The secondary defect should be self-closing.

INFERIOR DESIGNS

A final section must be devoted to those flaps of ill-conceived design which bring the methods under discussion into bad repute. Some of these useless designs are copied from textbook to textbook and thus survive, even in these enlightened days, to mislead the unwary. A summary in relation to figs. 8 and 9 should suffice:

(1) Relaxation incisions (except rarely on the scalp) are unsound and dangerous; this applies particularly to the limbs. The resultant sloughing, however, may still be seen as an occasional but needless complication of orthopædic repair (fig. 8*a*).

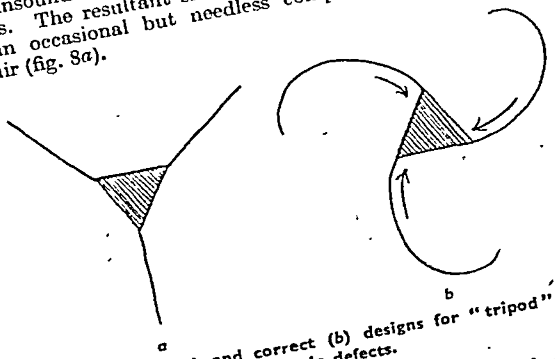

Fig. 9—Incorrect (*a*) and correct (*b*) designs for "tripod" closure of scalp defects.

(2) The Z-plasty, when misapplied to an elliptical defect, does not relieve lateral tension but only increases it.

(3) The inadequate "rotation" flap which is too short and too narrow is always a menace, especially near the ankle (fig. 8*b*).

(4) The *straight-legged* tripod incision for scalp defects is a futile procedure which is still figured in some modern textbooks. Harvey Cushing's three-flap operation succeeds admirably by virtue of the curve of its limbs (fig. 9).

SUMMARY

The repair of skin defects with local skin flaps as a primary operation has great advantages which are often overlooked.

A variety of designs are available, and there are wide indications for the use of these flaps, particularly for primary repair in operations for malignant disease.

The special problem of simultaneously providing lining and skin cover may often be solved by a single manœuvre

I am much indebted to my colleague Mr. R. H. Dale for h diagrams and to Mr. G. Clemetson for the photographs.

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TABLE IV—EXCRETION OF P.S.P. BY PATIENTS WITH HYPERTENSION AND HEART-FAILURE

Case no.	Age (yr.)	Sex	P.S.P. % in 2 hr.	Blood-pressure (mm. Hg)		Diagnosis
				Early	Now	
59	63	M	39	180/115	160/95	C.I.
60	39	M	45	220/145	130/110	H.H.F. & ? C.I.
61	59	M	32	210/110	130/85	C.I.
62	49	M	22	220/130	190/110	H.H.F.
63	68	M	38	180/130	160/100	H.H.F.
64	70	M	61	200/125	160/90	H.H.F.
65	67	M	38	240/130	170/110	H.H.F.
66	53	F	22	220/145	175/110	H.H.F.
67	68	F	25	—	225/130	H.H.F.
68	63	M	30	220/110	175/95	H.H.F.
69	57	M	37	230/130	205/100	H.H.F. & A.F.
70	42	M	43	200/110	190/95	C.I.
71	65	F	37	210/110	180/110	H.H.F.
72	73	F	36	220/120	180/85	H.H.F. & A.F.
73	69	M	31	230/140	210/120	H.H.F. & A.F.
74	72	M	25	210/110	150/85	C.I.
75	67	F	25	—	210/120	C.I.
76	59	F	35	—	240/140	H.H.F.
77	76	F	21	—	170/110	C.I. & A.F.
78	70	F	38	—	190/115	H.H.F.
79	73	F	38	220/105	120/60	H.H.F.

A.F., auricular fibrillation.
C.I., cardiac infarction.
H.H.F., hypertensive heart failure.

The bladder was emptied and the urine discarded. A glass of water (about 150–200 ml.) was given by mouth. 1 ml. of a sterile solution containing 6 mg. of P.S.P. was injected intramuscularly. At one hour and two hours urine was voided and saved. The output of P.S.P. in each specimen of urine was estimated separately. The estimations on the first half of the patients in each group were made by technicians at the London Hospital by visual colorimetry against a freshly prepared standard; the later ones were made by me with an Evans photo-electric colorimeter with an Ilford green no. 404 filter.

In the patients tested at the London Hospital the urea-concentration test was done simultaneously, 15 g. urea in 100 ml. water being given by mouth instead of the water alone. Cottet and Courjaret (1946) showed that urea did not affect the output of P.S.P., but they pointed out that oliguria and polyuria caused an error in the test. The volumes of urine in the present series were 60–180 ml. per hour, most of them being 100–140 ml. per hour.

RESULTS

Controls

The percentage excretion in two hours of the administered dose of P.S.P. in the controls is recorded in tables I and II. In all these the excretion exceeded half the dose given, with a mean excretion of 68% in those aged 15–40 and 62% in those aged 45–75.

Ageing caused a slight but significant reduction in the excretion of P.S.P. over two hours and must be taken into account when considering the subsequent groups. Sex made no difference to the amount of P.S.P. excreted.

TABLE V—EXCRETION OF P.S.P. BY PATIENTS WITH HEART-FAILURE AND WITH A PREVIOUSLY NORMAL BLOOD-PRESSURE

Case no.	Age (yr.)	Sex	P.S.P. % in 2 hr.	Blood-pressure (mm. Hg)		Diagnosis
				Early	Now	
80	60	M	50	165/90	160/80	M.S.
81	64	M	49	130/95	110/95	C.I.
82	[illegible]	M	60	160/80	110/75	C.I.
83	54	F	53	160/85	110/80	C.I. & A.F.
84*	74	F	48	—	170/80	Cor pulmonale
85	56	M	[illegible]	145/80	100/60	C.I.
86	60	F	52	150/80	160/80	M.S.
87	70	F	47	155/90	150/90	Cor pulmonale
88*	75	F	46	—	150/90	A.S.D. & M.S.
89	24	F	64	—	110/70	M.S.
90	47	M	[illegible]	—	130/80	M.S. & A.I.
91	71	M	41	150/90	120/80	C.I.
92	61	F	57	160/85	150/80	Cor pulmonale
93	51	M	50	110/60	160/60	A.I. & A.S.
94	49	M	[illegible]	150/90	120/80	A.S. & C.I.
95	47	M	65	145/60	110/60	M.S., A.I., & A.S.

A.F. auricular fibrillation.
A.S. aortic stenosis.
C.I. cardiac infarction.
A.I. aortic incompetence.
A.S.D. atrial septal defect.
M.S. mitral stenosis.
* The diagnosis was confirmed at necropsy, which showed no evidence of hypertension.

Hypertension Without Heart-failure

The percentage of P.S.P. excreted in this group is recorded in table III. In all except two patients it was less than 50% in two hours, with a mean value of 41.5%. All these patients were aged more than 45 except two who were aged 39 and 33.

Hypertension With Heart-failure

The percentage of P.S.P. excreted in two hours in this group is recorded in table IV. It was less than 45% in all but one of the patients, with a mean value of 34.3%. With only one exception the patients were aged more than 40.

Heart-failure Without Hypertension

The percentage of P.S.P. excreted in two hours is recorded in table V. It was greater than 45% with one exception; the mean value was 54%. All the patients were aged more than 45 except for one aged 24.

CONCLUSION

There is a clear difference between the amount of P.S.P. excreted by the controls and that excreted by the patients with uncomplicated essential hypertension, both in the mean and in the individual values. Similarly the amounts of P.S.P. excreted by the patients with heart-failure and hypertension were significantly lower than those excreted by the patients with heart-failure without antecedent hypertension. These findings are summarised in table VI and the accompanying figure.

TABLE VI—SUMMARY AND ANALYSIS OF RESULTS

Group	No. in group	Mean P.S.P. % in 2 hr.	Standard error of mean	
Controls 15–40 yr.	18	68	1.95	
Controls 45–75 yr.	15	62	1.78	$t = 8.9$, $p < 0.001$
Uncomplicated hypertension	25	41.5	1.43	
Hypertension with heart-failure	21	34.3	1.98	$t = 7.6$, $p < 0.001$
Heart-failure with no hypertension	16	54	1.65	

DISCUSSION

From these results it appears that the P.S.P. excretion test over two hours can be of definite assistance in diagnosing previous hypertension, whether or not heart-failure is present, provided the latter is not severe. For, although the excretion is decreased in heart-failure alone, there is a further significant reduction if hypertension is or has been present, and this can usually be detected by the test.

P.S.P. is eliminated both by glomerular filtration and by tubular excretion, and the latter is believed to be the more important (Goldring et al. 1936). However, when 6 mg. of P.S.P. is injected intramuscularly the plasma P.S.P. levels do not reach the range where self-depression of the tubular excretion of P.S.P. is important. Thus, at the plasma levels obtaining by this method of P.S.P. loading, the excretion of P.S.P. depends mainly on renal plasma flow. Heart-failure reduces renal plasma flow (Merrill 1946), and hypertension by itself also reduces it (Goldring and Chasis 1944). Moreover, where cardiac failure and hypertension coexist, each causes its own reduction in renal plasma flow; hence lower figures are obtained than when either condition exists alone (Brod and Fejfar 1950).

In this way the present results can be explained. Nevertheless it is difficult to reconcile them with those of other workers who have found normal values for the two-hour P.S.P.-excretion test except relatively late in the course of hypertensive disease (Goldring and Chasis 1944).

CLINICAL FINDINGS

All our patients, except cases 6 and 12, showed high glucose tolerance, 8 shallow insulin-tolerance curves (diminished insulin sensitivity), as is usual in pituitary overactivity, and 5 normal glucose tolerance. The basal metabolic rate (B.M.R.) and the specific dynamic action of protein showed no definite changes in any direction; nor was the serum-cholesterol level instructive. The serum-potassium and serum-sodium levels and the urinary excretion of 17-ketosteroids were not helpful in assessing the adrenal cortical function.

All our patients had, of course, high red-cell counts. A count of less than 6,000,000 per c.mm. was found only in case 2 (pituitary obese), case 3 (obese diabetic), and case 6 (erythræmic). The hæmatocrit values were also high—between 46·5 and 79. Six cases of erythræmia showed moderate leucocytosis (above 10,000 per c.mm. in cases 6, 9, 10, 12, 13, and 14); and the differential count in all the cases showed a slight shift to the left, as is usual in erythræmia. The blood volumes, determined by the dilution method with Evans blue, in all the cases examined (cases 2, 3, 4, 7, 8, 9, 11, 12, and 14) were increased owing to the enlargement of the red cells (Heilmeyer 1931). It was moderately increased (7·5–8·46 litres) in the patients with symptomatic pituitary polycythæmia (cases 2, 3, and 4), and greatly increased (12·7–17·0 litres) in the patients with erythræmia (cases 11, 8, 12, and 9). Heilmeyer gives similar values. There were only two patients with erythræmia (cases 7 and 14) who had blood volumes as low as 8·2 and 9 litres.

CLINICAL AND LABORATORY FINDINGS BEFORE AND AFTER TREATMENT

Case no.	Age (yr.) and sex	Spleen	Blood-pressure (mm. Hg)		Erythrocytes per c.mm. Hæmatocrit. Hæmoglobin. Leucocytes per c.mm.		Blood-sugar (mg. per 100 ml.)		Glucose-tolerance curve		Insulin sensitivity		Serum-potassium. Serum-sodium (mg. per 100 ml.)		*Urinary 17-ketosteroids* (mg. per 24 hr.)		Duration of treatment (days)	Total dosage (g.)
			Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After		
1	43 M	Not palpable	175/128	130/90	6,090,000 61 135% 7800	4,380,000 42½ 94% 6200	118	92	High	Normal	Diminished	Normal	18·5 359·0	17·8 327·0	20·0	6·2	70	63
2	52 M	Not palpable	240/135	170/110	5,980,000 57½ 130% 9100	4,870,000 48½ 107% 10,800	152	124	High	High	Diminished	Diminished	18·0 319·0	20·4 309·0	4·75	9·9	98	220
3	20 F	Not palpable	130/95	125/85	5,510,000 46½ 103% 4800	4,570,000 40 89% 4100	220	149	High	High	..	..	24·8 324·0	22·4 314·0	..	..	30	56
4	46 M	Not palpable	120/70	130/85	6,190,000 53 118% 8700	4,720,000 44 98% 8600	110	109	High	High	Diminished	Diminished	21·6 397·0	20·2 367·0	14·0	8·0	21	29
5	,,	Not palpable	130/75	130/85	6,040,000 50½ 112% 8600	5,050,000 48 106% 8600	..	..	High	..	Diminished	..	..	..	..	..	21	56
6	38 M	Palpable	120/85	125/85	5,780,000 52 114% 13,900	4,890,000 45 100% 8200	98	92	Normal	Normal	Normal	Normal	..	..	2·25	8·2	23	23
7	52 F	Palpable	170/120	150/105	6,270,000 61½ 136% 8400	5,370,000 52 114% 6100	99	..	High	..	Normal	..	24·9 314·0	21·3 338·0	9·0	7·0	59	158
8	51 M	Palpable	125/95	117/75	8,000,000 79 175% 8500	5,810,000 59 130% 11,700	90	..	High	High	Normal	Normal	18·8 291·0	18·2 308·0	15·0	12·0	148	1167
9	44 M	Palpable	130/90	135/85	7,310,000 74 164% 11,800	6,220,000 65 144% 13,300	110	96	High	Normal	Diminished	Normal	22·4 307·0	18·8 297·0	13·2	8·5	100	986
10	52 F	Not palpable	160/100	130/90	6,780,000 62 138% 12,700	5,960,000 56 124% 13,100	105	95	High	Normal	Diminished	Normal	..	..	11·7	11·0	43	43
11	43 M	Palpable	130/90	135/90	7,170,000 75½ 167% 5300	6,560,000 69 153% 5500	106	..	High	..	Normal	..	24·8 318·0	21·6 316·0	13·5	9·2	37	91
12	64 M	Palpable	115/80	125/80	8,010,000 74½ 165% 10,800	7,140,000 68½ 151% 8100	90	..	Normal	..	Normal	..	..	..	..	..	52	166
13	61 F	Palpable	160/100	160/100	7,200,000 70 155% 11,100	6,640,000 65½ 145% 6100	110	106	High	Flat	Diminished	Normal	..	..	8·5	3·8	32	32
14	65 M	Palpable	140/90	140/85	7,500,000 56½ 126% 12,800	7,080,000 52 114% 9900	107	..	High	..	Diminished	..	17·6 324·0	18·8 336·0	11·0	7·8	14	32

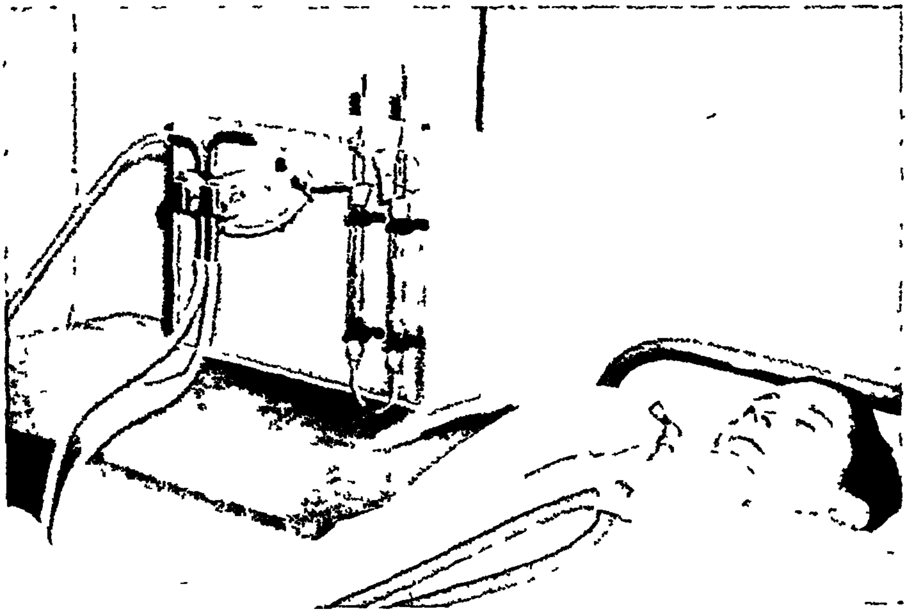

Fig 1—The respirator

the connection occurring, an electrical impulse is sent through the "booster" (O) to the corresponding coil on the valve, and the piston moves to the opposite side

Movement of the fluid from one tube to the other is through the connecting-tubes I and II By means of these connecting-tubes it is possible to vary the time-ratio between inspiration and expiration—a ratio that should be 1 2 During inhalation the fluid moves (fig 2) from L_1 to L_2, partly through I, where the flow is reduced by the screw-valve P, but mainly through II, where the flow is not checked A small light ball at the bottom of L_2 is lifted by the inflow through II and does not hinder it, so that it takes place quickly and easily During inhalation, II thus functions as a shunt, and the rising of the fluid in L_2 is not retarded in relation to the rise in pressure in the patient's air-passages

On the fall in pressure in L_1 that takes place during expiration, the flow of the fluid will be reversed, and the two floats move back to the position of equilibrium (fig 4), but the ball will now prevent a flow back through II, and allow passage only through I The rise of the fluid in L_1 can therefore be retarded in relation to the fall in pressure on the fluid by the use of the screw P, and the exhalation phase made as long as may be desirable

OPERATION OF THE RESPIRATOR

A coherent impression of the working of the apparatus is best obtained by following its operation through the three phases of inspiration, expiration and expiratory pause

Inspiration begins with the piston at the extreme left (fig 2) The rubber bag now distended, presses its contents through the valve, the inspiration tube, and the Y connection down into the lungs Here the pressure rises and this passes over through the side tube K to L_1, and presses the fluid over into L_2, while the little ball is raised by the inflow Inspiration is ended when the floater in L_2 closes the electric circuit between the electrodes there (fig 3) At the same moment the current flows through the right-hand coil and the piston moves over to the extreme right position

Now *expiration* begins (fig 4) The elasticity of the thorax presses the gas out through the valve to the outer air, and at the same time the pressure over the fluid in L_1 falls Because of the screw-valve P, the fluid flows slowly back through I from L_2 to L_1—so slowly that there is time for both complete expiration and the *physiological* expiratory pause This ends when the float comes back to its electrodes and closes the circuit between them (fig 5), which starts off the next inspiration

REGULATION OF THE RESPIRATOR

In artificial respiration such as this only three factors appear to need regulation (1) the rate of respiration, (2) the time-relation between inhalation and exhalation, and (3) the maximal pressure in the lungs at the end of the inhalation phase (inspiration pressure)

Rate of respiration—If the inspiration pressure is kept constant (by maintaining the position of the electrodes in L_2) the respiratory rate can be increased, in the first place, by shortening the inspiratory phase If the same pressure in the lungs is to be obtained in a shorter time, this must be done by filling the lungs in a shorter time Therefore the rate must be increased by increasing the flow from the oxygen cylinder If the time ratio between

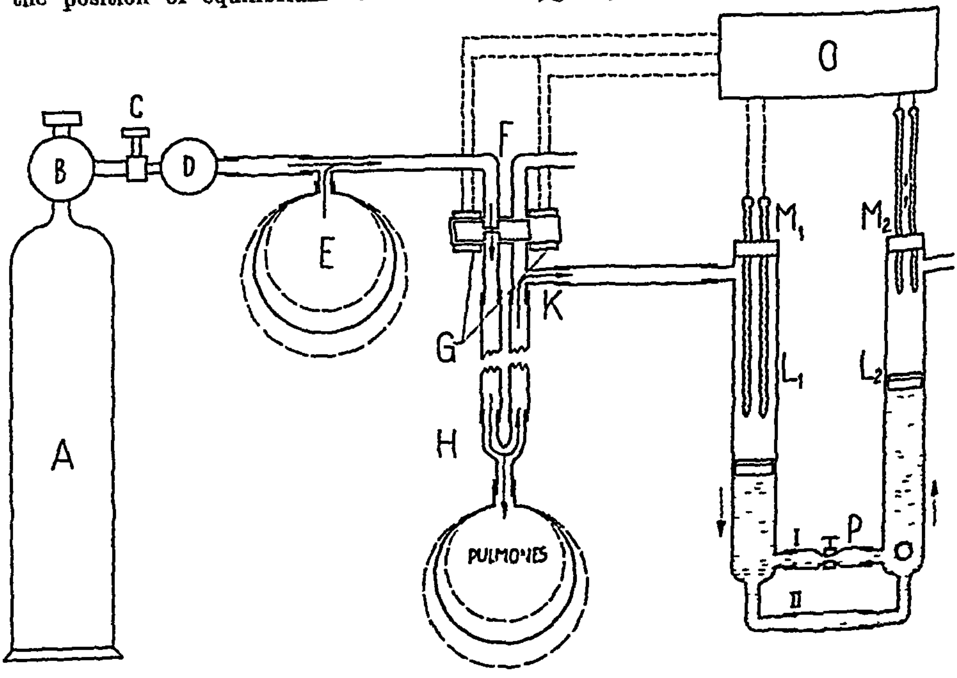

Fig 2—Diagram of respirator, during inspiration

clinical findings show, a considerable part in blood formation.

Though Flaks et al. (1937, 1938) and A. Querido and G. A. Overbeek (cited by Aschkenasy 1952) assume the existence of a specific pituitary erythropoietic hormone, and the latter workers also that of a specific hæmolytic one, their findings need confirmation; if they are right, *p*-hydroxypropiophenone might act on these hormones.

The hæmopoietic or hæmolytic action of the target glands of the pituitary seems not to be due to specific hormones, for there is no certain proof of their existence. For instance, Mansfeld's (1943) myelotropic hormone is hypothetical. Changes in the formation and destruction of the blood might be due to decreased activity of the target glands brought about through the depressant action of *p*-hydroxypropiophenone on the secretion of the pituitary hormones which act on those glands.

Our experiments show that the decrease of the red cells and of the hæmatocrit does not proceed pari passu, but that the decrease of the hæmatocrit lags behind that of the red cells at least in some cases, producing a tendency to hyperchromia and macrocytosis of the red cells. This suggests that *p*-hydroxypropiophenone affects primarily the formation of the red-cell stroma, perhaps through the inhibition of nucleoproteid synthesis, and only secondarily th[illegible] of action of *p*-hydroxypropiophenone, we think that our therapeutic results support our theory of the pathogenesis of symptomatic pituitary polycythæmia and erythræmia (Haynal and Gráf 1950) and refute Aschkenasy's (1952) objection based on the failure of our previous therapeutic experiments with sex hormones, thiamine, and radiotherapy.

The treatment of erythræmia and symptomatic pituitary polycythæmia with *p*-hydroxypropiophenone is aimed at the cause of these diseases as opposed to the alleviation of their symptoms, such as has been provided hitherto by the dietetic reduction of materials necessary for blood formation, the diminution of erythrocytes and the blood volume through venesection, hæmolysis with phenylhydrazine, and the inhibition of the erythropoietic action of the bone-marrow with arsenic, radiotherapy, benzene, or radioactive phosphorus.

SUMMARY

On the assumptions that (1) symptomatic polycythæmia and erythræmia are due to overactivity of the pituitary gland, and (2) *p*-hy[illegible] depresses the pituitary gland, four ca[illegible] and nine of erythræmia were treated with *p*-hydroxypropiophenone. Treatment in six of the cases of erythræmia was incomplete because the drug became unobtainable.

Undesirable effects were seen in two cases of incompletely treated erythræmia: nausea and vomiting in one, and toxicoderma in the other.

Therapeutic effects were observed on the red cells, hæmatocrit, and hæmoglobin, but were not permanent without a maintenance dosage. The results were obtained without hæmolysis and without histological signs of toxic effects on the bone-marrow.

It is claimed that these results support the theory that symptomatic polycythæmia and erythræmia are due to overactivity of the pituitary gland, and that treatment with *p*-hydroxypropiophenone aims at the cure of these diseases by the abolition of their cause—i.e., the overactivity of the pituitary—rather than the alleviation of their symptoms, such as has been provided by other remedies hitherto.

Grateful acknowledgment is made to the staff of our laboratory and especially to our clinical chemists Dr. Lily Pollák and Dr. Maria Stützel.

References at foot of next column

MECHANISM AND TREATMENT OF SPINAL-CORD DISORDERS ASSOCIATED WITH CERVICAL SPONDYLOSIS

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DISORDERS of the spinal cord associated with cervical spondylosis have received intermittent attention since the beginning of this century. Bailey and Casamajor (1911) described five cases, and further contributions were made by Parker and Adson (1925), Krabbe (1928), Junghagen (1929), Beadle (1931), Mixter and Barr (1934), Morton (1936), and others.

In recent years there has been greater recognition of the clinical syndromes associated with spondylotic changes in the cervical spine, and Kahn (1947), Bucy et al. (1948), Spillane and Lloyd (1951, 1952), Allen (1952), Bedford et al. (1952), and Russell Brain et al. (1952) have reviewed the subject from the standpoints of pathology, ætiology, clinical presentation, and treatment. From these reviews there emerges a clear and complete clinical picture, but the way in which the lesions of the spinal cord are produced remains somewhat obscure. As a result opinions differ about the best line of treatment.

It remains to be satisfactorily explained how a syndrome commonly associated with compression of the spinal cord is produced without apparent naked-eye compression of the cord visible at operation or post mortem. Queckenstedt's test for obstruction of the subarachnoid pathways is usually negative, and the protein content of the cerebrospinal fluid (C.S.F.) is seldom increased to the amount of that commonly observed caudal to an obstruction.

In this paper an attempt is made to show that in cervical spondylosis the spinal cord is compressed not by the disc protrusions alone but also by the ligamenta flava, which move forward as the neck is extended. Treatment is considered in the light of this hypothesis. In the interests of simplicity "disc protrusion" is taken to signify either simple nuclear extrusion, which is relatively uncommon, or ligamentous and annular thickening, with secondary osteophyte formation, which together form the transverse bars found in about 80% of cases.

CLINICAL SYNDROMES

Cervical disc protrusions cause symptoms referable to the nerve-roots, to the spinal cord, or to both. The neuritic syndromes caused by root compression are familiar and will not be described here. Spinal-cord compression is manifest as spastic paraparesis, with or without involvement of one or both upper limbs, or as hemi-cord dysfunction—variants of the Brown-Séquard syndrome. The clinical variations were well described by Stookey (1928) associated with ecchondromata, which disc lesions were then thought to be. Further good descriptions have been given by Allen (1952), Spillane and Lloyd (1952), and Brain et al. (1952). These observers agree that the

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The third patient, a 25 year old woman had no spontaneous respiration at all She has used the apparatus since Jan 20 She is pleased with it, and her clinical condition has been satisfactory

Blegdam Hospital, after an observation period, has ordered a further 12 respirators, to replace the students (still numerous) who supply manual respiration

POSSIBLE FURTHER USES OF THE RESPIRATOR

This apparatus has proved suitable for poliomyelitis patients, and can be adjusted to help patients who are either wholly incapable or can manage only a modicum of spontaneous respiration

It seems natural, however to consider also the possibility of using the apparatus in other cases where the patient's own respiration has stopped or is not functioning adequately Here one is in the sphere of hypothesis, since such other uses have not yet been tested

Poisoning

Cases of poisoning—particularly in patients who have taken morphine or other drugs with a gross depressive effect on the respiratory centre—are at present where spontaneous respiration is inadequate, treated by manual pressure ventilation after intubation—perhaps tracheotomy The use of the respirator in such cases might be considered

Accidents

Carbon-monoxide poisoning, drowning accidents, and similar conditions where artificial respiration is indicated seem, in theory at any rate, suitable for treatment with automatic pressure ventilation, applied through a closed mask

Operations

In thoracic operations where the pleura is opened and the negative Donders's pressure is removed, and oxygen and an anæsthetic are given by manual pressure ventilation after intubation, the use of the respirator seems possible The current that flows between the electrodes in the tube L_1 is so small that no electric spark is produced The danger of explosion in cases where the anæsthetic used is an explosive mixture is thus infinitesimal By a slight modification in the design, however, the apparatus may be made absolutely safe in this respect

Deep anæsthesia, alone or combined with curare injection to secure complete relaxation of the muscles, seems to provide a field where it is important to ensure respiration The capacity of the apparatus to "cooperate" with the patient would seem to be of value here The same may perhaps be true in the post anæsthetic phase

Deficient Oxygenation

Finally—to mention other and more remote possibilities—it may be possible, for short periods and by the use of a closed mask, to try the effect of such moderate pressure ventilation in cases where the oxygenation of the blood is insufficient because of superficial respiration This may arise in connection with reduction in efficient lung tissue—e g serious pneumonia lung œdema from uncompensated heart failure, shock traumatic and spontaneous pneumothorax

This, however, is only guessing which still has to be checked

SUMMARY

A new principle of automatic artificial respiration has been applied to the construction of a respirator, which has so far proved satisfactory in cases of poliomyelitis

This respirator, which is easily and cheaply made, operates in response to variations in pressure in the respiratory system, with which it has an airtight connection

The apparatus may also prove useful in the treatment of conditions other than poliomyelitis

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THE BIOLOGICAL ACTIVITY OF TRIIODOTHYRONINE

E G Tomich
B Sc Lond F R I C

E A Woollett

From the Pharmacology Unit, Glaxo Laboratories, Greenford Middlesex

THE finding of Gross and Pitt-Rivers (1952) that 3 5 3'-L triiodothyronine was three or four times as active as L thyroxine in preventing goitre in thiouracil treated rats prompted us to repeat their experiment and to determine the relative potencies by two other methods

A comparison by the goitre prevention assay was performed in duplicate, 74 rats being used in the two experiments Groups of rats received daily subcutaneous injections of the two compounds at two dose levels for ten days and a control group was injected with saline solution alone Throughout the experiment all five groups were offered ad lib tap-water containing 0 1% thiouracil A sixth group, of uninjected rats, got plain tap water On the eleventh day the rats were killed and their thyroid glands were removed and weighed The combined results from the two experiments were statistically analysed and showed L-triiodothyronine to be 7 4 times as active as L thyroxine

A second comparison, by a mouse anoxia method (Smith et al 1947), was made in triplicate, each experiment involving eight groups of 9 mice each Three groups were treated with L thyroxine at different dose levels, and the remaining five groups received graded amounts of L triiodothyronine Subcutaneous injections were given on the first, third, and fifth days of the experiment On the seventh day individual survival times were measured The combined results of the three experiments gave an activity ratio of 4 5 1 in favour of L triiodothyronine

Finally the effects of the two compounds on the rate of consumption of oxygen were compared in rats by a modification of the technique of Maclagan and Sheahan (1950) In one experiment the materials were injected subcutaneously at three dose levels to six groups of 4 rats each Daily injections were given on seven consecutive days, and individual oxygen consumption rates were determined daily throughout the experiment L triiodothyronine was found to be 5 1 times as active as L thyroxine A similar experiment, in which the drugs were given by mouth, gave a ratio of 5 3

During the course of absorption and excretion studies in rats and cats with labelled L triiodothyronine it was found that recoveries measured by the Blau (1935) isolation technique were similar to those obtained with thyroxine This technique has been widely used in the past by workers interested in the metabolism of thyroxine If exogenous thyroxine is deiodinated to triiodothyronine in the body, those who have used the Blau method for recovering thyroxine from animal tissues may well have been estimating triiodothyronine alone or a mixture of both substances

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produced evidence (not present in flexion) of obstruction of C.S.F. In one of the cases reported by Bucy et al. (1948) myelography showed obstruction of the oil column at the C5–C6 interspace only when the neck was hyperextended. Spillane and Lloyd (1952) observed that at the site of disc protrusion obstruction occurred in most cases only during hyperextension. This position was used routinely in [illegible] patients. Brain et al. (1952) noted greater deformity of the oil column in the extended position of the neck. Kaplan and Foster Kennedy (1950) drew attention to obstruction of the C.S.F., judged by Queckenstedt's test, in the extended position of the neck in eight patients who had either cervical disc protrusion or cervical arachnoiditis. A control series of more than 200 patients without such lesions showed no obstruction to the C.S.F. in any position of the neck.

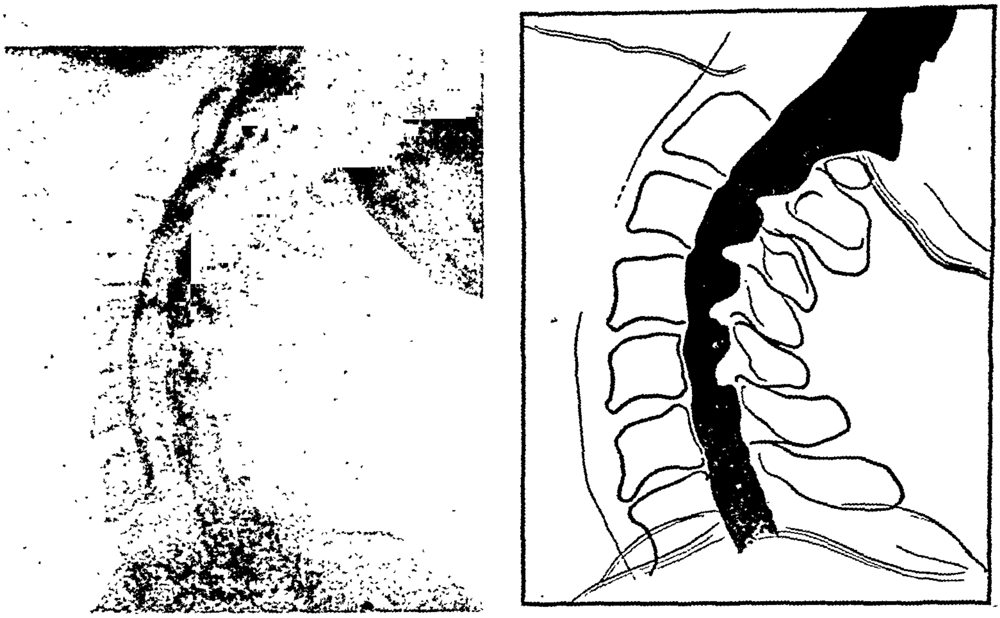


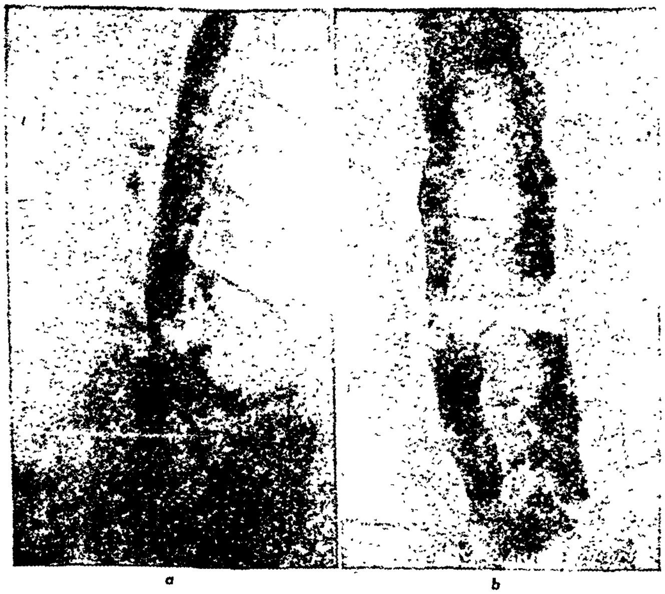
Fig. 3—Myelogram of cervical spine in cadaver showing compression between disc protrusions between C5 and C6 and between C6 and C7 and ligamenta flava bulging forward in hyperextension.

It is therefore suggested that the ligamenta flava, compressed and bulging intraspinally as the neck is extended, act as an intermittent compressing agent capable of producing gradual changes in the vasculature of the spinal cord, the precise nature of which is uncertain. The cord is held in position to receive each impact of recurring compression by the spondylitic elevation in front of it.

TREATMENT

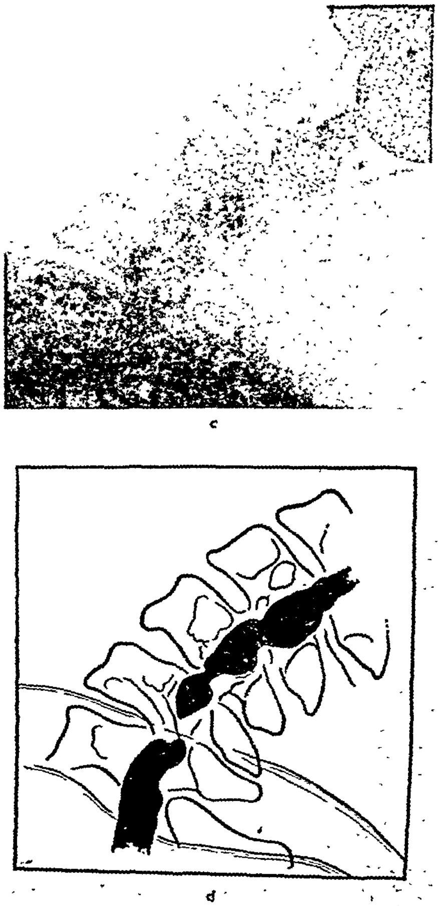
If the evidence for the compressing rôle of the ligamenta flava is held to be adequate, a rational line of treatment can be planned accordingly.

[illegible] took place in patients treated [illegible] et al. (1952) and by Spillane and Lloyd (1951). Immobilisation limits extension and prevents recurring trauma from the ligamenta flava. It cannot create any more room for the embarrassed spinal cord, because there is no inflammation to subside with rest. To be effective, immobilisation must continue for life. Whenever movement is restored, intermittent compression recurs with each movement of extension.



a b

Fig. 4—Myelogram of cervical spine in living patient with disc protrusion between C5 and C6: a, lateral view in normal position of neck; b, anteroposterior view in normal position of neck; and c and d, lateral view in forced extension of neck.



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Reviews of Books

Frontal Lobotomy and Affective Behaviour

A Neurophysiological Analysis JOHN F FULTON, M D, Sterling professor of physiology, Yale University London Chapman & Hall 1951 Pp 159 21*s*

Professor Fulton has an outstanding claim to write on this subject—or rather speak on it, for these were the Salmon lectures of 1950—for it was observations made by him and Carlyle Jacobsen on chimpanzees that led Egas Moniz to try interrupting the frontal projections in man as a method of treating mental disorder He writes with masterly selection and control of his material After reviewing the historical background, he considers the advances lately made in relating structure to function in the cerebral cortex and its connections, and some recent studies of behaviour in primates after section of various pathways The final division of the book is concerned with the effect upon mental disorders of more limited procedures than radical leucotomy Dr Fulton believes that the radical operation should now be abandoned, because of the intellectual impairment which follows from any lesion of the lateral surface of the frontal lobe or section of its projections on this the evidence is perhaps less conclusive than he believes

Management of Abdominal Operations

Editor RODNEY MAINGOT, F R C S London H K Lewis 1953 Pp 1253 £6

Mr Maingot expresses the hope that the title of this large book adequately explains its scope but the reader—and indeed some of the 33 contributors—may think it errs on the side of conservatism

Much of the book is concerned with physiological factors which have a bearing on abdominal operations—such as water and electrolyte balance, thrombosis, acidæmia and alkalæmia—and the parts played by vitamins, antibiotics, and so on Then there is a full consideration of anæsthesia, of chest complications, of thrombosis, and of early ambulation In this part of the book a great amount of knowledge has been collected, and it is all up to date though there seems to be no account of water intoxication, nor mention of proctoclysis But a judicial summing-up and an assessment of the value of many procedures recommended would really have been of more use than the encyclopædic methods used by most contributors in the section on anæsthesia for gastrectomy, for instance, the author carefully conceals his predilection, if he has one, for any particular method

The second part deals with regional abdominal disease Some of these chapters—those on the biliary tract, the œsophagus and gastric surgery in general—are excellent, and the discussion on vagotomy is helpful and illuminating, but some chapters suffer from the inability of the writers to make up their minds Thus some describe operative procedures while others do not Detailed technique from an experienced operator would have been welcomed, for example, in the account of herniorrhaphy—still an unsolved problem The simple steps of an interval appendicectomy are described, but no guidance is given on how to avoid injury to the nerves of the bladder in the excision of a carcinoma of the rectum Suction drainage is advised after all major abdominal operations on the gastro-intestinal tract, indeed, surgeons just now seem obsessed with suction drainage For intestinal obstruction it is recommended in all cases except those of strangulation But what indubitable signs of strangulation are there? We are not told There is an extraordinary recommendation to stretch the sphincter ani (to paralyse it) after operations in acute appendicitis for the avoidance of gaseous distension But why not pass a rectal tube, should the need arise? Why tear the fibres of the sphincter ani?

The third part consists of two chapters only—an elementary account of aseptic surgery and a very useful dictionary of clinical pathological values in health and disease

The editor admits repetition, dogmatism overlapping, lack of balance, different opinions, and lack of style, and he makes out a good case for the freedom of the contributor But a little less licence would have made the book more readable and comprehensible

Metabolic Interrelations

With Special Reference to Calcium Transactions of the 4th Macy Conference Editor E C REIFENSTEIN, M D, director, Oklahoma Medical Research Institute New York Josiah Macy, Jr, Foundation 1952 Pp 262 $4 60

AT the conference reported here 27 participants discussed 20 papers, dealing with different aspects of bone structure and formation The reporting is of the literal type common to this large series, so that closely argued theses, obviously destined for separate publication, are interspersed with the unbuttoned trivia of peripheral experts

The first five papers deal with the collagenous matrix of bone and cartilage, then comes a group of papers dealing with calcification and the crystal structure of calcium salts, sodium, fluoride, and sulphur in bone are each discussed in one paper Perhaps the two contributions of most general interest are the introductory paper by R H Follis on the structure, formation, and distribution of calcium and bone matrix, and J Gross's account of the in vitro fibrogenesis of collagen, beautifully illustrated by electron photomicrographs The final paper in the series has the inviting title, "Composition of teeth in relation to caries susceptibility", but it is a one page account of a small series of animal experiments and there was no discussion

This volume can be recommended to anyone interested in a fundamental approach to the structure and mineralisation of bone matrix, collagenologists should welcome the first five papers, and the paper on the turnover of bone sodium doubles previous estimates of the amount of sodium in this metabolically inaccessible situation

Practical Dermatology

GEORGE M LEWIS, M D, F A C P, professor of clinical medicine (dermatology), Cornell University Medical College Philadelphia and London W B Saunders 1952 Pp 328 37*s* 6*d*

THIS is designed as a text for medical students, a practical guide for general practitioners, and an aid in orientation for other specialists Professor Lewis confines himself to a description of the clinical features and management of the more common skin disorders, and has purposely omitted histology, mycology, bacteriology, and other subjects only indirectly related to dermatology The book is profusely illustrated in monochrome with 90 pages of photographs of uniformly good quality These are displayed in groups, with relevant textual details placed, as often as possible on the opposite page The chapter on animal infestations is particularly good, and supported by a veritable picture gallery—including everything from the commonplace if rarely photographed ova of *Pediculus vestimenti*, to the more rarely seen facies of the patient with trichiniasis Few of the author's opinions are controversial, but surely it is surprising to see seborrhoeic keratoses classified among the premalignant and malignant tumours Psychological factors are given adequate consideration and Professor Lewis rightly stresses that sympathetic history taking is often an important part of treatment He gives a short but useful bibliography of general texts and special monographs The chapter on dermatological formulæ is not of great value to doctors practising in the British Isles, since many of the proprietary preparations mentioned are not available in this country

The author has carried out very well what he set out to do

Anatomy of the Nervous System (9th ed Philadelphia and London W B Saunders 1953 Pp 581 42*s* 6*d*)—Dr S L Clark's latest revision of Ranson's well known textbook follows the pattern of the last edition Our knowledge of the structure and function of nervous pathways is growing so rapidly, under the stimulus of modern methods of study, that no textbook can include all that is known or surmised about them at its moment of publication, and Dr Clark is modestly aware of this Nevertheless, he has done his best, by adding new material and illustrations and by blending the account of structure with that of function, to grapple with his expanding subject

THE RENAL EXCRETION OF PHENOLSULPHONPHTHALEIN AS AN AID TO THE DIAGNOSIS OF PREVIOUS HYPERTENSION

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THIS investigation arose from the difficulty of diagnosing hypertension in older patients when the blood-pressure had fallen for any reason, notably following cardiac infarction. In such cases the signs of heart-failure often overshadow those of hypertension; and, although radiology will show considerable enlargement of the heart, such enlargement could be the outcome of cardiac infarction with or without failure. Again, the evidence of ventricular preponderance in the electrocardiogram may mask the changes of cardiac infarction, and a past history or record of hypertension is available in only a few cases. The changes in the retinal vessels, although of great value, are not always easily recognisable. The need for additional evidence of previous hypertension in these circumstances has been apparent for some time; for, although the treatment, usually that of heart-failure, is unaffected by this lack of information, the ultimate prognosis depends largely on an accurate diagnosis of the underlying ætiology.

TABLE I—EXCRETION OF P.S.P. BY YOUNG CONTROLS

Case no.	Age (yr.)	Sex	P.S.P. % in 2 hr.	Blood-pressure (mm. Hg)	Diagnosis
1	35	F	75	120/70	Fibroids
2	38	M	74	130/80	Healthy
3	16	F	70	130/70	Healthy
4	39	M	78	125/85	Healthy
5	34	F	56	105/65	Healthy
6	23	F	56	120/70	Enuresis
7	30	F	73	140/80	Pregnancy
8	29	M	61	120/80	Duodenal ulcer
9	31	F	75	115/80	Diabetes mellitus
10	27	F	75	130/80	Healthy
11	25	M	77	110/70	Healthy
12	27	F	58	115/75	Healthy
13	17	M	54	145/80	Healthy
14	23	F	62	130/80	Recent acute pyelitis
15	38	M	64	110/70	Pneumonia
16	28	F	80	130/80	Migraine
17	39	M	64	140/70	Gastric ulcer
18	34	M	70	150/80	Healthy

Further, some patients present with heart-failure and cardiac enlargement but without clinical or electrocardiographic manifestations of infarction, signs of a valvular lesion, or increase in the blood-pressure. The cause of the failure in this group is often difficult to determine and all too frequently ascribed to past hypertension, often on extremely slender grounds. In studying the results of routine renal efficiency tests made in the clinical laboratory of the London Hospital on patients with essential hypertension, an appreciable decrease below normal of phenolsulphonphthalein (P.S.P.) excretion in two hours was often noticed, although the urea-concentration test, blood-urea level, and catheter specimens of urine were almost invariably normal.

TABLE II—EXCRETION OF P.S.P. BY OLDER CONTROLS

Case no.	Age (yr.)	Sex	P.S.P. % in 2 hr.	Blood-pressure (mm. Hg)	Diagnosis
19	57	M	74	140/80	Pneumonia
20	56	F	57	120/70	Healthy
21	56	M	60	160/80	Healthy
22	52	F	60	130/90	Healthy
23	67	F	61	150/80	Mild thyrotoxicosis
24	53	M	56	130/85	Orthostatic albuminuria
25	56	M	78	140/80	Prostatic hypertrophy
26	45	F	56	120/80	Healthy
27	75	M	72	150/90	Abdominal aneurysm
28	68	M	57	140/80	Bronchial neoplasm
29	49	M	59	120/80	Duodenal ulcer
30	59	M	64	130/75	Gastric ulcer; Hodgkin's disease
31	46	M	62	130/85	Gastric ulcer
32	70	F	54	160/90	Hiatus hernia
33	52	F	60	130/85	Healthy

MATERIAL

The present investigation was made to determine the value of the P.S.P.-excretion test as an indication of antecedent hypertension; for this purpose tests were made in four groups of patients:

(1) *Controls.*—This group comprised thirty-three persons: eighteen aged 15–40 and fifteen aged 45–75. All were either considered healthy or were ambulant patients with no disease referable to the renal tract or to the cardiovascular system, and none had hypertension.

(2) *Hypertension without heart-failure.*—This group was made up of twenty-five patients with essential hypertension having no evidence of heart-failure and no significant albuminuria. The retinal arterioles showed irregularity and narrowing of their lumen, and in some cases there were also scattered flame-shaped hæmorrhages. Patients with papillœdema were excluded from the series.

(3) *Hypertension with heart-failure.*—In this group there were twenty-one patients in whom heart-failure complicated essential hypertension. None had valvular heart-disease. Several of the patients had normal blood-pressures on admission, although previously they were known to be hypertensive.

(4) *Heart-failure without hypertension.*—Sixteen patients with heart-failure from rheumatic heart-disease, cor pulmonale, or cardiac infarction, but with a normal blood-pressure, made up this group. In allocating patients to this group care was taken to establish the fact that, before the onset of cardiac failure, the blood-pressure had been within normal limits. This was most readily told by reference to previous case-notes in most cases; and, when these were not available, by study of the retinal, electrocardiographic, and cardioscopic findings. Even then the cases were accepted only if these tests provided unequivocal evidence.

TABLE III—EXCRETION OF P.S.P. BY PATIENTS WITH HYPERTENSION WITHOUT HEART-FAILURE

Case no.	Age (yr.)	Sex	P.S.P. % in 2 hr.	Blood-pressure (mm. Hg)
34	60	F	36	220/120
35	45	F	41	200/120
36	70	M	34	230/130
37	45	M	38	205/115
38	70	F	46	210/110
39	76	F	35	200/110
40	58	M	23	260/120
41	54	F	46	190/105
42	45	M	32	200/130
43	48	F	43	230/130
44	43	M	43	220/135
45	71	F	35	230/125
46	51	M	57	170/110
47	59	F	45	220/140
48	52	F	39	250/130
49	46	F	55	195/115
50	55	M	44	190/120(a) 150/90 (now)
51	49	F	46	190/125
52	65	M	50	180/110
53	59	M	38	230/140
54	66	M	39	210/110
55	50	F	47	260/140
56	70	M	42	170/120(b) 130/80(now)
57	39	F	37	185/110
58	33	F	45	200/115

(a) = 18 mos. ago. (b) = 5 mos. ago.

The signs of heart-failure in the last two groups included a raised jugular venous pressure, an enlarged tender liver, and œdema of the feet. In no patient could the failure be called severe.

METHOD

The P.S.P. test of Rowntree and Geraghty (1910) was made on the patients, and the procedure was as follows:

air results in the most severe and most long-continued headache This immediate headache, which usually lasts about forty-eight hours, is attributed by VON STORCH et al[10] to the irritant effect of the air It may be followed by the low-tension headache, and total replacement seems again most likely to produce this second headache Most therapeutic agents now introduced into the theca have been tested thoroughly in advance The early sulphonamides, and the early forms of penicillin, carried their own special risks, now happily eliminated, but care should be taken in the use of any new drug Streptomycin has a definite irritant effect on the meninges and causes an alteration in the constitution of the C S F which persists for some weeks

If drugs or other agents are to be introduced into the theca they should be known to be harmless There is much sense in KENNEDY's[9] plea that spinal anæsthesia should be used only when general anæsthesia is absolutely contra-indicated Pneumo-encephalography can be performed humanely and efficiently with the introduction of 30–40 c cm of air, provided that this is combined with painstaking positioning of the patient in order to display all the ventricular system It seems unnaturally savage to insist on complete replacement in order to obtain complete ventricular visualisation with only two or three films, at the expense of twelve hours of acute agony for the patient and a severe enough headache lasting several days With regard to the actual technique of puncture, is it too banal to suggest that the operator should approach this with the care and precision which he would like to have exercised on himself? Strict asepsis, and careful insertion of a sharp, small-bore needle into the correct space, with the minimum of trauma to intrathecal and extrathecal tissues, will avoid all the hazards in groups one and two, and will, in addition, do much to reduce the risk of headache HART[11] reports favourably on the use of a pencil-point needle The occurrence of headaches in 40% of ambulant patients in SCIARRA's[7] series confirms the idea that twenty-four hours' rest in bed is advisable after lumbar puncture Elevation of the feet perhaps has little to commend it, but there seems to be some point in increasing the fluid intake

Despite all care, however, the typical headache will develop in some cases The time honoured technique of keeping the patient in bed and horizontal, since it is the most comfortable position, should immediately be adopted, and the return to the vertical made gradually over the next few days CROSBY[12] suggests the use of β-pyridyl carbinol tartrate ('Roniacol Tartrate') for the long-term headache after pneumo-encephalography, and this substance may possibly alleviate the low-tension headache from lumbar puncture and spinal anæsthesia PFEFFER[13] records good results from treating post-lumbar-puncture headache with deoxycortone acetate by mouth He gives this, in a polyethylene glycol wax base, in doses of 2 mg six-hourly for one to four days Some workers recommend raising the C S F pressure by a second puncture and introduction of saline intrathecally Patients tend to resist this idea, and indeed the second lumbar puncture may result in further ill effects DEUTSCH[14] speaks well of the administration of 5% ethyl alcohol in 5% glucose for the treatment of post-lumbar puncture headache, he attributes the beneficial effects of the alcohol to dilatation of the choroid plexuses and increased formation of C S F These new remedies need to be further assessed, but meanwhile the clinician should aim, by perfecting his technique, to prevent the state of affairs that calls for such measures

Epidemiology of Accidents

IN 1950, 13,363 people in England and Wales were killed by accident Such was the compelling figure behind the recent discussion on the epidemiology of accidents by the epidemiology and preventive medicine section of the Royal Society of Medicine The section's mission is partly apostolic in propagating the use of epidemiological method in non-infectious disease, and partly educational in emphasising the urgency of the medical and social problem of death by violence In the section's discussion, on March 20, Dr W P D LOGAN, chief medical statistician to the General Register Office, said that violence had now supplanted infectious disease as the major cause of death in childhood, in 1950 about a third of all the deaths among schoolboys and young men were due to accidents, and the age distribution of accident mortality was marked by another rise among people of both sexes over the age of 65 Dissection of the tables of the Registrar-General's vital statistical report is the inevitable preliminary in social pathology, and the usual epidemiological concepts of host, agent and environment form a useful framework for the synthesis of ideas on this subject

Mr WILLIAM GISSANE, director of the Birmingham Accident Hospital, pointed out that agent virulence may be affected by coincidental changes in habits and environment, the danger of gas and electric fires is enhanced by the contemporary fashion of crinoline dresses made of inflammable fibre mixtures Host variation in susceptibility and exposure is reflected in many facets of the statistical tables The distribution of deaths in road accidents reveals the risk to the young and the inexperienced as pedestrians, cyclists, and motor-cyclists But experience is not all, in 1950 eight of the pedal-cyclists killed were over 80 years of age, and since the number of octogenarian cyclists seriously exposed to risk on the highway is small, the hazard to them must be great Women, on the other hand, are particularly prone to death by burning in the home both in early life and in old age There are sex differences in the nature of injuries, even in deaths due to falls In men 31% of the deaths from falls in 1950 were due to fractures of the skull and 38% to fractures of a limb, whereas among women the corresponding proportions were 8 and 74% The frequency of fracture of the femur among elderly women may be accounted for by the type of shoe worn and the bone fragility among the very old, who are more often women The male predilection for fracturing the skull is less easily explained, particularly as the adverse sex ratio is present throughout working life and even in childhood, indeed six times as many boys as girls are killed by falling objects fracturing

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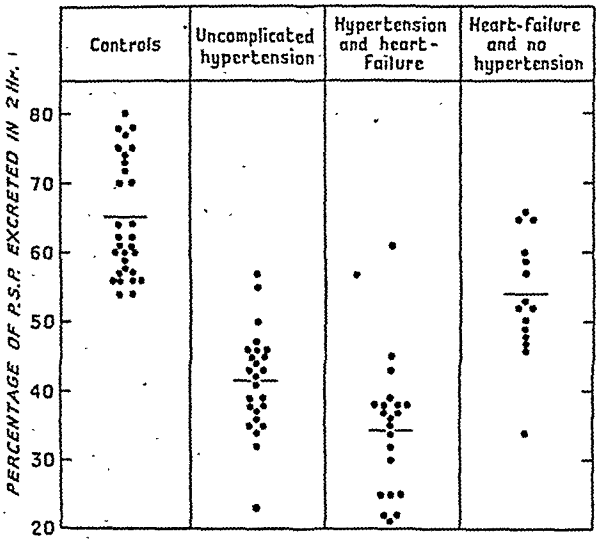

Percentage excretion of P.S.P. in 2 hours in four groups of patients. Horizontal bar indicates mean for each group.

SUMMARY

The excretion of P.S.P. after two hours in patients with hypertension was significantly lower than in healthy subjects.

It was also lower in patients with hypertensive heart-failure than in patients with heart-failure from other causes, irrespective of the state of the blood-pressure at the time.

Excretion of less than 50% in the absence of heart-failure, or 45% if heart-failure is present, strongly supports the diagnosis of hypertension.

This test helps to establish the diagnosis of hypertension in cases where the blood-pressure value for any reason, especially because of cardiac infarction, is natural at the time.

I wish to thank Dr. William Evans for his encouragement and criticism, and the physicians at Hammersmith Hospital for access to patients under their care.

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A NEW RESPIRATOR

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IN the autumn of 1952 we had in Denmark a poliomyelitis epidemic of the utmost severity, as regards both the type of illness and the numbers affected. There was a high proportion of cases with bulbar involvement, and the treatment of patients with respiratory paralysis proved a difficult problem.

At Blegdam Hospital, Copenhagen, where treatment was largely centralised, it soon became necessary to supplement the ordinary methods of applying artificial respiration to these patients. In coöperation with the anæsthetists, good results were obtained by positive-pressure ventilation (Lassen 1953). The method is briefly as follows:

> A high tracheotomy is performed, and a rubber tube with an inflatable cuff is fitted closely into the patient's trachea. The lungs are then insufflated by manual compression of a rubber bag filled with oxygen or a mixture of oxygen and nitrogen. The gas circulates in a closed system; exhaled gas passes through an absorber, which removes the carbon dioxide, and back to the rubber bag. The oxygen consumed is replaced from an oxygen cylinder.

Manual ventilation was performed by medical students of Copenhagen University. They worked 8-hour shifts, so the treatment of each patient needed three students every 24 hours. This method was adopted elsewhere in Denmark, including the medical department of the County Hospital, Skive. Its use here, however, was more difficult, since no students are available, and manual respiration had therefore to be carried out by the nurses. Replacement of human labour by some automatic method was thus highly desirable.

A respirator constructed here has proved an effective alternative (fig. 1). It is simple to make, and, compared with other respirators, it is very cheap. The essence of its function is that it depends on variation in pressure *in the patient's respiratory system, with which the* apparatus has an airtight connection. The highest pressure in the lungs at the close of the inspiratory phase sets off expiration. Not till the pressure in the lungs equals atmospheric pressure can the next inspiration start. There is thus a constant action and reaction between patient and respirator.

CONSTRUCTION OF THE RESPIRATOR

The respirator is shown diagrammatically in fig. 2.

The energy necessary to insufflate the patient's lungs is delivered by a cylinder of compressed gas (A), fitted with a manometer (B), a tap (C) for regulating the flow, and a flow-meter (D) by which the flow can be measured in litres per minute. The flow amounts to 7–10 litres a minute. Pure oxygen may be used, or a mixture of oxygen and nitrogen, or, in suitable cases, compressed air. On its way from cylinder to patient the gas is humidified by passage through water. With poliomyelitis patients an airtight connection is established through a high tracheotomy opening.

In a rubber bag (E) which acts as a reservoir container, the flow from the cylinder collects while the patient is exhaling into the outer air. During the subsequent inhalation the rubber bag, now distended, presses some of its contents into the patient's lungs under moderate pressure (130–190 mm. water).

Both inspired and expired gas pass through a single valve (F). In the valve-chamber is a piston which fits closely to the inside of the chamber except in the middle, where there is space for the gas to pass through the chamber. The piston is actuated by the magnetic fields produced by two coils (G). When the piston is at the extreme left position (fig. 2), allowing the gas to pass from the rubber bag to the patient, the valve is closed for connection to the outside air. Conversely, the piston at the extreme right position (fig. 4) allows exhalation while cutting off the flow from the rubber bladder, which therefore fills during this phase.

From the valve two tubes lead to the patient, with a Y-connection (H) just above the patient's trachea. On the valve is yet another tube (K) through which the pressure obtaining in the patient's lungs is transferred to the tube L_1.

L_1 and L_2 are two connected tubes; L_1 is in airtight connection with the patient's air-passages, while L_2 is open to the outer air. These tubes contain a fluid of very low volatility and of viscosity equal to that of water. When this fluid touches the electrodes M_1 and M_2 it makes an electrical connection between them. In figs. 3 and 5 this is shown as taking place through two floats on the surface of the fluid.

The electrodes marked M_1 are set so that they are connected by the float in L_1 when the two columns of fluid are standing at the same height—i.e., when they are in equilibrium (fig. 5). The height of the electrodes M_2 is variable. This pair of electrodes is connected when a certain pressure in tube L_1 has sent the float in L_2 up to the electrodes (fig. 3). This pressure, which is equal to that in the lungs, is therefore controlled by the height of the electrodes above the position of equilibrium. On so far reached in these social experiments will create a demand for further and more sustained, efforts to improve their techniques

If the social scientist has sometimes been less successful than we, and he, had hoped, is it not perhaps because we are not clear what we can reasonably expect him to offer? He comes to us from a background of academic freedom where he has always enjoyed the right of free and lively discussion, and one of the most important things he can teach is respect for facts and tolerance for other cultures In the long run, said Professor **Myrdal**, irrationality cannot stand up to facts, and the social scientist who can persuade us to give up social superstitions and admit that our prejudices, though cherished, are probably ill founded, has made the world a safer and pleasanter place to live in (The local need for tuition in the technique of rational discussion is made equally clear by any newspaper correspondence, parliamentary discussion, or conversation in a bus on a controversial subject, such as capital punishment, the death penalty, education, or racial segregation) Again, though we offer the social scientist opportunities for collecting facts and amassing data which are closed to the academic worker, are we sufficiently jealous of his integrity? As Professor **Myrdal** pointed out, "science is criticism, and social sciences imply criticism of society" Will the State, he asked, continue to grant the social scientist the freedom he needs and enjoys? He must be at liberty to state the truth even when it is inopportune, and he must not be allowed to grow shy of broader issues

These are ways in which we can help the social scientist But some of his difficulties are technical and beyond our aid His fellow scientists, indeed, have always been somewhat suspicious of the purity of his methods They have an uneasy and not unjustified feeling that he is at least as interested in what *should be* as in what *is* And it is true that the social scientist (like the doctor) stands in more intimate relation to his material than most scientists, for he is a participant observer of actual social processes He is willy nilly a part of the process he is observing and of the national cultures against whose values the facts must be assessed This brought Professor **Myrdal** to the social scientist's greatest handicap The more closely facts are associated with people, the more difficult they are to present objectively hence the social scientist would be hard put to it to produce a collection of facts untinged by judgment, and indeed they would probably be valueless if he did There are no answers without questions and by the selection of his questions the social scientist shows his interest But this difficulty Professor **Myrdal** maintained must be faced not evaded Valued premises must be explicit and deliberately chosen, not implicit and concealed Furthermore there are, he averred, in most situations several sets of perhaps conflicting valuations It is small wonder then that the sociologist with his present inefficient tools is sometimes at a loss to offer firm prognoses and plans in the face of these imponderables Yet he has certainly moved a long way from the days when the politicians were content to listen politely to his advice Today he already shares in administration and legislation tomorrow he may well find that he is holding the restless baby called international tensions

Annotations

COSTS AND VALUES

Just before the House of Commons adjourned last week the Minister of Health announced the formation of a new committee to review the cost of the National Health Service The terms of this announcement were such as to disturb not only members of the Opposition but also a good many people who are working in one way or another to make the service a success The committee's terms of reference (see p 749), with their emphasis on control of Exchequer funds, on the burdens on the Exchequer, and on the avoidance of a rising charge, and their remark about "the maintenance of an adequate service" sounded as though they were framed by some one who regarded the N H S as primarily a liability, which must now be reduced they suggested that this was a Treasury committee appointed to propose or justify cuts Fortunately Mr Macleod's replies to his questioners were reassuring in at least one important particular—the absence of haste Cuts which are made hastily are too often made blindly, and at the tender age of 5 the National Health Service really must be spared any further slapdash surgery The Minister, however, made it plain that the committee will not be pressed for time, and we may hope therefore that it will be able to study the implications of any changes it may recommend We cannot yet tell whether it will be well qualified to form "value judgments" on, for example, the proportion of the national income which the service can properly claim, or the distribution of funds between the different parts, but it should certainly be in a position to display the close association between finance and policy, and to discuss both incentives to economy and disincentives such as excessive central control Though ad hoc committees are not an ideal substitute for a consistent policy, few will deny the very real need for dispassionate inquiry into the matters which Mr Guillebaud and his colleagues will have to consider

MAINTENANCE TREATMENT IN PERNICIOUS ANÆMIA

Not long ago we noted that vitamin B_{12} (cyanocobalamin) was being increasingly used for the treatment of pernicious anæmia[1] Further reports have confirmed the value of this substance in maintaining a proper level of red cells and hæmoglobin Murphy and Howard[2] treated 8 patients with 1 μg of crystalline vitamin B_{12} daily, given intramuscularly, for 21–39 months They found that this treatment gave effective control and maintained the blood counts at satisfactory levels One of their patients already had locomotor difficulties caused by involvement of the central nervous system this disability was neither aggravated nor improved Murphy and Howard suggest that 1 3 μg of crystalline B_{12} is equivalent to 1 *U S P* "anti anæmic unit" of liver extract Meacham and Heinle[3] carried out a more elaborate survey They had previously shown that a vitamin B_{12} concentrate given intramuscularly once every 3–4 weeks in doses equivalent to 1 μg per day did not suffice for proper maintenance[4] They took 21 patients and increased the dose to 3 μg daily, before the increase 14 had red cell counts of less than 4 million per c mm, after 11–16 months' treatment all 21 had counts of a higher level The "concentrate" they were using has proved to be a mixture of vitamin B_{12} (cyanocobalamin) and vitamin B_{12b} (hydroxocobalamin) So far inspiration and expiration is to be kept at 1 : 2, then expiration must likewise be shortened by easing the screw of the valve P. A reduction of the rate is obtained, conversely, by reducing the flow, which causes inspiration to take place more slowly. By tightening the screw at P, expiration can be kept at the correct ratio to inspiration.

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[1] *Lancet* 1952 ii 1165

[2] Murphy W P Howard I *New Engl J Med* 1952 247 539

[3] Meacham G C Heinle R W *J Lab clin Med* 1953, 41 [illegible]

[4] Meacham G C Vignos P J Heinle R W [illegible] Epstein M *Ibid* 1950 35 711

The *time-relation between inspiration and expiration* is regulated as described above, by means of the screw at P.

Maximal pressure in the lungs at the end of inspiration is controlled by the height of the electrodes in L_2, and may thus be varied from patient to patient, and according to the needs of each individual from time to time. It is possible, for example, for the space of a couple of inhalations, to raise the electrodes a little above the normal, and so, as prophylaxis against atelectasis, to give the patient a couple of higher-pressure " sighs."

CLINICAL EXPERIENCE

Two respirators, constructed on the principles already described, have been used since the middle of January, 1953, in the medical department of the County Hospital, Skive, on two boys with poliomyelitis.

The first, 13 years of age, is completely quadriplegic and up to the time of writing (end of February) has been quite incapable of spontaneous respiration. The second, 8 years of age, has had extensive paralysis in all four extremities but power of movement in certain groups of muscles is greatly improving. This patient, after a fortnight of total paralysis of the respiratory system, has for the last three weeks shown signs of a return of respiratory movement—at first in the form of contractions of the auxiliary respiratory muscles. Later, the diaphragm and the intercostal musculature began to work, but only for short periods and to a very limited extent, quite inadequate for effective ventilation of the lungs.

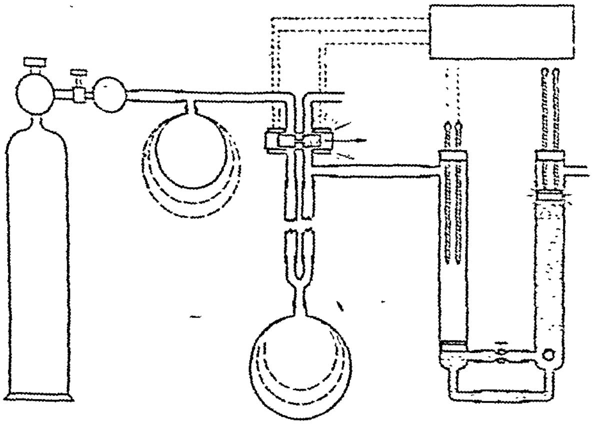

Fig. 3—Diagram of respirator, at the start of expiration.

High tracheotomy was performed on both these patients on arrival; and respiration was given manually, since at that time the construction of the new respirators was not finished. When these were fitted, the condition of both boys—in their own judgment and in ours—visibly improved. It should be remembered that manual respiration had had to be undertaken by our nurses, who in this matter were quite without experience. Immediately after the change both boys fell asleep, colour and pulse improved, while their blood-pressure steadied at a lower and more satisfactory level.

It would seem that with this respirator it is possible to give some training in spontaneous respiration when this shows signs of returning. In the case of the 8-year-old boy, who has begun to make spontaneous respiratory movements, we are gradually lowering the inspiratory pressure, and at the same time training him to work in step with the respirator. The result of this close collaboration between patient and respirator will be that an increasingly effective spontaneous breathing eventually gives the patient the upper hand so that the respirator will come to work in step with him. A later example will show this.

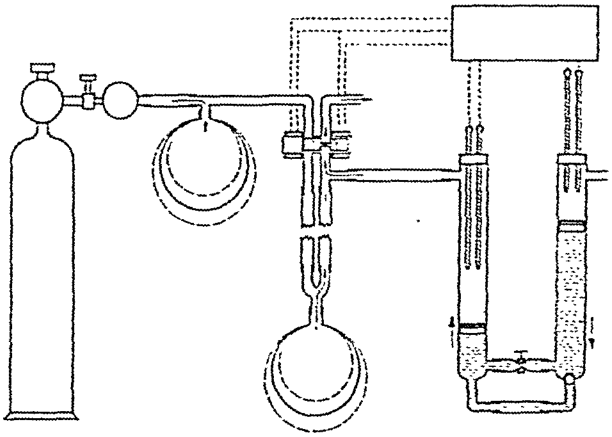

Fig. 4—Diagram of respirator, during expiration.

On Jan. 20, 1953, a third respirator was demonstrated at the Blegdam Hospital, Copenhagen, on three patients with paralysis of the respiratory system.

The first, a man about 30 years of age, with no spontaneous respiration, was satisfied with the apparatus and found it better than the " student " method.

The second, also a man, had at the time of the demonstration so much spontaneous respiration that he could manage without help for 18–20 hours out of the 24. His unaided respiration was quick and superficial, with a rate of about 40 per min. When the respirator was first fitted to this patient, it was set with a quite high inspiration pressure and a rate of about 20 per min. The patient's own weak respiratory movements seemed to have little or no influence on the variations in the pressure in the lungs thus obtained, but the difference between the slow pace of the apparatus and the patient's own respiratory movements seemed unpleasant to him. The inspiration pressure was therefore reduced and the rate increased, so that the respirator worked in time with the patient's spontaneous respiratory movements. Then, as the patient put it, it was he that breathed in, but the respirator helped him.

The accompanying figures show how the respirator can support a spontaneous effort at respiration. Such an effort will draw air into the lungs. This suction will transfer itself to the tube L_1, where consequently the float will connect the electrodes, and the respirator will momentarily support the patient's own superficial inhalation with a fuller, higher-pressure inhalation.

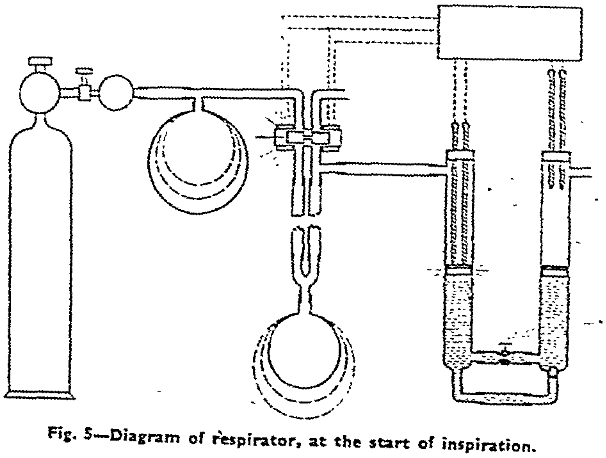

Fig. 5—Diagram of respirator, at the start of inspiration.

measuring the tensile strength of wounds In control rabbits, week-old wounds had twice the tensile strength of wounds from cortisone treated animals Administration of ascorbic acid with cortisone did not materially affect this result, nor did it influence the histological appearance of depressed fibroplasia In scorbutic guineapigs cortisone treatment, though it seemed to ameliorate the scurvy, did not further impair the tensile strength of wounds

Thus although both scurvy and administration of cortisone lead to defective collagen formation, the relationship between ascorbic acid and cortisone cannot be simply defined As Bourne points out, the failure of development of collagen fibres from these two mechanisms cannot be attributed to their action at the same level Cortisone has many known effects on connective tissue—cells, fibres, and ground substance—but at present these effects cannot be linked with the biological action of vitamin C

CONFERENCE ON ENDEMIC GOITRE

ALMOST every country has areas of endemic goitre This was therefore a particularly appropriate subject for debate at a conference of experts arranged by W H O and held last December at the National Institute for Medical Research, London The findings of this conference have now been reviewed by J B Stanbury[1]

On the theoretical side endemic goitre presents no problems the thyroid needs iodine to make its hormone, if insufficient iodine is present in the diet the thyroid enlarges and forms a goitre The normal daily output of thyroid hormone contains about 0 2 mg of iodine Much of this iodine, however, is re-used after breakdown of the hormone, so the actual minimum iodine requirements of the body are of the order of 0 1 mg per day If all persons living in iodine deficient areas were provided with an extra ration of 0 1 mg of iodine daily, there should be no goitre

This theoretical expectation is largely borne out in practice, and in several areas—notably Switzerland and Michigan—the incidence of endemic goitre has been strikingly reduced by the provision of iodised salt It would be too much to hope that this simple expedient will entirely eliminate goitre, since it is by no means uncommon in areas where iodine is abundant Nor does extra iodine have much effect on established goitre, even in deficient areas, its usefulness lies in prevention rather than cure But a great deal would be achieved by applying in every area of endemic goitre the prophylactic measures successfully used in Switzerland and Michigan This aim has so far been thwarted by various factors—political, economic, and chemical Legislatures are—rightly—wary of compulsory contamination of foodstuffs In backward countries the supply of salt is often not refined, hence iodine would have to be added by hand, at a prohibitive cost Finally, iodide proves unstable and unwilling to remain uniformly mixed with salt under very hot or very damp conditions A proposal before the conference was that, instead of iodide, iodate should be used, since this is much more stable Studies with labelled iodate have shown that its iodine is available to the thyroid, while its toxicity appears to be very low This may prove to be the most useful form in which to distribute iodine in tropical countries

These practical difficulties have caused some people to wonder whether iodine prophylaxis is worth the effort and expense Most goitres are quite harmless Although there is some evidence in endemic areas of an increased incidence of thyrotoxicosis and (more doubtfully) of thyroid cancer, the disadvantages of having a goitre are more often æsthetic than medical, and would not justify any great effort at prophylaxis The strongest argument for a determined effort to eradicate endemic goitre comes from the load of endemic cretinism which so often accompanies it The case would be greatly strengthened if it were proved that the feeblemindedness, deaf-mutism, retardation of growth, and economic unproductiveness which are often found in endemic goitre areas are also causally related to iodine deficiency So far such claims have not been properly substantiated If they were, the argument for insisting on iodine prophylaxis, despite all practical difficulties, would be overwhelming

TRACING THE STAPHYLOCOCCUS

THE investigation of staphylococcal infections has been greatly aided by the development of new methods, including the coagulase test, the typing of strains by serological and bacteriophage techniques, and the recognition of penicillin-resistant strains Phage typing of *Staphylococcus aureus* differs from Vi phage typing of typhoid bacilli in that it depends, not on the more or less specific lysis of a strain by one of the phages in critical test dilution, but on the pattern of lysis produced by the series of typing phages Precise typing is of special value in tracing the sources and paths of cross-infection, and Hood[1] has described a way of facilitating large numbers of tests for the purposes of a burns research unit

The essence of this method is the preliminary testing of strains with a small number of pools of phages, each of which rarely cross reacts with the other pools and contains single phages usually forming associated patterns of lysis Staphylococci can adsorb the phages in the pool to which they are resistant, but they still give the same pattern of lysis with those in the pool to which they are sensitive as they do with single phages The reliability of the method was confirmed in an extensive trial It was also found that the phages of serological group A, whether single or pooled, were stable at their test dilution for at least a month at 0°–5°C, but that those of group B were usually stable for only 2–3 weeks The method adopted by Hood as a routine is to test new strains first against five phage pools, each containing 5–10 single phages, the results are read after 18 hours at 30°C or 6 hours at 37°C They are then tested against the single phages in any pool giving a positive result, the broth culture of staphylococci used for inoculating the plates for the preliminary test can be used again for this purpose

The prevalence and spread of *Staph aureus* in the noses of infants and mothers not in hospital has been studied by Ludlam[2] in five child-welfare clinics In the first 2 months of life the organism was more often present in infants who had been born in hospital than in infants born at home, in the last half of the first year the same difference was observed The prevalence fell steadily with age from its early high levels of about 70–86% in the hospital-born infants and 60% in the home born infants to a level much below that of the normal adult population In the mothers of these infants the prevalence (40–60%) was higher than the adult normal level only in the first 2 months after delivery, at that time the prevalence in those delivered in hospital was also higher than in those delivered at home In contradistinction to previous observations made in maternity hospitals there was an association between nasal carriage of staphylococci in infants and in mothers, but only during the first few months Penicillin resistant staphylococci were much commoner in infants up to 5 months of age and their mothers who had been delivered in one hospital than in another hospital or at home but swabs taken after this was known showed a high proportion of resistant strains from the nurses and infants and the dust of the nurseries at both hospitals The investigation yielded many phage types Of 35 instances

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[1] Stanbury J B *Chron World Hlth Org* 1953 7 61

[1] Hood A M *J Hyg, Camb* 1953, 51 1
[2] Ludlam G B *Ibid* p 64

Preliminary Communication

THE RENAL DUCTS OF BELLINI

OBSERVATIONS IN NEWBORN BABIES

In examining routine sections of kidneys of adults or of children one very rarely sees what appears to be a communication between the pelvis and the openings of the ducts of Bellini in the renal papillæ. One always has the impression that the histological section has missed the place where the duct opens into the pelvis.

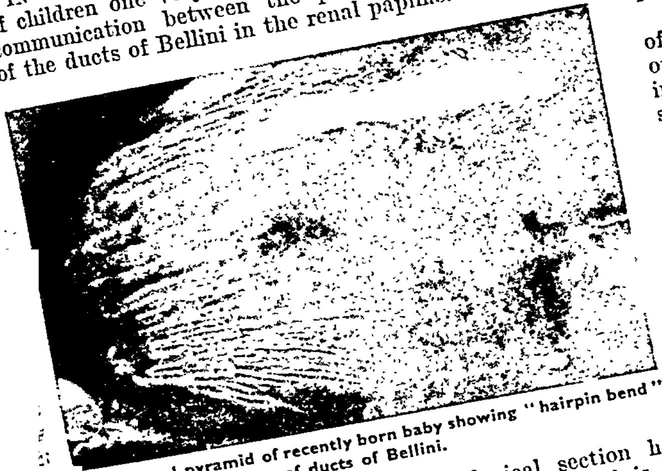

Fig. 1—Renal pyramid of recently born baby showing "hairpin bend" of ducts of Bellini.

Experimentally it has been possible to inject the whole circulatory system, both arterial and venous, of the kidney, but no-one has succeeded in injecting its secretory system. Two facts are very striking about the physio-anatomy of the collecting tubes:

1. If, when making retrograde pyelograms, the operator exerts pressure to fill the whole pelvis, instead of injecting the ducts of Bellini, as is to be expected, he injects the pelvic veins—the phenomenon of pyelovenous back flow (Hinman and Lee-Brown 1924).

2. Aseptic renal calculi are formed at the tips of the papillæ as though there were a barrier between the renal pelvis and the secretory system of the kidney (Randall 1940, Scheele 1951).

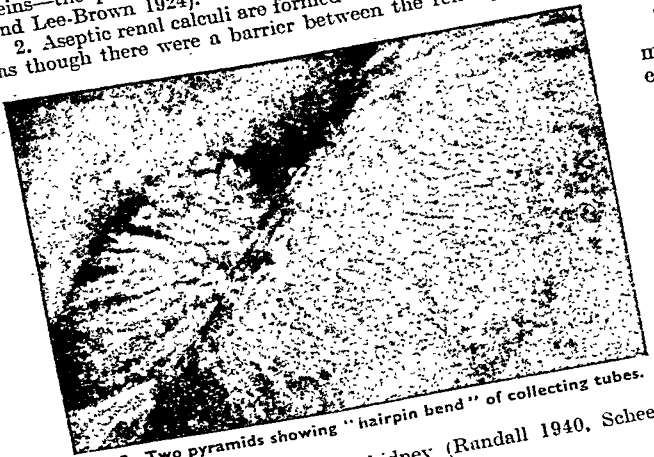

Fig. 2—Two pyramids showing "hairpin bend" of collecting tubes.

Physiologically we can study the excretory system of the kidney by examining those of babies recently born at term. In some of these cases it can be seen that the whole of the pyramids of the kidneys contain a "uric-acid precipitate" which fills the terminal collecting tubes (figs. 1 and 2), and by studying these kidneys under the low power we can see that the ducts of Bellini do not end in the renal pelvis. They seem to join another duct of Bellini and to finish in what appears to be a "hairpin bend." If the kidney is examined when very fresh, we see what looks like epithelium with some small vessels covering the tip of the papillæ. By sectioning these kidneys we can observe how the uric acid fills the terminal ducts, but these do not appear to be in actual contact with the renal pelvis (fig. 3).

Encouraged by this observation, I am now studying different kidneys to ascertain (1) if this absence of openings of the ducts of Bellini is to be seen only in babies recently born at term; (2) if this absence is peculiar to some papillæ and not to the whole of the renal pyramids; and (3) if at a later age the ducts of Bellini develop openings and drain the urine directly into the renal pelvis.

After having examined a few hundred routine sections of kidneys of all ages, and some serial sections of this organ from different animals, especially the cat (because in this animal the kidney has only one pyramid) I am sceptical of accepting the existence of openings of the ducts of Bellini, and I am considering the possibility that in the normal kidney the urine is dialysed through a pelvic epithelium and not excreted by the ducts of Bellini into the renal pelvis.

I am now studying this anatomical detail by serial sectioning of different kidneys and by taking a photomicrograph film of the sections to show, objectively, the existence or not of openings of the ducts of Bellini.

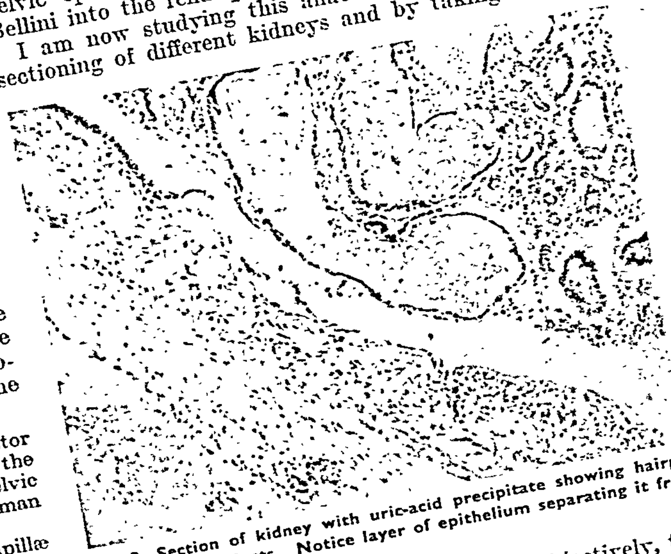

Fig. 3—Section of kidney with uric-acid precipitate showing hairpin tip of Bellini ducts. Notice layer of epithelium separating it from renal pelvis.

Thanks are due to the medical staff of Booth Hall Hospital and the Duchess of York Hospital for Babies for the use of their material, and to Mr. T. Walsh, A.I.M.L.T., and Miss A. J. Orrell for the histological preparations. The Endowment Fund of Booth Hall Hospital gave a grant towards the expenses of this research.

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"The method of scientific publication in this country is notoriously somewhat peculiar. Although much research is entirely paid for from public funds, little money is available from this source for the publication of the results, and without publication such work is usually abortive. Publication of the results of research work is largely undertaken by what are, in effect, coöperatives of the research workers themselves and the spare-time labours of unpaid editors and officials. Scientific societies are able to make claims on the Government grant in aid of scientific publications (which is administered by the Royal Society), but this fund is proving inadequate. The long-term solution is the rationalisation of the publication of research. In the meantime there is need for the grant in aid of scientific publications to be increased and for a similar fund to be made available to students of the humanities."
—G. C. AINSWORTH, *Times*, March 19, 1953, p. 9.

Special Articles

EPIDEMIOLOGY OF STREPTOCOCCAL INFECTIONS AND THEIR NON-SUPPURATIVE COMPLICATIONS *

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IN the past fifteen years knowledge of the behaviour of streptococcal infections has increased greatly, thanks primarily to the work of Griffith,[1] Lancefield, and their co-workers[2] on the serological grouping and typing of streptococci It is now known, for example, that group-A β hæmolytic streptococci are the important group in human infections More than forty type strains have been identified in this group By serological techniques it is now possible to study the many factors related to the spread of these organisms in a population and to confirm the association of group-A streptococci with the non-suppurative complications—rheumatic fever and acute hæmorrhagic glomerulonephritis

General Aspects of Epidemiology of Human Streptococcal Infections

Much has been written about the epidemiology of β hæmolytic streptococcal infections in man Our intention here is to summarise some current concepts and to point out some deficiencies in knowledge

SOURCE OF INFECTING AGENT

Man is the only known natural reservoir of group A streptococci These organisms may occasionally be found in certain animals and in dust food and other substances In the latter circumstances, however the presence of streptococci may almost always be traced to human contamination and cannot be attributed to a biological requirement for survival of the organisms The ultimate source of streptococcal infections is thus the human reservoir

With few exceptions the habitat of the streptococcus in man is the upper respiratory tract One may ask, "What is known about the residence of the organisms at this site?" Perhaps the best answer is obtained by reviewing the sequence of events when a person acquires a new type of streptococcus

There is some evidence[3] that the organisms are first found in the anterior nares, which are presumably the site of deposition most readily available If the local factors are favourable at this site, a state of "parasitism" develops The streptococci multiply and spread with the result that large numbers are found in the nose, the throat, and probably the accessory sinuses In such circumstances clinical illness usually occurs but, as the acute symptoms subside, the number of streptococci in the nose rapidly decreases, and after two or three weeks few persons harbour the organisms in the anterior nares Likewise the number of streptococci in the throat decreases, but here the organism may persist for months[3,4]

An example of such persistence of the organism in the throat is found in the study of 53 "convalescent carriers" who acquired their streptococcal infections at the Francis E Warren Air Force Base in Wyoming[4] All were in the convalescent phase of untreated acute tonsillitis and pharyngitis due to group A streptococci At the end of three months' observation 90% of these men still harboured the infecting type of streptococcus in their throats

As the result, presumably, of acquisition of, and parasitism by, the group A streptococcus, type specific immune bodies appear in the serum within three to eight weeks, according to the type of streptococcus[5] Such antibodies are believed to be protective against the subsequent development of infection with the same type of organism[6]

During the period of parasitism, which here is considered to include the "convalescent carrier" state, a loss of type specificity may occur, presumably owing to a decrease in, or disappearance of, the M substance, or type specific protein, elaborated by the organism[4] That this may be so is shown by the fact that the production of M protein by carrier strains may be restored to apparently full capacity by animal passage[4,7]

This then, is the possible sequence of events when a person acquires a new type of group-A streptococcus Many questions, however, remain to be answered particularly regarding the significance of the observation thus far made For example, how long does the organism remain infectious in terms of spread in man (a qualitative attribute)? Or, what role does the numerical decrease in numbers play in the ability of the organism to spread (a quantitative attribute)? The answers to these two questions are not clear today The loss of M protein may mean a loss of virulence or a loss of the capacity to spread, or both Hamburger et al[8] have shown that the nasal carrier, excreting large numbers of organisms may induce spread of infection But all nasal carriers do not induce spread of infection or cause secondary cases[3] The only fact that seems clear is that "spread" indicated by secondary cases decreases as time elapses from the point of initial parasitism, regardless of whether the organism is harboured in the nose or in the throat[3,9]

MECHANISM OF SPREAD

The usual concept regarding spread of streptococci involves two general routes of transfer of organisms from the initial carrier to the recipient (1) directly between the two persons through physical contact or by droplets passing through the air for short distances, and (2) indirectly through fomites or via the air by means of droplet nuclei and dust[10] This classical theory of spread is considered to apply also to the agents causing other types of respiratory diseases

In fact, however, there is little if any direct evidence indicating the relative importance of these various modes of spread or even whether any of them is epidemiologi

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* This investigation was sponsored by the Commissions on Acute Respiratory Diseases and Streptococcal Diseases, Armed Forces Epidemiological Board and was supported in part by the Offices of the Surgeons General Departments of the Army and Air Force and by grants from the Helen Hay Whitney Foundation the Brush Foundation the Cleveland Foundation the S P Fenn Trust and Mr Philip R Mather

THE LANCET

LONDON: SATURDAY, APRIL 11, 1953

Hazards of Lumbar Puncture

LUMBAR punctures, like crimes, are seldom committed in the contemplation of failure. If the operator reflects on his state of mind as he presses the needle into the theca, he is not likely to perceive in the foreground of his consciousness any clear image of the hazards attending the next few millimetres of forward progress. As he gains experience, his appreciation of the possible complications becomes keener; but, paradoxically, lumbar punctures are usually left to the most junior members of the hospital medical team.

The hazards of lumbar puncture fall into certain definite groups. In the first of these groups are the numerous effects of direct trauma from inexpert introduction of an unsatisfactory instrument. Ligaments, vessels, nerve-roots, spinal cord, and even the intervertebral discs have all suffered damage in this way; DRIPPS and VANDAM[1] have seen gelatinous material drip from a needle which had entered a nucleus pulposus. The second group comprises the infections that may follow septic technique or the injudicious introduction of the needle through an infected area of subdermal or deeper tissue. How often infection occurs one cannot know, since it attracts little publicity. It may result in either generalised meningitis or else an epidural abscess. There is the large third group of hazards, associated with disturbance of the dynamics of the cerebrospinal fluid (C.S.F.). The danger of herniation of the brain through tentorium or foramen magnum from puncture in the presence of increased intracranial pressure is well known, but not everyone is so familiar with the sudden exacerbation of symptoms and signs of a spinal-cord tumour from this procedure.[2] Such a mishap calls for fairly rapid surgical intervention since without relief of the increased pressure on the cord vessels irreversible changes may take place in the neurones. Furthermore, SCHUBE and RASKIN[3] point out that the withdrawal of as little as 10 ml. of fluid may result in sufficient vascular dilatation to induce intracerebral or meningeal hæmorrhage from diseased structures such as aneurysms or sclerotic vessels. Ocular palsy, usually an external rectus affection, is another possible sequel of lumbar puncture, and may be due to alteration in dynamics leading to stretching of the abducens nerve at some point in its long course. HUGHSON[4] has shown that pressures in the C.S.F. and in the auditory labyrinth are closely related; and the impairment of hearing that occasionally follows lumbar puncture, particularly in the presence of severe headache, may be due to lowering of C.S.F. pressure.

These dramatic incidents are not very common; but it is in this third group, of dynamic disturbance, that there falls the common problem of the post-lumbar-puncture headache. There is always doubt as to the nature of this headache. On the one hand the patient who is unaware of the possibility of it is less likely than others to become a victim; and on the other hand the doctor is naturally reluctant to ascribe head pains to his own efforts. This headache is precipitated or aggravated by the assumption of the erect posture; and it may be relieved by abdominal compression. It may come on as long as seven days after puncture; and, if untreated, it may continue for weeks. WOLFF,[5] among others,[1] believes that this headache results from the loss of C.S.F. and subsequent traction, displacement, or swelling of those parts of the cranial contents most susceptible to pain—the venous sinuses, the dura and its arteries, and the basal arteries. MARSHALL[6] has adduced evidence which seems to show that reduced C.S.F. pressure is not absolutely related to the headache; but most workers hold that relative lowering of the pressure, by initial withdrawal of samples and subsequent slow leakage from the puncture-hole, is the real cause. SCIARRA and CARTER[7] showed that headache is almost as common after simple puncture of the theca without withdrawal of C.S.F. as after withdrawal of 10–12 ml. of fluid: this point is corroborated by many reports that the use of small-bore needles greatly reduces the risk of headache. Occasionally, in addition to headache there may be vertigo, vomiting, and other symptoms of intracranial hypotension, including disturbed consciousness.[8]

These are the dangers of the simple diagnostic tap. If in addition anæsthetic, diagnostic, or therapeutic compounds are introduced into the theca a fresh chain of events is set up and new hazards arise. These constitute the fourth group. It may sometimes be difficult to decide whether symptoms following spinal anæsthesia are due to the lumbar puncture or to an unusual reaction to the anæsthetic. Most such headaches are of the leakage type already described, but occasionally there is a response that can be interpreted only in terms of meningeal irritation. Sphincter disturbance and even paralysis of the limbs may follow spinal anæsthesia.[9] Myelography, requiring the introduction of radio-opaque material into the theca via the cisternal or the lumbar route, invariably produces both headache and backache. Subsequent examination of the C.S.F. almost always reveals an increase in cells and protein, and it seems probable that almost all agents at present in use for myelography provoke some meningeal reaction. Pneumo-encephalography has complications of its own. The first few cubic centimetres of gas to reach the brain produces an immediate crashing headache which builds up as the volume of the gas in the subarachnoid space increases; maximum replacement of the C.S.F. with

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of streptococcal infection with rheumatic fever Nephritis has been reported to occur after upper respiratory infections and infection with organisms such as the pneumococcus [24, 25] Moreover nephritis has only rarely followed epidemics of streptococcal infection, in contrast to rheumatic fever Examples of this are seen in a food-borne outbreak of type 5 streptococcus infection at Fort Bragg,[21] in which there were 3 instances of rheumatic fever among 100 cases of streptococcal infection, but no instances of acute nephritis Similarly, at Francis E Warren Air Force Base there were 1206 persons infected with typable group A streptococci, of whom 32 developed rheumatic fever but only 1 had nephritis [26]

Annual variations have been noted in the occurrence of nephritis At the Cleveland City Hospital,[27] for example, the number of admissions for acute nephritis varied from 29 to 85 in 1922–31 (see table) In 1921, however, there were 105 admissions, the year previously only 58 It is well known that hospital admissions reflect the influence of many factors, but the degree of variation here suggests the possibility of an identifiable factor

ADMISSIONS FOR ACUTE NEPHRITIS AT THE CLEVELAND CITY HOSPITAL *

Year	Number	Year	Number
1920	58	1926	41
1921	105	1927	29
1922	34	1928	29
1923	37	1929	29
1924	40	1930	38
1925	85	1931	38

* From Seegal et al [27]

Any epidemiological association of acute nephritis with hæmolytic streptococci must take into account such apparent discrepancies as these On reviewing the data obtained from 16 sporadic cases of nephritis in Cleveland and elsewhere [28] it was noted that type 12 streptococci were definitely or presumably the cause of the preceding infection in 14 instances, and type-4 streptococci in 2 instances One of the cases of nephritis, which developed after a type-12 streptococcal infection, was observed at Warren Air Force Base, where type-12 infections had been few, accounting for only 42 of the 1206 cases In Cleveland, where most of the sporadic cases were found, the results of weekly cultures were available over a three year period from a population of about 260 persons During this period type-12 streptococci had accounted for about 20% of the acquisitions of group A streptococci in the population Presumably, therefore, about 80% of the streptococcal infections in this area were caused by serological types other than 12, and yet nephritis was associated with the type-12 infections

The question therefore arose "Is acute nephritis associated only with a specific type or possibly with certain strains of a few types of streptococci, and can its occurrence be explained on this basis?" Several outbreaks or small epidemics of nephritis have been observed [28] In four of those in which the strains were typed,[26] type-12 streptococci were found in the patients or as the predominant streptococcus in the population in which the cases occurred

Recently in a recruit-training camp there has been an outbreak of streptococcal infections during which more than 100 cases of nephritis were observed [28] The type 12 streptococcus was the predominant organism in this outbreak A high attack-rate of nephritis followed the type 12 infections but not infections caused by other types Moreover some rheumatic fever also followed the type 12 illnesses

It therefore seems that the epidemiology of acute hæmorrhagic nephritis is basically the epidemiology of certain strains of group-A streptococci that are nephritogenic Studies are now in progress to define further this relationship

Summary

The epidemiology of the group-A hæmolytic streptococcal infections appears to account for the epidemiological behaviour of both rheumatic fever and acute hæmorrhagic glomerulonephritis

Rheumatic fever is not apparently associated with infection by any particular type of group A β hæmolytic streptococcus Nephritis, on the other hand, may follow infection only by certain types, here called nephritogenic

Further knowledge of group-A streptococcal infections should contribute greatly to our understanding of the behaviour of their non-suppurative complications

Typing and grouping sera were obtained through the New York State Department of Health, the Army Medical School, and the Communicable Disease Center, U S P.H S

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"Government only works at all satisfactorily when you can go and talk to the man who is personally responsible for the decision that has been taken Remove this opportunity of personal contact and government becomes diffused and abstract We become numbers, black marks on white paper We fall into the diagnoses of the International Statistical Code, with a social group attached The person responsible becomes a 'they,' whose behaviour can never be observed directly, but can only be inferred 'They' are always polite, imperturbable 'They' attach great store to precedent 'They' do not grow old and resign age does not seem to weary them In this way individual human responsibility is being slowly lost Have we not the courage to restore it and allow the boards in touch with hospitals to take more of their own decisions?"—*Dr W I Card, Spectator*, March 20, 1953, p 336 their skulls. It does not need two people to generate a road accident; of about a thousand motor-cyclists (including passengers) who were killed on the road in 1950, 178 were killed by falling off their cycles, by running off the road, or in some way other than by a collision.

This raises the question of host susceptibility which, under the name of "accident-proneness," has excited the interest of many epidemiologists and psychologists since the report by GREENWOOD and WOODS appeared in 1919.[1] Studies by ADELSTEIN [2] on accidents among shunters in the South African railways has rekindled this interest, for he criticises the rather slipshod thinking that has distorted the original precision of the pioneers in this field. Accident-proneness—defined as an innate and immutable characteristic of the individual whereby some in a group sharing the same environmental risks have an unduly high share of the accidents—has been largely discounted as a major source of accident causation. If 50% of accidents are sustained by 40% of the workers, this does not mean that there exists an accident-prone minority, since if accidents were distributed at random among the group the distribution might be similar. The demonstration of individual excessive accident liability is fraught with difficulties, since it requires the continued observation of apparently similar people working long in the same environment. Such conditions are seldom found, particularly as the truly accident-prone may change his job after having had an accident. In flying, for example, the potentially accident-prone's first accident is liable to be his last, and there is no further opportunity for demonstrating that "repeating" which is the hall-mark of the condition. Despite the difficulties of isolating and defining accident-proneness, some clinicians are inclined to believe that temperamental qualities affect liability to error and accident. Sometimes this inference is soundly based on the objective tests designed to measure skill of performance under harassing circumstances.[3] Other workers venture into theories about the unconscious death wish as a cause of accidents. Commenting on this ADELSTEIN points out that the fatal-accident rate was much higher among shunters than among clerks; but there was no compensating rise in the number of suicides among the clerks.

However intriguing such theories of host variability may be, they should not blind us to the importance of environmental conditions. Crowding, for example, may be an important feature of what GORDON [4] has called "the reservoirs of infection" in accidents—the home and the highway. The frequency of reported accidents in factories with different degrees of congestion certainly suggests that overcrowding may have some bearing on the problem; but here again it is difficult to be sure that we are not measuring frequency of reporting rather than frequency of accident. Curiously enough, the rural roads seem to be more dangerous than those in the city, at least for males; and the same trend has been noted in the U.S.A.[4] Anyone who has served in a R.A.F. flying-station will remember the prevalent belief that accidents always happen in threes. Are accidents infectious? No-one seems to know; but new simple and sensitive tests [5] for detecting changes in the distribution of accidents in time and in space may throw clearer light on the relation of accidents to a changing environment.

GISSANE remarked at the meeting that the total loss inflicted on the community through death or injury by violence brooks no delay. We need, he said, special hospitals for treatment and reablement. But, as he also suggested, we need as part of the team field epidemiologists, based on the hospital, who can relate injury to circumstance, reveal the foci of special risk, and plan the measures of prevention.

The Social Scientist

OUR national way of meeting a crisis is to draw together; and the almost continuous crisis we have faced during the last forty years has led us more and more to club our resources and entrust to the State their fair distribution. But we should hardly have accepted the consequent interference with our private lives if we had not already been inclined to accept a modification of our society. This changing climate of opinion is largely traceable to the influence of the social scientist, and speakers at the first annual conference of the British Sociological Association, held in London at the end of last month,[6] showed a lively sense of their responsibilities.

In his opening address Prof. GUNNAR MYRDAL, who admitted to being himself an escaped economist, went back to the early sheltered days of social science, when its adherents were limited to a few university dons and a "restricted amateur fringe." This small group, he pointed out, brought forward big ideas: if the views of MALTHUS on population began as an academic abstraction, they certainly ended by affecting social policy. For a very long time, however, the social scientist's influence was ideological and he did not begin to emerge from his seclusion until the first world war, when the economist was summoned to help the politician and the Civil Servant. To begin with he was encouraged only to advise his more worldly colleagues in planning the new industrial controls made necessary by war; but he remained to share in administration. Nor after the war did he withdraw to his academic retreat; indeed he extended his work and called some of his fellow social scientists, such as the psychologists, to his side. Large business concerns were beginning to recognise, as Professor MYRDAL put it, "that their contacts with the public went beyond buying and selling," and they, too, now turned to the social scientist for help. The depression of the '20s, when facts about nutrition, health, and unemployment were urgently called for, gave the social scientist further opportunities, and the late war completed his emancipation. Such war-time devices as evacuation, rationing, and propaganda were largely dependent on his help, and in the years of so-called peace the anthropologist and the educator have taken an increasingly active part in such work as the democratisation of Japan, the occupation of Germany, and Colonial administration. Professor MYRDAL would not claim that they have been entirely successful with these unfamiliar tasks, but he believes that the results

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1. Greenwood, M., Woods, Hilda M. Industrial Fatigue Research Board, report no. 4. H.M. Stationery Office, 1919.
2. Adelstein, A. *J. R. statist. Soc.* 1952, 115, 354.
3. Davis, D. R. Pilot Error. Air Ministry, A.3139A. H.M. Stationery Office, 1948.
4. Gordon, J. E. *Amer. J. publ. Hlth*, 1949, 39, 504.
5. Maguire, B. A., Pearson, E. S., Wynn, A. H. A. *Biometrika*, 1951, 39, 168.
6. See *Lancet*, April 4, 1953, p. 692.

over a number of years of H C TROWELL, who was unfortunately not able to attend the conference in person In a paper on the clinical aspects and treatment of kwashiorkor Trowell stressed that the disease develops in children fed a diet low in protein but relatively high in carbohydrate, this distinguishes it from general malnutrition, in which calorie deficiency predominates (In parenthesis, it may be remarked that though the theory of relative carbohydrate excess has been widely held, as is shown by names such as "sugar baby" and "starchy food dystrophy" applied to conditions of this type, and although it is in keeping with theoretical expectations based on the experimental work of Best and of Griffith, it has never received direct proof by measurements of actual dietary intake The difficulties of this are obvious, there is clearly an urgent need to surmount them) Trowell described how in kwashiorkor the main damage is inflicted on the organs with the highest protein turnover—not only liver, but also pancreas and gut Workers at Kampala have shown that in the pancreas both structural and functional lesions occur at an early stage In the subsequent discussion it became apparent that here is one point where studies in man seem to be in advance of those in the laboratory Although a reduction in enzyme content of pancreatic juice has been brought about in dogs and in rats by dietary means, there has so far been little success in producing experimentally the structural changes—atrophy and fine fibrosis—found in kwashiorkor The acute necrosis produced by the antimetabolite ethionine is not a characteristic lesion of that disease

Although Trowell underlined the importance of protein deficiency, he could not, in the present state of knowledge, regard this as the sole cause of kwashiorkor What other causal factors there may be is not known, the workers in Uganda regard skimmed milk as the treatment of choice, and do not feel that either choline or vitamin B_{12} has any specific therapeutic action Vitamin B_{12} may, however, play a supplementary part in preventive diets based on vegetable proteins To elaborate such diets is a problem of urgent importance, since, although in theory kwashiorkor could be eradicated by the provision of cow's milk, in practice there is not enough to go round As P GYORGY (Philadelphia) pointed out, the most economical source of protein for the infant is human milk Normally it is thought that if a diet is to be adequate at least 14% of its calories must be derived from protein In human milk this figure is only 6%, and yet it is a complete food—a very remarkable fact

Two papers were devoted to the metabolic and biochemical changes in human fatty liver and cirrhosis J C WATERLOW and S J PATRICK (University College of the West Indies Jamaica) have studied in infants the activity of a number of enzymes in liver tissue obtained by needle biopsy Although the results so far are negative, in the sense that no specific biochemical lesion has been found in the malnourished liver, it has been shown that this approach is technically feasible, it is possible to do six or seven different enzyme assays together with a number of other chemical measurements, on 3–4 mg of tissue These workers have found that the pattern of enzymes in the human liver is very different from that in the rat, which makes caution necessary in applying to one species conclusions derived from the other The enzymes that they have studied are very well preserved even in the most severely fatty livers nor have they been able to find any relation between the amount of fat in the liver as measured quantitatively in the biopsy specimen, and the general condition of the baby or its response to treatment These findings support the clinical conclusion of Trowell and others that in kwashiorkor the fatty liver is not the dominant feature

An enzyme that might well repay study in malnourished persons is xanthine oxidase W W WESTERFELD (Syracuse) described experiments in which the concentration of this enzyme in liver and gut was reduced almost to zero by protein starvation Moreover, for full activity xanthine oxidase needs a cofactor which has been identified independently by Westerfeld and by a group at the Lederle Laboratories as molybdenum This is of interest, since many tropical soils are deficient in that, as in other, trace elements The possibility of a trace element deficiency in man has been little investigated It may be that such a deficiency would manifest itself by a change in activity of enzyme systems many of which need metals in minute amounts either as activators or as constituents of prosthetic groups

Negative results were also reported by G J GABUZDA and C S DAVIDSON (Boston) from a study of nitrogen metabolism in patients with cirrhosis They could find no deviation from normal in nitrogen absorption, nitrogen balance, or amino acid tolerance Possibly these investigators were thwarted in their search for a metabolic disturbance by the enormous functional reserve of the liver If these two studies—that on nitrogen metabolism and that on enzymes—are representative, it must be admitted that we have a long way to go before we can characterise in biochemical terms either the lesion in the liver itself or its effect on the rest of the body

The last three papers of the first day were devoted to alcoholism and its treatment J MARDONES (Santiago, Chile) discussed the complex causal relations that may exist between alcoholism and vitamin deficiency First, alcohol, either by a pharmacological action or by increasing the calorie intake, may reduce the appetite there is no evidence that it causes an increased vitamin requirement Secondly, both Mardones and R J WILLIAMS (University of Texas) have shown experimentally in rats that deficiency either of known B vitamins or of some unknown factor may cause an increased craving for alcohol When vitamins are given, this craving disappears Lastly, both clinically and experimentally there seem to be great individual differences in the desire for alcohol These differences may result from a genetically determined disorder of metabolism, perhaps a difficulty in the initial stages of carbohydrate oxidation Thus, in Williams's view alcoholism results from a deviation, inherited or acquired, in nutritional requirements and metabolic pattern from that which we have come to regard as normal His approach can be followed in the study of any disease, not only alcoholism an emphasis on the importance of individual variability, which should be regarded not as an unavoidable evil, but as a focal point for research

Liver Necrosis

On the second day of the conference, when dietary liver necrosis was discussed, all the papers were concerned with experimental work, since there is no evidence that in man this lesion arises from malnutrition alone Nevertheless, it is possible that human dietaries may be lacking in some of the factors deficiency of which causes liver necrosis in rats Although in man this deficiency may never culminate in massive necrosis, it may be enough to make the liver more vulnerable to other insults, such as infections or toxins This point of view which dates back to the early work of Whipple, derives support from the experiments of P GYORGY (Philadelphia) He has shown that antibiotics notably aureomycin, confer a partial protection, delaying the onset of liver necrosis The inference is that bacteria from the gut play some causal part A crucial experiment on this point is now in progress, and was described by T D LUCKEY, of the Germ-free Laboratory, Notre Dame University Indiana Preliminary trials show that Gyorgy's necrogenic diets do not produce liver damage in rats which throughout their lives are kept germ free

of 60 ft. straight past number two; fortunately their belay held firm, and he was left swinging in the abyss.

At that distance his movements were reminiscent of those of a water-boatman (*Corixa geoffroyi*) and at the third swing he made contact with the rock and continued his upward course. At this point number two's voice, quite unruffled, floated across the corrie: "Ye' maun go it again, Jimmy; me, I couldna' manage." Jimmy went it again, this time with success; but, as I strolled round to the top of the climb, I saw both number two and number three miss their footing at the mauvais pas, and swing similarly for a time, though on a shorter pendulum, in space. When eventually they all came over the lip of the crag, I inquired whether they had had an enjoyable climb. "Ach fine," they said.

Then number three, who took blackouts, was a cause of some concern even to the Hasheaters; but I have since heard with relief that he is now safely in the Royal Air Force.

* * *

Did general practitioners contribute more to advances in medicine in the past than the present? I found myself pausing in my researches among the medical journals of last century to ask this question. I opened my mouth to say "Yes, of course," and then I stopped to reflect. I am glad I did so, for I would otherwise have fallen into the ever-open trap, better recognised by statisticians than by us lesser mortals, of comparing incomparables.

General practice and its place in medicine have greatly changed during the past century. A hundred years ago consultants with hospital beds had no particular advantage over general practitioners in their opportunities for advancing medical knowledge. But today specialists (the term now seems more appropriate than consultants) have access to many facilities denied to the general practitioner—junior staff, records staff, first-class nursing, a laboratory, an X-ray department, and so on. But the general practitioner is not without his own advantages; he can still advance knowledge by clinical study of the natural history of diseases, especially short-term febrile illnesses seldom seen in hospital practice, and by study of familial, social, and environmental aspects of disease. His better title—family doctor—shows where his real opportunities lie.

* * *

Many commemorative lectures tail off towards the end and we are brought back to consciousness by the handclaps of those in the front row. How pleasant it was by contrast the other evening when, at the end of his discourse, the lecturer turned from the discussion of diseases of an important organ to recall how when he was a little boy his father used to entertain him and his small friends to a magic-lantern show in the consulting-room. The lecturer has treasured ever since one of the slides which ended these shows, and he now had pleasure in putting it on the screen. It was a picturesque scene such as would appeal to the young of all ages, and across the top of it in beautiful lettering were the words "Good Night." I shall remember this when I have long forgotten what the lecture was about.

* * *

The other day I came across this inscription in Southwark Cathedral:

> Here Lockyer lies interr'd: enough, his name
> Speakes one hath few competitors in fame;
> A Name soe Great, so Generalle may scorne
> Inscriptions wh. doe vulgar tombs adorne.
> A diminution tis to write in verse
> His eulogies wh. most mens mouths reherse.
> His virtues and his PILLS are soe well knowne
> That envy can't confine them under stone.
> But they'll survive his dust and not expire
> Till all things else at th' universall fire.
> This verse is lost, his PILL Embalmes him
> To future times without an Epitaph.
> This April 26, 1672, aged 7[illegible]

I wonder who Lockyer was, and whether his pills still survive under different names to the Universal Fire.

* * *

I wonder what river my fellow peripatetic of March 28 was fishing when he saw a pair of yellow wagtails disporting themselves on the bank beside him. The yellow wagtail is not usually a water bird, and it is surely quite an ornithological event for him to be seen in this country before the end of March.

Letters to the Editor

PHARMACEUTICAL ADVERTISEMENTS

SIR,—The letter from Dr. Elek (March 28), written apparently with authority from St. George's Hospital Medical School, is so seriously misinformed that a reply is needed. He complains that British pharmaceutical firms are not fair or just—he even uses the word pernicious—because they do not return financial rewards to medical research. Has he bothered to confirm his facts? Does he know, for example, that one alone of these firms spends half a million pounds every year on medical research?

He urges, as if it were a new idea, that manufacturers should "spend at least part of their profits on financing research projects in universities and other suitable establishments—not in their own laboratories where a bias could be suspected." Does he know that approximately 100 research fellowships in universities are maintained by these British commercial firms with complete freedom from control; and that one single firm makes grants to other research workers in universities of well over £100,000 a year? Does he know that these firms are promoting a department of pharmacology in the Royal College of Surgeons of England at a cost of many thousands of pounds, again with complete freedom to the college?

And finally—this really is the last straw—he compares British firms unfavourably with American firms in their devotion to advertisement rather than to research. I would like to be kind to Dr. Elek, but surely never before did misinformation lead to such wanton misrepresentation.

London, W.1. REGINALD WATSON-JONES.

FLOUR

SIR,—The explanations offered by Professor Frazer (March 28) for our patient's allergic response to chemically treated flour appear to be based on the assumption that the flour or bread this patient was given had always received either chemical or physical (aeration) treatment.

Whereas the use of flour improvers is a miller's process, the aeration treatment is a baker's process, applied during the making of the dough. It was stated in our paper that the patient was given a 7 lb. bag of chemically untreated flour for cooking purposes. This flour had received neither chemical nor physical (aeration) treatment. She consumed the whole 7 lb. of flour with no skin disturbance. Moreover, since then she has used four more 7 lb. bags of chemically and physically untreated flour for cooking. The products have been shared with her family, but she estimates that she has eaten about one third (or 9 lb.) of the flour herself, and there has been no reaction in her skin.

Since Dr. Frazer's letter appeared, the patient has been given bread made by the straight dough process (i.e., without aeration) from chemically untreated flour. Her skin has shown no reaction to this bread.

Reigate. G. C. SHELDON.
London, W.1. ALLAN YORKE.

SIR,—At the end of their article of March 21, describing a case of eczema associated with the ingestion of chemically "improved" flour, Dr. Sheldon and Dr. Yorke pose the question: "Is this a rare case of allergy, or merely the first recognition of a common disorder?" The following is an account of an almost exactly similar syndrome whose association with flour I recognised in 1946 but which hitherto I have not reported publicly.

A married housewife, then aged 41, developed in December, 1942, a severe facial eczema. (In contrast to Sheldon and Yorke's case, the extremities were not affected. The menopause did not occur till ten years later.) In its most developed form the eczema occurred in phases, or cycles, which had a periodicity of about 7–9 days. The onset of each phase was characterised by a sense of localised prickling and tightness. In about 24 hours angry red splashes appeared symmetrically where mother and infant carried staphylococci, the type was the same in 19.

Ludlam concludes that, though some of the observations are difficult to explain, there is little evidence of transfer of nasal staphylococci from the mother to the infant in hospital, but that [illegible] staphylococci are liable to be acquir[illegible]ant. The hospital-delivered mother probably picks up the resistant strain from her infant after her return home. There is also some risk that penicillin-resistant strains may be further spread in the community by transfer to home-born infants at the clinics or possibly by midwives recently associated with the hospitals. Resistant strains do not yet seem to be becoming much more prevalent in the general population; but it is important to watch the routes by which such prevalence may be increased.

INSURANCE CLAIMS AND INFLUENZA

THOSE who have laboured to produce statistics of weekly claims on the Ministry of National Insurance for sickness benefit probably never dreamt that their figures would be useful to students of the epidemiology of influenza. Today almost all who earn are entitled to sickness benefit; and during an epidemic of influenza, particularly one caused by virus A, the usual high incidence of infection is rapidly reflected in a sharp rise in the claims for sickness benefit. No other disease produces a comparable rise in morbidity figures; and a rise in the number of claims above 175% of the weekly average can be taken as evidence of influenza. By following the rise and fall in the figures for claims in different parts of the country the path of an influenza epidemic can be accurately mapped out.

This technique was first successfully applied in the 1950–51 epidemic of influenza,[1] where it was shown that the outbreak began in three port areas—Aberdeen, Tyneside, and Falmouth-Truro—and was followed by an independent focus in Merseyside. Corresponding information for this year's epidemic is not yet available, but a recent report[2] summarises some essential features shown by preliminary figures. In the first week of January of this year influenza had reached a moderately heavy prevalence in two areas—the Eastbourne district, and an area which contains many Service establishments and stretches from Camberley, Aldershot, and Farnham up to the Thames between Egham and Walton. The London area became involved in the third week of January, and thereafter the epidemic wave spread outwards from London growing fainter as it spread further north. There is a clear indication that areas heavily involved in 1950–51 were dealt with more leniently in the present epidemic. If we take the hint, protective vaccination for the next epidemic should be concentrated on populations in the Midlands and further north who were less densely infected this year.

Each new successful technical advance seems to answer some of the questions for which it was designed and then to pose new problems. One problem brought out by the investigation of the 1950–51 outbreak was the strange way in which the epidemic seemed to advance across country like a wave, ignoring the well-worn lines of communication. This unusual type of progress has been reported before, and there seems at present to be no obvious explanation. Another problem concerns the origin of this year's epidemic; the early involvement of port areas in the 1950–51 epidemic showed that virus had entered this country by sea—a fact that was strongly supported by antigenic studies of viruses isolated here and abroad. This year, however, the epidemiological data suggest either that the virus had sneaked quietly into the country and waited for a favourable moment, or that it had remained in this country in a latent phase during the past two years. Epidemiologists would much like to know by which of these ways the epidemic originated.

A RARE COMPLICATION OF CHICKENPOX

Saslaw and his colleagues[1] at the Ohio State University Hospital have recently, within a period of five months, seen 3 adults with chickenpox and associated pneumonia. Radiographs of the chest in each case showed diffuse bilateral nodular or miliary infiltration, scattered evenly throughout both lung fields. Radiographic clearing ran parallel with the improvement of the skin lesions, although in 1 patient some infiltration was still present in the lower lobes two months after the onset of the pneumonia. Blood-cultures were negative in every case. Results of sputum examinations did not suggest a bacterial pneumonia. The leucocyte-count was only moderately elevated in 2 patients and was normal in the 3rd. Serological investigation for primary atypical pneumonia, psittacosis, and Q fever was negative. The clinical and radiological features in the 3 patients were closely similar. The pneumonic illness was in each case severe, and although dramatic recovery took place, this was not attributed to any specific action of antibiotics on the varicella virus. The authors could find only 8 similar reported cases—all in adults in the United States.

NEW REGULATION

THE new arrangements proposed by the Working Party[2] for distributing the central pool to general practitioners in the National Health Service came into force on April 1. The principal [illegible] the increase of the capitation fee to [illegible]; [illegible] of the maximum size of a doctor's list from 4000 to 3500; and an extra payment of 10*s.* for each patient from the 500th to the 1500th on a doctor's list. Doctors with 4000 patients will have twelve months in which to adjust their lists. Initial allowances[3] (£600 in the first year, £400 in the second year, and up to £200 in the third) have been introduced to encourage doctors to set up in practice in under-doctored areas. Hardship allowances will be available for elderly doctors who may lose their "fixed annual payment" and not be eligible for the new initial allowance. Doctors of sixty-five and over with lists of at least 500 persons may claim these supplementary payments which will not exceed £350 per annum; claims should be submitted if possible by June 30. Full details of the scheme were issued to executive councils last week.[4]

The regulations officially making these charges were published on March 27. (The allocation of the sum reserved by the Working Party for stimulating the growth of group practices is still under consideration.) It is unlikely that they will be challenged; but a group of Labour M.P.S. headed by Mr. Aneurin Bevan, have tabled a prayer for the annulment of the rules issued last month[5] amending the cost of pay-beds and the medical and surgical fees for private patients.

ON March 30 Sir RUSSELL BRAIN was re-elected president of the Royal College of Physicians of London.

THE 121st annual meeting of the British Medical Association will be held in Cardiff from July 9 to 17 under the presidency of Mr. Tudor Thomas. Coronary Disease, Fibrositis, and Overweight have been chosen as the subjects of the three plenary scientific sessions.

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1. Third Annual Report of the Ministry of National Insurance. H.M. Stationery Office, 1952.

1. Saslaw, S., Prior, J. A., Wiseman, B. K. *Arch. intern. Med.* 1953, 91, 35.
2. See *Lancet* 1952, i, 1155.
3. *Ibid*, ii, 1029.
4. [illegible]

the available evidence is consistent with it Otherwise, the pharmacopœia would be burdened with every new "remedy" which was not proved to be actively harmful We have found no evidence that vitamin E increases the exercise tolerance of patients with intermittent claudication, and we have shown that its possible effect under the conditions of our trial is at most, small We believe, therefore, that the null hypothesis should be assumed to be true

M HAMILTON
G M WILSON
P ARMITAGE
London W 12 J T BOYD

SENIOR REGISTRARS

SIR,—It is time that something was done to help senior registrars who cannot help themselves There must be many hundreds of us throughout the country, growing yearly more hopeless a stagnant pool of cheap specialists deliberately created by the National Health Service A great many of us have been qualified for more than twelve or fourteen years, but we are paid less than newly settled general practitioners, we are liable to dismissal at short notice and at regular intervals, we cannot settle anywhere and we cannot plan anything Successive Ministers of Health or their underlings have blandly assured us for years that they are deeply concerned and the position is being explored

It is obvious that we cannot all become consultants overnight—indeed some of us may never be suitable But two immediate measures could be adopted to help us meet our financial and domestic insecurity We could be given some certainty of tenure of our posts beyond three years, and we could be given some annual increment of pay when we have reached the present maximum of £1300, which is so very much less than that of the most recently appointed consultant

Ipswich EDWARD ELMHIRST

POSITION FOR TONSILLECTOMY

SIR,—I would like to comment on the remarks of *Mr Ballantyne and Dr MacDermott (March 14)*

Although the risk of spinal-cord damage during tonsillectomy must be extremely remote, the cases cited by Sir Charles Symonds are a warning against hyperextension of the neck As your correspondents point out, the reason for the extended position is to prevent blood entering the bronchial tree St Clair Thomson and Negus[1] say that 40% of a series of post tonsillectomy cases were found to have blood in the bronchi Yet pulmonary complications from this cause are rare it is probable that they occur *only after the inhalation of tonsillar* tissue or blood clot Small quantities of blood entering the trachea in a liquid form will be spread over the surface in a thin film and removed by ciliary action before bronchial plugging occurs Thus, the risk is slight if flooding of the laryngeal opening during the operation is prevented, if complete hæmostasis is attained, if all blood clots are removed from the nasopharynx and pharynx at the end of the operation, and if the patient is rapidly moved to the lateral position Flooding of the laryngeal opening can be prevented by intratracheal intubation with a large-bore tube and by the use of an efficient suction apparatus by an assistant if the hæmorrhage is brisk *Hyperextension of the neck* is not necessary In my experience the use of a pillow under the shoulders is liable to cause excessive extension in short necked subjects My practice is to lower the head rest, after the patient has been placed on the table and a gag inserted to an angle just sufficient to cause the blood to drain away from the larynx In all but the rare case no strain on the neck results, particularly if the anæsthesia is on a light plane In the rare case, some degree of Trendelenburg position can be added The careful removal of clots at the end of the operation is probably of greater importance in the prevention of pulmonary complications than the degree of hyperextension of the neck I know of a near fatality caused by laryngeal occlusion by a large clot dislodged from the nasopharynx after the patient was moved from the table

Finally, I consider that there is some risk of injury to the neck when the patient is moved from the table and turned on his side

Swindon, Wiltshire COLIN M JOHNSTON

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[1] Thomson St C Negus V E Diseases of Nose and Throat. London 1948 p 443

REMEDY FOR ANÆMIA

SIR,—It is with regret that I note in your column an advertisement for a new hæmatinic which recalls the palmy days of polypharmacy It is said that each capsule of this preparation contains 192 mg ferrous sulphate, 10 µg vitamin B_{12}, 0 85 mg folic acid, 50 mg ascorbic acid, 100 mg powdered stomach and 350 mg of an insoluble liver fraction, and it is recommended as "*the greatest step forward yet made in the treatment of common anæmia*," and "invaluable in the treatment of nutritio[illegible] post-infectious anæmia, the [illegible] of pregnancy, infancy, pellagra and sprue and allied dyscrasias"

Whatever may be the situation in the United States, this polypharmacy is not needed in Britain The megaloblastic anæmias of pregnancy, infancy, pellagra and sprue are so rare that full scale investigation is needed before any such diagnosis can be accepted treatment may then be with folic acid, vitamin B_{12} and ascorbic acid, nicotinic acid, &c, whichever is indicated Nutritional hypochromic anæmia—an elegant term for iron deficiency—can be treated quite efficiently by simple iron salts or by injection of saccharated iron hydroxide

Further, such blunderbuss preparations are dangerous, because they prevent accurate diagnosis Only the other day I was asked to study an anæmic patient who had received iron salts, folic acid, liver extract (parenteral and *oral*), vitamin B_{12}, and a mixture of other B vitamins This treatment had effectually destroyed the clues on which I depend, and I could not help the patient Another patient, referred to a colleague for diagnosis of a suspected pernicious anæmia, received *oral* and parenteral liver extract only 24 hours before reference *to hospital for* investigation—making the diagnosis unnecessarily difficult No one can exaggerate the importance of diagnosis in anæmia, or the difficulty of establishing it after treatment has started In more than 9 cases out of 10, a simple history and simple laboratory tests suffice to establish the diagnosis—and laboratory tests are becoming available to more and more practitioners

One must conclude that the manufacturers of the new confection are hoping to divert a larger proportion of the nation's drug bill into their own *pockets* This is a lawful—and perhaps even a *commendable*—aim but the money available for the health service is limited and the cost of curing a patient with the new remedy is likely to exceed that of curing him with some simpler and less elegant preparation It is difficult to escape the conclusion that to order so elegant a preparation is against the best interests of patients and of the country

Such sentiments are spreading among the younger consultants and their registrars Our task today is to restore to health (and work) as *many patients* as possible and to do this at the minimum of expense Recently it was pointed out that about £240 000 has been wasted by *ordering a proprietary* preparation in place of its official equivalent *d* amphetamine

When public moneys are wasted on this scale those who encourage such expenditure are challenging the Government of the day, one of whose chief tasks is to cally the important route of spread. Moreover, indirect evidence, obtained from attempts to prevent "airborne" spread by way of droplet nuclei and dust, suggests that, at most, such spread is of only secondary or minor importance. Repeated attempts to control the environment with ultraviolet light, aerosols, and the oiling of floors and blankets have had little effect on the spread of hæmolytic streptococci or of other forms of respiratory disease.[11 12] It may be argued that all important places of spread have not been controlled in such studies, but the fact remains that these procedures, as used, have not been effective.

The hypothesis that seems most tenable is that intimate contact, such as occurs, for example, in the home and possibly in the school-room, is required for effective spread. Elucidation of the factors involved in intimate contact is difficult, but it seems reasonable that physical contact and transmission by larger droplets for short distances are operative. Presumably time-dosage relationships are important. Transmission may be effected along single or multiple channels which are not yet defined.

There are, of course, other factors that correlate with the occurrence of group-A streptococcal infections, such as age, climate, season, and degree of crowding. Such correlations have been given causal significance in the past, but it now seems desirable to re-examine their interpretation. For example, the age-specific incidence-rates for streptococcal infections, usually greatest in the age-group 5–9 years, primarily may reflect not susceptibility but simply the opportunity to acquire infection. In a study of illness in Cleveland families[13 14] the peak of all respiratory infections was in young school-children. Moreover the height of the attack-rate in pre-school children depended on the presence or absence of school-age siblings in the home. Thus the level of occurrence of respiratory illnesses in the pre-school child depended primarily on his opportunity to acquire infection from an older sibling. Likewise the high infection-rates which have persisted for years at certain military posts may indicate that the troops at such posts have a greater opportunity to acquire streptococci and not that the troops stationed there have an increased innate susceptibility. A true interpretation remains to be established.

Similarly, correlations of infection-rates and carrier-rates with climate, season, and crowding may reflect merely the relation of these factors to the opportunity to acquire and carry the streptococcus, rather than the more subtle effects of these factors on the organism or the host. Thus, in the study of 53 "convalescent carriers" mentioned previously, 27 were transported by airplane to the Florida coast and the remaining 26 were kept at the 6000-ft. altitude of Cheyenne, Wyoming.[4] The number of streptococci decreased at the same rate in these two groups of carriers. Here, at least, geographic location and the differences in climatic conditions, comparable to seasonal change, did not affect the quantitative aspects of the host-parasite relation during convalescence.

For reasons such as these it seems desirable to re-examine our accepted concepts of the epidemiology of β-hæmolytic streptococcal infections and, in so doing, to seek fuller interpretations of the importance and significance of factors apparently related causally to high or to low incidence and prevalence levels.

Non-suppurative Complications of Group-A Streptococcal Infections

It is now generally accepted that there is a temporal and probably causal relation between group-A streptococcal infections and rheumatic fever. In contrast, the relation between streptococcal infection and acute hæmorrhagic glomerulonephritis has been less definite. If the association of rheumatic fever and nephritis with streptococcal infections is truly one implied by the term "non-suppurative complications," that association should be supported by a consideration of the epidemiological aspects of both the initial infection and of the complicating sequelæ.

RHEUMATIC FEVER

There now seems to be little question of the relation of a group-A streptococcal infection, or perhaps of multiple infections, to the development of rheumatic fever. Justification for this conclusion comes from such evidence as: (1) the serological demonstration of type-specific streptococcal infection preceding the onset of rheumatic fever in the individual case[15]; (2) the epidemiological association of "outbreaks" of rheumatic fever with outbreaks of streptococcal disease[16]; and (3) the virtual eradication of rheumatic fever by prophylaxis or early treatment of streptococcal infections.[15–18]

Moreover the epidemiological features of rheumatic fever may be likened to those of group-A streptococcal infections, when such factors as age, season, climate, geographic distribution, and crowding are considered. Until established beyond reasonable doubt, however, it does not necessarily follow that similarities with respect to such factors prove that the two types of illness are causally related. But closer inspection of these factors in the light of the available data leads to the concluson that the epidemiological features of rheumatic fever are indeed those of group-A streptococcal infections in general.

Rheumatic fever, for example, is principally a disease of childhood. The assumption has therefore been made that children are more susceptible to rheumatic fever than are adults, and that such susceptibility explains the age-distribution. Yet, when streptococcal infections occur in young adults, as in the military forces,[19] the incidence of subsequent rheumatic fever is not significantly different from that occurring after streptococcal infections in children—i.e., about 3%. Therefore susceptibility to rheumatic fever does *not* appear to decrease with age, at least during the first three decades. If one now compares the age-distributions of streptococcal infections and of rheumatic fever in civilian populations, one finds that they can be superimposed, and that the peaks of both are in the same age-group of 5–9 years. Thus the relation of age to the occurrence of rheumatic fever is the same as the relation of age to streptococcal infections.

Geographic distribution provides another example, although the data are more limited. The areas of high prevalence of rheumatic fever are usually those having a high prevalence of streptococcal infections. Moreover, the frequency of occurrence of rheumatic fever as a complication of group-A streptococcal infections, regardless of the route of transmission, is about 3% in Boston,[20] North Carolina,[21] Wyoming,[19] Denmark,[22] and other areas.[19]

As regards the relation of housing and poverty to the recurrence of rheumatic fever, Hewitt and Stewart[23] obtained no evidence that the disease was associated either with bad housing or with poverty per se. They pointed out that the opportunity for infection appeared to be the overruling factor determining its incidence.

In further support of the close epidemiological association of rheumatic fever and group-A streptococcal infections in general is the fact that rheumatic fever follows streptococcal infection without apparent regard for the type-specificity of the infecting streptococcus.

ACUTE GLOMERULONEPHRITIS

The relation of acute hæmorrhagic glomerulonephritis to infection with β-hæmolytic streptococci has not been as clear, nor as generally accepted, as the association the available evidence is consistent with it Otherwise, the pharmacopœia would be burdened with every new "remedy" which was not proved to be actively harmful We have found no evidence that vitamin E increases the exercise tolerance of patients with intermittent claudication, and we have shown that its possible effect under the conditions of our trial is at most, small We believe, therefore, that the null hypothesis should be assumed to be true

M HAMILTON
G M WILSON
P ARMITAGE
J T BOYD

London W 12

SENIOR REGISTRARS

SIR,—It is time that something was done to help senior registrars who cannot help themselves There must be many hundreds of us throughout the country, growing yearly more hopeless, a stagnant pool of cheap specialists deliberately created by the National Health Service A great many of us have been qualified for more than twelve or fourteen years, but we are paid less than newly settled general practitioners, we are liable to dismissal at short notice and at regular intervals, we cannot settle anywhere and we cannot plan anything Successive Ministers of Health or their underlings have blandly assured us for years that they are deeply concerned and the position is being explored

It is obvious that we cannot all become consultants overnight—indeed some of us may never be suitable But two immediate measures could be adopted to help us meet our financial and domestic insecurity We could be given some certainty of tenure of our posts beyond three years, and we could be given some annual increment of pay when we have reached the present maximum of £1300, which is so very much less than that of the most recently appointed consultant

Ipswich EDWARD ELMHIRST

POSITION FOR TONSILLECTOMY

SIR,—I would like to comment on the remarks of Mr Ballantyne and Dr MacDermott (March 14)

Although the risk of spinal cord damage during tonsillectomy must be extremely remote, the cases cited by Sir Charles Symonds are a warning against hyperextension of the neck As your correspondents point out, the reason for the extended position is to prevent blood entering the bronchial tree St Clair Thomson and Negus[1] say that 40% of a series of post tonsillectomy cases were found to have blood in the bronchi Yet pulmonary complications from this cause are rare it is probable that they occur only after the inhalation of tonsillar tissue or blood clot Small quantities of blood entering the trachea in a liquid form will be spread over the surface in a thin film and removed by ciliary action before bronchial plugging occurs Thus, the risk is slight if flooding of the laryngeal opening during the operation is prevented, if complete hæmostasis is attained, if all blood clots are removed from the nasopharynx and pharynx at the end of the operation, and if the patient is rapidly moved to the lateral position Flooding of the laryngeal opening can be prevented by intratracheal intubation with a large bore tube and by the use of an efficient suction apparatus by an assistant if the hæmorrhage is brisk Hyperextension of the neck is not necessary In my experience, the use of a pillow under the shoulders is liable to cause excessive extension in short necked subjects My practice is to lower the head rest after the patient has been placed on the table and a gag inserted to an angle just sufficient to cause the blood to drain away from the larynx In all but the rare case no strain on the neck results, particularly if the anæsthesia is on a light plane In the rare case some degree of Trendelenburg position can be added The careful removal of clots at the end of the operation is probably of greater importance in the prevention of pulmonary complications than the degree of hyperextension of the neck I know of a near fatality caused by laryngeal occlusion by a large clot dislodged from the nasopharynx after the patient was moved from the table

Finally, I consider that there is some risk of injury to the neck when the patient is moved from the table and turned on his side

Swindon Wiltshire COLIN M JOHNSTON

REMEDY FOR ANÆMIA

SIR,—It is with regret that I note in your columns an advertisement for a new hæmatinic which recalls the palmy days of polypharmacy It is said that each capsule of this preparation contains 192 mg ferrous sulphate, 10 µg vitamin B_{12}, 0 85 mg folic acid, 50 mg ascorbic acid, 100 mg powdered stomach, and 350 mg of an insoluble liver fraction, and it is recommended as "the greatest step forward yet made in the treatment of common anæmia" and "invaluable in the treatment of nutritional hypochromic anæmia post-infectious anæmia, the megaloblastic anæmias of pregnancy, infancy, pellagra and sprue and allied dyscrasias"

Whatever may be the situation in the United States this polypharmacy is not needed in Britain The megaloblastic anæmias of pregnancy, infancy, pellagra and sprue are so rare that full scale investigation is needed before any such diagnosis can be accepted, treatment may then be with folic acid, vitamin B_{12} and ascorbic acid, nicotinic acid, &c, whichever is indicated Nutritional hypochromic anæmia—an elegant term for iron deficiency—can be treated quite efficiently by simple iron salts or by injection of saccharated iron hydroxide

Further, such blunderbuss preparations are dangerous because they prevent accurate diagnosis *Only the other day I was asked to study an anæmic patient who had received iron salts, folic acid, liver extract (parenteral and oral), vitamin B_{12}, and a mixture of other B vitamins This treatment had effectually destroyed the clues on which I depend, and I could not help the patient Another patient, referred to a colleague for diagnosis of a suspected pernicious anæmia, received oral and parenteral liver extract only 24 hours before reference to hospital for investigation—making the diagnosis unnecessarily difficult No-one can exaggerate the importance of diagnosis in anæmia, or the difficulty of establishing it after treatment has started In more than 9 cases out of 10 a simple history and simple laboratory tests suffice to establish the diagnosis—and laboratory tests are becoming available to more and more practitioners*

One must conclude that the manufacturers of this new confection are hoping to divert a larger proportion of the nation's drug bill into their own pockets This is a lawful—and perhaps even a commendable—aim, but the money available for the health service is limited and the cost of curing a patient with the new remedy is likely to exceed that of curing him with some simpler and less elegant preparation It is difficult to escape the conclusion that to order so elegant a preparation is against the best interests of patients and of the country

Such sentiments are spreading among the younger consultants and their registrars Our task today is to restore to health (and work) as many patients as possible and to do this at the minimum of expense Recently it was pointed out that about £240 000 has been wasted by ordering a proprietary preparation in place of its official equivalent, *d* amphetamine

When public moneys are wasted on this scale those who encourage such expenditure are challenging the Government of the day, one of whose chief tasks is

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[1] Thomson St C, Negus V E Diseases of Nose and Throat. London 1948 p 443

Medical Conferences

NUTRITIONAL FACTORS AND LIVER DISEASES

Conference in New York

FROM A CORRESPONDENT

The biology section of the New York Academy of Sciences on Feb. 13 and 14 held a conference under the chairmanship of Dr. Klaus Schwarz, with the ambitious object of reviewing modern knowledge on dietary liver injury, and particularly the relation of animal experiments to conditions in man. Progress in the study of liver disease is especially notable in the tropics, where diets are poor and malnutrition comes high on the list of suspects as a cause of liver damage. For this reason the Academy generously made it possible for several workers from overseas to attend the conference. Nevertheless, the main emphasis was inevitably on experimental work: of 27 papers, only 7 dealt with liver disease in man. In the printed report, however, the balance will be restored by the inclusion of communications from J. N. P. Davies (Uganda), J. Gillman and T. Gillman (Johannesburg), and B. M. Nicol (Nigeria).

Fatty Liver and Cirrhosis

In an introductory paper F. S. Daft (National Institutes of Health, Bethesda) emphasised the differentiation, first made by the workers at Bethesda, of two completely distinct pathological entities: on the one hand fatty liver, caused by deficiency of choline or its precursors, and leading ultimately to cirrhosis; on the other hand *necrosis resulting from deficiency of sulphur-amino-acids.*

C. H. Best (Toronto) discussed the nutritional significance of choline, and suggested that the term "lipotropic" should be restricted to describe substances which accelerate the rate of removal of excess liver fat; it cannot logically be applied to the other effects of choline, such as the prevention of hæmorrhagic kidneys in growing rats, or of slipped tendons in chicks. Choline has been shown to have lipotropic activity in a wide variety of animal species, but whether the list includes man is not yet certain. Even in animals it is difficult to produce a diet deficient only in lipotropic factors, because of the dual rôle of methionine as a precursor of choline and as an essential sulphur-containing amino-acid. In man the difficulties are even greater, and the crucial experiment to test the lipotropic effect of choline has not yet been performed.

This point recurred in a later paper by G. J. Gabuzda and C. S. Davidson (Boston), on the treatment of alcoholic cirrhosis. This disorder responds well to dietary treatment in hospital; the improvement cannot be attributed simply to hospitalisation and withdrawal of alcohol because it does not occur when only glucose-saline is given. The results of adding choline to the glucose-saline were *not impressive.* This experiment, however, does not fulfil the criterion that the diet should be deficient only in lipotropic factors and in nothing else.

It was clear from subsequent papers that we have still much to learn about the mechanism of lipotropic activity. Two lines of approach have a fundamental bearing on this problem. One is to study the mechanism of transmethylation and the metabolism of one-carbon compounds. This topic was touched on, but not developed in detail, in discussion of a paper by V. A. Drill (Wayne University, Detroit). His work re-emphasises the point originally developed by McHenry—that the lipotropic effect of various substances does not depend only on their choline content. Drill has shown that liver extract has a greater lipotropic activity than stomach powder, although the latter contains much more choline. Liver extract contains vitamin B_{12} and folic acid, both of which play some part in transmethylation reactions. These vitamins by themselves had *no lipotropic action under* the conditions of his experiments; but together, in combination with small amounts of choline, they were partially though not completely effective. Drill suggests that liver extract may contain some as yet unidentified lipotropic factor; it may be this that is responsible for the beneficial effect of milk in human fatty liver (kwashiorkor), in which choline and methionine are, from all reports, ineffective.

The second approach to the problem is the measurement of turnover-rates under various dietary conditions. W. E. Cornatzer (University of North Dakota) has studied this problem extensively. He described phospholipid synthesis in the liver as a very primitive function only altered by severe stress. In man the rate of synthesis is very little changed in cirrhosis or hepatitis; in animals it appears to be constant, whether the liver is fatty, fibrosed, or normal, and is not affected by the dietary protein intake. According to the classical theory, choline deficiency causes fatty liver by slowing down the formation of phospholipids and hence causing a failure of fat transport. Turnover studies appear not to support this view, although the intricacies of this experimental approach are not readily grasped by the uninitiated, who include your correspondent.

From biochemistry the conference went on to consider the sequelæ of fatty liver, and the long-term results of the diets which produce it. The histogenesis of fibrosis was described by W. S. Hartroft (Toronto). An important transition stage is the formation of fatty cysts by the fusion of cells overloaded with fat. This paper produced some interesting topics for discussion. The general feeling seemed to be that there is not sufficient evidence to postulate an invariable causal relationship between fat and fibrosis, although the degree of fatty change is very important. It is a puzzling fact, and one not sufficiently appreciated, that whereas in the rat both fat and fibrosis appear first and are most severe at the centre of the lobule, in man—at least in kwashiorkor—both lesions begin peripherally. Whatever the reason for this difference, it is noteworthy that in both species the fibrosis develops at the site of the fatty infiltration. There is no preceding necrosis in the usual sense of the word; but the presence of fatty cysts, produced by rupture of cell-membranes, is evidence that those cells which have fused were degenerate. Fibrosis or cirrhosis is not the only sequel of choline deficiency: as D. H. Copeland and W. D. Salmon (Auburn, Alabama) have shown, if sufficiently prolonged it leads to the formation of tumours, both benign and malignant, in the liver and other organs. J. W. Wilson (Brown University, Providence, Rhode Island) has also produced neoplasia in mice by feeding a base exchange silicate, which probably acts by removing choline from the intestinal contents.

The relevance of this experimental work to problems of human medicine and pathology was well illustrated by J. F. Brock (Cape Town). He presented maps showing the reported distribution, throughout the world, of kwashiorkor, cirrhosis of the liver, and primary hepatic carcinoma. Although the distributions seem not to be identical, all three conditions have a high prevalence in the tropics and in countries where *there is much* malnutrition. Reliable information about prevalence is, however, very scanty; Brock's paper emphasised the part that epidemiological studies can play in elucidating the pathogenesis of these forms of liver injury and their relation to diet.

Although information may be scanty from many parts of the world, this cannot be said of Uganda. From that territory outstanding contributions have been made to our knowledge of kwashiorkor, mainly through the work mechanism by which the results are achieved is often a matter for conjecture The important thing is to have achieved by manipulation the relief no other treatment could have produced

London, S W 3 JOHN EBBETTS

HALLUX VALGUS

SIR,—You have often commented on the high prevalence of hallux valgus (which even in school children is as great as 80%[1 2]) and you referred in your leading article of Feb 14 to the unsatisfactory results of treatment

For the past twelve years I have studied this condition in detail, and I should like to set out my conclusions on its cause, on the probable reasons for failures in treatment, and, most important, on how hallux valgus can be prevented

Cause

The normal hallux should be quite straight, and the angle of the metatarsophalangeal joint should be 180° But a normal hallux is rarely seen in the adult by the age of two 10% of children have a valgus deformity, and at sixteen the figure is 80%

The normal position is the position in which there is maximum efficiency in weight transmission This is the position the hallux will always assume when weight bearing, unless deformed or restricted by footwear The earliest sign of hallux valgus is slight adduction of the hallux when the foot is at rest and not weight bearing

Seat the patient so that his feet rest comfortably on the floor The toes are adducted, forming a slight angle instead of being in contact throughout their length When the patient stands up an inward thrust accompanies the well known forward thrust and corrects the deformity (fig 1) In early cases the correction is complete, but it becomes less and less effective as the deformity progresses

But this natural corrective action of the deformed foot is *not* possible in most kinds of shoe

Once the inward thrust becomes ineffective severe hallux valgus is inevitable *from this point onwards the foot deforms itself*

Hardy and Clapham[3] confirmed my view[1] that the cause of hallux valgus is not hereditary Hallux valgus can only be caused by wearing wrongly designed footwear The presence of some hereditary factor in no way alters this fact The only cause is pressure on the inner side of the phalanges which is greater than that exerted upon the inner side of the first metatarsal—in other words, a pressure that causes adduction of the hallux When the hallux is held for long periods in the adducted position a vicious circle is created which leads to considerable deformity

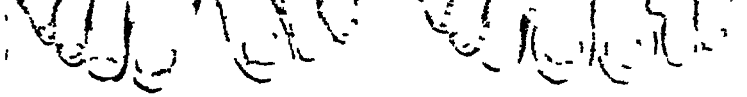

Fig 1—(Left) feet of 13-year-old child at rest showing 13° of hallux deformity (right) same feet when bearing weight, showing correction of deformity

Examination of all adults' and most children's footwear will show that it cannot accommodate the hallux in its normal position When the foot is shod the hallux is adducted

Adduction approximates the origin and insertion of the long flexors and extensors of the toe because they arise on the outer side of the long axis of the toe Prolonged adduction causes a shortening of these slackened structures which, when complete, alters the action of these muscles

In a normal foot or in one only slightly deformed, the command "bend your toes up or down" produces a pure flexion or extension of the toes As soon as shortening occurs pure movements are impossible Voluntary flexion and extension is thereafter always accompanied by adduction of the hallux The adduction producing a lateral movement of as much as half an inch

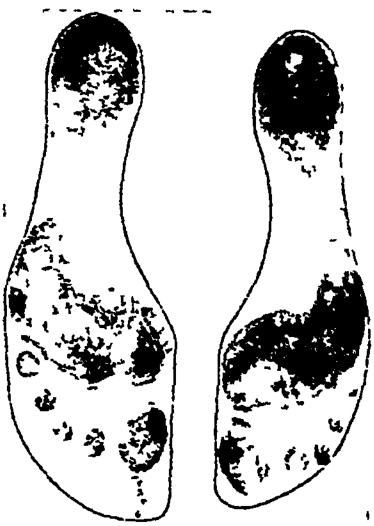

Fig 2—Correctly designed footwear Foot prints of a child with insole patterns superimposed Both shoes have a straight inner border and accommodate the toes in their normal position (Left) correct fitting with allowance for thrust and growth, (right) incorrect fitting

The abductor hallucis offers no effective opposition, and from this point onwards every movement of the hallux includes unopposed adduction and further shortening, leading to obvious valgus deformity Ultimately the degree of deformity exceeds that of the shape of the shoe

It is not generally realised how very early these changes occur There does not appear to be any fixed point beyond the 180° at which these changes commence X ray examination has shown that rearrangement of the trabeculæ of the cancellous bone of the hallux occurs quite early One case with only 18° of deformity showed a definite radiation pattern forming at the point where the exostosis later developed

Treatment

Cases can conveniently be divided into three groups self-correcting, correctable, and operation cases

Self-correcting—In early cases where an effective inward thrust is still present the provision of correctly designed footwear, permitting the toe to resume its normal position, will ultimately effect a cure

Correctable—Cases where the inward thrust, if present is ineffective, where there is no gross joint or bone change, and where with the aid of manipulation under anæsthesia, restoration of mobility and normal position are obtainable, can be corrected without operation These cases respond well to corrective strapping over a long period The strapping must maintain correction without restricting foot function and I have suggested a method of doing this which gave encouraging results[4] But the method is of little use, for if the toe is strapped quite straight the patient cannot wear his shoes—not because the strapping is too bulky but because his shoes are not designed to accommodate his foot with the hallux straight

Operation cases—It is useless to attempt to cure by operation without removing

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[1] Pratt, C A Your Children's Feet London, 1951

[2] British Boot Shoe and Allied Trades Research Association Research report April, 1949 p 107

[3] Hardy, R H Clapham J C R *Lancet*, 1952 i, 1180

[4] Pratt C A [illegible] of Chiropody [illegible] 1949

A remarkable feature of this necrosis, and one that contrasts strongly with the fatty liver, is the suddenness with which it develops. Nevertheless, as F. W. Hoffbauer (University of Minnesota) showed, it is possible to abort the acute attack by testing the urine daily for bilirubin, and giving protective substances as soon as bile appears. In this way recurrent non-fatal episodes can be produced. In the livers of these rats Hoffbauer found the pathological picture first described by Himsworth and Glynn—a coarse, so-called post-necrotic, scarring, which cannot be regarded as a true cirrhosis. It was agreed in the discussion that this lesion in the rat is a good counterpart of the Marchand type of coarsely nodular cirrhosis in man. However, H. Popper (Chicago) pointed out that a pure Marchand's cirrhosis, in which the surviving tissue between the scars is normal, is rare in human pathology. Usually the remaining tissue shows a diffuse fibrosis, perhaps caused by damage to the vascular tree.

A puzzling characteristic of dietary liver necrosis is that it can be prevented by two apparently unrelated substances—cystine or sulphur-amino-acids, and vitamin E. The rôle of tocopherol was first discovered by K. Schwarz (National Institutes of Health, Bethesda); his work was done in Germany during the war, and was not known at the time in England or America. In these countries attention had been concentrated on deficiency of sulphur-amino-acids as the causative factor. Great variability was found, however, in the incidence of the lesion in different laboratories—a variability that was explained when Gyorgy independently discovered the part played by vitamin E and the need for controlling its level in the necrogenic diet. These difficulties have now been overcome, and M. Goettsch (University of Puerto Rico) described how the lesion can be produced with extreme regularity if the mother is depleted of vitamin E during pregnancy and lactation, being given only just enough to prevent resorption of the fœtus. G. Klatskin (Yale University) reported that in cirrhosis in man there is evidence that the tissues are depleted of tocopherol.

Disturbance of metabolism of sulphur-containing substances was mentioned by several speakers. H. Popper (Chicago) described the lesions produced in rats by the anti-metabolite ethionine, and by bromobenzene, which acts as a drain on sulphur reserves because it is detoxicated by combination with cysteine. Neither of these poisons produce massive necrosis; the former causes fatty liver, the latter zonal degeneration. J. M. R. Beveridge (Queen's University, Kingston, Ontario) reported that thyroidectomy protects against dietary necrosis; this may be because it increases the number of available sulphydryl groups in the tissues. Finally, in experiments on enzyme activity R. E. Olson (University of Pittsburgh) showed that though—surprisingly—zymes are well preserved in the necrotic liver, there is decreased concentration of the sulphur-containing oenzyme A.

Obscure though the picture is, it is further complicated by Schwarz's discovery that there is a third protective substance, present in commercial casein and in some strains of yeast. This has provisionally been called 'factor 3.' Its identity has not yet been elucidated, although over 800 different fractions have been tested on some 10,000 rats. These figures illustrate the immense scale of the work that has to be done in the isolation and biological testing of a new protective factor.

Conclusion

The conference demonstrated the advantage of such n exchange between clinical and experimental workers. t should not be assumed that only the clinicians gained; or it seems clear that in this field medicine retains its rôle as a spur to the biological sciences.

In England Now

A Running Commentary by Peripatetic Correspondents

I do not set myself up as the discoverer of the ubiquity of the guilt feelings in the anxiety neuroses, but now I come to think of it I certainly did come upon it independently of its original discoverer.

It was this way. About thirty years ago I was in practice in a small village where I was the parish doctor. Like all parish doctors I was sorely troubled by the usual little clutch of neurotics who, entitled to free treatment, saw no reason for putting any bounds to their demands. Every day and all day the wearisome squad laid siege to my consulting-room. The chief of my tormentors was a long-faced spinster of forty, who for the wind in her stomach had drunk deep of every bottle on my shelves, to whose back I had applied every species of plaster, and even—my most powerful charm—on the nape of whose neck I had stuck the most avid and bloodthirsty of my leeches. All to no avail; I cured one pain only to arouse ten others in its place. At last when my bottles were dry, my leeches gorged, and my purse empty I turned upon her. With anger in my voice I broke in on the thousandth variation on her theme of aches and pains with: "What wickedness have you committed that the Lord should afflict you in this way?" And then I stopped. with qualms of conscience. Surely I had gone too far, and she would turn on me with the outraged innocence of a vestal virgin accused of a miscarriage. But no. she was silenced . . . for the first time in many years. Embarrassed and confused she gathered her things together, and mumbling something almost inaudible about being no worse than a lot of people she could name but wouldn't, she went away. And what is more she stayed away, avoiding me as one who had read her guilty secret and whom she had better not annoy.

Well there it is. With my little one-and-only discovery I shall pass with my betters into the limbo of the forgotten. I cannot even dream of my name figuring in a little italic footnote in some authoritative textbook of the future: "A similar observation was made independently twenty years later by Smithers of Great Squelching."

* * *

I was taking advantage of the premature spring to mow the lawn. My two nieces. Christine, aged six, and Gabrielle, aged four, were both working on their own vegetable patch. I heard a shout, and looked up to see Gabrielle running towards me holding her forehead from which trickled a thin stream of blood.

"Hallo, nipper, what's happened?"

"Christine hit me with her spade."

I strode over to Christine and said: "Christine, did you hit Gabrielle with your spade?"

She went on turning the earth and said "No."

"Christine, tell me the truth, did you hit Gabrielle with your spade?"

She picked up a worm and threw it away and, without turning round, said: "No."

By this time I was pretty hypertensive. "Christine," I thundered, "I will give you one more chance. DID YOU HIT GABRIELLE WITH YOUR SPADE?"

The tears were spurting out of her eyes as she turned the earth. "No. It was *her* spade."

* * *

The Hasheaters (*Homo sapiens* var. *caledoniæ*), who were oddly ignored by Dean Swift, live in the North of Scotland, and are distinguished by two principal characteristics; the habit, whence their name derives, of mixing soup, joint, and pudding together in a basin and eating the result with a large wooden spoon; and a propensity for reckless rock-climbing.

I first became aware of their existence on a shimmering summer's day last year; I was sunning myself in a safe corner in the Grampians, when the silence was disturbed by a rich, if untrained, baritone voice singing *When I'm cleaning windows.* I trained my glasses on the corrie whence the sound came, and saw a party of three climbers about half-way up an exposed buttress some 500 feet high. I had just noted that the leader was wearing a bright blue jersey, when to my horror he fell a matter the œsophagus and I did a gastrectomy below the ulcer, the only time I have used the device, the patient has not bled since, and is well two years later I have no use for total gastrectomy for a non-malignant lesion

London, W 1 HENEAGE OGILVIE

A DESIGN FOR FAMILY PRACTICE

SIR,—In my article of March 21 I had no intention of involving the College of General Practitioners in medical politics, with which as Dr Hunt (March 28) points out, it is not concerned

Four years' experience of good working conditions in general practice have shown me that the family practitioner is discouraged from making full use of such conditions because of the basic economic factors operating in the National Health Service In my view, this is the biggest obstacle to the realisation of the ideals of the new college Whether or not it is removed altogether is of course a matter for the General Medical Services Committee

Burley near Ringwood ROBERT HOWARD

MENTAL HEALTH RESEARCH FUND

SIR —The Mental Health Research Fund was founded in July, 1949, and last year you were good enough to draw attention to it in a leading article and by your report of the inaugural conference at Oxford[1] Many of your readers will have seen, in the *Times* of March 10, a letter making the fund known to the public and inviting contributions In launching this public campaign it seems appropriate to recall our purposes and hopes to the minds of doctors

That research in mental health is needed is abundantly clear from the high incidence of mental illness in the community and from the growing population of our mental hospitals Fortunately research methods are full of promise and yearly become more accurate and delicate We hope the fund will be able to offer grants to approved research projects, and wish to remind your readers that its outlook is catholic as we stated in the *Times*, it is not wedded to any particular approach to this many-sided subject The governing body is composed mainly of people who are already active in fields bearing on the mind, and the fund works in close touch with the National Association for Mental Health

If as we hope, there are those among your readers who would wish to give this fund their support, we are in a position to assure them that any contributions which they can secure for the fund would be used to good advantage We shall be glad to send further particulars of the fund to any doctors or laymen who may be interested

IAN T HENDERSON
Chairman Executive Committee
GEOFFREY VICKERS
Chairman Research Committee

D R MACCALMAN
W E LE GROS CLARK
DAVID HENDERSON
PRISCILLA NORMAN
DEREK RICHTER

Maurice Craig House
39 Queen Anne Street
London W 1

INFLUENCE OF LANGUAGE ON MEDICINE

SIR —Prof J Z Young (March 28) quotes the motto of the Royal Society (*nullius in verba*) and states that it seems to suggest that we ought to try "to escape from the persuasive effect of language on our observations and instruments" But the motto is an abbreviation of a line in which Horace describes himself as *nullius addictus iurare in verba magistri* (not bound over to swear allegiance to any master)

That "Don't be a slave to words" is good counsel no one will deny but here we have a far more important injunction don't be a slave to anyone's ideas even if he is "the best authority", ask what his evidence is

Nullius in verba is surely the finest motto a scientific society could have Can any of your readers say who adopted it for the Royal Society ?

London W 1 JOHN PRYNN

Public Health

The Salford Survey

THE survey of the population of Salford by mass radiography is the largest study of its kind yet undertaken in the United Kingdom The six mass-radiography units of the Manchester Regional Hospital Board are to operate in Salford for at least six months, with the object of examining as many as possible of those who live or work in the city The target is set at 100 000 volunteers, but it is hoped that this number will be greatly exceeded It is expected that a considerable number (perhaps up to 200) new cases of pulmonary tuberculosis as well as of other chest abnormalities of significance will be discovered In order that patients suffering from infective tuberculosis shall receive hospital treatment as quickly as possible, additional tuberculosis beds have been made available at the Ladywell Hospital Salford, and elsewhere

Apart from the removal of coats and jackets, undressing before examination has been dispensed with and open public sessions have been arranged at which anyone may attend without appointment For those unable to attend at the open sessions, appointments will be made for convenient days and times, including evenings Special arrangements have been made for the examination of school children All householders will receive a personal letter from Dr J L Burn the medical officer of health, inviting their cooperation and explaining the aims and the scope, and relevant details of the survey All the larger employers of labour in the city have been invited to participate and certain periods have been set aside for units to operate in industrial premises Details of the survey have been notified to all trade unions and the large majority have already promised their aid Other publicity will be given through posters pamphlets, bookmarks short advertising films, slides, and newspaper advertisements The British Broadcasting Corporation has promised to cover the survey in its news service, while religious leaders and all the secretaries of local organisations, such as the W V S the Boy Scouts organisations and old people's clubs have been invited to help

Units are housed in vans 27 ft long, weighing approximately 11 tons Five units are allotted to five main areas of the city, while the sixth which operates indoors on mains electricity supply, will be used for examining special groups—including patients referred by family doctors, expectant mothers, hospital staffs, and inmates of old people's homes and Darby and Joan clubs Besides the use of mass radiography, special tuberculin surveys will be made, particularly in children under 5 years of age A start has already been made in children's Homes and Corporation Nurseries

In a recent statistical survey it was found that of twenty large county boroughs in England and Wales Salford had the second highest death-rate from respiratory tuberculosis, and a random sample of at least 1% of the population will be studied in an endeavour to isolate the social, occupational, and epidemiological factors responsible for infection

Medical and administrative working parties have been set up The former, which deals with the medical, clinical and social approach to the problem, includes Dr Norman Kletz (chairman) Prof Fraser Brockington Prof Wilfrid Gaisford Prof Ronald E Lane Dr Burn and Miss Nancy Goodman with Dr F C S Bradbury, Dr William Lee Dr M Greenberg Dr J S B Mackay, Dr Ronald Walshaw Dr Randal Staller, and Dr J O Fegan

Examination of the general public will begin next Monday

Smallpox

A further 5 cases of smallpox have been confirmed in the outbreak in Lancashire and the West Riding, bringing the total to 21 by April 7 There have been 2 more deaths making 4 in all a 19 year old youth died on April 1 and a 44-year old Todmorden woman on April 3 on the skin adjacent to each side of the nose and on the nasolabial folds. The middle of the forehead and chin were involved to a lesser degree. This red phase, which was attended by intense burning sensations, continued for about 2 days and then subsided, being replaced by desquamation. By about the 7th day the active disturbance seemed to cease, but within a day or two the prodromal prickling would return and the cycle of events was repeated. The patient's mental state, especially during the prodromal and red stages, was one of extreme nervous irritability with alternating moods of depression in which her only wish was to withdraw. These psychological features may have been at least in part a response to the painful discomfort and the disfigurement, but this is not necessarily the complete explanation.

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[1] *Lancet* 1952 i 681

The patient was examined by several dermatologists who thought the condition might be a neurodermatitis. A variety of applications were suggested and tried but none proved beneficial. X-ray treatment was also given but this seemed to aggravate. She was also seen by a physician, who carried out a series of tests for allergy; but these revealed nothing definite. She was then referred for psychological investigation, but no association could be determined between "the disease" and any disturbing emotional events. The patient herself began to study the reactions to various articles of diet, with negative results except that the attacks seemed to be less severe, and even occasionally to abort, when she used bread made by a certain baker, which, in those days of war (1943–44), seemed to be definitely lighter in colour than the standard loaves of the times. In pursuit of this possible clue I wrote to my friend, the late Sir Jack Drummond, who caused inquiries to be made. He reported that there was no difference in the flour used in the lighter-coloured bread from that particular baker and the loaves made by others. I replied that this seemed odd, inasmuch as the colour of this bread was as distinct from the loaves of other bakers as the two shirts in the advertisement for 'Persil.' In any case this lighter-coloured bread soon after ceased to be obtainable and the dermatitis resumed its relentless course.

In 1945 the eruption, for some reason or other, began to subside; at any rate it was much less troublesome. But it returned abruptly in October, 1946, and the state of the patient again became desperately unhappy. Remembering the 1943 experience of the apparently whiter loaf, we decided to try the effect of excluding from the diet all products containing flour. The effect was immediate and dramatic. The exclusion began at a time when the cycle was just entering its red phase. This subsided at once, desquamation was minimal, and further eczematous manifestations ceased. From then on the patient used potatoes and home-made oatcakes in place of breadstuffs. From time to time an experimental addition of small quantities of bread was made to the diet but only minute amounts could be tolerated. I approached the Ministry of Food on behalf of the patient and provided them with an account of the occurrence. They generously secured for her, in return for the surrender of her bread coupons, a supply of imported white flour which differed (but in what chemical aspects I do not know) from the high-extraction flour in general use in Britain at the time. This supplement to her diet enabled the patient to maintain weight and keep the dermatitis in abeyance. If, however, at any time she was on holiday and partook of the usual breadstuffs the dermatitis reappeared. In the course of the following years she came to acquire a certain and increasing tolerance to limited amounts of breadstuffs, but even to this day great care has to be exercised.

Other points of interest are that during the illness the patient was found to be extremely susceptible to nicotinic acid. Also, after a second injection of penicillin a fortnight after a first, the skin responded by the not unusual german measles type of reaction, and at a later date a small plug of penicillin inserted into a socket after a tooth had been extracted produced an alarming dermatitis of the hands which looked like crocodile skin and were exceedingly swollen, stiff, and painful for several weeks. I wondered if the sensitisation to the allergen in flour had in some way facilitated an increased sensitivity to other allergens.

The point that impressed me most was the *dramatic* nature of the response. Seldom have I seen such a clear-cut instance of immediate "cause" followed by immediate "effect." Much, of course, remains to be understood. There is no information as to the frequency of such occurrences; no information about the "kind of person" who responds to flour in this way: no real understanding of the bodily mechanisms involved. All that can be said at this stage is that in respect of at least two cases of obscure and distressing eczema it has become a little clearer as to why they took ill when they did and recovered when they did. Yet because of the dramatic nature of the response, both to the provocation and its withdrawal, a vista of investigations opens out—as, for instance, into the various disorders which have definitely or seemingly increased during the last twenty or thirty years. For example, if one took a series of patients with active duodenal ulcer and treated every second case with complete withdrawal of modern flour under its various guises, one would soon secure an answer to what part, if any, was likely to be played in its ætiology by at least one of our common foodstuffs.

Glasgow S.1. J. L. HALLIDAY.

VISITS TO CHILDREN IN HOSPITAL

SIR,—Professor Moir, whose remarks at a meeting of the Leeds Regional Hospital Board were reported on March 28 (p. 656), is a busy consulting surgeon who probably has not the time to observe children in hospitals where daily visiting is allowed and to compare them with children whose parents are excluded from the ward. The evidence of those who have had the time to make such observations shows that his belief that children forget their parents if they are left alone for a day or two lacks any basis in fact.

It is doubtful if the professors of child health in the Universities of London, Sheffield, and Newcastle, to name but a few, are swayed by "sloppy sentiment" in their condemnation of the old practice of depriving sick children of parental love. Let Professor Moir read the evidence in Dr. John Bowlby's *Maternal Care and Mental Health* [1] or see the Tavistock Clinic's film, *A Two Year Old goes to Hospital*,[2] and he will soon realise that sound sense and realism underlie the humane changes that many pædiatricians are eager to bring about.

Newcastle upon Tyne J. G. NEVILLE.

VITAMIN E AND INTERMITTENT CLAUDICATION

SIR,—Dr. Loxton (March 28) criticises us for trying to prove a null hypothesis (that vitamin E has no more effect on intermittent claudication than an inert substance); and he asserts that this null hypothesis has, in fact, already been disproved by other workers. We cannot accept as *disproof* the results of trials, however extensive, which have not been adequately controlled, and we have already emphasised that previously reported results fall into this category. Had the efficacy of vitamin E been previously established by an adequately controlled series, our trial would have been unnecessary.

We completely agree, of course, that the null hypothesis cannot be *proved*, and we are sorry if the condensation required in the summary of our paper, and in our subsequent letter, has led Dr. Loxton to think otherwise. Indeed, we were careful to state in our article (Feb. 21, p. 369):

> "The rather small numbers of patients available in this trial may have led to moderate effects of vitamin-E treatment not being detected owing to the considerable variability between patients."

And we proceeded, in table VIII, to give confidence limits for the mean effect of vitamin-E treatment in comparison with the controls. We found, for example, that it is most unlikely that vitamin E increases the average exercise tolerance after the treatment period by as much as 2·3 circuits, or about 12%, since the mean exercise tolerance is about 19 circuits.

Although a null hypothesis can never be *proved*, it must often be right to act as though it were true when

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1. Bowlby, J. Maternal Care and Mental Health. W.H.O. Monograph Series, no. 2. Geneva, 1951; see *Lancet*, 1951 i, 1165.
2. See *Lancet*, 1952, ii, 1122.

might mutilate the National Health Service? Everybody knows that he is the avowed enemy of the service, as he has publicly declared, and in his own hands it has already received many grievous blows The best service he could render it would be to resign

Mr **MACLEOD** It is true that this matter has been considered at the highest levels of Government, but we consider—and it is possible to disagree on this—that it is essentially a departmental matter and therefore, that this announcement should be made by myself and not by the Chancellor of the Exchequer as part of the Budget speech This is a long-term problem which in the view of most people remains essentially unsolved

When the right hon gentleman suggests that we should remit this question to the Central Health Services Council—or that we should take account of their views on this kind of matter—I entirely disagree It is because the council are representative of wide interests within the health service that I do not consider them to be the proper body for an inquiry of this nature In my view, what is needed is an entirely independent inquiry It should not in any sense be a political one nor one which is linked in any way, through the membership of the committee, to any of the professions concerned in the health service

With regard to the accusations that the right hon gentleman was good enough to end his speech with in the first place I should not have agreed to a committee—nor would Mr Guillebaud have accepted the chairmanship of a committee—which was designed to mutilate the National Health Service

Mr **BEVAN** May I call the Minister's attention to the first error that he made in the course of his statement? I never suggested that these terms of reference should be sent to the Central Health Services Council I suggested that they might be asked for their advice about any organisational modifications Is an expenditure equal to £100 million in the National Budget, and which concerns the welfare of all the citizens of Great Britain, a fit subject to be remitted to a committee of inquiry? If so, why does not the Chancellor of the Exchequer remit to a committee of inquiry the question whether taxes should be lower or higher Why does not the Chancellor of the Exchequer hand his Budget to a committee of inquiry?

Mr **RICHARD FORT** Many inside this House and outside will welcome the statement and the opportunity to have a large amount of information about costs and expenditure brought together in a form in which we can really appreciate its value In putting this matter before the committee, will he ask their opinion about the effect of making block grants to the hospitals, which would give regional boards greater independence?

Mr **MACLEOD** Block grants come within the terms of reference That is a subject on which people hold strong views and on which there may conceivably be considerable saving I have no doubt that the points of view for and against block grants will be put to the committee

Mr **ARTHUR WOODBURN** May I ask the Minister whether he is aware that a reading of the terms of reference creates the impression that they are tendentious and that they are suggesting to the committee what the committee should report? Since an economist is being put in charge of the committee, is it its purpose to find out as the Organisation and Methods Department of the Treasury might find out, whether the existing service can be more economically worked? Is the Minister aware that there is a Select Committee of this House which inquires into these matters and which may have been examining this question already? Has he considered that this may be a reflection upon them? If this committee is to give a balanced report to the House will it be called upon to find out what was the cost of preventable disease in this country before the health service was introduced? If my memory is correct, before the war the Minister's Department estimated it at £550 million a year May I ask him whether he will broaden the terms of reference so that if the committee is to report on the economics of the health service it will report on them comprehensively as they affect the whole country?

Mr **MACLEOD** I do not agree with the right hon gentleman in his reading of the terms of reference This is a general inquiry into the function, structure, a[nd] policy of the service and not an economy-cuts committee It is true that the Select Committee have done admirable work in this field but that touches only the fringe of the very much bigger problem Many countries have made experiments in social welfare and we ourselves have had this splendid experiment going on now for five years But not everybody is satisfied that we and other countries have found the ideal way of running the service and the ideal way of financing it We can honestly differ about this, but in my view a committee not tied to any profession in the health service or to any political party is the best way in which we can seek answers to these difficult questions This is a very long-term business It will take many months and perhaps a year

Later in an adjournment debate on a personal case in which it was alleged that N H S hospital authorities offered a patient insufficient help on a long railway journey, Mr. **ARTHUR BLENKINSOP** asked whether there could be any connection between a case of this kind and the drive for the general reduction of expenditure in the National Health Service There must be a good deal of misunderstanding about the cost of our health service, he continued It seemed to be evident that the Minister was accepting without question as a fact that it was costing far more than was necessary, and that great economies could be carried out without danger to the service and to the treatment provided for patients within it He was anxious as to whether this drive for economy might not cause countless more cases of this kind He could not emphasise too strongly that, far from the over-all expenditure on the health service being too great we must examine the point as to whether or not extra additional expenditure was urgently required for the benefit of the community He agreed that economies could still be made in the health service but there were fields in which large sums of new expenditure were required Over these last few years owing to the imposition of an over-all ceiling upon health expenditure, at the same time as costs had been rising the services given within the service had had to fall As this became more severe, especially this year, the pressure upon every hospital authority to deal with rather less than its customary good will with individual cases was bound to grow Because the costs of the service were rising, including food costs, the hospitals like other sections of the service were having to face all the time the need to cut down what they could provide and this at a time when in our interests as a community we should expand many of the services that richly needed expansion What was more, there was a lot of loose talk as though the total sums that we spent upon our health service were in some way astronomical and quite beyond our ability to pay Was that really true? No one had attempted to examine our total costs today as against the total costs of health care in the days before the health service was introduced Certainly, we spent a much smaller percentage of our national income on health care than was done in America In his view hospitals were not being given sufficient funds to enable them to maintain properly the fabric of their buildings As the years went by and if not enough money was put into the work, we would be faced with enormous costs There were great jobs of work that needed to be done that in the interests of economy ought to be carried out If the present procedure was carried on, if we maintained this artificial ceiling that had been running for some four years he ended we were in effect denying to the health service the finances that it must have if it was to devel[op] properly

QUESTION TIME

Drugs, Dressings, and Appliances for Private Patients

Sir **EDWARD KEELING** asked the Minister of Health how much it would cost the taxpayer to give drugs dressings and appliances to private doctors' patients after deducting the 1s prescription charge, but without allowing for the transfer of many National Health Service patients to private doctors which would follow such gift —Miss M P **HORSBRUGH** replied If the net cost per person were the same as for persons under the National Health Service (which assumes the private doctors would be bound to observe the same conditions as National Health Service doctors) the total cost to the taxpayer might be nearly £1½ million per annum secure value for money. The introduction of unnecessary high-priced polypharmaceutical mixtures encourages waste of public money, and must bring forward the day when practitioners are allowed to prescribe only from a standard formulary and manufacturers will have to secure a licence to use a proprietary name for their preparations. The introduction of such mixtures is against the best interests of the medical profession and of the pharmaceutical industry.

Central Middlesex Hospital,
London, N.W.10. GEORGE DISCOMBE.

POLIOMYELITIS

SIR,—I was surprised to see that Dr. Ritchie Russell and several of your correspondents state that a pillow or a board at the foot end of the bed are sufficient to prevent drop-foot. This may look satisfactory enough when a patient has been neatly arranged for an official ward round; at all other times we find that the feet are simply not up against the support. Unless a child is very severely paralysed it will move about in bed a little, and its position is in any case frequently disturbed for bed-making, toilet, &c. We find that club-foot shoes are necessary to prevent equinus deformity.

This brings me to another point. We have several children in this hospital in whom muscle spasm has persisted for more than a year after their acute illness; at least this is how it appears to us. In most cases the calf muscles are affected but in one patient it is the biceps. The affected muscles can be stretched to their full extent by firm, sustained pressure, so we are not dealing with a true contracture. If left unsplinted the limb takes up a position of pronounced deformity. The stretching causes a good deal of pain, and this is worse when the patient fails to coöperate. If he can be taught to relax there is less difficulty in stretching the muscle, and once fully stretched it seems to become painless. In some of these cases the opponents of the painful muscles are completely paralysed, in others they have a fair power of contraction; the exact strength is difficult to assess under the circumstances.

I would be most interested to hear views on the true nature of this condition and its prevention. Should passive stretching be performed more vigorously and earlier? At present we do little in the first three weeks; after that patients are treated once daily. I might add that the patients thus affected are not necessarily those that have been rigidly splinted. In fact, as far as we can see, rather the reverse is the case, and the patient with the spastic biceps was certainly never splinted at all.

King Edward VII
Orthopædic Hospital, Sheffield. E. G. HERZOG.

POLIOMYELITIS IN DENMARK

SIR,—Although Dr. Anderson and his colleagues (March 28) object vigorously to my letter of March 14, it is, I think, obvious that both they and I are advocating the same need to enlist assistance to maintain a free airway in patients suffering from acute poliomyelitis with bulbar and/or respiratory paralysis.

They favour strongly Dr. Lassen's method of tracheotomy with positive-pressure breathing, whereas I would urge that this is not the best way to keep these patients alive. In the 50 paralytic patients dealt with from this department at Stoke Mandeville Hospital during 1952, all survived (except one infant aged 2 weeks) without any having a tracheotomy; and at least 6 of these cases would have qualified for the Copenhagen treatment.

We were probably lucky, but we also had a most careful nursing drill for maintaining the airways clear. The vital importance of frequent changes of posture (every 2 hours) was emphasised in this recent experience by the fact that, though none of the patients developed atelectasis while under special nursing care, 2 with severe intercostal paralysis developed atelectasis when this care was relaxed 3–4 weeks after the onset of the illness. The longest period of complete paralysis of swallowing was 2 weeks. Removal of secretions with a sucker is a traumatic procedure, and we were glad to find that the sucker is rarely required when postural drainage is efficiently maintained. In this connection Dr. Anderson and his colleagues scoff at my emphasis on the prone posture, but in this they betray a common failure to understand that postural drainage of the lungs can only be effective for anatomical reasons if the prone posture is used freely. Tank respirators must be so designed that the patient can lie prone; and both of the latest respirators, now manufactured respectively by Messrs. Siebe, Gorman Ltd. and Messrs. Stanley Cox Ltd., fulfil this requirement satisfactorily. The cuirass respirator fails in this respect, and in any case does not give sufficient tidal air for acute cases.

It is gratifying that the Copenhagen experience has made it so very apparent that saving life in the acute stage depends on preventing atelectasis, but the uncritical advocacy of the Danish emergency measures as the method of choice is surely somewhat unwise. Their mortality-rate for cases of bulbar and/or respiratory paralysis (about 40%) can, I believe, be improved upon by other well-tried and safer methods.

Department of Neurology,
Radcliffe Infirmary, Oxford. W. RITCHIE RUSSELL.

OSTEOPATHY

SIR,—In the discussion of this subject by correspondents, one vital point seems to have been overlooked. The positioning of the vertebræ depends primarily on muscle action. Muscle action, in the absence of an obvious lesion, is primarily a behavioural manifestation which involves the whole organism. No amount of "re-positioning of the vertebræ" either by gentle or by forcible manipulation will get around the fact that when a person is accustomed to using his body in a certain way, he will return to this way after the manipulation. It is no help to give specific exercises to "maintain the osteopathic correction": it is the total behaviour pattern which usually needs re-educating, not the individual muscles.[1]

This is not to deny that manipulation may on occasions dramatically remove symptoms of pressure; but a predisposition to set up a faulty vertebral alignment will remain until the total behaviour pattern has been re-educated.

London, S.W.7. WILFRED BARLOW.

SIR,—Spinal-nerve-root compression, it seems, may be due to a displaced fragment of the annulus of an intervertebral disc (Dr. Cyriax, March 21) or to narrowing of the intervertebral distance, with sometimes pressure on the radix from the displaced disc, or from its extruded nucleus pulposus (Dr. Turner, March 28). For the practical purpose of treating the condition, it is unimportant which explanation one accepts, for the result does not depend on a particular pathological theory.

The Cyriax manœuvres can be successful: Dr. Turner admits this, but insists with understandable prejudice that osteopathic methods are better. He who advises manipulative treatment for this condition, however, has often to choose between an osteopath (who may or may not have the same training and use the same method as Dr. Turner, who may in fact have received his diploma from a correspondence school, or who may have had no training at all) and a physiotherapist of the St. Thomas's school, all of whom use the Cyriax technique. The latter will often be the safer choice.

It seems pointless to argue the merits of the rival schools: both methods have their successes, and the will consider, among other things, the effect of noise in relation to human efficiency The harmful effects of noise on the individual can be reduced to some extent by the wearing of protective ear coverings and by eliminating injurious noise at its source by improved designs of machines and their mountings and the sound insulation of walls and ceilings, but the subject has been found to bristle with practical difficulties

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[1] Barlow, W. *Ann. phys. Med.* 1952, 1, 77.

Dr STROSS Is the Minister aware that protective ear coverings appear to be very much in their infancy and that there is not a satisfactory type available? Could he tell me if scientific research is to be conducted into finding the right type of protective ear covering for these men? Mr WATKINSON Yes, that is so

Obituary

CECIL HOLMES LYON

O B E, F C I I

THE death of Mr C H Lyon, clerk of the London Executive Council on March 22 while still in office, brings a sense of loss to very many London doctors He joined the service of the London Insurance Committee in 1913, becoming its registrar at the end of the first world war In 1932 he was promoted to be deputy clerk, and he succeeded Mr Gilbert as clerk of the infant London Executive Council in 1919 So highly were his services valued that when his retiring age approached, his council unanimously asked him to continue his work

J A S writes "Lyon's efficiency and quiet friendliness were always at the disposal of individuals as well as of the professional bodies whose work was linked with his council At the meetings of the London Medical and Dental Committees and their subcommittees his interventions were rare but his advice, leavened always with a quiet humour, was always welcome and often sought The same unobtrusive friendliness marked his dealings with doctors who sought his guidance on the problems of practice in the National Health Service His warm humanity was fortified by his Masonic activities and by his interest in Hayes Parish Church, where he was for many years organist and choirmaster"

Appointments

GRAHAM A N M B Durh D P M physician superintendent St Crispin Hospital near Northampton

HUGHES E W M D Lond M R C P resident physician Tehidy Chest Hospital, Camborne Cornwall

[illegible] J M B A Camb M B Edin, F R C S E senior surgical registrar thoracic unit Hawkmoor Chest Hospital Bovey Tracey, Devon

Antrim County Health Committee

CASTLES WINIFRED M B Belf D P H M O and M O H Larne borough Carrickfergus borough, Whitehead urban and Larne rural districts

SHERRARD ELIZABETH M B Belf D P H D OBST asst county M O

[illegible] I C M D Belf D P H M O and M O H, Ballymena borough and rural district

Birmingham Regional Hospital Board

EGAN THOMAS M D N U I, D P M consultant psychiatrist and deputy medical superintendent St George's Hospital Stafford

HEFFERNAN, D J L R C P I D L O consultant E N T surgeon Birmingham (Dudley Road) and Lichfield Sutton Coldfield and Tamworth groups of hospitals

WHITEHEAD J P M R C S asst pathologist (S H M O) South Warwickshire group of hospitals

Manchester Regional Hospital Board

[illegible] C F M B N U I D A asst anaesthetist, Preston and Chorley hospital centre

DAVIES C ST J M R C S D M R D asst radiologist Bolton and district centre

[illegible] I M M B Manc D A consultant anaesthetist South Manchester hospital centre

JONES R G G M B Lond D A consultant anaesthetist, South Manchester hospital centre

North East Metropolitan Regional Hospital Board

[illegible] HELEN M R C S part time psychiatrist (consultant), West Essex Child Guidance Clinic Walthamstow

[illegible] M R C S D M R D part time radiologist (consultant) Harold Wood Hospital and Goodmayes Hospital

[illegible] I H N F R C S part time orthopaedic surgeon (consultant) Mildmay Mission and Queen Elizabeth Hospital for Children

[illegible] M R C S M R C O G part time obstetrician and gynaecologist (consultant) St Andrew's Hospital, Bow Hospital and Poplar Hospital

Notes and News

ASSOCIATION OF CLINICAL BIOCHEMISTS

THE inaugural meeting of the Association of Clinical Biochemists was held at the Postgraduate Medical School of London on March 28 The formation of the association springs from a meeting in May, 1952, at which representatives of societies of clinical biochemists in Glasgow, the Midlands and north western and southern England set up an interim committee under the chairmanship of Prof F J [illegible] The association will be both scientific and professional in scope On the professional side it will concern itself with the status of qualified biochemists working in hospital and allied laboratories who have not hitherto been specifically provided for by professional associations In the scientific sphere it will work in the rapidly expanding field of clinical biochemistry, where pathology, clinical medicine, and biochemistry overlap, and which is not systematically covered by any of these branches of science The association will hold regional and national meetings at which papers will be read and demonstrations given Joint meetings with other societies will be arranged both locally and nationally The association hopes also to cooperate with the member societies of the International Association of Clinical Biochemists in a scheme for standardising and periodically checking analytical methods used in hospital laboratories

The inaugural meeting accepted a set of rules submitted by the interim committee, who are to hold elections not later than Aug 31 The association will be directed by a president and a council composed of chairman, secretary, treasurer and two nationally and five regionally elected members The interim committee is acting as a provisional council with Dr A L Tarnoky (Royal Berkshire Hospital, Reading) as secretary

The following papers were read at the inaugural meeting E B Love (Preston), laboratory control of anticoagulant therapy, I D P Wootton (London), quartz spectrophotometer in clinical chemistry; H Bickel, J Gerrard, and E [illegible] Hickmans (Birmingham) influence of phenylalanine intake on phenylpyruvic oligophrenia, and A L Latner (Newcastle upon Tyne), quantitative paper strip electrophoresis of serum proteins

HEALTH REGULATIONS FOR WORKERS

THE International Labour Organisation has reported a division of opinion among governments in regard to a set of proposed international regulations to safeguard the health of workers in their places of employment The proposed regulations constitute one of the eight items on the agenda of the I L O 's general conference that opens at Geneva on June [illegible]

The question was first discussed by the general conference last year,[1] when it was agreed that this year's conference should pursue it further on the basis of a report to be prepared by the I L O after consultations with governments It was also decided that the 1953 conference should determine whether the proposed regulations should take the form of (1) a recommendation or (2) one or more conventions supplemented by a recommendation

The I L O report, lately published, proposes two alternative sets of texts for consideration by the conference One of these is a proposed recommendation, the other comprises two proposed conventions supplemented by a recommendation One of these conventions would regulate the medical examination of workers and the other would require the notification of cases of occupational disease The proposed recommendation deals with the technical measures for the control of health hazards, medical examinations, and the notification of occupational diseases The proposed supplementary recommendation which deals with the same subjects, is intended to serve as a guide to governments in the event of the conference deciding on the adoption of conventions supplemented by a recommendation The suggested provisions for medical examinations are restricted to workers in occupations involving special risks to health The notification of occupational disease would, in principle, apply to cases and suspected cases, and the competent authority in each country would be left to draw up a list of notifiable diseases

The report discloses that 24 governments have no general comment to make and that they consider the proposed texts suitable for discussion by the conference Nine governments favour the adoption of a recommendation alone T secure value for money. The introduction of unnecessary high-priced polypharmaceutical mixtures encourages waste of public money, and must bring forward the day when practitioners are allowed to prescribe only from a standard formulary and manufacturers will have to secure a licence to use a proprietary name for their preparations. The introduction of such mixtures is against the best interests of the medical profession and of the pharmaceutical industry.

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[1] See *Lancet*, 1952, ii, [illegible]

Central Middlesex Hospital,
London, N.W.10. GEORGE DISCOMBE.

POLIOMYELITIS

SIR,—I was surprised to see that Dr. Ritchie Russell and several of your correspondents state that a pillow or a board at the foot end of the bed are sufficient to prevent drop-foot. This may look satisfactory enough when a patient has been neatly arranged for an official ward round; at all other times we find that the feet are simply not up against the support. Unless a child is very severely paralysed it will move about in bed a little, and its position is in any case frequently disturbed for bed-making, toilet, &c. We find that club-foot shoes are necessary to prevent equinus deformity.

This brings me to another point. We have several children in this hospital in whom muscle spasm has persisted for more than a year after their acute illness; at least this is how it appears to us. In most cases the calf muscles are affected but in one patient it is the biceps. The affected muscles can be stretched to their full extent by firm, sustained pressure, so we are not dealing with a true contracture. If left unsplinted the limb takes up a position of pronounced deformity. The stretching causes a good deal of pain, and this is worse when the patient fails to coöperate. If he can be taught to relax there is less difficulty in stretching the muscle, and once fully stretched it seems to become painless. In some of these cases the opponents of the painful muscles are completely paralysed, in others they have a fair power of contraction; the exact strength is difficult to assess under the circumstances.

I would be most interested to hear views on the true nature of this condition and its prevention. Should passive stretching be performed more vigorously and earlier? At present we do little in the first three weeks; after that patients are treated once daily. I might add that the patients thus affected are not necessarily those that have been rigidly splinted. In fact, as far as we can see, rather the reverse is the case, and the patient with the spastic biceps was certainly never splinted at all.

King Edward VII
Orthopædic Hospital, Sheffield. E. G. HERZOG.

POLIOMYELITIS IN DENMARK

SIR,—Although Dr. Anderson and his colleagues (March 28) object vigorously to my letter of March 14, it is, I think, obvious that both they and I are advocating the same need to enlist assistance to maintain a free airway in patients suffering from acute poliomyelitis with bulbar and/or respiratory paralysis.

They favour strongly Dr. Lassen's method of tracheotomy with positive-pressure breathing, whereas I would urge that this is not the best way to keep these patients alive. In the 50 paralytic patients dealt with from this department at Stoke Mandeville Hospital during 1952, all survived (except one infant aged 2 weeks) without any having a tracheotomy; and at least 6 of these cases would have qualified for the Copenhagen treatment.

We were probably lucky, but we also had a most careful nursing drill for maintaining the airways clear. The vital importance of frequent changes of posture (every 2 hours) was emphasised in this recent experience by the fact that, though none of the patients developed atelectasis while under special nursing care, 2 with severe intercostal paralysis developed atelectasis when this care was relaxed 3–4 weeks after the onset of the illness. The longest period of complete paralysis of swallowing was 2 weeks. Removal of secretions with a sucker is a traumatic procedure, and we were glad to find that the sucker is rarely required when postural drainage is efficiently maintained. In this connection Dr. Anderson and his colleagues scoff at my emphasis on the prone posture, but in this they betray a common failure to understand that postural drainage of the lungs can only be effective for anatomical reasons if the prone posture is used freely. Tank respirators must be so designed that the patient can lie prone; and both of the latest respirators, now manufactured respectively by Messrs. Siebe, Gorman Ltd. and Messrs. Stanley Cox Ltd., fulfil this requirement satisfactorily. The cuirass respirator fails in this respect, and in any case does not give sufficient tidal air for acute cases.

It is gratifying that the Copenhagen experience has made it so very apparent that saving life in the acute stage depends on preventing atelectasis, but the uncritical advocacy of the Danish emergency measures as the method of choice is surely somewhat unwise. Their mortality-rate for cases of bulbar and/or respiratory paralysis (about 40%) can, I believe, be improved upon by other well-tried and safer methods.

Department of Neurology,
Radcliffe Infirmary, Oxford. W. RITCHIE RUSSELL.

OSTEOPATHY

SIR,—In the discussion of this subject by correspondents, one vital point seems to have been overlooked. The positioning of the vertebræ depends primarily on muscle action. Muscle action, in the absence of an obvious lesion, is primarily a behavioural manifestation which involves the whole organism. No amount of "re-positioning of the vertebræ" either by gentle or by forcible manipulation will get around the fact that when a person is accustomed to using his body in a certain way, he will return to this way after the manipulation. It is no help to give specific exercises to "maintain the osteopathic correction": it is the total behaviour pattern which usually needs re-educating, not the individual muscles.[1]

This is not to deny that manipulation may on occasions dramatically remove symptoms of pressure: but a predisposition to set up a faulty vertebral alignment will remain until the total behaviour pattern has been re-educated.

London, S.W.7. WILFRED BARLOW.

SIR,—Spinal-nerve-root compression, it seems, may be due to a displaced fragment of the annulus of an intervertebral disc (Dr. Cyriax, March 21) or to narrowing of the intervertebral distance, with sometimes pressure on the radix from the displaced disc, or from its extruded nucleus pulposus (Dr. Turner, March 28). For the practical purpose of treating the condition, it is unimportant which explanation one accepts, for the result does not depend on a particular pathological theory.

The Cyriax manœuvres can be successful: Dr. Turner admits this, but insists with understandable prejudice that osteopathic methods are better. He who advises manipulative treatment for this condition, however, has often to choose between an osteopath (who may or may not have the same training and use the same method as Dr. Turner, who may in fact have received his diploma from a correspondence school, or who may have had no training at all) and a physiotherapist of the St. Thomas's school, all of whom use the Cyriax technique. The latter will often be the safer choice.

It seems pointless to argue the merits of the rival schools: both methods have their successes, and the

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1. Barlow, W. *Ann. phys. Med.* 1952, 1, 77.

Nursing Fellowship

The University of Edinburgh has appointed Miss G B Carter, B SC, S C M, S R N, to the Boots Research Fellowship in nursing, tenable in the department of social medicine

Dental Service

On March 26 the Minister of Health, the Minister of Education, and the Under Secretary of State for Scotland received a deputation from the British Dental Association, the purpose of which was to discuss the difficulties of the school dental service.

Naval Medical Compassionate Fund

A meeting of the subscribers will be held at 3 P M on Monday, May 4, at the Medical Department of the Navy, Queen Anne's Mansions, St James's Park, London, S W 1, to elect six directors of this fund

Exhibition of Medical Photography

An exhibition entitled 100 Years of Medical Photography is to be held at the Royal Photographic Society, 16, Princes Gate, London, S W 7, from April 7 to 30 (Mondays to Fridays 9 30 A M to 5 30 P M, Saturdays 9 30 A M to 5 P M)

Medical Award

Dr Dorothy Meiklejohn has been appointed M B E *in* recognition of her bravery when Mau Mau terrorists attacked her and her husband in Kenya last November Her husband later died from his injuries

Mental After Care Association

The annual meeting of this association will be held at the apartments of the Royal Society, Burlington House, Piccadilly, London, W 1, on Friday, April 17, at 3 P M when the speakers will include Dr Henry Yellowlees, chairman of the association

W H O Conference on Health Education

Between April 10 and 18 the World Health Organisation is holding in London a regional conference on health education, which is being attended by experts from the United Kingdom and eighteen countries of Western Europe The joint chairmen are Prof J M Mackintosh and Dr Aujaleu (France)

Laboratory Animals Bureau Congress

The sixth Laboratory Animals Bureau Congress, held at the Royal Veterinary College London on March 27 and 28, was attended by some 250 technicians The congress was opened by Sir Harold Himsworth secretary of the Medical Research Council The proceedings will be published in the *Journal of the Animal Technicians Association*

Conference on the Family

The second British National Conference on Social Work, organised by the National Council of Social Service, is to have as its theme The Family The meetings, which will start at 9 30 A M on Thursday, April 16, and continue for three days, are to be held at Bedford College for Women, Regent's Park, London, N W 1 Medical speakers will include Dr John Bowlby and Dr Rene Sand (Belgium)

Anniversary of Harvey's Birth

A commemoration of the 375th anniversary of Harvey's birth held in his native town of Folkestone on April 1 (*Times*, April 2, p 5) was attended by the Mayor of Folkestone and Dr T Hare president of the Harveian Association The Rev J V Hooper, Vicar of Hempstead where Harvey is buried, announced that last year's ceremony had brought such public support to the fund of his church that the Harvey tomb and chapel were now almost restored

CORRIGENDUM *Rothschild Hadassah University Hospital, Jerusalem*—In our advertisement columns (March 28, p 35) applications were invited for the posts of head of the E N T department and head of the ophthalmological department at this hospital The salary for a full time appointment in each case is I£270 (pounds Israeli) per month, plus family allowance A corrected notice appears in this issue

EMERGENCY BED SERVICE.—In the week ended last Monday applications for general acute cases numbered 1043 The proportion admitted was 91 2%

Dr C J Austin is shortly to retire from the post of medical superintendent of the Fiji Leprosy Hospital at Makogai which he has held for nearly twenty two years

Diary of the Week

APRIL 12 TO 18

Monday, 13th

ROYAL EYE HOSPITAL, St George's Circus Southwark S E 1
5 15 P M Dr T H Whittington Astigmatism and its T-
ment Factors Affecting Binocular Vision
MEDICAL SOCIETY OF LONDON 11, Chandos Street W 1
8 30 P M Dr Kenneth Harris Dr Samuel Oram E
Manifestations of Coronary Disease

Tuesday, 14th

ROYAL COLLEGE OF PHYSICIANS
5 P M Dr L A Carmichael Hemiplegia of Early Onset
Results of Hemispherectomy (First of two Lum
lectures)
ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
8 P M *Section of Psychiatry* Dr Denis Leigh Psychiatr
General Practice

Wednesday, 15th

ROYAL SOCIETY OF MEDICINE
8 15 P M *Section of General Practice* Dr Marion Ray
Mr Alan Brews Vaginal Discharge
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE 28 Portl
Place W 1
3 30 P M Dr B L Schlesinger Tuberculosis in Childhood
INSTITUTE OF UROLOGY St Paul's Hospital Endell Street W C
5 P M Dr E G B Calvert Surgery and the Diabetic

Thursday, 16th

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee) Prof W C
Nixon Physiological and Clinical Aspects of Ute
Action
ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S W 1
5 P M Dr Carmichael Hemiplegia of Early Onset and Res
of Hemispherectomy (Second of two Lumleian lectur
ROYAL EYE HOSPITAL
5 30 P M Miss J M Dollar Problem of Iridocyclitis and
Investigation
ST GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Cor
S W 1
5 P M Dr J Hamilton Paterson Neurological Demonstrati
BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street, W 1
8 P M Dr A E Jones Clinical Aspects of Carcinogenesis Dr
Glücksmann Histological Aspects of Carcinogenesis
Histogenesis of Epidermal Tumours Induced by Carcino
genic Hydrocarbons and by Beta Rays
LONDON JEWISH HOSPITAL MEDICAL SOCIETY
8 30 P M (11 Chandos Street W 1) Dr Michael Krem
Modern Views on Epilepsy and its Treatment

Friday, 17th

FACULTY OF RADIOLOGISTS 45 Lincoln's Inn Fields W C 2
4 P M Prof R J V Pulvertaft Study of Radiosensitivity i
Vitro Dr Edith Paterson Factors Influencing Recov
After Whole Body Radiation Dr W M Court Brown
Aspects of Water and Electrolyte Metabolism in Radia
Sickness
ROYAL SOCIETY OF MEDICINE
9 A M (Queen Elizabeth Hospital, Birmingham, 15) Sect
of Surgery
4 30 P M *Section of Epidemiology and Preventive Med*
Dr H J Trenchard Dr R Grenville Mathers C
of Tuberculosis—Preventive Measures in Chest Cl
Dr J C N Westwood Psittacosis—Recent Vir and
Epidemiological Observations
8 15 P M *Section of Radiology* Dr Constance Wood Its
Decade and Next—an Appraisal (Presidential a
ROYAL EYE HOSPITAL
4 30 P M Mr A J Cameron Problem of Retinitis Pigmen
BRITISH ASSOCIATION OF PHYSICAL MEDICINE
10 30 A M (University College Hospital Medical School W C 1)
Start of two day annual meeting
BRITISH INSTITUTE OF RADIOLOGY
6 30 P M Prof J Rotblat D SC Study of Distributi of
Thorotrast in Body by Autoradiography
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION
8 30 P M (Royal Free Hospital School of Medicine 8 Hunter
Street, W C 1) Mr C E Shattock Lumps in Breast
MANCHESTER MEDICAL SOCIETY
8 P M (University of Manchester) *Section of Anæsthetics*
Dr A J Gray Man's Inventions Dr M Saunders
Milestone in Relaxation?

Births, Marriages, and Deaths

BIRTHS

BRITTAIN—On March 21, at the Christopher Nursing H
Wigan, Lancs to Dr Ina Brittain (formerly Eakin) wife
Dr George Brittain—a daughter

MARRIAGES

BICKFORD—GODFREY—On April -, at Caxton Hall
Bickford, lieut-colonel R A M C to Maud Godfrey

the cause. This is the reason for the failures of surgical treatment—not bad surgery, not bad luck, but failure to remove the cause. The straightened toe is immediately deformed again when the patient wears shoes.

With the patient standing upright with the feet close together, the normal, or restored to normal, feet make contact with each other throughout their length. There is no angle or gap between the big toes. Only shoes that have a straight inner border and no gap between the inner side of the toes can therefore accommodate the feet in this shape (fig. 2).

Which is the most effective operation for advanced hallux valgus I am not competent to say. I suggest, however, that the best method will only be effective if the patient wears correctly designed footwear after the operation.

Prevention by Correct Footwear

I do not myself wear correctly designed shoes, for I do not know where I can buy them, and I cannot afford to have them specially made. Some children's shoes are correctly designed but most are not.

Through my Member of Parliament, I have asked the Minister of Health to create a Seal of Approval which manufacturers under licence could emboss on their footwear to show that it is correctly designed—the first requirement of design being that the footwear must accommodate the straight hallux. The Minister seems to favour the idea of a seal but he is unwilling or unable to do anything about it himself. In my view it is the duty of a Minister of Health to take immediate action to reduce the crippling prevalence of hallux valgus.

The first requirement is official medical approval of a correct design; and this would form the basis of whatever further action is necessary. Surely the medical profession is prepared to tell the shoe manufacturers what are the medical requirements for satisfactory footwear? Only when this has been clearly stated can we expect manufacturers to comply with these standards; and upon their action successful treatment and prevention depend.

Neither apathy nor opposition should delay action, for only when we have revolutionised the design of footwear can we confidently recommend an operation for advanced hallux valgus and look forward to the day when hallux valgus will be of interest only to the historian.

London, S.E.22. **CHARLES A. PRATT.**

MENTAL ACTIVITY IN INFANCY

SIR,—Mrs. Collis (March 28) misses the point of our argument. We agree that "mental and motor defects both affect physical activity, though in differing ways." We cannot, however, agree that the tests recommended by Mrs. Collis can be relied upon to separate mental deficiency in cerebral palsy from mental retardation due to the motor defect. We argued that all the tests for mental development were motor tests only. The term "release phenomena" as applied to tonic neck and tonic labyrinthine reflexes is, we believe, common neurological usage. We used this term as it seemed to us relevant to the problem for at least two reasons. First, the degree of release is a direct indicator of the severity of the motor handicap. Secondly, the released motor phenomena, by their persistence and strength, are responsible for the non-appearance of a higher integrated motor behaviour that may well be, and often is, potentially present.

London, W.1.

KAREL BOBATH
BERTA BOBATH.

SIR,—Professor Illingworth agrees, in his letter last week, that it is through its physical expressions that we judge mental development. As he himself admits, however, assessment of this through alertness, interest (or awareness), social responsiveness, response to sound, grasping reactions, and vocalisations (all mentioned in my original text) relies upon the infant's neuromuscular coördination. At the time when this "is not quite ready" for mature expression, and in cases where it is impaired, assessment by these means is impracticable. It was for these reasons that I ventured to select some other neuromuscular reactions of infants and to suggest that their modification may also be linked with mental advance.

Cerebral Palsy Unit,
Queen Mary's Hospital for Children,
Carshalton, Surrey.

EIRENE COLLIS.

THE PROBLEM OF PEPTIC ULCERATION

SIR,—I must agree with most of Mr. Downie's criticisms last week of my "annual lecture." I can only plead that it was the best I could do under the circumstances—an hour in which to cover a large topic before a mixed audience, few of whom were surgeons. I have, however, a few comments on each of his paragraphs.

Mr. Downie seems to have found some political or social implications in my views on the ætiology of ulcer. I can assure him none were intended. Certainly most of my ulcer patients are both intelligent and ambitious, but they are all "just ordinary chaps," and quite a few of them are bus drivers. I find out if a bus driver is ambitious by talking to him as a man rather than a patient, by discussing with him his job, his home, his family, and his pals as well as his pain. I am not sure that the word "stress" is really a "meaningless phrase"; I prefer it to the "adaptation syndrome" which has the semblance of meaning without the reality. The struggle for existence is not new, but the constant awareness of the struggle is a phenomenon of the present century, as is duodenal ulcer.

With the views on the indications for operation that Mr. Downie expresses in his second paragraph I feel less happy. He says: "I hope Sir Heneage will agree that in the treatment of peptic ulcer there must be one law for the rich and another for the poor." I could not agree less. I feel very sorry for the German who lost his motorcycle because he had a month of medical treatment for his duodenal ulcer, but the implication that he might have kept it had he been admitted to the surgical wards seems to err on the side of optimism. The figure "40" has no more magic than 400 or 0·4; but merely represents my opinion which, on this occasion, I had been asked to give. We must all operate earlier sometimes. I have recently been forced to do a gastrectomy on a boy of 14. But, in my view, we should remember that gastrectomy, successful as it is, is a gross mutilation, a wholesale sacrifice of normal tissues and of one of the most important phases of normal digestion. The man who has lost the major part of his stomach has lost most of his reservoir, most of his mechanical kneading apparatus, most of his mechanism for dealing with meat-fibres, and most of his protection against swallowed bacteria. How sure are we that a man so deprived will not eventually suffer some hormonal or nutritional disturbance? We know already that he appears to suffer no ill effect in twenty years. Have we any right to assume that this immunity will hold good for forty or sixty years?

I did not discuss the treatment of high gastric ulcers, because I was not speaking to those who were interested in technical details. In any case my experience is nothing to that of Norman Tanner. I agree, however, that the high gastric ulcers, particularly that group that Mr. Downie has recently discussed so ably,[1] the high lesser-curve ulcers that cannot be demonstrated by X rays or the gastroscope but that bleed *torrentially*, present a problem of real difficulty. I personally have only found one in which it was not possible to do a high Billroth-I gastrectomy of the Pauchet type, cutting round the ulcer with scissors. In one the ulcer involved passive antibody which will prevent paralysis and that inhibiting alimentary infection Bodian (1952b) states that a level which is barely detectable in neutralisation tests can protect cynomolgus monkeys from paralysis, whereas titres five hundred times as great still permit alimentary infection in the chimpanzee In the cynomolgus monkey specific serum antibody can prevent paralysis after alimentary infection (Bodian 1952c)

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[1] Downie, V. J. *Brit. med. J.* 1952, ii, 24.

It should be mentioned here that, though in these experiments the borderline titre appeared to be about 0 01 ml gamma-globulin per kg, Wood et al (1952) have shown that in man only very small amounts of Lansing antibody appear in the serum after the inoculation of gamma-globulin in doses of 0 1–0 4 ml per lb body weight The two series of experiments are not strictly comparable, because Wood used larger amounts of virus in the neutralisation tests than did Bodian

On the basis of his findings, and those of other workers whose reports did not at the time fit in with current theory, *Bodian suggests a reconsideration of the pathogenesis of poliomyelitis* He postulates that there are three phases of virus growth—alimentary, vascular, and neural His hypothesis is that the vascular phase, responsible for high antibody titres, may be initiated by penetration of the virus from the alimentary tract into the blood stream or the regional lymph glands The virus then enters the central nervous system via the bloodstream—possibly, on the basis of histological findings, by the area postrema in the floor of the fourth ventricle

ACTIVE IMMUNISATION OF MAN

Koprowski et al (1952) fed a monkey-adapted Lansing type strain to 20 volunteers, who were then studied clinically, serologically, and by the examination of stools for the presence of virus In no case was any illness observed in the volunteers

At the beginning of the experiments the sera of 3 volunteers contained neutralising antibodies and 2 others gave equivocal results, 12 of the remaining 15 excreted virus after feeding, and in all 15 a high titre of neutralising antibodies was then found In 12 cases the process was repeated, and in 2 of them alimentary reinfection was achieved The remainder neither excreted virus nor showed any change in antibody titre In 1 of these 2 cases a third feeding yet again produced alimentary infection, but a fourth attempt gave negative results in both On the second feeding their antibody levels were similar to those of the remaining 10, but a further increase in antibody took place in 1 In the other, whose stools were negative after a third feeding, an increase in antibody was nevertheless then detected In 2 of the 3 volunteers whose sera showed significant antibody levels at the beginning of the experiments a carrier state was again established, but none of them showed any further increase in antibody at any time No search was made for virus in the blood stream of any of these volunteers

PASSIVE IMMUNISATION OF CHILDREN

Almost 55 000 children were inoculated with either gamma globulin or a control gelatin solution during September, 1951 and July, 1952, in four epidemic areas of the United States (Hammon et al 1952) The dosage of gamma globulin was high, averaging 0 14 ml per lb body-weight The children were carefully followed up particularly from ten to thirty days after inoculation By October, 1952 90 children who had been followed for at least thirty days were considered to have contracted paralytic poliomyelitis Of these, 26 had gamma globulin and 64 gelatin—a statistically significant difference

In 28 cases which occurred during the first week after inoculation 12 children had received gamma globulin and 16 gelatin During the second week, however there were 3 cases in the gamma-globulin group and 23 in the controls and this striking difference persisted until the fifth week From the second to the fifth week there were 6 cases in children who had received gamma globulin and 38 in children who had received gelatin—a highly significant difference After the fifth week the difference between the two groups was slight

Up to now the only results available are those based on clinical grounds, and no laboratory examinations have been reported Hammon et al suggest that the gamma globulin should not have interfered with inapparent infection and development of active immunity This is, of course, the crux of the problem, and, should there be no such interference, there may well be a field of usefulness for this method

Lymphoid Tissue and Blood

There is considerable evidence that poliomyelitis affects lymphoid tissue No time relationship has yet been established but, obviously, studies of regional lymph glands during the incubation period of the experimental disease might be rewarding Sommers et al (1951) have pointed out that in the paralytic disease the most consistent and most severe lesions of any outside the central nervous system are in lymphoid tissue Wenner and Paul (1947) and Wenner and Rabe *(1951) have isolated the virus from lymph glands* at necropsy I would enter a plea for more critical study of the ileum Sabin and Ward (1941) and Wenner and Paul (1947) have isolated the virus from its wall, and it does seem that in this region the anatomical requirements both for growth and antibody production are all present

Direct evidence that poliomyelitis virus is to be found in the blood stream of man is meagre Two isolations have already been mentioned, and 13 cases of poliomyelitis in the first fortnight of life have been recorded (Baskin et al 1950, Wright and Owen 1952) There is also evidence of *myocarditis in the early stages of* infection (Laake 1951)

In spite of this lack, there is so much suggestive indirect evidence that in discussing Bodian's hypothesis it seems legitimate to go further and to adduce evidence from other virus diseases In some of these it has been found that the virus travels from the site of entry to the regional lymph-glands where it multiplies This is followed by invasion of the blood stream, by which other lymphoid tissues, including probably the spleen, are infected After a further period of growth here there is a secondary viræmia, during which the virus travels to those cells which, when attacked, give the clinical picture of the disease This sequence can be modified by existing antibody or the administration of gamma globulin

Spread of Virus

The first question that arises is the function of circulating antibody in poliomyelitis, and it is now accepted that in laboratory animals immunity runs parallel with the titre of neutralising antibody One can reasonably suggest that in man also the function of antibody is the provision of *immunity* Howe (1951) has pointed out that alimentary infection appears to be the essential part of natural immunisation For the regular production of antibody in any quantity it seems that the virus must appear in the blood stream If it does, is it there as part of the disease pattern or as an *incidental leak* from the intestine? Proof of its presence in the blood is lacking but we have not even begun to study the incubation period in man

It is tempting to think that, when we do study it we may find a picture similar to that outlined, in which entering through the nasopharynx or alimentary tract after local and then generalised growth in lymphoid tissues the virus travels in the blood stream to settle in cells of the gastro intestinal tract In some cases the virus may also enter the central nervous system and in some of these it may cause paralysis whether this is a function of the virus or of the host we do not know This hypothesis of generalised spread may be supported

The 5 new cases are all in the direct line of contact with earlier cases; 4 of these patients live in Halifax and 1 in Oldham. So far there have been 11 confirmed cases in Todmorden, 2 in Bacup, 2 in Oldham, 2 in Bury, and 1 in Halifax.

Tuberculosis in Scotland

The report for 1952 of the Department of Health for Scotland [1] describes the decline in tuberculosis mortality which we referred to last week (p. 702). The reduction in the death-rate from respiratory tuberculosis was shared by all the age-groups of both sexes, with the exception of males at the extremes of life. In 1952 there were 1404 deaths—a rate of 27 per 100,000. Among young women aged 20–24—a particularly susceptible group—the death-rate fell from 122 per 100,000 in 1950 to 45 per 100,000 in 1952. These improvements were "due to improved medical and surgical treatment, together with the fact that the disease is now being brought under treatment at a much less advanced stage." Notifications of tuberculosis in Scotland were also fewer: the provisional total for 1952 was 7259, compared with 7776 in 1951. In the last quarter of the year, however, the number of notifications showed very little change from the corresponding figure for 1951. The report says that the number of hospital beds for patients suffering from respiratory tuberculosis rose from 5967 at the end of 1951 to 6098 a year later. During the same period the waiting-list fell from 3129 to 1711. By the end of 1952, 412 patients had gone to Switzerland under the Swiss-Sanatorium Scheme.

The South Eastern Regional Hospital Board has been operating a scheme for seconding student nurses from the general training-schools in Edinburgh for a period of work in tuberculosis wards; and this scheme has enabled additional beds to be opened during 1952. The arrangement has proved successful and has been welcomed by the nurses themselves. A similar scheme is starting in Aberdeen. So far it has not been possible to do the same in the western region, where the need is greatest, but, the report remarks, "it is hoped that fuller co-operation from the main training hospitals will shortly be forthcoming."

Colour-vision of School-children

In his report for 1952, Dr. J. F. Warin, school medical officer for Oxford, describes the results of colour-vision tests performed on children between 10 and 11 years of age. During the past four years 4973 Oxford children have been examined, and 67 of them, all boys, were found to have some degree of colour-blindness. The majority of those affected had a slight red-green defect. The prevalence of colour-blindness among the boys tested was approximately 2·6%.

De-salting Brackish Water

Under the auspices of O.E.E.C. a working party was set up last year to study the de-salting of brackish water. De-salting concerns many countries where water-supplies are short or are likely to become so, including the Netherlands, South Africa, the West Indies, and Pakistan.

The working party appointed a group of experts to study four processes which were thought to merit further investigation. These are ion-exchange, separation by freezing, electrolysis, and vapour compression distillation. The group is now drawing up its report. Later the working party should be able to recommend one or more processes for coöperative development to countries of O.E.E.C., including the United Kingdom. These countries will be free to collaborate or not, as they choose.

The idea of a working party on de-salting came originally from the Netherlands, where the underground water level is falling and the water getting brackish. Although de-salting is not yet a serious problem in Britain there is a tendency for certain London supplies to become slightly brackish.

Those interested in the progress of the work on this subject should apply for further information to the Department of Scientific and Industrial Research, Charles House, 5, Regent Street, London, S.W.1.

Dangerous Drugs Regulations

The Dangerous Drugs Regulations, 1953,[1] which came into force on March 31, consolidate and amend the earlier regulations. They apply to all substances to which the Dangerous Drugs Act, 1951, applies, with the exception of certain drugs listed in a schedule to the new regulations. The main amendments include a provision for midwives to possess and administer medicinal opium, tincture of opium, and pethidine procured upon an order signed by the medical officer of health, or a person authorised by him, up to the amount specified in the order. Hitherto a midwife was required to produce her personal register of cases to the chemist supplying the drugs. A relaxation order,[2] which also came into force on March 31, recognises that morpholinylethylmorphine is now of medical value by freeing it from the restrictions on sale and manufacture imposed by the Dangerous Drugs Act, 1951, on certain alkaloids and their derivatives which are not used for medical or scientific purposes.

Parliament

Review of Cost of N.H.S.

On April 1 at the end of question time Mr. Iain Macleod, the Minister of Health, announced the appointment of a committee to review the cost of the National Health Service.

The Secretary of State for Scotland and I, Mr. Macleod said, have had under close review the whole problem of the present and future cost of maintaining a proper and adequate National Health Service, and we have already initiated a number of administrative and other measures designed to alleviate the considerable cost to the taxpayer without impairing the quality of the service provided. But these are, inevitably, measures of detail and the general long-term problem remains essentially unsolved.

After a great deal of thought, the Secretary of State and I both feel that the many issues involved in this problem are so complex that the wisest course will be to refer the whole matter for an independent and objective inquiry by a committee. We therefore propose to appoint a small committee with the following terms of reference:

> "To review the present and prospective cost of the National Health Service; to suggest means, whether by modifications in organisation or otherwise, of ensuring the most effective control and efficient use of such Exchequer funds as may be made available; to advise how, in view of the burdens on the Exchequer, a rising charge upon it can be avoided, while providing for the maintenance of an adequate Service; and to make recommendations."

Mr. C. W. Guillebaud, the Cambridge economist, has accepted our invitation to be chairman of the new committee. I will inform the House as soon as possible of the names of the other members.

Mr. Aneurin Bevan: May I ask whether the Cabinet, as a whole, seriously decided that this was an issue that should be remitted to a committee of inquiry. Is it not in fact a matter primarily for the House of Commons, for political decision, and is it not an act of the most unprecedented political cowardice to send to a committee a matter which is at the centre of British politics? Not only modifications to the organisation are to be discussed but, in the words of the terms of reference, "or otherwise." In other words, the whole central question whether there should be any longer a free health service in Great Britain is to be remitted to a committee of inquiry. If the Minister is going to have advice upon the question whether any modifications in the organisation of the health service ought to be made, why does he not ask for the views of the Central Health Services Council, which is exactly suited to that purpose, and which is a repository of expert knowledge on this subject? Is it not a fact that what he is doing, as a consequence of struggles between himself and the Treasury, is seeking another instrument by which he

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[1] Reports of the Department of Health for Scotland and the Scottish Health Services Council, 1952. H.M. Stationery Office. Pp. 126. 4s.

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[1] The Dangerous Drugs Regulations, 1953. S.I., 1953, no. 499. H.M. Stationery Office. Pp. 25. 1s.

[2] The Dangerous Drugs Act (Relaxation) Order, 1953. S.I., 1953, no. 397. H.M. Stationery Office. 2d.

papilloma $^1/_4$ in in diameter, on the upper part of the anterior wall The patient looked and felt well and had no symptoms I can recall only two of the many cystoscopic occasions when the bladder was free from papilloma

Case 2 —A woman, aged 67, has been treated by me for twenty four years by cystoscopic diathermy for vesical papilloma and is keeping very well, though when last examined, on Oct 24, 1952, there was still a patch of sessile papilloma on the left side of the bladder base

Although these two cases had several features in common, they differed in the following respects in case 1 the recurrences were widespread and sometimes pedunculated, and they rapidly reappeared , in case 2 the reappearances were *consistently at the left side* of the bladder base, were never pedunculated, and did not recur rapidly

It is a point of interest that I cannot recall any female case of vesical papilloma that became malignant after many years of cystoscopic fulguration On the other hand malignant disease has appeared in three of my male patients treated for simple growths by cystoscopic fulguration over periods of thirteen, fourteen, and twenty three years The danger is always there Nor *does a long lapse of time give complete security against* a reappearance of a simple growth, which may afterwards become malignant

I have the records of a case whose treatment was concluded by a late and able colleague, and who came to me twenty eight years later with a quite small papilloma—an obviously recent recurrence He was last seen by me with a further recurrence simple in appearance, thirty one years after the original discovery

Once a bladder has been rendered free from growth by cystoscopic diathermy, the intervals at which subsequent inspections are made will vary from case to case, according to how often recurrences are found But all these cases should be inspected at least once a year indefinitely

CYSTOSCOPY

Cystoscopic appearances of carcinoma should present no difficulty to the expert eye In fact, it is essential that the cystoscopist train himself to recognise the characters of malignancy

The following are the signs which have guided me to this diagnosis

(1) Ulceration of the growth surface

(2) The presence of a firm smooth nodule of growth or of a firm bulge of the vesical mucosa in the vicinity of the growth The firmness is estimated by probing with a diathermy electrode

(3) Hyperæmia of adjacent vesical mucosa This obliterates the outlines of individual blood vessels and is generally widespread

(4) Œdema of or surrounding, the new formation This sometimes results in bullæ

(5) A firm base to a sessile proliferation when probed with a diathermy electrode

(6) A lack of progress from treatment by several well conducted cystoscopic diathermy applications

(7) *A precipitate edge to a necrotic area of the proliferation* This is the only cystoscopic sign which has enabled me to distinguish between simple and non invasive malignant papilloma

Calculous deposit adherent to a necrotic area of growth must be considered with circumspection and a necrotic surface—short of ulceration—of a papilloma will also create a doubt , but in either case one or two vigorous diathermy treatments, followed by careful cystoscopy should settle the question

Suspicious appearances must be thoroughly investigated by a second cystoscopy after a suitable interval following a vigorous diathermy Inspection within about two weeks of diathermy application may reveal surrounding œdema which is entirely attributable to the treatment

A new case of bladder growth presenting with persisting dysuria or increased frequency, as well as hæmaturia which is not terminal, probably is a case of carcinoma , and the patient should be admitted to hospital for the first cystoscopy, so that, if fulguration is necessary to aid the diagnosis, it may be given on this occasion This is important because a quickly repeated cystoscopy in such a case may find the bladder so irritable as a result of the first examination that a satisfactory opinion must be delayed

BIOPSY

It is my practice not to rely on a cystoscopic biopsy As I have already emphasised, it is only the exceptional case of infiltrating carcinoma that cannot be recognised at once cystoscopically When one is able to make such a definite decision, it is certainly a waste of valuable time to delay further action until a laboratory report comes to hand Moreover where the report is negative one may still doubt whether the right piece of tissue has been removed

Even in a difficult case which has required a delayed inspection following a fulguration the uncertainty is generally cleared up at the second cystoscopy Where the diagnosis in such circumstances is still doubtful, or positive, I prepare to open the bladder on a subsequent early occasion to apply radium treatment, at the same time taking the biopsy specimen In fact, as will be shown later, an excellent result may be expected from implanting radium into a non-infiltrating papilloma

It sometimes happens that, by following the above rules of treatment, a biopsy report of tissue taken on the occasion of the opening of the bladder to implant radium shows that the case is one which might well have been left to cystoscopic diathermy treatment That is a hazard which the above routine always holds but which becomes reduced to a negligible size as the experience of the surgeon increases

Three of my early cases fell into this category, and it is of great interest to me to be able to record their after history They had the common features of single sessile papillomatous growths, 1–1$^1/_2$ in in diameter, they were treated with radium , and the patients were alive and well seventeen, fourteen and eight years afterwards One tumour was of non invasive anaplastic malignancy the second was reported to be non malignant , and in the third no biopsy was made In the eight year case the patient died at the age of 83 without signs of recurrence or metastasis, and in the fourteen year and seventeen-year cases both patients are still alive and well at the ages of 74 and 77

I have two reasons for reporting these cases (1) the bladders of all 3 patients remained free from post radium irritation , and (2) there was no reappearance later of even a simple papilloma I believe the explanation of the *latter fact to be that radium implanted into* a non invasive malignant or a simple papilloma where there has not yet been more than one mass of growth present, allays the tendency towards further reappearances of papillomata

This is in striking contrast with the course of events in two other separate groups of papilloma of the bladder

1 Radium implanted into a single papilloma of low malignancy when simple papillomata are present elsewhere in the bladder

2 Either single or multiple papillomata treated by diathermy only

In both these groups there is a tendency towards recurrence

The way in which, in the less malignant growths, the use of radium inhibits reappearance elsewhere in the bladder has been emphasised by Frankson (1950) It may well be that we are approaching an era when some simple form of radiation will be a regular part of the treatment of simple papilloma

TOTAL CYSTECTOMY OR RADIUM ?

Both cystectomy and radium have had a fair trial and it is now possible to compare the results Those of

Hospital Salary Awards

Replying to a question, Mr. Iain Macleod stated that the estimated cost in 1953–54 of wage and salary awards made to all full and part time hospital staff during the last 12 months was approximately £6¼ million.

Training of Oral Hygienists

Mr. Blenkinsop asked the Minister why he had decided to close the training-school for oral hygienists early in 1954.—Miss Hornsby-Smith replied: The school was organised solely for the purpose of an experiment, now completed, in the training and use of oral hygienists and was financed wholly from public funds. The final report on the results of the experiment was published in the annual report of the Central Health Services Council for 1951.

Control of Cortisone

Replying to a question, Mr. Peter Thorneycroft, president of the Board of Trade, said licences permitting private commercial imports of finished cortisone were not at present being issued. Supplies were purchased by the Ministry of Health for continuing clinical research and for use in selected hospitals where treatment could be strictly supervised.

Mr. Bence: It is not much use giving people this excellent treatment in hospital if it is to be discontinued as soon as they leave hospital.—Mr. Thorneycroft: I understand that the Ministry of Health still consider it necessary to control the use of this drug very carefully as the knowledge of its long-term effects is so far incomplete. In the view of the Ministry adequate supervision of treatment can only be ensured if the treatment is carried out in this way for the present.

Capital Expenditure on Mental Hospitals

Replying to a question, Mr Macleod, the Minister of Health, stated that the estimated capital expenditure on mental hospitals and mental deficiency institutions during 1948–49, 1949–50, 1950–51, and 1951–52 was respectively 13, 17, 15, and 21% of the total capital expenditure on hospitals.

University Grants

Replying to a question, Mr. J. A. Boyd-Carpenter, financial secretary to the Treasury, said that the total of recurrent grants to universities and university colleges in Great Britain for the academic year 1952–53 was £20 million. Of this sum, Oxford University would receive £1,215,000, Cambridge University £1,325,000, and London University £6,280,000. In addition, non-recurrent grants were made in response to specific applications. Non-recurrent grants paid in the academic year 1951–52 amounted to £7,002,095, of which Oxford University received £311,191, Cambridge University £297,005, and London University £1,821,221.

Coalminers and Pneumoconiosis

In answer to a question, Mr. L. W. Joynson-Hicks, arliamentary secretary to the Ministry of Fuel and Power, aid that about 80 coalminers in 1950, and 101 and 112 in the wo following years, were advised to leave the industry, or suspended, on account of having pneumoconiosis with tuberculosis.

Sick Pay in Government Departments

In answer to a question, Mr. Boyd-Carpenter stated that a report by the Medical Research Council revealed no evidence that there was any serious abuse of sick-pay schemes in Government industrial departments, but departments were continuing to watch sick-absence rates carefully to determine whether any modifications appear desirable.

Post-war Loaf

In answer to a question, Major Gwilym Lloyd George gave the following details of the investigations made on the points raised in paragraph 65 of the report of the Conference on the Post-War Loaf (Cmd. 6701).

The nutritional value of the “reinforced” flour which is available in the United States is not strictly comparable with that of the “restored” flour which will be available in this country. There is, however, no evidence that the “token” nutrients added in the processes of either “reinforcement” or “restoration” differ from those naturally present in the wheat grain. Investigations have shown that no means are available to determine with certainty whether the “token” nutrients in flour are of natural origin or have been added.

The policy of the Government is to allow complete freedom to the milling industry to produce flours of any level of extraction for any purpose, subject to the restoration of the “token” nutrients to all flours below 80% extraction. This question does not therefore arise. Flour of 80% extraction (which will be used among other purposes for the National loaf) will automatically contain the required levels of token nutrients, and in these circumstances producers of National flour will need no safeguard beyond that which they can themselves provide by milling to 80% extraction. Flour milled at lower rates of extraction will have to be fortified by the addition of the quantities of token nutrients required to restore the level to the minima recommended by the Conference on the Post-War Loaf.

A review has been made of wheat varieties from the point of view of their “token” nutrient content as well as their milling and baking qualities, but no useful action appears to be practicable. The question in this subparagraph does not arise as there will be no restriction on the rate of extraction of flour imported into the United Kingdom.

British Hertford Hospital, Paris

Replying to a question, Mr. H. A. Nutting, under-secretary for foreign affairs, said that no decision had yet been taken by the committee of the hospital on the hospital's future; but it was likely that it would have to be closed unless it could continue to be maintained either from local income or from donations from this country towards its running expenses.

Fluorine Gas Contamination

Dr. Barnett Stross asked the parliamentary secretary to the Ministry of Works, as representing the Lord President of the Council, what research was being made into the problem of fluorine gas contamination of the atmosphere, resulting from the firing of sanitary and other ware in continuous kilns; and whether he would make a statement on the effects of the inhalation of this gas by human beings.—Mr. A. H. E. Molson replied: In 1947 the British Pottery Research Association, which is now part of the British Ceramic Research Association, completed a thorough investigation of this problem. Their recommendations for the avoidance of the nuisance were agreed to and published by the Chief Inspector of Alkali Works in his report for that year. Fluorine gas does not occur free in Nature and when given off in an industrial process quickly combines with the moisture in the air to form hydrogen fluoride. If hydrogen fluoride is present in sufficient concentration it causes irritation of the eyes and respiratory system. I am advised that no record can be found of cases of hydrogen fluoride poisoning in this country.

Tuberculosis in Glasgow

Replying to a question, Commander T. D. Galbraith said that in 1952 the death-rate from respiratory tuberculosis was 49 per 100,000 population for Glasgow, and 22 for the rest of Scotland excluding Glasgow.

Replying to a further question. he added that at the end of 1952 there were in the Western Region 3303 staffed beds for respiratory tuberculosis. More beds could have been brought into use had there been nurses available to staff them. The waiting-list for sanatorium treatment in the region at Feb. 28 was 1230. Half this number of additional beds would enable the waiting-list to be cleared quite quickly.

Spastic Children in Scotland

In an answer to a question, Mr. J. Henderson Stewart stated that there is 1 residential school in Scotland which provides exclusively for spastic children, the Westerlea School of Spastics, Edinburgh. In addition there are 5 residential schools for physically handicapped pupils which take some spastic children. There is no hospital unit set aside solely for spastic children. Those who need hospital care are dealt with in local general hospitals or in orthopædic units in larger central hospitals. Educational facilities are available to children who have to stay long in hospital.

Deafness Caused by Industrial Noise

Dr. Barnett Stross asked the Minister of Labour whethe he had noted that about half the number of men employe in chipping, riveting, stamping, plating, and heading becam deafened to speech at more than three feet after 20 yea exposure to the noise created at their work; and what ste were being taken to protect them from this type of deafne —Mr. Harold Watkinson replied: My Department is aw of the recent report of a committee of the Medical Rese Council on the medical and surgical problems of deaf and that exposure over many years to noise above cer intensities may cause deterioration in hearing. Much rese is being carried out into this question. and a committe been set up jointly by the Department of Scientific Industrial Research and the Medical Research Council

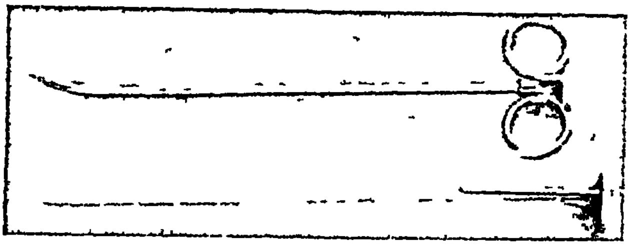

Fig 3—Radon seed introducer with guide-pin on handle

For accurate placing I do not withdraw the inserted instrument until the next one is placed in position In this way proper spacing is not difficult I find it best to work with three introducers, the third holder is necessary to ensure rapid working There is an obvious advantage if the operator can make the insertion with either hand The instrument I use (fig 3) has been made for me by the Endoscopic Company, of London

The considerable amount of intravesical sepsis which follows radium insertion prevents immediate or early closing of the bladder, but with radon the bladder is closed as part of the operation, and the patient is soon about on his feet again This advantage offers an obvious temptation in favour of radon But there is a significant absence of published figures to support any claim that this method can give comparable results to radium in the treatment of infiltrating growths

In this group of cases, after radon has been used, early local recurrence has been my regular experience, and when this happens, the resulting bladder discomfort may call for palliative ureteric transplantation As a contrast with local recurrence after radium, irritation of the bladder is strikingly absent, and the patient at least has a comfortable end

OTHER METHODS

Radioactive wire (tantalum) and fluid are both at present being tried in the bladder, and time is required to show what place these modifications of existing radiation methods will take in the treatment of vesical carcinoma

The practical difficulties of applying X ray therapy to the bladder have so far rendered this method ineffective, except sometimes for controlling hæmorrhage, but there is scope for further efforts

MEASURING THE GROWTH

It has been our custom in this country to have a physicist present in the theatre to estimate the dosage required in relation to the size of the growth When the growth is extensive and occupies an arc of a circle, the dimensions can only be accurately estimated with a malleable measure Callipers are useless I use a piece of lead tape about 8 cm long and graduated in 0 5 cm lengths (fig 4) This, too, was made for me by the Endoscopic Company

SUMMARY

All patients with vesical papillomata should undergo regular cystoscopic inspection indefinitely

Papillomata without cystoscopic features of carcinomata ascertained after careful investigation, should be treated by cystoscopic diathermy

It is generally not possible to distinguish cystoscopically between simple papilloma and non invasive papillary carcinoma

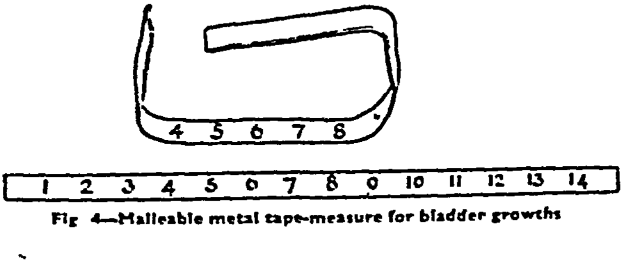

Fig 4—Malleable metal tape-measure for bladder growths

It is essential that a cystoscopist should be able to recognise the early signs of invasive carcinoma

The lack of biopsy details, showing whether the growths in question are infiltrating or not, is a weakness in many statistical reports

It is not possible to assess immediate prognosis merely on a histological grading classification of already infiltrating tumours

Is the growth infiltrating or not ? This is the question of overriding importance in prognosis If the growth is infiltrating, the extent to which it infiltrates is the next most important factor

In trying to balance the claims of one form of treatment against another, it should be borne in mind that the substitution of the large bowel for the urinary bladder generally shortens life

The results of radium treatment are better than those of cystectomy

Evidence is lacking that radon seeds have any more than a palliative action on invasive growths

Metals and fluids rendered radioactive artificially are being used experimentally

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SOME DEVELOPMENTS IN THE TECHNIQUE OF TRIGEMINAL INJECTION

JOHN PENMAN
M B Lond, M R C P

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THIS paper is a sequel to one about radiological location of the trigeminal needle (Penman 1949) With the exceptions implied below, that technique is unaltered, the approach used is still the anterior, the X ray apparatus is still of the Lysholm Schonander type, the basal and oblique projections are those recommended before, and where Harris's guide lines are mentioned the previous nomenclature will be retained

Choice of Puncture Point

PRE-SELECTION RADIOGRAMS, OR GRID FILMS

Härtel (1912) recognised that the correct puncture point might prove to be anywhere in quite a large area, but stated that the needle should usually enter the cheek opposite the second upper molar tooth This is a difficult instruction to follow in the living, even when the teeth of that region are present, and many patients requiring trigeminal injection are edentulous

Harris (1937) recommended that downwards from the most lateral part of the bony margin of the orbit one should draw a line parallel to the median plane of the face, and take the highest point on that line at which one could conveniently press a finger tip inwards and upwards beneath the lower border of the maxilla The puncture point thus defined is usually at a height about midway between those of the alæ nasi and the angle of the mouth, it is widely used serves extremely well in average cases, and in this paper will be called the conventional puncture point There are two opposite extremes, however, at which it becomes ineffectual Sometimes the anterior surface of the petrous bone is so steep and the foramen ovale faces so much downwards that a needle inserted at the conventional point will either fail to enter the foramen at all or enter it but immediately jam on the petrous bone, or at best lie so close against the petrous bone as to be underneath the trigeminal sensory root Less often the anterior petrous are Australia, Costa Rica, Greece, India, Lebanon, New Zealand, Switzerland, the United Kingdom, and the United States. Six governments—those of France, the Federal Republic of Germany, Israel, Italy, Luxembourg, and Yugoslavia—favour the alternative of two conventions and a supplementary recommendation. Belgium, Egypt, and Sweden prefer a single convention supplemented by a recommendation, while Poland suggests the adoption of three conventions together with a supplementary recommendation.

Conventions adopted by the conference are not binding on a country until ratified but must be considered for possible ratification. Recommendations are not subject to ratification, but countries have the obligation to consider giving effect to them.

APPROVED NAMES FOR DRUGS

The British Pharmacopœia Commission has issued the following new supplementary list of approved names:

Approved name	*Other names*
Benethamine Penicillin ..	N-Benzyl-2-phenylethylamine salt of benzylpenicillin.
Bismuth Glycollylarsanilate	Bismuthyl N-glycollylarsanilate. Milibis.
Cetrimonium Chloride ..	Hexadecyltrimethylammonium chloride.
Hexachlorophane	Di-(3 : 5 : 6-trichloro-2-hydroxyphenyl)methane. Hexachlorophene.
Hyaluronidase	Enzymes which depolymerise hyaluronic acid.
Iodothiouracil	4 - Hydroxy - 5 - *iodo* - 2 -mercaptopyrimidine. Itrumil is the sodium derivative.
Iopanoic Acid	2-(3-Amino-2 : 4 : 6-tri-iodobenzyl)-butanoic acid. Telepaque.
Methylpentynol	3-Methylpent-1-yn-3-ol. Oblivon. Somnesin.
Nitrofurazone	5-Nitrofuran-2-aldehyde semicarbazone. Furacin.
Pentaerythritol Tetranitrate	2 : 2-Bishydroxymethyl-1 : 3-propanediol tetranitrate. Pentaerithrityl Tetranitrate.
Phenylephrine	(−)-1-m-Hydroxyphenyl-2-methylaminoethanol. Neophryn is the hydrochloride. Neosynephrine is the hydrochloride.
Procainamide	4 - Amino - 2 - (diethylaminoethyl) - benzamide.
Procyclidine	1 - *cyclo*Hexyl - 1 - phenyl - 3 - pyrrolidinopropan-1-ol. Kemadrin is the hydrochloride.
Sulphasomidine	6 - p - [illegible]

University of London

Mr. A. d'A. Bellairs, lecturer in anatomy in the University of Cambridge, has been appointed to the readership in anatomy at St. Mary's Hospital Medical School. Dr. K. W. Cross, senior lecturer in human physiology at St. Mary's Hospital Medical School, has been appointed to the readership in human physiology at the school. The title of reader in anatomy has been conferred on Dr. J. T. Aitken in respect of the post held by him at University College.

University of Glasgow

On June 17 the honorary degree of LL.D. will be conferred on Sir Harold Himsworth, secretary of the Medical Research Council.

Royal College of Surgeons of England

The college is to hold a course of surgery lectures and clinical conferences during April. Further particulars may be had from the deputy secretary, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

Royal College of Physicians of Ireland

On March 27 the following candidates, having passed the final examination of the Conjoint Board in Ireland, were admitted licentiates in medicine and midwifery:

Jehangir Manek Anklesaria, C. P. Carey, T. H. Chillingworth, J. A. Davies, I. H. C. Lynch, E. A. Moore, Ishverlal Parbhoo, W. V. Reynolds, Denis Ryan, J. F. L. Watson.

Conjoint Board in Ireland

At recent examinations the following were successful:

D.O.M.S.—G. E. C. Hewson.

D.P.M.—S. Lennon, D. E. Munro, E. O. Lundholm, B. G. Fleming, C. McP. Smith, M. A. Rahill, J. W. Sandler, R. A. Robinson, B. A. O'Connell, D. H. A. Irwin.

D.C.H.—G. Bheek, F. P. S. le Roux, Margaret Magill, A. J. MacDonald, A. J. Edwards, E. O'Connor, T. D. Shanahan.

Royal College of Physicians of London

Dr. E. A. Carmichael will deliver the Lumleian lectures at the college, Pall Mall East, S.W.1, on Tuesday and Thursday, April 14 and 16, at 5 P.M. He will speak on Hemiplegia of Early Onset and the Results of Hemispherectomy.

Hunterian Society

The gold medal for 1952 of this society has been awarded to Dr. Douglas French (Kidsgrove, Staffs) and a *proxime accessit* award has been made to Dr. A. E. de la T. Mallett (Wimborne, Dorset). The subject for the 1953 essay is the Management of Peptic Ulceration in General Practice. Further details may be had from the hon. secretary, Mr. Alec W. Badenoch, 110, Harley Street, London, W.1.

Hastings Lecture

Dr. F. A. E. Crew, F.R.S., professor of public health and social medicine in the University of Edinburgh, is to deliver the Hastings lecture at B.M.A. House on Wednesday, May 6, at 6.30 P.M. He is to speak on Medicine and Social Policy. Mr. Walter Elliot, F.R.S., M.P., will be in the chair.

The Hastings lecture of the British Medical Association is intended for the general public, and medical readers are asked to bring this function to the notice of lay people who might be able to attend. Admission is free by ticket obtainable from the Public Relations Department, B.M.A. House, Tavistock Square, London, W.C.1.

Society of Anæsthetists of South Wales

The following officers have been elected: president, Dr. F. Pearson; vice-president, Dr. W. W. Mushin; hon. secretary, Dr. K. S. Thom (41, Caerau Road, Newport, Mon.); and hon. treasurer, Dr. D. S. Jones.

International Congress on Rheology

The second International Congress on Rheology will be held at Oxford from July 26 to 31 under the presidency of Sir Geoffrey Taylor, F.R.S. Further particulars may be had from Mr. G. W. Scott Blair, The University, Reading, Berkshire.

International Congress of Pædiatrics

The seventh International Congress of Pædiatrics will be held from Oct. 12 to 17 in Havana, Cuba. The following subjects have been chosen for discussion: Epilepsy in Infancy and Childhood, Diagnosis of Congenital Malformations of the Heart and Great Vessels Susceptible of Surgical Treatment, Problems of the Premature Infant, Complications of Primary Tuberculosis, and Metabolism and Nutrition Problems. Further particulars may be had from the general secretariat of the International Pædiatric Association, Kinderspital, Zürich, 32, Switzerland.

Opposition to Proposed Sheffield Health Centre

A further attempt to set up a health centre at Firth Park, Sheffield (see *Lancet*, 1952, ii, 346), has ended in failure, according to a report received on April 2 by Sheffield Executive Council of a meeting last month that was attended by Miss E. M. Russell-Smith, an under-secretary to the Ministry of Health. Three doctors, representing their colleagues in the Firth Park area and the Sheffield local medical committee, opposed the project on the ground that coöperative arrangements—partnerships, mutual assistance, and other action to promote group practice—could lead to services equalling those that could be provided by a health centre. The possible loss of freedom and independence by doctors entering a health centre in such matters as the purchase and selection of instruments and equipment was also emphasised. Moreover they would occupy premises as tenants. Other disadvantages included: concentration of a large number of patients in one centre; expense to the taxpayer and ratepayer in providing domestic and secretarial staff, compared with the help now given by many doctors' wives; the unwillingness of patients to attend a centre; and the likelihood of a doctor returning home and finding another set of patients waiting for him. The chairman suggested that the "real and immediate need" was for experimental schemes; but it was pointed out, on behalf of the doctors, that they did not feel the Firth Park district was suitable for an experiment of this kind. Furthermore they did not consider it practicable for a doctor to divide his practice so as to take only a proportion of his patients to the centre. Practitioners in the Firth Park area were unanimous in their opposition to the centre, and it was not possible to say that any of the doctors could agree to work there without incurring the resentment of their colleagues.

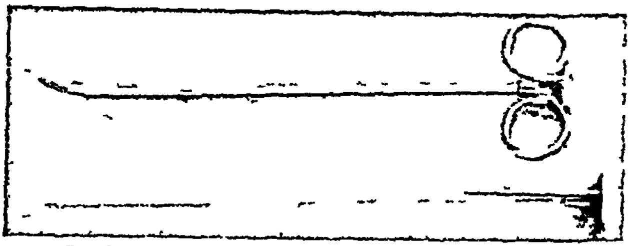

Fig 3—Radon seed introducer with guide-pin on handle

For accurate placing I do not withdraw the inserted instrument until the next one is placed in *position*. In this way proper spacing is not difficult. I find it best to work with three introducers, the third holder is necessary to ensure rapid working. There is an obvious advantage if the operator can make the insertion with either hand. The instrument I use (fig 3) has been made for me by the Endoscopic Company, of London.

The considerable amount of intravesical sepsis which follows radium insertion prevents immediate or early closing of the bladder, but with radon the bladder is closed as part of the operation, and the patient is soon about on his feet again. This advantage offers an obvious temptation in favour of radon. But there is a significant absence of published figures to support any claim that this method can give comparable results to radium in the treatment of infiltrating growths.

In this group of cases, after radon has been used, early local recurrence has been my regular experience, and when this happens, the resulting bladder discomfort may call for palliative ureteric transplantation. As a contrast with local recurrence after radium, irritation of the bladder is strikingly absent, and the patient at least has a comfortable end.

OTHER METHODS

Radioactive wire (tantalum) and fluid are both at present being tried in the bladder, and time is required to show what place these modifications of existing radiation methods will take in the treatment of vesical carcinoma.

The practical difficulties of applying X-ray therapy to the bladder have so far rendered this method ineffective, except sometimes for controlling hæmorrhage, but there is scope for further efforts.

MEASURING THE GROWTH

It has been our custom in this country to have a physicist present in the theatre to estimate the dosage required in relation to the size of the growth. When the growth is extensive and occupies an arc of a circle, the dimensions can only be accurately estimated with a malleable measure. Callipers are useless. I use a piece of lead tape about 8 cm long and graduated in 0.5 cm lengths (fig 4). This, too, was made for me by the Endoscopic Company.

SUMMARY

All patients with vesical papillomata should undergo regular cystoscopic inspection indefinitely.

Papillomata without cystoscopic features of carcinomata, ascertained after careful investigation, should be treated by cystoscopic diathermy.

It is generally not possible to distinguish cystoscopically between simple papilloma and non-invasive papillary *carcinoma*.

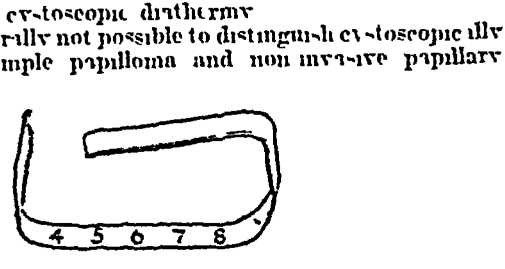

Fig 4—Malleable metal tape-measure for bladder growths

It is essential that a cystoscopist should be able to recognise the early signs of invasive carcinoma.

The lack of biopsy details, showing whether the growths in question are infiltrating or not, is a weakness in many statistical reports.

It is not possible to assess immediate prognosis merely on a histological grading classification of already infiltrating tumours.

Is the growth infiltrating or not? This is the question of overriding importance in prognosis. If the growth is infiltrating, the extent to which it infiltrates is the next most important factor.

In trying to balance the claims of one form of treatment against another, it should be borne in mind that the substitution of the large bowel for the urinary bladder generally shortens life.

The results of radium treatment are better than those of cystectomy.

Evidence is lacking that radon seeds have any more than a palliative action on invasive growths.

Metals and fluids rendered radioactive artificially are being used experimentally.

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SOME DEVELOPMENTS IN THE TECHNIQUE OF TRIGEMINAL INJECTION

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THIS paper is a sequel to one about *radiological* location of the trigeminal needle (Penman 1949). With the exceptions implied below, that technique is unaltered; the approach used is still the anterior, the X-ray apparatus is still of the Lysholm Schonander type, the basal and oblique projections are those recommended before, and where Harris's guide lines are mentioned the previous nomenclature will be retained.

Choice of Puncture Point

PRE-SELECTION RADIOGRAMS, OR GRID FILMS

Härtel (1912) recognised that the correct puncture point might prove to be anywhere in quite a large area, but stated that the needle should usually enter the cheek opposite the second upper molar tooth. This is a difficult instruction to follow in the living, even when the teeth of that region are present, and many patients requiring trigeminal injection are edentulous.

Harris (1937) recommended that downwards from the most lateral part of the bony margin of the *orbit* one should draw a line parallel to the median plane of the face, and take the highest point on that line at which one could conveniently press a finger tip inwards and upwards beneath the lower border of the maxilla. The puncture point thus defined is usually at a height about midway between those of the ala nasi and the *angle of the mouth*; it is widely used, serves extremely well in average cases, and in this paper will be called the conventional puncture point. There are two *opposite* extremes, however, at which it becomes ineffectual. Sometimes the anterior surface of the petrous bone is so steep and the foramen ovale faces so much downwards that a needle inserted at the conventional point will either fail to enter the foramen at all, or enter it but immediately jam on the petrous bone, or at best lie so close against the petrous bone as to be underneath the trigeminal sensory root. Less often the anterior petrous

NEW CONCEPTS OF POLIOMYELITIS *

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> "POLIOMYELITIS is a common virus disease which usually runs a mild course characterised by upper respiratory or gastro-intestinal symptoms but occasionally the picture is complicated by signs indicating invasion of the C.N.S. . . ." (Howe 1952).

This definition, which may still appear unusual to some, underlines the change of emphasis in the study of poliomyelitis in the last few years. The accident of paralysis has been placed in its proper perspective, and we now view the whole disease—or what we think is the whole disease—instead of concentrating too much on one facet of it.

Three different immunological types of poliomyelitis virus have so far been described—namely, Brunhilde (type 1), Lansing (type 2), and Leon (type 3). The adaptation of the Lansing type to mice has enabled antibody surveys to be made with relative ease by means of neutralisation tests, and the results have confirmed recent ideas about the epidemiology of poliomyelitis (Meenan 1951). The virus is widely distributed and occurs in all climates. Antibodies to all three strains have been demonstrated among communities as remote from one another as Eskimos (Paul et al. 1951) and Africans (Howe 1952).

These surveys have usually been made with the Lansing strain only, but there is reasonably good evidence that the distribution of antibodies to it closely parallels the distribution of poliomyelitis virus, independent of strain differences. The average age at which poliomyelitis is acquired in any given community seems to be the same as the average age of acquisition of Lansing antibodies (Gear et al. 1951). The relationship cannot be taken as absolute, and one cannot use survey results as a universal index of the immunity of any given population. In future surveys more than one type of antibody should be tested.

Large epidemics of paralytic poliomyelitis seem to be a reflection of the improved living and sanitary conditions of the countries which suffer them. In most parts of the world poliomyelitis epidemics are small or unimportant; and paralysis, when it occurs, is almost limited to children under 5 years old. As the virus is liberally distributed, nearly everybody comes in contact with it before that age, and progressively acquires enough resistance to make a paralytic illness unlikely. On the other hand, in a person not protected by previous exposure to the virus, the likelihood of paralysis rises during childhood, being lowest in infancy and reaching a peak in early adult life. As research on the virus has been almost exclusively carried out in countries where the disease *is* epidemic rather than endemic, we have come to think of epidemics as the natural host-virus relationship. But the reverse appears to be actually the case. Instead of coming recently to prey on man, the virus seems rather to have lived in more or less harmonious relationship with us for centuries; and it is we who, by altering our living conditions, have upset the balance.

To offset this gloomy picture it is commonly held that there is a mechanism of natural immunisation, even in those countries which are now subject to epidemics. Turner et al. (1950) suggest that there are a thousand subclinical infections with the Lansing strain for every clinical case of poliomyelitis, and Howe (1952) says that for every paralytic case amongst those reaching the age of 20 there have been a hundred non-paralytic or abortive cases. Brown et al. (1952), however, hold that the distribution of virus, even during epidemics, is confined to close contacts of cases, such as members of their families. If this is so, the need for a safe and efficient method of prophylaxis is even greater than was thought.

Prophylaxis

The use of vaccines and of gamma-globulin in the prevention and control of paralytic poliomyelitis has been discussed in academic fashion for several years. So satisfied, however, were all workers in this field of the strict neurotropism of the virus that there seemed to be little theoretical justification for their use. It is true that Enders et al. (1949) had grown the virus in tissue culture free from neural elements, but it remained for Horstmann (1952) and Bodian (1952a) to give fresh direction to our study of the disease pattern. By the demonstration of a viræmia in the experimental disease they may have brought poliomyelitis into line with what we know of some of the other virus diseases instead of its being a complete enigma. The virus had, of course, been looked for in the blood of patients, but the finding that antibodies were present to a high titre at the onset of paralysis was taken as confirmatory evidence that it did not travel by this route. Two isolations from the blood of patients have been reported (Ward et al. 1946, Koprowski et al. 1947) in one of which the virus was recovered less than six hours after the onset of an abortive illness. In retrospect it looks as though in many cases virus was not isolated because it was sought too late.

EXPERIMENTS ON MONKEYS

Most of the recent work on poliomyelitis has been done on chimpanzees, which seem to react to infection much as man does. Simple feeding of the virus to these animals leads to a high rate of alimentary infection and a low rate of paralysis, and the clinical and pathological features of poliomyelitis appear to be the same in both species. In Horstmann's (1952) work virus was isolated from the blood of 5 of 8 chimpanzees which, after feeding, had no apparent disease. It was recovered between the fourth and the sixth day. Bodian (1952a) infected 4 chimpanzees, with very interesting results:

> 2 of them became paralysed after thirteen and seventeen days, and virus was isolated from the blood-stream on the eighth and fifteenth days respectively. In a 3rd chimpanzee the virus was present in the blood on the eighth day and again on the eleventh day; the chimpanzee showed no clinical sign of infection, but histological lesions were present in the central nervous system on the fifty-ninth day. In the first 2 chimpanzees antibody was present to a high titre at the time of paralysis. The response was lower in the 3rd chimpanzee but by no means negligible by the fifteenth day. In all 3 the virus was present in the fæces.
>
> The 4th chimpanzee reacted differently. No virus was isolated from the blood on the eighth day, the antibody response was slow, and no evidence of involvement of the central nervous system was found after sacrifice on the seventy-second day. On the other hand, the excretion of virus in the fæces appeared to be greater and more prolonged than in the 3 other chimpanzees. A high titre of antibody did not seem to affect virus excretion. This animal, the only one in which a viræmia could not be demonstrated, was the only one in which the central nervous system was not affected.

Other evidence, from experiments in cynomolgus monkeys, is also available (Bodian 1952b):

> After 23 were fed virus on three consecutive days 12 became paralysed and 11 remained well. A viræmia was demonstrable on the seventh day in 6 of those 12 which subsequently became paralysed but in none of the 11 others. Later bleedings, on the day of paralysis, in 7 of the monkeys revealed no viræmia.

Further experiments can be summarised to show a striking and suggestive difference between the level of porates a device introduced by Luer about 1860 but long regarded as unnecessary on ordinary syringes—a *threaded stem and a milled runner*, which can be used as a check against injecting more than a predetermined quantity of liquid (Dr Wilfred Harris has for many years used the same device on a shorter, broader 1-ml syringe)

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* Based on a paper read before the section of pathology of the Royal Academy of Medicine in Ireland on Jan. 16, 1953. The full text will appear in the *Irish Journal of Medical Science*.

Location of Injected Alcohol

MIXTURE OF ALCOHOL WITH RADIO-OPAQUE MEDIUM

While one is using radiography to guide the needle, an opportunity would be missed if one did not also try to gather some evidence of the situation of the injected alcohol A mixture of 4 parts by volume of absolute ethyl alcohol with 1 part of a synthetic iodine compound ('Myodil') has been manufactured for that purpose In the presence of even a trace of water the two ingredients separate, and the syringe into which the mixture is drawn must therefore be carefully dried, for the special syringe described above a handy drying implement is an ordinary pipe cleaner, autoclaved For drawing up the mixture it is best to use a short fine intradermal needle, its socket must be dried out before it is fitted to the syringe, which must next be used to force air outwards through the needle shaft until that also is dry

After injection of 0 10 ml of this mixture, radiograms in the basal and oblique projections may show a variety of appearances Not infrequently the opaque medium is seen scattered in the posterior fossa, in that event, even though for the first five or ten minutes there may have been satisfactory trigeminal sensory loss, one can be sure that no lasting success has yet been achieved In other cases the opaque medium forms a close network of minute globules within a small and roughly circular area anteromedial to the needle tip, in which event one can be fairly sure that the sensory loss will be permanent As soon as the mixture leaves the needle its ingredients separate, the alcohol tending to float upwards and the opaque medium to sink, with the result that there is only indirect evidence of the location of the alcohol, nevertheless the empirical value of this method is considerable

A serious danger must be mentioned the mixture may be mistaken for the pure opaque medium and offered as such to a doctor to inject intrathecally before myelography This has happened once, when only exceptional *vigilance prevented a presumably* lethal injection of absolute alcohol into the cisterna magna The following precautions should be observed

(1) The mixture must be supplied in ampoules containing not more than 1 ml (media for myelography are usually supplied in 3-ml ampoules)

(2) Each ampoule, not merely each box containing a batch of them, must be labelled "Absolute alcohol with myodil [or whatever the trade name may be] for trigeminal injection only," the more dangerous ingredient being mentioned first

(3) Preferably the whole stock of the mixture in a hospital should be under lock and key apart from stocks of other substances kept in the operating theatre

Conclusion

With these supplementary aids injection of the trigeminal sensory root remains a difficult and often a lengthy procedure, but its chief object—lifelong trigeminal anæsthesia for relief of tic *douloureux*—is achieved with less discomfort to the patient and greater certainty.

The mixture of alcohol with a *radio opaque medium* is the invention of Dr James Bull, to whom I am most grateful for his help and encouragement in all radiological aspects of trigeminal injection In the initial construction of the trigeminal grid Miss Susan Browne gave valuable assistance, for which I take this opportunity of thanking her For the rest of these aids to injection I am solely responsible

The grid films and the mixture of alcohol with a radio-opaque medium were first described publicly, though only *orally, at a meeting of the Society* of British Neurological Surgeons on July 22, 1949[†] None of the other aids has been described before

The ten millimetre stop is an extremely simple device which can be manufactured by any good surgical instrument maker The special 1 ml syringe is made by Messrs Down Brothers, Mayer & Phelps The mixture of alcohol with myodil is supplied by Messrs Glaxo with precautions (1) and (2) recommended above

CORRECTION

This is an appropriate place for pointing out an inaccuracy in my earlier paper (Penman 1949), in which ossified ligaments adjoining the foramen ovale were referred to as if they were all of one type Chouké (1946, 1947, 1949) has shown conclusively that there are two ligaments, the pterygospinous and the pterygo alar, which differ in origin, frequency among white people and Negroes, angle, and relation to the foramen I am much obliged to Dr Chouké for personally drawing my attention to this distinction

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ALCOHOL PAIN IN HODGKIN'S DISEASE

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FOUR years ago a patient with Hodgkin's disease, whose tolerance to alcohol was considerably reduced, was admitted to the Radium Centre, Aarhus At *that time the lymphogranulomatous processes* were mainly localised in his lungs The patient said that ingestion of very small quantities of alcohol, such as a glass of mild beer (alcohol content about 1%), produced pain in the left side of the chest The pain developed a few minutes after the ingestion and persisted for about an hour.

Since that time we have invariably questioned our patients with Hodgkin's disease or other hyperplastic disorders of the lymphoid tissue about their tolerance of alcohol We found this symptom, which we have termed "alcohol pain," in 9 of 62 patients with Hodgkin's disease We were at a loss to explain the mechanism of production of alcohol pain, and were for a long time *in doubt whether it was a specific symptom* of Hodgkin's disease Since similar findings have been published by other workers (Hoster 1950, Verbeeten 1952), we report these 9 cases here

CASE-RECORDS

Case 1 —A *man, aged* 29, noticed enlargement of his cervical lymph nodes for the first time in 1945 Histological examination of an excised lymph node in 1946 revealed Hodgkin's granuloma At that time radiography of his chest did not show any abnormalities Six months later he complained of a sense of oppression in the chest and radiography revealed a slightly blurred pulmonary *pattern but* by those cases which show the "illness of infection," and some such course of events could explain the early appearance of antibodies. In the chimpanzee antibodies can sometimes be detected before virus can be recovered from the stools (Melnick 1951). As already mentioned they have often been found by the time paralysis supervenes. Alternatively, the infection may be entirely peripheral and superficial, with virus growing in the nasopharynx and the intestine, and sufficient virus being absorbed from these sites to produce immunity or to enter the central nervous system.

[†] A reproduction of a grid film without any account of its use was published in *Radiography* 17 157 This was done without my agreement and by an error for which apology has been made

[‡] Aided by grants from the Anders Hasselbalch Anti Leukæmia Foundation and C P Schepler and Wife's Bequest the Irma Foundation

The fundamental difficulty is to know how far experimental findings can be applied to natural infection in man. What is the relation between the disease in animals produced by large doses of laboratory-adapted strains and that in man produced by small doses of naturally occurring virus? Whether or not alimentary reinfection can be established in the immune subject may be a question of dosage.

The experimental action of gamma-globulin suggests that spread by the blood-stream to the central nervous system may be important, because quite low levels will prevent paralysis; but the findings in man are still too few to be significant. Not all chimpanzees with viræmia develop paralysis (Bodian 1952b). At a maximum of 50, the number of second attacks is very small by comparison with the vast number of paralytic cases reported, and it is generally accepted that they are due to an antigenically different strain from that which caused the first. Be that as it may, it has been accepted for years that poliomyelitis virus can travel in nerves, and we have no right to assume that virus found in them is always travelling centrifugally. What has not, perhaps, been demonstrated so convincingly is that in natural poliomyelitis the virus does travel by the nerves.

To conclude, however, I must point out that, though theoretical musings are refreshing, and the need to remove poliomyelitis from the vacuum in which it has too long languished away from other virus infections is urgent, they remain theoretical. In no disease is it so difficult to see the wood for the trees, and all one can do is to point out lines of research which must be interesting and may well be rewarding. In the half-century of poliomyelitis study we have discarded the theory of lymphatic spread. We now seem to be reaching a phase where the theory of neurotropism is weakening and hæmatogenous spread is coming to the front. Perhaps, as so often happens, the truth lies in a synthesis of all three, as already outlined.

Basis for Control?

One of the attractions of the theories under discussion is that they provide a rational basis for the control of paralytic poliomyelitis by ordinary immunological means. Indeed, the work on vaccines and gamma-globulin is an act of faith in them. Antibodies so produced or provided will be of little value unless they come in contact with the virus, and the blood-stream seems a far more likely place for this to happen effectively than the central nervous system. These theories must also derive support from recent epidemiological findings. Widespread and completely silent immunisation seems more likely to be, as in other infections, a function of the usual mechanisms than of completely peripheral infection with only incidental immunity.

Before we build on these foundations, however, let us recognise that they are incomplete. In an attempt to compress a very large subject into small compass it is impossible to examine all its implications; and there are solid reasons why we should not be led too far and too fast. One crucial question has not yet been answered. Is the pathogenesis of poliomyelitis in man the same as in the chimpanzee? We know that the chimpanzee closely simulates man in its reaction to the virus, and that, once infection has been established, the distribution and characters of the lesions in the central nervous system are identical. What we do not know is whether the passage of virus from the intestine to the central nervous system follows the same pattern in the two species. Among the primates, resistance to the virus varies at different portals, although the final picture is the same (Howe 1952). For instance, is the human intestine more or less permeable to the passage of virus than that of a chimpanzee? If there is a viræmia in man, is it easier or less easy for the virus to enter the human central nervous system than that of the chimpanzee? Is the distribution of the virus in space and time within the body the same in both species?

The pace at which poliomyelitis research is moving is almost frightening. With recent technical advances bringing it within the reach of many more laboratories one may expect the near future to be as productive and stimulating as the recent past. If that be so, we may confidently look forward to an era in which man and virus may yet again live happily together, and in which the only apparent complication of infection—paralysis—may be controlled.

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TREATMENT OF CARCINOMA OF THE BLADDER

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THE treatment of vesical carcinoma begins with the regular supervision of simple bladder growths. This is because the danger of malignancy threatens all bladders which have been the seat of merely simple papillomata. This fact is obvious from an analysis of a consecutive series of my own cases, for of 205 of these which were thought not to be malignant and were treated by cystoscopic diathermy 21% ultimately proved carcinomatous.

The passage of time, even of many years, is no safeguard against this menace. On the other hand, there are cases in which simple growths keep on reappearing for years and years without developing invasive characters, as shown by the two following cases.

Case 1.—A woman, aged 68, has been treated by me for papilloma of the bladder by cystoscopic diathermy for more than twenty-three years, having had 65 applications. The last cystoscopy, on Aug. 13, 1952, showed a single pedunculated obtained at another hospital revealed typical Hodgkin's granuloma. X-ray treatment of the involved lymph-nodes evoked a good response. On admission to the Radium Centre in Aarhus in October, 1952, the patient complained of tenderness over the manubrium sterni, where a diffuse and rather firm tumour was palpable. There was moderate enlargement of the axillary and inguinal lymph-nodes on both sides. Chest radiograms did not reveal any infiltrative processes or enlargement of mediastinal nodes, but an area of necrosis the size of a plum, was disclosed in the left upper quadrant of the manubrium sterni. The general condition was good, E.S.R. 19 mm. in 1 hr. (Westergren), Hb 110%. X-ray therapy to the sternum was given, but the tumour did not decrease appreciably in size.

Reactions to Alcohol.—On one occasion during his stay in hospital the patient had a glass of lager with his luncheon. Immediately afterwards acute pain developed over his manubrium and persisted for about ten minutes, radiating down the arms, and was superseded by paræsthesiæ. A few days later the patient again tried to take a glass of lager with his luncheon. An attack of such intense pain developed that he asked for morphine. The character of the attack was as on the previous occasions. At the time of writing no information about the patient's tolerance to alcohol after his discharge has been received.

Case 9.—A young man, aged 20, was called up for military service in August, 1952. About that time he noticed for the first time an asymptomatic swelling in the left supraclavicular fossa. The swelling was rather tender, but as he was otherwise in good health he did not apply for medical aid. While he was on leave in October, 1952, acute pain developed in the region of the tumour and in the entire left side of his chest shortly after he had drunk a glass of lager. He had to go to bed, and a doctor was sent for. He was then admitted to a military hospital; a biopsy specimen from the tumour showed a typical Hodgkin's granuloma, and the patient was transferred to the Radium Centre in Aarhus. On admission here a tumour in the left supraclavicular fossa, the size of two clenched fists, was revealed. Chest radiograph showed no abnormality, and no enlargement of lymph-nodes, liver, or spleen was present. The patient had no fever and the general condition was good; E.S.R. 12 mm. in 1 hr. (Westergren), Hb 83%. The patient is still under treatment.

DISCUSSION

In all the 9 cases reported here the diagnosis of Hodgkin's disease was verified by histological examination of a lymph-node, and the microscopical picture was in all cases typical of Hodgkin's granuloma.

In all the cases pain developed in some part of the body after ingestion of alcohol. The pain was localised to the sites of lymphogranulomatous foci, such as the peripheral lymph-nodes, the mediastinum, and bones. Clinically, it seemed that the pain was localised to the focus which was active at the time. The pain was often very intense and in some cases developed after very small quantities of alcohol, such as a glass of mild beer. The pain invariably appeared a few minutes after the ingestion of the alcohol and persisted for thirty to sixty minutes—i.e., it began as soon as the ingested alcohol was absorbed and persisted until the greater part of it was oxidised. In 2 of the cases it was stated that the tolerance to alcohol was considerably increased after a course of treatment which led to an improvement of the general health. Only alcoholic beverages were stated to induce the pain.

We are at a loss to explain the mechanism by which this pain is produced in Hodgkin's disease. To detect if the pain was excited by the vasodilating effect of alcohol we treated case 7 with various vasodilators (glyceryl trinitrate ointment, histamine hydrochloride, and nicotinic acid amide) but these substances did not produce any pain.

Among many patients with lymphomata of various types the symptom of pain after ingestion of alcohol was found only in those with Hodgkin's disease. At present it is impossible to appreciate the value of the "alcohol test" as a diagnostic aid in Hodgkin's disease. However, in cases where it is impossible to obtain material for a histological examination—e.g., if the disease is localised to the mediastinal lymph-nodes—the presence of the symptom may point to the correct diagnosis, although it must be emphasised that it was only in a small proportion of our patients with Hodgkin's disease that this symptom was present.

SUMMARY

In Hodgkin's disease the ingestion of alcoholic beverages, even in small quantities, often produces severe pain.

The pain is confined to the lymphogranulomatous foci active at the time.

This reaction, which we term "alcohol pain," may sometimes be the initial symptom of Hodgkin's disease and seems to be of some diagnostic value.

Nine illustrative cases are briefly reported.

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PHLEBOTOMY FOR HÆMOCHROMATOSIS

EFFECT OF REMOVING 52 PINTS OF BLOOD IN SIXTEEN MONTHS

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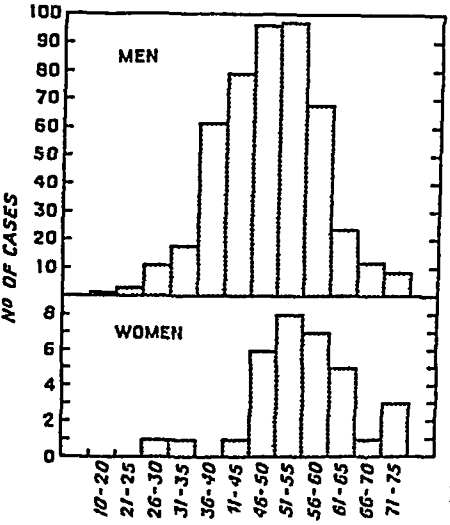
IT is now known that only negligible quantities of iron can be excreted by the body, and that normally there is a mechanism which prevents excessive absorption of iron from the gut (McCance and Widdowson 1938, Hahn et al. 1943, Granick 1946). The evidence has been summarised by Houston and Thompson (1952). In hæmochromatosis there is probably a congenital defect in the mucosal block for iron. In consequence slightly more iron is absorbed than can be excreted, and the progressive accumulation of iron in the tissues is accompanied, usually about middle age, by the characteristic pathological changes of the disease.

It has been suggested that the rarity of hæmochromatosis in women may be explained by their having, in menstruation and pregnancy, a means of excreting the iron which is absent in men. In patients with hæmochromatosis the tissues contain some 25–50 g. of iron, compared with 3–5 g. in normal people. During the thirty years of reproductive life the average loss of iron through menstruation and pregnancy is probably about 10–15 g. In women with the underlying metabolic defect of hæmochromatosis this loss of iron might be sufficient to delay or suppress the clinical expression of the disease.



Age-distribution of 479 men and 33 women with hæmochromatosis.

Study of the age incidence of hæmochromatosis lends some support to this hypothesis. Women get the disease later in life than do men, and almost always after the

Jacobs, who has practised both methods extensively, are perhaps the most informative. The Glasgow school of urologists (Jacobs et al. 1947) put forward figures which made it abundantly clear that radium implantation was the better method. Fresh data presented by Jacobs at the annual meeting of the British Association of Urological Surgeons in 1952 (not yet published), and at the International Congress of Urology in New York, gave further emphasis to the superiority of radium.* His results are particularly valuable because they embrace the two principal methods—cystectomy and radium—of treating invasive carcinoma. Of his 110 patients treated with radium 33·6% survived five years, whereas the estimated number of five-year survivors after cystectomy (B.A.U.S. series 1952) is 20·5% of 705 cases.*

But other surgeons in this country, who are not practised in the use of radium, have become very expert in the cystectomy-plus-ureter-transplantation technique, and it is with a sympathetic understanding that one notes the rearguard action they continue to fight in this losing battle to support cystectomy.

Comparative figures in different grades of carcinoma, from published results generally, give no satisfaction, because of the lack of information about biopsy. This omission becomes important where many growths are included in which the cellular anaplasia has not yet reached the bladder wall but is confined to the papillomatous protuberance; and it is interesting to note the regularity with which this matter is not discussed.

Moreover the anaplastic non-invasive papillomata are satisfactorily treated by cystoscopic diathermy; so to include these in a statistical report in support of a method of treatment, without any indication as to how many such are included, throws no light on the real problem, which is—what is the best method of treating infiltrating growths of the bladder?

This criticism applies equally to reports on all methods of treatment. Nevertheless, this fault, because it is commonly present, still allows a helpful comparison to be made between the two chief methods of treatment—total cystectomy and radium implantation—which comparison, as has already been pointed out, discriminates so much in favour of radium.

For many years the carcinoma registry of the American Urological Association was content to designate non-invasive papillomata of the bladder as grade-I carcinoma. Although this claim was recently retracted (quoted by Higgins 1952), the mischief of the original classification has been done. The result is that the value of many operative statistics is difficult to assess.

In studying results in relation to higher grades of carcinoma, determined histologically, I can find little encouragement to feel that the lower grades of the invasive groups necessarily give better prognoses than the higher. An obviously important factor is the extent to which infiltration has taken place when the treatment is started, which varies so much in different cases; and the question seems to me to arise whether the lower-grade ones do not give rise to symptoms later than the higher-grades.

To exclude the non-invasive carcinomata from a series of cases is to present undisguised the formidable nature of the problem of treatment of infiltrating growths of the bladder. This is reflected in a series of 57 of my own cases of carcinoma of the bladder which are presented in this form and were all treated by radium implantation or radon. So far as I know, this is the first report of carcinoma of bladder cases made in this way.

Half of the patients were dead before twelve months had passed after the operation; and only 7% survived more than four years, although some have survived three or four years and seem likely to reach the five-year mark. One of them has survived eleven and a half years. I could add a patient who survived twelve years, a man, aged 63, who had a typical early infiltrating carcinoma with ulceration and surrounding thickening; but no biopsy was made, and therefore I prefer to leave him out.

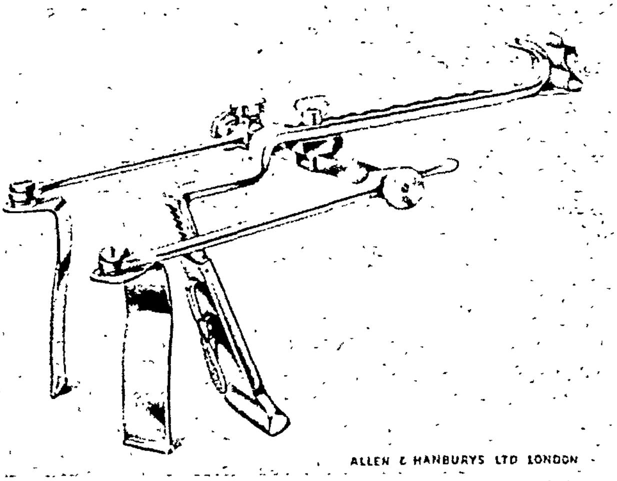


Fig. 1—Bladder retractor. The posterior blade moves up and down on a ratchet, and its lower end does not curve forwards. The lower ends of lateral blades curve outwards.

RADIUM TECHNIQUE

Bladder Retractors.—In recent years, in Great Britain, these have developed along entirely wrong lines for good exposure of bladder growths; they encroach too much on the bladder base, where most growths are situated. Fig. 1 shows a different type of retractor which obviates this defect. It was made for me by Messrs. Allen & Hanburys, of London.

Radium Introducer.—The other point which has worried me is the lack of any sound means of judging whether the encircling needles completely enclose the growth. In the higher grade of malignancy this uncertainty is a potential weakness in radium treatment which requires further research. Palpation through the open bladder often reveals the growth to be very much larger than could be estimated by cystoscopy. The Endoscopic Company, of London, have made for me a long-handled radium introducer with pointed and cupped ends, which are a great advantage for complete insertion of the needles over the old pattern (fig. 2).

RADON

My experience with radon is limited, but I have used it with advantage on occasions. I have never attempted to use it cystoscopically.

Unlike radium, unused units are wasted; often, when the bladder is opened, more seeds are needed than appeared to be required when the growth was viewed cystoscopically; and the chances of success with an infiltrating growth when the radon-seed supply is inadequate are nil.

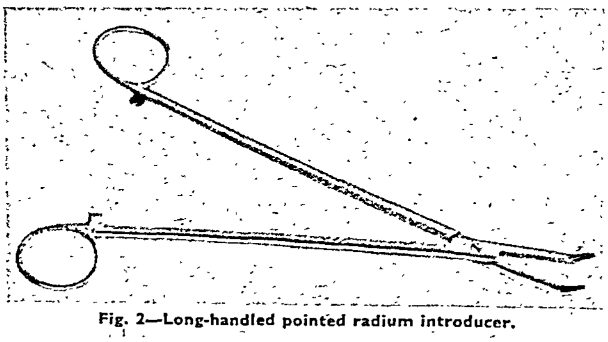


Fig. 2—Long-handled pointed radium introducer.

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* This figure is reached by combining the 28 patients who have survived five years or more with others still surviving from two to four years whose prospects of surviving for five years are considered to be good.

way of removing iron from the body except by removing blood, which contains 500 mg of iron per litre Hence it is logical to try repeated venesection in patients with the disease

TRIAL OF THE METHOD

A man aged 39, with hæmochromatosis proved by liver biopsy, whose case has already been briefly reported (Houston and Thompson 1952), was bled by venepuncture a pint a week from Nov 22, 1951, to July 3, 1952, since when a pint has been taken every fortnight Throughout this period he has continued at work as a chartered accountant, and at no time has he noticed any ill effects from loss of blood Up to now 52 pints of blood has been withdrawn in sixteen months The patient has not been given any hæmatinics

Table II shows the results of weekly examinations of blood and estimations of the serum-iron and plasma-protein levels None of these has shown any significant alteration The serum-iron level has shown a downward trend but is still above the normal range

DISCUSSION

Granick (1949) was probably the first to suggest that repeated venesection might be beneficial to patients with hæmochromatosis Finch et al (1950) reported that the weekly removal of about a pint of blood for seven weeks caused a progressive fall in hæmatocrit and serum-iron levels in 4 normal men but not in 4 patients with hæmochromatosis Their conclusion is that the rate of blood regeneration after phlebotomy depends chiefly on available body stores of iron Davis and Arrowsmith (1950) and Beyers and Gitlow (1951) have also subjected patients with hæmochromatosis to repeated bleeding without causing anæmia The patient reported here has so far had 52 pints of blood withdrawn in sixteen months, and his blood picture remains normal

Possibly the iron used by the hæmochromatotic in this remarkably rapid blood regeneration may come partly from increased absorption of iron from the gut In the present experiment the patient could not be kept on a low-iron diet, because this would have necessitated a long stay in a metabolic ward However, in sixteen months he has lost 12 g of iron in the blood removed, and not more than a fraction of this can have been made up from his food It seems fair to conclude that his enormous iron stores have been reduced to some extent

Whether he has derived any benefit is a question more difficult to answer There are no satisfactory criteria by which this can be decided But, as patients with hæmochromatosis die from the effects of their disease on vital organs, such as the liver and the heart, and as these pathological effects are probably related to the amount of iron deposited, repeated phlebotomy, started early, might improve the prognosis considerably Bleeding, if properly controlled, is probably free from danger and as no alternative treatment is available, merits at least a long trial Only if a sufficient number of patients so treated are satisfactorily followed up and reported—necessarily by different observers, in view of the rarity of the disease—can its effect ever be finally assessed

SUMMARY

Evidence is presented that repeated phlebotomy may be useful in the treatment of hæmochromatosis

52 pints of blood was withdrawn in sixteen months from a man with proven hæmochromatosis without causing anæmia or other ill effect

Such bleeding may reduce the enormous iron deposits and perhaps improve the prognosis It might with advantage be adopted as the treatment of choice for all early cases, at least until sufficient data have been collected to enable its long-term effects to be assessed

My thanks are due to Prof Max Rosenheim for permission to carry out this therapeutic experiment on his patient , to Dr R. L Waterfield for the blood counts and to Prof R H S Thompson for the serum iron estimations

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surface is so close to the horizontal that the same needle, having entered the foramen easily enough, will inevitably pass above the sensory root. There are also less extreme cases in which the conventional puncture point either is a little too high and brings the tip of the needle a little too low in relation to the sensory root, or vice versa. Such cases, whether of the less or of the more extreme kind, are not merely conjectural; radiograms in the oblique projection have often proved their existence.

What we require, then, is a first puncture point which shall at least give the needle a clear run through the foramen ovale and bring it approximately into the right relation with the petrous bone. To this end two devices are combined.

(1) *Härtel's Point and Associated Points*

Härtel (1921) wrote that the axis of a correctly placed needle, if produced backwards, would pass through the vault of the skull at a point which could be found by measuring from the lambda 4 cm. forwards along the sagittal suture and then 2 cm. laterally away from the side of injection. This, which I call Härtel's point, is a reliable guide. In the present procedure it is marked on the scalp with two other points in a plane parallel to the plane of the sagittal suture: one 4 cm. anterior to it, and one 4 cm. posterior to it or 2 cm. lateral to the lambda.

(2) *Trigeminal Grid*

Five straight fine wires, each 4 cm. long, are placed parallel 1 cm. apart; a second set of five similar wires is placed at right angles to the first to form a square 4 × 4 cm., subdivided into sixteen squares 1 × 1 cm. Where the middle wire of each set crosses the other, at the centre of the larger square, a small lead-shot is placed, and the whole is fixed between two layers of washed X-ray film or other suitable transparent material. The grid is then ready for use.

Next, Harris's guide lines are drawn on the patient's face, and the grid is fastened onto his cheek with sticking-plaster. The lead shot must lie over the conventional puncture point, and one of the two middle wires must lie over the elevation line—i.e., the line joining the puncture point to the zygoma point. Three radiograms are now taken in three slightly different projections, for all of which the patient's face rests

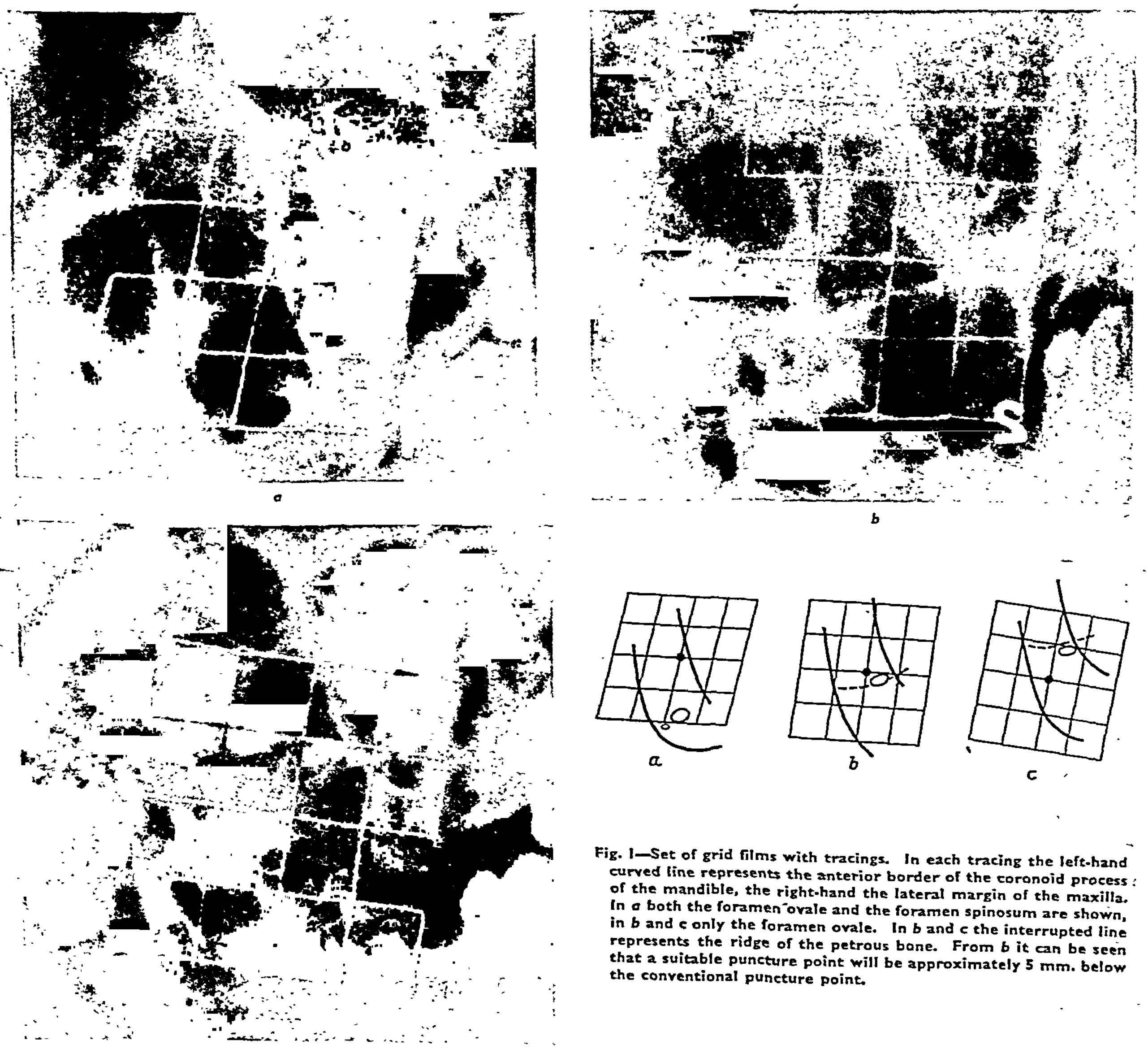

Fig. 1—Set of grid films with tracings. In each tracing the left-hand curved line represents the anterior border of the coronoid process of the mandible, the right-hand the lateral margin of the maxilla. In *a* both the foramen ovale and the foramen spinosum are shown, in *b* and *c* only the foramen ovale. In *b* and *c* the interrupted line represents the ridge of the petrous bone. From *b* it can be seen that a suitable puncture point will be approximately 5 mm. below the conventional puncture point.

TABLE II—MAXIMUM RATE OF URINE FLOW IN PATIENTS THOUGHT TO HAVE ADRENAL DEFICIENCY

Case no.	Diagnosis	Volume of water taken (ml.)	Maximum rate of urine flow (ml. per min.)
7	Anorexia nervosa	1000	6.9
20	"	840	8.4
1[illegible]	Primary ovarian deficiency	900	7.4
21	" "	1000	15.3
22	Myxœdema	1000	6.8
26	"	1000	8.4

(4) The water should be drunk when the oral cortisone activity is greatest, measured by eosinophil depression, and in adrenal deficiency this is about four to eight hours after the cortisone has been taken. If the water is taken when cortisone activity is not greatest, a full diuresis will not result (Oleesky and Stanbury 1951).

As can be seen from table II, in the conditions likely to be confused with hypopituitarism or with Addison's disease, such as myxœdema, primary gonadal deficiency, and anorexia nervosa, the maximum rate of urine-flow after ingestion of a litre of water exceeds 2 or 3 ml. per minute and is normal. Thus these conditions can be clearly separated from adrenal deficiency. The test has been very valuable in establishing or excluding the diagnosis of hypopituitarism.

Conditions in which there may be a failure to eliminate the water load—e.g., heart failure and cirrhosis of the liver (Adlersberg and Fox 1943, Ralli et al. 1951)—hardly enter into the differential diagnosis of adrenal insufficiency. In normal people given cortisone the rate of urine flow in a water diuresis can be increased above the control value (Rosenbaum et al. 1951), but the dose required is huge, 200–500 mg. a day, whereas the dose used in the adrenal-deficient is only 50–75 mg.

The rare salt-losing type of chronic renal disease described by Thorn et al. (1944) can be confused with Addison's disease; in fact it is usually mistaken for Addison's disease. There is a failure of water diuresis, and the Kepler test is positive but usually the blood-urea level is very high, and there is an inability, absent in adrenal deficiency, to produce a concentrated urine. The renal tubules are resistant to 'Pitressin,' deoxycortone, and parathyroid extract and clinically, on the one occasion on which it was given, cortisone failed to alter the course of the disease (Nussbaum et al. 1952). No one has specifically tried to rectify the failure of water diuresis with cortisone, and I have not had the opportunity of trying this, but the available evidence suggests that cortisone will not restore the water diuresis. Thus the salt-losing type of nephritis can probably be separated from Addison's disease by the test as described.

ADVANTAGES

The advantages of the test devised by Soffer and Gabrilove (1952) and of the one described here over the Kepler test are as follows:

(1) They are simpler to perform and less arbitrary.

(2) They do not require any chemical analysis and so can be done in the ward.

(3) They are more specific for adrenal deficiency in that not only is a defect (failure of water diuresis) present in the adrenal-deficient assessed but also the ability of the adrenal hormone known to rectify this defect can be shown.

The test described here has advantages over the test described by Soffer and Gabrilove (1952) in that less time is required and the volume of water drunk can be adjusted to suit each patient. A patient of even moderate intelligence can coöperate by collecting the specimens and noting the times at which they are passed. The only calculation involved—that of the urine flow—is very simple.

SUMMARY

A simple test for adrenocortical insufficiency is described. It is similar to that of Soffer and Gabrilove (1952) but does not require consumption of a large volume of water.

It is suggested that tests of this type should supersede the Kepler test because they are simpler to perform and are more specific indicators of adrenal insufficiency.

Thanks are due to the physicians at the Manchester Royal Infirmary and the Royal Infirmary, Sheffield, for permission to study their patients.

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PARATHYROID TUMOUR WITH HYPERPARATHYROIDISM AND COEXISTENT GASTRIC AND DUODENAL ULCERATION

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IT is generally accepted that primary hyperparathyroidism is the result of hypersecretion of one or more of the parathyroid glands, caused usually by an adenoma, occasionally by hyperplasia and hypertrophy, or rarely by a carcinoma of the gland. It is, however, not widely known that an adenoma of the parathyroid may sometimes reach considerable size and may even contain calcium deposits. Some of these large tumours, particularly those located in the upper mediastinum, have been mistaken for substernal thyroid (Hirsch 1937) or aneurysm of the innominate artery (Bergstrand 1931).

In primary hyperparathyroidism the patient's life depends on the diagnosis being made before irreparable damage has been done, particularly to renal function. The following case is recorded (1) because it illustrates the fallacies which may arise in diagnosis; (2) because of the unusually large parathyroid tumour in the upper mediastinum; and (3) because of the coexistence of gastric and duodenal ulceration.

CASE RECORD

A widow, then aged 46, had her left kidney removed in 1941 for multiple renal calculi and hydronephrosis. In February, 1949, she felt a sharp pain in her right upper arm, and radiography revealed a pathological fracture of the upper third of the right humerus. This lesion was attributed to metastases, because radiography showed a round well-defined opacity as large as a big plum in the right upper mediastinum believed to be the primary tumour. The tumour and the fracture were treated by deep radiotherapy 2000r, but neither the size nor the density of this tumour responded to

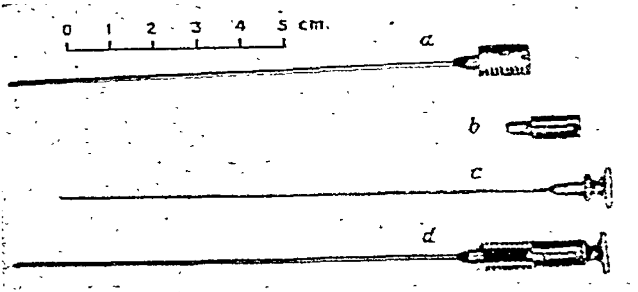

Fig. 3—*a*, 100-mm. needle ; *b*, 10-mm. stop ; *c*, stylet ; *d*, the above three parts assembled.

This difficulty is overcome by means of a stop or distance piece, drilled to allow the stylet of the needle to pass through it, which fits into the needle mount, receives in turn the mount of the stylet, and holds the tip of the stylet exactly 10 mm. short of the tip of the needle (fig. 3). If a film is exposed in the basal projection with this stop in place, the terminal 10-mm. portion of the needle shaft, being hollow, throws a fainter shadow than the rest, from which it can be easily distinguished. The length of the intracranial portion of the shaft is now estimated by comparison with the 10-mm. portion, and this can be done by eye to the nearest millimetre. The intracranial depth required for successful injection is usually 10–15 mm. Before the basal exposure the distance from the zygoma point to the mount of the stylet is measured and written down, and after it the measurement is repeated in case the needle has moved.

The stop must be left in place only during the basal exposure, for there is always a possibility that a small quantity of blood may collect in the hollow terminal portion and clot there. Similarly, needles must not be stored with their stops in place, lest traces of blood should be left in their terminal portions.

The stop enhances the value of the basal projection and shows that even a fairly experienced injector, estimating needle depth merely by touch, may make a large error. The first needle to pass the foramen ovale seldom secures adequate sensory loss ; but, when its depth is so accurately known, a second needle can be inserted beside it to a depth no less accurate. A recent improvement, not shown in fig. 3, is a longitudinal slot in the stop, which enables one to fit and remove it without withdrawing the stylet from the needle.

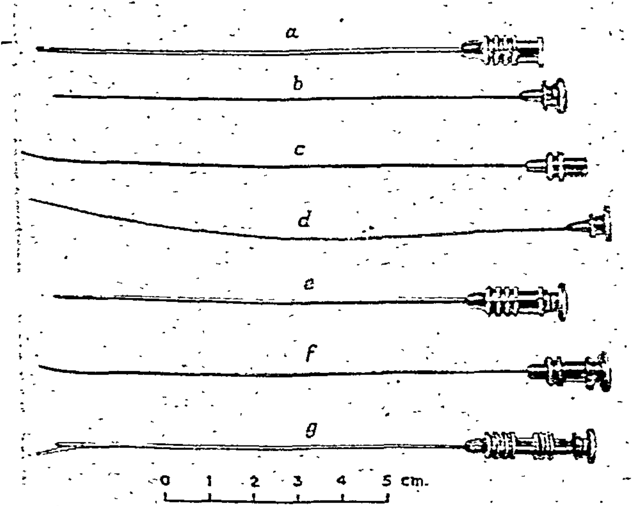

Fig. 4—Double needle : *a*, outer component ; *b*, outer stylet ; *c*, inner component ; *d*, inner stylet ; *e*, assembly of *a* and *b* ; *f*, assembly of *c* and *d* ; *g*, assembly of *a*, *c*, and *d*.

In some cases the sensory root lies so far medial to the foramen ovale that a successful injection can only just be achieved by passing the needle as close as possible to the ramus of the mandible, and in others the sensory root lies so far lateral that the needle has to pass equally close to the maxilla. Hence one can infer that there are also still more extreme cases in which the sensory root lies too far medial or lateral to be reached at all by an ordinary needle.

An analogous difficulty may occur in the vertical plane : the axis of the foramen ovale may be so much steeper than the anterior surface of the petrous bone that a needle passing through the foramen is bound to go above the sensory root. The double needle shown in fig. 4 is designed to reach the root in such cases ; the outer component is first fitted with the outer stylet and passed through the foramen, after which its depth is checked radiologically and adjusted if necessary. Next, the mouth of the outer component is turned in the direction most likely to prove favourable and the outer stylet is replaced by the inner component and inner stylet, which are advanced very cautiously from the moment when they begin to emerge from the outer component. The inner stylet is then withdrawn, and a trial dose of procaine is injected. If success does not follow, the inner component is half-withdrawn, both components are rotated slightly, the inner is advanced as before, and another trial dose is injected.

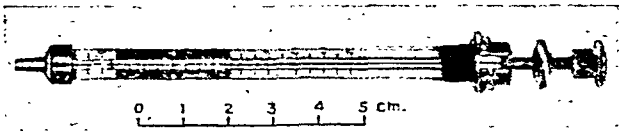

Fig. 5—1-ml. syringe graduated in units of 0·01 ml., with threaded stem and runner.

This needle has succeeded after prolonged failure with ordinary trigeminal needles, and has done so by reaching further medially, laterally, or downwards than they could reach, thus confirming the hypothesis which led to its invention. In so far as it has a greater diameter than they, it may be expected to cause more pain, and therefore it should seldom be used unless there is already analgesia or hypalgesia of the mandibular division. It might also be expected to be more liable to cause hæmorrhage, but that has not been observed. Its rigidity makes it easy to aim. One might well have hoped that it would lend itself to routine use, since the tip of its inner component can be moved in three dimensions without being withdrawn from the foramen ovale, and so ought to stand an improved chance of encountering the sensory root ; but in that respect it has proved disappointing and it by no means supersedes the single straight needle.

Measurement of Small Doses of Procaine and Alcohol

SPECIAL SYRINGE

For injection of the sensory root it is essential to measure the injected fluids to the nearest 0·01 ml. A suitable trial dose of 2% procaine is 0·03 ml., and a suitable individual dose of alcohol (though it may be repeated five or ten times in all) is 0·05 ml. With such doses one must know, and allow for, the exact capacity of the mount and shaft of the needle, which in the case of 100-mm. needles is usually 0·06 or 0·07 ml.

The syringe shown in fig. 5 is new only in the limited sense of being a fresh combination, so far as I know, of two earlier designs. As regards capacity and shape, it is of the type known as Waller's long vaccine syringe, which holds 1 ml. and is long and narrow enough to be graduated in units of 0·01 ml. In addition it incor-

11 tumours in the anterior and 5 in the posterior mediastinum Thus, the differential diagnosis of a round mass in the upper anterior or posterior mediastinum should include parathyroid tumour

In the present case the malignant character of the mediastinal mass was doubted by me for the following reasons (1) the tumour was well circumscribed and had a calcified rim, (2) it had displaced the trachea below the sternum, but there was no evidence of infiltration into the neighbouring structures, (3) comparison with previous chest radiographs showed no appreciable change in size and density of the tumour, and (4) the tumour had shown no response to deep X-ray therapy These findings, combined with general osteoporosis, fibrocystic changes in some bones, healed pathological fractures, and a history of multiple renal calculi of the left kidney and of calcified deposits in the right kidney led to the diagnosis of hyperparathyroidism This was confirmed by the high serum-calcium level of 22 mg per 100 ml and the lowered plasma phosphate level of 2 5 mg per 100 ml

In the final stage parathyroid poisoning (serum-calcium 22 mg per 100 ml) with renal failure (blood-urea 312 mg per 100 ml) were present However, the clinical picture was complicated by severe epigastric pain, the cause of which was gastric and duodenal ulceration Rogers (1946), Rogers et al (1947), and Robinson et al (1951) have drawn attention to the common occurrence of duodenal ulcers in hyperparathyroidism These workers suggest that the association of hyperparathyroidism with duodenal ulcer is too common to be merely coincidental, but so far they have been unable to explain the relationship The severe calcification of the abdominal aorta found in this case and the occurrence of arteriosclerosis in hyperparathyroidism may perhaps offer a clue to this association My radiological investigations of the pathogenesis of gastric ulcer in patients over 50 years of age have suggested that arteriosclerosis plays an important part in its pathogenesis (Elkeles 1949, 1950) In a high proportion of gastric ulcer cases calcification of the abdominal aorta was found I pointed out that, although the same does not apply to duodenal ulcer in general, those ulcers which develop in later life may also be due to arteriosclerosis I therefore suggest that a causal relationship exists between arteriosclerosis and the occurrence of gastric or of duodenal ulcer in hyperparathyroidism

Peptic ulceration is an important complication in hyperparathyroidism from the therapeutic standpoint In the present case the patient had been kept, for three months before admission to hospital, on a strict milk diet Albright and Reifenstein (1948) emphasise that a high blood-calcium level may easily lead to parathyroid poisoning when a high-calcium diet is given In this patient, therefore, the milk diet may have precipitated parathyroid poisoning with renal failure

SUMMARY

A case of primary hyperparathyroidism with a large partly calcified parathyroid tumour in the upper mediastinum and coexistent gastric and duodenal ulceration is described

The difficulties which may arise in the diagnosis of hyperparathyroidism are discussed

Parathyroid adenoma should be included in the differential diagnosis of tumours located in the upper mediastinum

Attention is drawn to the common association of hyperparathyroidism with gastric or duodenal ulceration, and to the danger of a strict milk diet, which may precipitate parathyroid poisoning

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I wish to thank Dr J Browning Alexander for permission to make use of the clinical records of this patient, and Dr Donald Hunter for his keen interest in this case and for confirming the diagnosis The case was referred to as case 5 by Mr J E Richardson in his Hunterian lecture to the Royal College of Surgeons of England on Feb 19, 1953

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GROWTH OF BACTERIA IN INTRAVENOUS INFUSION FLUIDS

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JUNIOR CLINICAL PATHOLOGISTS, BRISTOL ROYAL INFIRMARY

COMPLICATIONS of intravenous infusion are not uncommon Overloading of the circulation, thrombosis of the vein (Bolton Carter 1951), and infection of cut down wounds are well recognised mishaps We draw attention here to the possibility of a dangerous reaction caused by bacterial growth in the infusion fluid during the infusion This complication we have met twice within two years Both patients developed serious pyrexia while on intravenous infusion therapy lasting several days, and in each case large numbers of coliform bacilli were found in the infusion fluid These organisms are unlikely to have been present originally in the fluid

CASE-RECORDS

Case 1 —In May, 1950, a woman, aged 43, after an operation for excision of rectum, received intravenous therapy consisting of glucose and physiological saline solution On the second postoperative day, while still receiving the infusion, she developed an increase of pyrexia, for which no obvious clinical cause could be found Her temperature reached 103 2°F and remained raised for thirty six hours, but when the infusion apparatus was taken down the temperature settled rapidly (fig 1)

Investigation —0 5 ml of fluid was taken with sterile precautions from the tube of the giving set and cultured immediately on 5% horse-blood agar A profuse pure growth of a coliform bacillus was obtained Fluid taken from the bottle at the same time gave a very scanty growth of the same organism

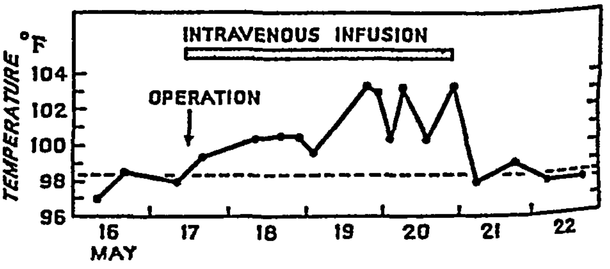

Fig 1—Treatment and temperature-chart of case 1

This organism grew both at room temperature and at 37°C, but better at 37°C It was non motile It fermented lactose saccharose maltose and mannitol with production of acid but not gas The Dulcitol was not fermented Indole was not produced The methyl red test was positive The Voges Proskauer reaction was negative The organisms grew in Koser's citrate medium

This organism therefore belonged to the anaerogenes group of coliform bacilli

The rubber tubing was opened throughout its entire length No flaws were detected and no clots were seen apart from some small ones in the shank of the needle

Case 2 —In June, 1952, a woman, aged 31, had intravenous infusion therapy continuously for three days during an no enlargement of the mediastinal lymph-nodes. A year later itching of the skin and a cough with production of sputum had developed. Radiography in 1948 showed enlargement of the lymph-nodes in the right hilar region. During the next few years the patient complained of progressive fatigue, dyspnœa, and lumbar pain radiating down the legs. Chest radiograms from March, 1950, revealed a wide mediastinal shadow. In 1951 dyspeptic symptoms developed, and a peptic ulcer was disclosed radiographically. Since the diagnosis of Hodgkin's granuloma the patient has for periods received treatment with X rays or with nitrogen mustards. The general condition has fluctuated, but each renewed course of treatment is still followed by a satisfactory remission.

Reactions to Alcohol.—Since 1944 the patient has been unable to tolerate alcohol. At first a sense of oppression in the chest developed, sometimes accompanied by retrosternal pain, when he drank a bottle of lager (375 ml., alcohol content about 3%). At the examination in 1951 he stated that ingestion of alcohol led to a sensation of suffocation and development of the aforementioned pain. He also complained of lumbar pain radiating down the right thigh posteriorly; the pain developed two or three minutes after he had had a glass of schnapps and persisted for about twenty minutes.

Case 2.—A woman, aged 26, noticed enlargement of her cervical lymph-nodes for the first time in 1944. Histological examination of a biopsy specimen from a lymph-node showed Hodgkin's granuloma. Before her admission to the Radium Centre in Aarhus she had received five courses of X-ray therapy to both sides of the neck, the thorax, the spine, and the left greater trochanter. On admission here in February, 1950, she was rather weak, with a fluctuating temperature and erythrocyte-sedimentation rate (E.S.R.) 120 mm. in 1 hr. (Westergren). Firm and slightly enlarged lymph-nodes were noticed on both sides of the neck, in the right axilla, and in the right inguinal region. Radiography revealed destruction of the right transverse process of the second thoracic vertebra and of the right clavicle, a defect of the third lumbar vertebra, a nodular density in the ilium, and large infiltrations in both lungs. Some improvement resulted from treatment with triethylene melamine. In September, 1951, she was rather weak and said she had been bedridden during the greater part of the period since admission to hospital. Radiography showed necrosis in the right humerus.

Reactions to Alcohol.—At this examination the patient said that for the last three years she could not tolerate alcohol. Immediately after the ingestion of a glass of wine or a bottle of lager intense pain developed in the affected areas, mainly on the anterior aspects of the lower extremities; the pain generally persisted for fifteen minutes.

Case 3.—A man, aged 26, fell ill in 1949 with enlargement of the lymph-nodes in the left axilla, pain in the right shoulder radiating to the arm, and itching. Histological examination of an excised lymph-node showed Hodgkin's granuloma. On admission in January, 1949, to the Radium Centre in Aarhus he had slight enlargement of the lymph-nodes of the neck and supraclavicular fossæ. Radiography revealed a mediastinal tumour but no infiltrations in the lungs. The E.S.R. was 34 mm. in 1 hr. (Westergren). During the next three years he was treated repeatedly, partly with nitrogen mustards and partly with arsenicals and X rays.

Reactions to Alcohol.—As early as a year before the patient fell ill he had noticed that the ingestion of alcohol caused immediate pain in the right side of his chest, rather liberal quantities being necessary to produce the pain at first. Immediately after a course of nitrogen mustards in 1951, during which his general health improved, he could again tolerate alcohol, but a month later small quantities of lager produced pain in the right side of his chest.

Case 4.—A woman, aged 24, noticed enlargement of the lymph-nodes of her neck and later also of her right axilla in 1947. In October, 1948, she was admitted to the Radium Centre in Aarhus. In addition to the enlarged lymph-nodes a mediastinal tumour was found by radiography. Histological examination of a biopsy specimen of a lymph-node showed Hodgkin's granuloma. The patient received a course of nitrogen mustards. In February, 1949, she was readmitted with a complaint of constant oppression in her chest and pain in her right arm. X-ray therapy was given. In January, 1950, the mediastinal tumour had increased, and a month later radiography showed necrosis in the sternum. At that time the patient stated that burning retrosternal pain developed whenever she drank wine or beer. Usually the pain developed in a few minutes and persisted for up to half an hour

Case 5.—A man, aged 34, noticed enlargement of the lymph-nodes of his right supraclavicular fossa for the first time in 1947. Examination at the Radium Centre in Aarhus in February, 1948, revealed enlargement of the lymph-nodes of the neck and the supraclavicular regions. Chest radiography showed enlarged hilar shadows with perihilar infiltrations. Histological examination of an excised lymph-node from the lateral cervical region showed Hodgkin's granuloma. The patient received a course of nitrogen mustards and, later, one of X-ray therapy. An examination six months later revealed atelectasis of the middle lobe of the right lung. A further course of nitrogen mustards was given. A year later gastric symptoms developed. The patient died in March, 1951. At that time there was generalised Hodgkin's disease with skeletal foci.

Reactions to Alcohol.—From October, 1948, the patient could not tolerate alcohol. Immediately after the ingestion of even very small quantities of alcohol intense pain developed over the lower thoracic region. He noticed this pain for the first time once when he had had a glass of mild beer with a meal. Thereafter pain developed whenever he took an alcoholic drink; merely one or two mouthfuls of lager could induce the pain, which persisted for half an hour. For prophylactic reasons he had occasionally taken two analgesic tablets when he intended to have a glass of lager. On one occasion when he had drunk a glass of red wine he had to lie down owing to intense pain. The pain was not accompanied by nausea or vomiting. Even immediately after the end of a course of nitrogen mustards he could not tolerate small quantities of alcohol.

Case 6.—A man, aged 28, fell ill in 1948 with enlargement of the cervical lymph-nodes. Shortly afterwards pain developed over the sacral and left gluteal regions. Radiography revealed enlarged lymph-nodes in the hilar regions but no osseous abnormalities in the pelvis and hips. Histological examination of an excised lymph-node showed Hodgkin's granuloma. During the next year dyspnœa on exertion and progressive lumbar pain developed.

Reactions to Alcohol.—At the time when the diagnosis was established the patient could drink a bottle of lager without any subsequent pain, but six months later intense pain developed in the lumbar region and over the sacrum after ingestion of even very small quantities of alcohol.

Case 7.—A woman, aged 52, fell ill in 1951 with swelling below the right clavicle and transitory swelling of the right arm. Six months later intense itching of the skin developed. On admission to Marselisborg Hospital in September, 1952, she had an ill-defined swelling below the right clavicle, the size of a clenched fist, and a slightly enlarged lymph-node in the right axilla. There were numerous scratch marks on the skin. Histological examination of an excised infraclavicular lymph-node showed Hodgkin's granuloma.

Reactions to Alcohol.—Shortly after the onset of the disease the patient had noticed that pain developed in the right arm almost immediately on ingestion of small quantities of alcohol; even beer with an alchol content of 1% could induce the pain. During her stay in hospital such an attack of pain was provoked by oral administration of 10 ml. of 50% alcohol. Five minutes later intense pain developed in the right shoulder and arm and persisted for an hour.

Investigation.—To find out if the pain might be due to vasodilation by the alcohol, various other vasodilators were administered. Glyceryltrinitrate ointment was applied to the skin over the enlarged lymph-nodes, but no pain developed. A subcutaneous injection of histamine hydrochloride 0·5 mg. produced a hectic flush of the cheeks and headache but did not excite pain in the shoulder. An intravenous injection of nicotinic acid amide 2 ml. gave similar well-marked symptoms of vasodilation but no pain in the shoulder.

Treatment and Progress.—The patient was subsequently transferred to the Radium Centre in Aarhus, where she was given X-ray therapy to the enlarged lymph-nodes. A month later she was completely well; the itching of the skin had disappeared, and she could tolerate alcohol; even after a large glass of whisky the usual pain in the arm and shoulder did not develop.

Case 8.—A man, aged 31, with a past history of good health, developed an attack of acute pain across the chest, radiating from the manubrium sterni, after having drunk a glass of lager in May, 1951. Shortly afterwards enlargement of the cervical lymph-nodes was observed, and a biopsy specimen through one of two rubber covered apertures in the screw cap of a sterile Winchester bottle containing a little solid mercuric chloride as antiseptic Through the other aperture passed a sterile needle attached, by a short length of rubber tubing on its outer end, to a glass tube containing sterile cotton-wool This acted as an outlet for air but prevented contamination of the apparatus Fluid from the bottle was allowed to run slowly through the tubing into the Winchester bottle at the rate of a slow infusion so that 1 litre bottle emptied in about twenty four hours after which it was changed for a fresh one At the beginning of the experiment and at intervals of twenty-four hours fluid was taken from the needle with aseptic precautions and the viable organisms were counted

Several experiments were made with large and small inocula, and showed that the organisms multiplied in spite of three or more changes of bottle in every case when the fluid was not acid Table III shows the results of several typical experiments As suggested above, the failure of the organisms to persist in the dextrose is presumably due to the low pH of that solution

DISCUSSION

Though it might be thought that the organisms isolated from the infusion apparatus in our cases were already present in the bottles before transfusion we consider this very unlikely The bottles are obtained from a reputable commercial source, and no other infected bottles were discovered during the widely separated periods when these incidents occurred It seems more likely that the infection took place during the infusion, either while the bottles were being changed or by contaminated air sucked into one of the bottles through the air-replacement tube

Coliform organisms are known to be present in the air and dust of wards, and can multiply in simple fluids It is well known that coliform bacilli can use ammonium salts as the sole source of nitrogen and simple carbon compounds as a source of energy Under certain conditions growth can take place in even simpler media Bigger and Nelson (1943) succeeded in growing coliform bacilli in distilled water to which had been added small quantities of talc or other inorganic substances, and they suggested that, under these conditions, the metabolic requirements of the bacilli were obtained from atmospheric ammonia and carbon dioxide We have shown that small numbers of coliform bacilli can multiply in Hartmann's solution with 5% dextrose or in physiological saline solution, under the conditions of an intravenous infusion Once they begin to multiply in the tubing of the infusion apparatus, coliform bacilli may continue to grow, even though the bottles are changed This would happen, however, only if the same giving set were retained In such a case a heavy concentration of organisms can be built up in the infusion set, with serious consequences to the patient

Such a sequence of events should be considered as a possible cause of an obscure pyrexia in a patient on prolonged intravenous therapy

Bolton Carter (1951) has suggested that in prolonged infusions the vein used should be changed periodically to reduce the incidence of thrombophlebitis We suggest that in the course of intravenous infusions likely to last several days a new giving set and a new needle should be used about every twenty-four hours However, if the patient has very few good veins, it would seem permissible to change the giving set but not the needle because the volume of possibly contaminated fluid in the needle and its attached short length of tubing is very small

We should also like to emphasise the importance of strict asepsis during the process of changing bottles as well as when setting up an intravenous infusion Further, we think that the addition of a sterile cotton wool filter to the air replacement tube of the infusion bottle is advisable, to prevent organisms from entering the fluid in the apparatus from the air

A common procedure in many hospitals is to change from a bottle of blood to a bottle of crystalloid solution by simply transferring the rubber bung with its attached clot-filter and giving set Such a procedure increases the risk of contamination of the infusion fluid, because blood is not a sterilised fluid In changing from infusion of blood to infusion of crystalloids, therefore, a fresh giving set should always be used

SUMMARY

Two cases are described in which a patient receiving prolonged intravenous therapy developed severe pyrexia due to growth of coliform bacilli in the infusion apparatus

Small numbers of coliform bacilli (about 10 in one experiment) were introduced into an intravenous infusion running in the laboratory under conditions similar to those of intravenous therapy in patients Considerable multiplication took place when crystalloid solutions such as Hartmann's fluid with 5% dextrose or physiological saline solution were used, in spite of changing bottles

In cases of pyrexia of unknown origin in patients receiving intravenous therapy a bacterial growth in the infusion set should be considered as a possible cause

Attention is drawn to the importance of aseptic precautions in the administration of intravenous fluids

During a long-continued intravenous infusion the giving set and, if possible, the needle should be changed at least once in every twenty-four hours

We wish to thank Mr R V Cooke, F R C S, for drawing our attention to this problem, and Dr W A Gillespie and Dr G K McGowan for their help and advice

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Medical Societies

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Abdominal Exploration and Re-exploration

ADDRESSING the section of surgery on March 10 Mr ROBERT COOKE observed that in cases of non penetrating injury of the abdomen exploration was too often deferred disastrously, because either the evidence of visceral injury seemed meagre or resuscitation was deemed inadequate Records of a large hospital showed a failure to recognise a second or third lesion from which death ensued

Diagnostic laparotomy was often a real necessity even today despite the most carefully taken history and the most complete examination, supported by diagnostic aids Even when the diagnosis of gall stones or appendicitis seemed well established, a properly conducted exploration might show that the symptoms were referable to another and more serious lesion Mr Cooke mentioned the tragedies that might result from ignoring the presence of occult blood in the fæces the cause must be ascertained promptly In the newborn intestinal obstruction demanded early exploration to determine the cau since multiple obstructions might be present the inc must be large enough to allow gentle, complete eventration of the bowel, so that the whole picture was seen before corrective surgery was undertaken

Mr Cooke laid much emphasis on the steady loss of life resulting from want of further resolute surgery when obstruction followed an abdominal operation This was due to a faulty conception of what was going on inside or to want of sufficient humility and courage to say that another operation was necessary because something had gone wrong the abuse of various suction tubes with the support of intravenous therapy too often gave rise to a false sense of security We talked of paralytic ileus, when we should be operating for mechanical obstruction

For twenty years Mr Cooke had been urging wider exploration in cases of very advanced abdominal neoplasm It was astonishing what could be accomplished enopause. In Sheldon's (1935) series the 277 male ases were fairly evenly spread on either side of the peak ncidence at 45–50 years; only 2 of his 14 female cases occurred before this age. He has since stated (Sheldon 1951) that 1 of his 2 young female cases did not have proven hæmochromatosis and was included in his chart of the age-incidence in error; hence of his 13 female patients only 1 developed the disease before the menopause.

In view of the small number of women in Sheldon's series I have investigated the age-incidence of a further 202 male and 20 female cases published since 1935.* Table I and the accompanying figure show the age-distribution of these patients (at the time of diagnosis when this is stated) and of Sheldon's patients. In the present series too the male cases were much more evenly spread throughout the adult years of life than the female cases, only 2 of the women being under 45 years of age. It is of particular interest that 1 of these 2 young women, whose case was reported by Murray-Lyon (1936), had had amenorrhœa for thirteen years before dying of hæmochromatosis at the age of 34.

TABLE I—AGE AND SEX DISTRIBUTION OF 512 CASES OF HÆMOCHROMATOSIS

Cases	Age-group (yr.)											
	10–20	21–25	26–30	31–35	36–40	41–45	46–50	51–55	56–60	61–65	66–70	71–75
Males:												
Sheldon (1935) ..	..	2	7	13	37	48	59	56	34	9	8	4
Houston ..	1	1	4	5	24	31	37	41	34	15	4	5
Total	1	3	11	18	61	79	96	97	68	24	12	9
Females:												
Sheldon (1935) ..	..	..	1	..	..	..	2	5	1	3	1	..
Houston ..	..	..	..	1	..	1	4	3	6	2	..	3
Total	..	..	1	1	..	1	6	8	7	5	1	3

Hæmochromatosis, then, probably results from excessive intake of iron, due either to an inborn error of metabolism or to multiple transfusions (Kark 1937, Schwartz and Blumenthal 1948); and there is no known

TABLE II—BLOOD PICTURE IN HÆMOCHROMATOSIS TREATED BY REPEATED VENESECTION

Date	Hb (%)*	Red cells (million)	Hæmato-crit (%)	Mean corpuscular volume (cu.μ)	Mean corpuscular diameter (μ)	Colour-index	Serum-iron (μg. per 100 ml.)	Plasma-protein (g. per 100 ml.)			Blood removed (pint)
								Total	Albumin	Globulin	
Nov. 22, 1951	117	5·8	53	91	7·2	1·0	325	..	..	..	1
Dec. 6 ,,	107	5·2	48	91	7·2	1·0	317	..	..	..	1
,, 13 ,,	107	5·4	49	91	7·1	..	254	..	..	..	1
,, 20 ,,	95	4·2	46	..	..	..	244	..	..	..	1½
,, 28 ,,	103	5·2	49	94	7·2	1·0	..	..	..	..	1
Jan. 3, 1952	99	4·9	48	99	7·4	1·0	250	..	..	..	1
,, 10 ,,	99	5·2	48·5	93	7·2	1·0	..	..	..	..	½
,, 17 ,,	101	4·9	48	98	7·3	1·0	..	..	..	..	½
,, 24 ,,	105	4·9	47·5	97	7·2	1·0	313	..	..	..	1½
,, 31 ,,	104	5·0	50	100	6·9	1·0	..	7·55	4·92	2·63	1
Feb. 8 ,,	94	4·7	48	102	7·0	1·0	262	..	..	..	1½
,, 14 ,,	98	4·4	46	104	..	..	218	..	..	..	1½
,, 21 ,,	101	5·0	49	98	7·0	1·0	255	..	..	..	1
,, 28 ,,	101	4·7	50	107	7·1	1·1	..	..	..	..	1
Mar. 6 ,,	111	5·1	49·5	96	..	..	..	6·43	4·00	2·43	1
,, 13 ,,	102	4·5	45	100	..	..	250	..	..	..	1
,, 20 ,,	96	4·3	48	..	..	..	242	..	..	..	1
,, 27 ,,	109	4·8	51	107	..	..	238	..	..	..	1
April 3 ,,	100	4·8	50	105	7·1	1·0	238	..	..	..	1
,, 10 ,,	98	5·0	48	96	7·0	1·0	..	..	..	..	1
,, 17 ,,	101	4·4	47	108	7·0	..	247	..	..	..	1
,, 24 ,,	104	5·2	51·5	99	7·1	1·0	..	..	..	..	1
May 1 ,,	96	4·9	48	98	..	..	..	..	..	..	
,, 8 ,,	100	5·3	49	93	7·1	1·0	204	6·35	4·70	1·65	1
,, 15 ,,	97	5·1	47·5	94	..	..	215	..	..	..	1
,, 22 ,,	100	5·0	50	100	7·0	..	..	..	..	..	1
,, 29 ,,	103	5·2	50	97	7·0	1·0	218	6·90	4·90	2·00	1
June 5 ,,	106	5·2	49	94	7·0	..	..	..	..	..	1
,, 12 ,,	104	5·2	47	90	7·0	1·0	242	..	..	..	1
,, 19 ,,	101	4·7	48	102	..	..	212	..	..	..	1
,, 26 ,,	99	4·5	46	102	7·0	1·1	224	..	..	..	1
July 3 ,,	109	5·0	47	94	..	..	218	7·50	5·10	2·40	1
Aug. 7 ,,	92	5·6	51	91	..	..	225	..	..	..	1
,, 14 ,,	108	5·1	50	98	..	..	245	..	..	..	1
,, 28 ,,	108	5·4	50	93	..	1·0	..	..	..	..	1½
Sept. 11 ,,	107	4·8	49	..	..	..	246	..	..	..	1
,, 25 ,,	99	..	47	..	..	..	224	..	..	..	1
Oct. 10 ,,	109	5·1	48	94	..	..	232	..	..	..	1
,, 23 ,,	106	5·2	49	94	..	..	208	..	..	..	1
Nov. 6 ,,	114	..	51	..	..	..	..	7·03	4·89	2·14	1
,, 20 ,,	114	5·7	49·5	87	..	..	220	..	..	..	1
Dec. 4 ,,	105	5·2	51	..	..	..	220	..	..	..	1
,, 18 ,,	109	5·2	49	..	..	..	..	..	..	..	½
Jan. 1, 1953	107	5·2	48	..	..	..	216	..	..	..	1½
,, 15 ,,	112	5·0	49	..	..	..	220	6·33	4·32	2·01	1½
,, 29 ,,	104	5·5	50	..	..	..	..	..	..	..	1½
Feb. 13 ,,	106	4·8	50	..	..	..	228	..	..	..	1½
,, 26 ,,	104	5·6	49	..	..	..	221	..	..	..	1½
Mar. 12 ,,	105	4·9	49	..	..	..	..	..	..	..	1
,, 26 ,,	101	5·2	49	..	..	1·0	223	..	..	..	1

* 15·6 g. = 100%.

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* In the list of references the papers reporting these cases are marked with an asterisk.

who emphasised the synthetic functioning of the mind and students of neurology and endocrinology, who showed the mechanisms linking mental activity with muscular or glandular responses, also contributed to the synthetic outlook Freud drew attention to hysteria as a symbolic response Gradually, too, it became clear that the vegetative neurosis, innervated by the autonomic, is the organism's physiological response to chronic or recurrent emotional states, and there is evidence of affinity between certain emotional conflicts and certain bodily tissues

Dr Alexander relates his outlook to various types of disease—gastro-intestinal, respiratory, cardiovascular, skin, metabolic, and endocrine, and disorders of the joints and musculature Disturbances of the sexual functions are discussed by Dr Therese Benedek There is a brief concluding chapter on therapy The book is clearly and sensibly written, and has a useful bibliography and indexes

Trichlorethylene Anæsthesia

GORDON OSTLERE, M A , M B Camb , D A , deputy first assistant, Nuffield department of anæsthetics, University of Oxford Edinburgh E & S Livingstone 1953 Pp 83. 7*s* 6*d*

A SURVEY of an extensive series of references can easily become tedious , but, though Dr Ostlere has scoured the literature of his subject, his book reads pleasantly There are no unnecessary repetitions, yet judicious cross-references reassure the reader that nothing important is being left out

Despite its title, the book includes, very properly, a chapter on analgesia—though it is a little confusing to find here the chief reference to cæsarean section In the same chapter the author misrepresents Seward, whose " requirements " referred to " anæsthetic mixtures suitable for intermittent self-administration " and not to " obstetrical analgesics " generally An impression is given that inhalation analgesia is the only sort available for use by midwives, whereas in fact they are now permitted to use pethidine, regarded by many as the most useful aid of all Of the various obstetric inhalers designed to overcome variability in vapour concentration, the only one described is the Epstein Macintosh, which, as the author admits, was not approved by the Medical Research Council

Though full references are given to dangers and accidents from the use of trichlorethylene, some anæsthetists will think too little has been made of the risks (e g , that of associating adrenaline with it), and the accidents are for the most part dismissed as due to wrong technique On the other hand Dr Ostlere states clearly what he regards as the limitations of this drug, and he gives a full account of its pharmacology

Vocational Services for Psychiatric Clinic Patients

THOMAS A C RENNIE, M D , Cornell University Medical College , MARY F BOZEMAN, Rehabilitation Project, National Association for Mental Health Cambridge, Mass Harvard University Press London Oxford University Press 1952 Pp 100 8*s*

THIS book describes a study of the vocational problems presented by 380 men and women, aged 15–72 attending six different psychiatric outpatient clinics in the United States of America The data have been analysed in an attempt to discover the extent to which such problems are presented by psychiatric outpatients, the vocational services needed to help in the solution of these problems, and the ways in which clinics and employment agencies can best cooperate in the patients' interests The problems are analysed in relation to age, social and educational background, and medical diagnosis Special groups such as school-leavers, university students the physically handicapped, and the aged are discussed Although the *social scene in America is somewhat* different from our own, the similarities are enough to make this study of interest here , but the book might be more simply written, and the modest conclusions presented less elaborately. Those of particular significance for us are the need to evolve better methods of vocational guidance, and to provide more suitable opportunities for employment for the psychiatrically handicapped and for the aged, and the need for closer coöperation between employment agencies and clinics, preferably by personal consultation between all concerned with the welfare of any patient

Visual Anatomy

Thorax and Abdomen SYDNEY M FRIEDMAN, M D , PH D , professor of anatomy, University of British Columbia Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1952 Pp 203 75*s* 6*d*

THIS is the second volume in Professor Friedman's series dealing with regional anatomy for the student who has already completed a dissection Unofficial trials with the first volume, on the head and neck, seem to show that he is succeeding in his intention, which is " to present briefly and forcefully that Anatomy which is essential for the practice of Medicine " In this volume the approach is again synthetic, starting with the bones and on these building up successive layers of soft tissues , as before, the emphasis is laid on the illustrations, of which there are 91 These illustrations are sufficiently unusual to compel attention, and in many cases their originality of viewpoint and construction is most helpful The accompanying text is clear and concise, and includes a great deal of information shorn of minutiæ Over these minutiæ trouble may of course arise, for there can be many opinions on what constitutes an " essential " detail Professor Friedman includes a brief section on the back and spinal cord, and another on surface anatomy The plan of these books is stimulating, and it is being energetically carried through , we shall look forward to the volume on the limbs when it appears The price, however, seems excessive

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New and Nonofficial Remedies (Philadelphia and London J B Lippincott 1952 Pp 838 27*s*)—To be admitted to the American pharmaceutical *What's What*, a new and non official remedy must survive a grilling by the council on pharmacy and chemistry of the American Medical Association The rules are formidable, and though the council emphasise that the acceptance of a particular preparation is not to be interpreted as an endorsement or a recommendation, it is hard to read the rules without admiring the drugs that get through and sympathising with those that fail The first part of the book includes monographs on the action and use of accepted preparations , and later on there are details of tests and standards for the drugs for which official standards are not available In small print at the end is a tremendous list of unaccepted products, with references to reports, presumably cautionary, that have been published about them Perhaps the manufacturers of ' Genuine Gluten Flour ' and a brand of nitrogen trichloride (agene) were not too disappointed at the rejection of their products

Diseases of Metabolism *Detailed Methods of Diagnosis and Treatment* (3rd ed Philadelphia and London W B Saunders 1952 Pp 1179 75*s*)—In this old friend, back *from a rejuvenating holiday with Prof Garfield G Duncan,* the editor, and his publishers, the form has not been changed, though some sections have been assigned to new authors and have in consequence been greatly modified or entirely rewritten A welcome chapter has been included on porphyrin metabolism, and the sections on water balance, diabetes, and vitamin disorders have been extensively revised Each chapter, as of old, concludes with a substantial list of original references No book is perfect, and there are some mistakes and omissions in this one , but the original aim was to help *to bridge the gap between the investigator and the practising* physician, and the new edition continues to do that, and to do it well

Recent Advances in Anæsthesia and Analgesia (7th ed London J & A Churchill 1953 Pp 410 30*s*)—The five years since the previous edition have provided *Dr C* Langton Hewer with so much new material that not only has the book increased by nearly 60 pages but the type is smaller and the pages fuller The new material ranges from apparatus and drugs to such new and controversial innovations as anæsthesia with hypotension Dr Langton Hewer *still retains* the habit of freely inserting his own comments These are always helpful though they are becoming noticeably, and perhaps justifiably, *more pungent with each edition* The book still remains one of the best reference sources to anæsthetic literature In future editions the author should perhaps set a narrower interpretation on " recent," for his work will soon be more accurately described as a textbook

SPECIFIC WATER DIURESIS TEST FOR ADRENOCORTICAL INSUFFICIENCY

S. OLEESKY
M.Sc., M.B.Manc., M.R.C.P.
LECTURER IN THERAPEUTICS, UNIVERSITY OF SHEFFIELD

THE diagnosis of adrenocortical insufficiency still resents many difficulties (de Mowbray and Bishop 953). The most useful laboratory aid is considered to e the Kepler test (Robinson, Power, and Kepler 1941). his test can be divided into two parts: the first is an ssessment not only of the ability to have a water diuresis ut also of the changes in diurnal rhythm which may be resent in adrenal deficiency; and the second part is guide to the ability to conserve chloride and to eliminate rea. Thus the test unites the results of many phenomena nd is not an analysis of one particular defect in adrenal leficiency.

The test as generally performed is tedious and comlicated. Often the patient is unable to drink the large olume of water required, and the second part of the est requires a relatively complicated analysis of blood nd urine. As regards the second part of the test, many ases have been published in which the Kepler factor A is igh, with the first part of the test positive—e.g., in 5* out of the 74 cases of Addison's disease of Levy, Power, nd Kepler (1946)—and some observers may then have rroneously excluded adrenal insufficiency. There may lso be false positive and false negative responses to the first part of the test (Levy et al. 1946); in fact in another 9 out of the 74 cases there was a false negative result to the first part of the test.

It is now well established that the failure of water diuresis in adrenal insufficiency due either to hypopituitarism or to Addison's disease can be restored with cortisone (Chalmers and Lewis 1951, Garrod and Burston 1952, Leaf and Mamby 1952, Oleesky and Stanbury 1951, Slessor 1951, Thorn et al. 1951). Relying on this, Soffer and Gabrilove (1952) have proposed a simplified version of the Kepler test. Briefly, after a water load of 1500 ml. the volume of urine produced is measured over the next five hours, and this volume should exceed 800 ml. and in the normal usually lies between 1200 and 1900 ml. If the volume is small, the test is repeated after oral cortisone. In adrenal insufficiency, either primary or secondary to hypopituitarism, the volume of urine produced is small but is increased to normal after oral cortisone.

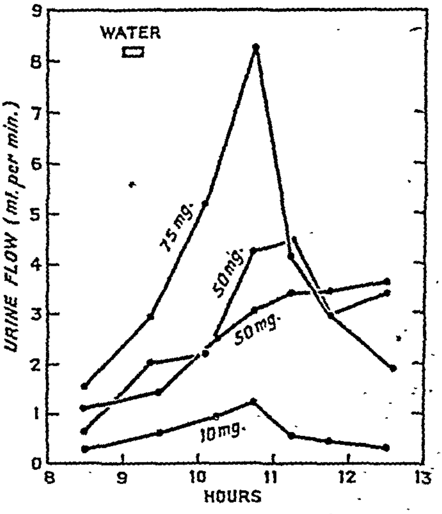
TABLE I—GREATEST RATES OF URINE-FLOW IN PATIENTS WITH ADRENAL DEFICIENCY WITH AND WITHOUT CORTISONE

Case no.	Diagnosis	Controls		Observations after cortisone		
		Volume of water taken (ml.)	Max. rate of urine-flow (ml. per min.)	Dose of cortisone (mg.)	Volume of water taken (ml.)	Max. rate of urine-flow (ml. per min.)
1	Hypopituitarism	1000	1·8	50	1000	13·6
2	,,	1000	1·8	50	1000	10·0
9	,,	900	0·6	50	880	8·7
10[1]	,,	800	0·72	75	870	1·8
14[2]	,,	1000	2·5	50	1000	7·3
16[3]	,,	600	1·2	75	600	8·2
24	,,	800	0·9	75	1000	16·3
3	Addison's disease	1000	0·5	50	920	4·1
18[4]	,,	650	0·73	—	—	—
27	,,	850	2·7	75	850	6·8

1. Patient was a pituitary giant with secondary hypopituitarism, and the dose of cortisone may have been too low, and so only a partial restoration to normal was achieved.
2. Diuresis under cortisone was cut short with intravenous pitressin. Otherwise a greater urine-flow would probably have been reached.
3. Control observation when the patient was on 10 mg. and the second observation when on 75 mg. of intramuscular cortisone daily.
4. Patient ill and died before second part of test could be performed.

AUTHOR'S MODIFICATION

The disadvantages of the test devised by Soffer and Gabrilove (1952) lie in the not infrequent inability, particularly of the adrenal-deficient, to ingest 1500 ml. of water without vomiting, and the fact that each part of the test lasts five hours. A procedure just as simple is for the patient, after overnight deprivation of fluid, to drink as much water as possible up to a total of 1 litre within twenty minutes. The urine-flow is then measured at intervals of fifteen to twenty minutes for two and a half hours. The test can be repeated next day with about the same volume of water, but this time 50–75 mg. of cortisone is given by mouth four hours before the water is taken. The results in any particular case can be reported by recording the maximum rate of urine-flow after taking a particular volume of water, and the maximum rate after the same volume of water but under the influence of a certain amount of cortisone. In adrenal insufficiency the maximum rate of urine-flow will be low—i.e., less than 2 or 3 ml. per minute, and will be restored to normal with cortisone. Table I shows the application of this test to 3 patients with Addison's disease and 7 patients with hypopituitarism. It is well known that treatment with deoxycortone does not affect water diuresis in man and so will not invalidate the results obtained.



A series of water diureses under differing daily doses of cortisone in case 16 with Simmonds's disease. The dose of cortisone is marked on each diuresis curve. The increase in the maximum rate of urine-flow with increasing dose of cortisone is clearly shown.

It is necessary to observe the following precautions:

(1) The patient's serum-sodium level must not be very low, because then even cortisone will fail to produce a normal water diuresis (Garrod and Burston 1952). At one time in case 16, with Simmonds's disease, there was a failure of water diuresis after 100 mg. of oral cortisone, although eosinophil depression had been achieved. At that time the patient's serum-sodium level was only 114 m.eq. per litre and serum-chloride 88 m.eq., though later she had a normal diuresis on 75 mg. of intramuscular cortisone per day, when her serum-sodium was 144 m.eq.

(2) The dose of cortisone must be not less than 50–75 mg., because sometimes a lower dose may fail to restore fully the rate of urine-flow (Thorn et al. 1951). The accompanying figure shows the effect of gradually increasing daily intramuscular doses of cortisone on the water diuresis in case 16. The water load was 600 ml. in each experiment, and each test was made at the same time of the day.

(3) It is essential to use the same time of the day for the control diuresis and the diuresis under cortisone, because the *maximum* rate of urine-flow likely to be achieved varies with the time of day in which the water load is taken (Stanbury and Thomson 1951, Papper and Rosenbaum 1952).

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* Levy et al. (1946) state that in 2 of these 5 cases there may have been technical errors.

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MA322a

PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD DAGENHAM treatment. The pathological fracture healed. In 1950 the patient had a pathological fracture of the superior ramus of the right pubis. A second course of deep radiotherapy 2000r. had no effect on the mediastinal tumour, but the pathological fracture of the pubis healed.

In March, 1951, she was admitted to hospital complaining of drowsiness, epigastric pain, nausea, and severe vomiting. For the last few years she had been suffering almost continuously from generalised aching pain, and for the last ten months she had had epigastric pain, which was brought on by food but not relieved by alkalis.

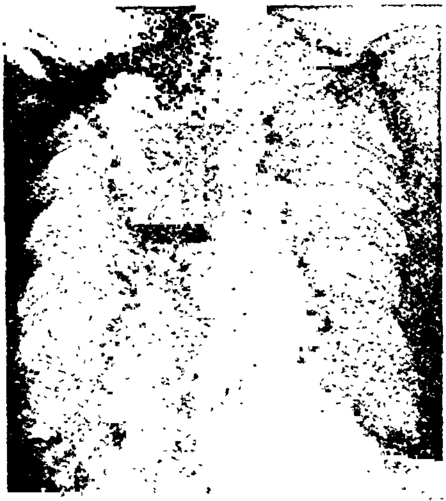

Fig. 1—Dense opacity with calcified rim in right upper mediastinum.

Investigations.—The cardiovascular system showed no abnormality except an extremely low blood-pressure. There were râles at both bases of the lungs. There was no palpable mass in the abdomen, but there was tenderness on pressure in the epigastrium. Plain radiography of the abdomen showed no fluid level and no evidence of intestinal obstruction. A few calcified shadows were seen in the region of the right kidney. A barium meal revealed an ulcer crater above the incisura angularis of the stomach. The duodenal bulb was deformed and showed an ulcer niche at its medial fornix. There was no delay in emptying of the stomach. Films taken in the right oblique position revealed much calcification of the abdominal aorta. A chest radiograph (fig. 1) showed a dense well-defined round shadow, as large as a big plum, with a rim of linear calcification. The trachea below the sternum was displaced to the left. A lateral view showed the tumour to be in the posterior mediastinum. Radiography of the skeleton revealed general osteoporosis; fibrocystic changes in the right humerus, with expansion and thinning of the cortex (fig. 2); fibrocystic changes in the right superior ramus of the ischium and pubis, with healed pathological fracture; and a moth-eaten appearance of the skull, and osteoporosis of the facial bones in contrast to the teeth, which were of normal density, but laminæ duræ were absent (fig. 3). A fractional test-meal showed achlorhydria with histamine response. The urine was acid and contained albumin and leucocytes. A blood-count showed red cells 4,590,000 per c.mm., Hb 94%, white cells 10,000 per c.mm. (polymorphs 89·5%, eosinophils 1%, monocytes 2%, lymphocytes 7·5%). The erythrocyte-sedimentation rate (Wintrobe) was 24 mm. at 1 hour. The blood-urea was 312 mg. per 100 ml., serum-calcium (repeated examinations) 22 mg. per 100 ml., the plasma-inorganic phosphate 2·5 mg. per 100 ml., and the plasma-alkaline phosphatase 17·5 King-Armstrong units.

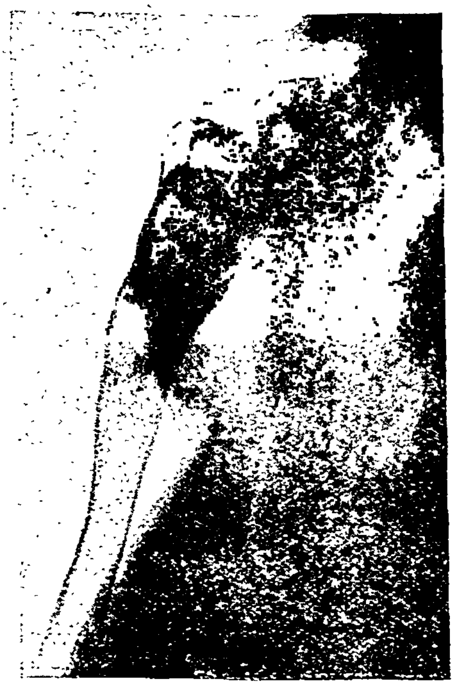

Fig. 2—Fibrocystic changes of proximal half of right humerus, with expansion and thinning of cortex and healed pathological fracture.

Treatment and Progress.—The patient's condition improved with stomach aspiration and intravenous saline solution, and she became more alert. Her blood-urea fell to 88 mg. Operation for parathyroid tumour was advised, but the patient refused and, against medical advice, she was taken home, where she died a few weeks later.

DISCUSSION

It is reasonable to assume that the multiple renal calculi found ten years earlier were due to hyperparathyroidism. Nephrolithiasis and nephrocalcinosis are common and dangerous complications of this condition: they may be present without any recognisable changes in the skeleton, or there may only be general osteoporosis without fibrocystic changes in the bones. The presence of multiple renal calculi should suggest hyperparathyroidism. Investigation of the blood chemistry in these cases should not be confined to estimation of blood-urea but ought to include examination of the calcium metabolism.

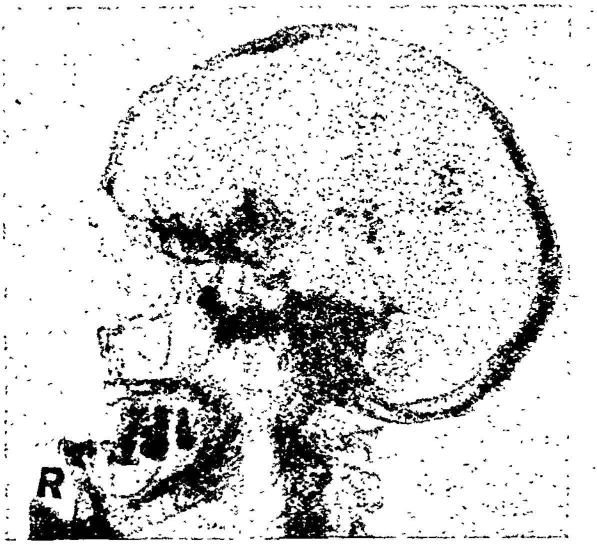

Fig. 3—Moth-eaten appearance of skull and osteoporosis of facial bones in contrast to teeth, which show no decalcification but absence of laminæ duræ, a sign of generalised decalcification.

The second stage of the patient's illness was dominated by involvement of the skeletal system, with pain in joints and bones and with pathological fractures. The clinical notes suggested that failure to recognise the bone lesions as a manifestation of hyperparathyroidism was probably due to the fact that the large tumour in the upper mediastinum had been mistaken for a malignant new growth. Indeed, most parathyroid tumours reported are small. However, Hunter and Turnbull (1931) published a case in which two parathyroid tumours were found, the larger one measuring 7·5 × 5·1 × 1·8 cm. and weighing 26·2 g., and Beyerinck (1932) reported a case in which three parathyroid tumours were found at necropsy, one of them being as large as a hen's egg. The location of parathyroid tumours in the upper mediastinum is not uncommon. Albright and Reifenstein (1948), reviewing 60 cases of hyperparathyroidism, found immune response will no doubt be answered in due course

Although this news sounds very hopeful, there are two points which should discourage over-optimism Firstly, a big effort has clearly been needed to prepare and test enough vaccine for quite a small number of people Each batch of vaccine will need rigorous tests before it can be safely used, and it may be some time therefore before these vaccines are available in any quantity Secondly, though some immunologists believe that the development of resistance to infection and the presence in the serum of antibody to the infecting agent (so often found in close association with one another) are in fact indissolubly linked, this has yet to be proved in poliomyelitis The low prevalence of paralytic poliomyelitis in the community means that very large numbers of people must be immunised before it can be confidently concluded that a vaccine not only produces an antibody response but also protects against paralysis

Radiology in Duodenal Ulceration

THE only satisfactory way of establishing the presence of a duodenal ulcer, other than by laparotomy, is by the radiographic demonstration of unmistakable changes These changes are usually limited to the first part of the duodenum, though they may occasionally be found in the second part[1] The radiographic evidence may be conclusive, when an ulcer crater is seen, inferential, when the duodenal cap is deformed but no ulcer crater is recognisable, or indirect and equivocal, when irritability of the duodenal cap, pylorospasm, radiographic evidence of "gastritis", or other unconvincing signs are present Only the conclusive and the inferential radiographic signs point with a high degree of probability to the presence of an ulcer Radiography, though revealing an ulcer may not reveal an unsuspected cause—for example, a pancreatic neoplasm Clearly radiographic examination is most useful as a check on medical treatment in cases where a crater has previously been seen It must be remembered, however, that duodenal ulcers are often multiple STURTEVANT and SHAPIRO[2] reported finding twenty-five ulcers in one case at necropsy, yet more than two craters are rarely recognised radiographically Thus a patient's symptoms may continue after the healing of an observed ulcer crater, because of the persistence of another ulcer, unrecognised radiographically

At the Royal Society of Medicine on March 20, Dr GEORGE SIMON and Dr G H DU BOULAY reported that, following stringent criteria, they satisfied themselves that an ulcer crater was present in 47% of 134 consecutive patients with clinical and radiographic evidence of duodenal ulceration They pointed out that mistaken identification of a crater may be followed by operation at which a supposed crater is found, and this may be a false confirmation of an inaccurate radiographic observation They examined their patients repeatedly for six months from the first examination In 38 of their 63 cases where an ulcer was present the crater size changed in parallel with the symptoms, but in others symptoms persisted despite apparent healing of the ulcer, or else the size of the ulcer remained the same though symptoms were relieved—in 1 instance symptoms disappeared but the ulcer crater became larger In the 71 cases where they demonstrated no ulcer crater at any examination, no association could be established between alterations in the shape of the deformed duodenal cap and relief or exacerbation of symptoms Their observations led them to doubt whether, once the patient has gained clinical relief, further radiographic examination is useful, for, even though this may show an ulcer crater, it is questionable whether further strict treatment is worth while With duodenal ulceration, radiography, they declared, is primarily a diagnostic procedure, but a further examination is justified possibly after treatment has relieved symptoms, and certainly if the pattern of symptoms changes Preoperative radiography they suggested, is of little value Mr HAROLD EDWARDS, as a surgeon, was concerned to see whether a patient had earned the right to an operation Structural change, not the presence of an ulcer, was the important factor in the decision From experience at operation he doubted whether radiological opinion on the presence of an ulcer crater was completely reliable Patients with duodenal ulcer do not as a rule come to the radiologist until symptoms have been present for some time, and possibly the duration has some influence on healing Dr F PYGOTT said that in a series of 104 cases observed for fifteen months he had observed healing in 17% of cases where symptoms had been present for less than 3 years, in 7% of cases where symptoms had been present for 3–10 years, and in none where symptoms had been present for more than 10 years

It would seem that little or nothing is to be gained by routine radiographic control of medical treatment of duodenal ulceration The main value of radiography is in diagnosis, in the detection of complications, and in the exclusion of a second lesion arising independently In selected cases occasional examinations after clinical cure, or after relapse has been controlled, may be justified, but the results must be interpreted with reserve A general policy on these lines would greatly alleviate the heavy pressure on radiology departments, and would enable more useful work to be done without detriment to the patient

Uterine Cancer and Vaginal Smears

THOUGH malignant cells had been detected in vaginal smears by PAPANICOLAOU[1] as long ago as 1928, the routine examination of smears as a means of recognising early or recurrent uterine cancer was not seriously proposed as a diagnostic aid until 1941 Since then a great deal of work has been done, and there is much evidence on which to base a judgment of the method

Superficial epithelial cells in the female genital tract are subject to cyclical changes and constant exfoliation, which is particularly evident when the cells are malignant and are therefore dividing rapidly In such cases, normal and abnormal cells, shed mainly from vaginal epithelium cervix, and uterine body with an occasional cell from fallopian tubes and ovaries, accumulate in the vagina, and they can be

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[1] Frenkel E Brit J Radiol 19[illegible] 25 132
[2] Sturtevant M Shapiro I L Arch intern Med 1926, 38 41

[1] Papanicolaou G N New Cancer Diagnosis In Proceedings of the 3rd Race Betterment Conference 1928 p [illegible] Quoted by Papanicolaou G N Amer J Obstet Gynec 1946 51, 316

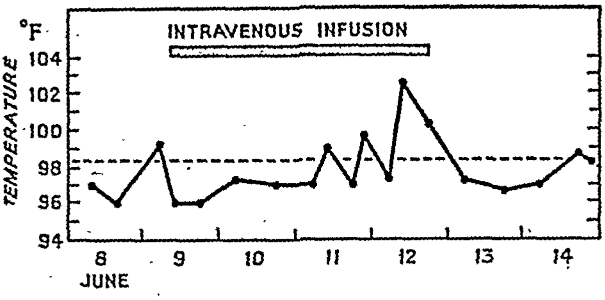

Fig. 2—Treatment and temperature-chart of case 2.

episode of anuria, which had come on after a period of hypotension during an ophthalmic operation. Over each twenty-four hours the patient received 1 litre of Hartmann's solution with 5% dextrose, followed by 1 litre of physiological saline solution with 5% dextrose, and then by 1 litre of 5% dextrose. On the third day she developed a temperature of 100·6°F, which rose to 102·6°F on the fourth day. On this day the infusion apparatus was taken down, after which the temperature settled rapidly (fig. 2).

Investigation.—A drop of Hartmann's solution with 5% dextrose from both the tubing and the bottle was cultured immediately after the drip had been stopped. The bottle, which had just been started, was sterile, but the fluid from the tubing gave a heavy growth of a coliform bacillus.

It grew both at room-temperature and at 37°C, but better at 37°C. It was actively motile. Dextrose, lactose, saccharose, maltose, mannitol, and dulcitol were fermented, with formation of acid and gas. Indole was not produced. The methyl-red and Voges-Proskauer tests were negative. Growth took place in Koser's citrate.

The organism was therefore an atypical member of the coliform group.

No flaws or clots were found in the tubing.

TABLE I—ANALYSIS OF 32 INTRAVENOUS INFUSIONS INVESTIGATED

Infusion fluid	No. of infusions cultured	
	Duration of infusion less than 48 hr.	Duration of infusion 2–4 days
Physiological [illegible]	8	1
[illegible] % dextrose	..	2
[illegible] xtrose	6	6
5% Dextrose	5	4

FURTHER OBSERVATIONS

In view of these findings an attempt was made to determine whether similar but less heavy, and therefore perhaps undetected, infection of infusion fluids occurred at all frequently in hospital practice. The infusion fluids being administered to 32 patients were investigated. The fluid from the tubing was cultured within forty-eight hours of starting the infusion in 19 cases, and from two to four days in 13 cases. The nature of the fluids cultured is shown in table I.

All 32 fluids were found to be sterile.

We then sought to ascertain whether coliform bacilli introduced into infusion fluids could multiply to an extent sufficient to perpetuate the contamination in the apparatus, even though a fresh uninfected bottle was substituted for a contaminated one. All the experiments were made at summer room-temperature (about 20°C). The organisms used were the coliform bacilli isolated from cases 1 and 2.

First it was necessary to determine whether the bacilli multiplied in four different commonly used infusion fluids at room-temperature.

5 ml. of a broth culture, incubated overnight with the organism to be tested, was centrifuged, washed twice in 20 ml. of sterile distilled water, and resuspended in 20 ml. of sterile distilled water. A standard drop (0·02 ml.) was added to a sterile container holding 20 ml. of the infusion fluid to be investigated. This bottle was shaken well and allowed to stand at room-temperature for twenty-four hours. The approximate numbers of live organisms in the infusion fluid were determined by the method of Miles et al. (1938) both directly after mixing at the beginning of the experiment and after twenty-four hours.

The results of typical experiments are shown in table II, which shows that growth took place in physiological saline solution and in Hartmann's fluid with 5% dextrose, but not in 5% dextrose or in physiological saline solution with 5% dextrose. A possible explanation for this was suggested to us by the fact that Bolton Carter et al. (1952) found that the mean pH of all the bottles of dextrose solution examined by them was 4·5. Using Gillespie's method for unbuffered solutions (cited by Fildes 1931) we determined the pH of three samples of each of the four infusion fluids, and the mean results were as follows:

TABLE II—RESULTS OF INFECTING INFUSION FLUIDS

Infusion fluid	No. of living coliform bacilli per ml.			
	From case 1		From case 2	
	At 0 hr.	At 24 hr.	At 0 hr.	At 24 hr.
Physiological saline ..	55,000	650,000	28,500	285,000
Physiological saline with 5% dextrose	45,000	20,000	28,500	Less than 5000
Hartmann's fluid with 5% dextrose	125,000	450,000	22,000	1,900,000
5% Dextrose	65,000	50,000	42,500	Less than 5000

Fluid	*Mean pH*
Physiological saline solution	6·3
Physiological saline solution with 5% dextrose	4·3
Hartmann's solution with 5% dextrose ..	6·1
5% Dextrose	4·1

The pH of the two solutions in which coliform bacilli multiplied was thus near neutrality. Evidently dextrose solutions become acid when sterilised and do not support growth. Hartmann's solution with 5% dextrose has a pH near that of physiological saline solution and allows growth. The acid produced from dextrose is apparently neutralised by the sodium lactate in Hartmann's solution.

The next step was to determine whether the coliform bacilli isolated from our two cases could multiply in the running fluid of an infusion apparatus under conditions similar to those of intravenous therapy.

Small volumes ranging from 1 drop to 1 ml. of a suspension containing a known number of coliform bacilli, washed as before, were introduced into a fresh litre bottle of infusion fluid. A sterile giving set with rubber tubing and needle was attached to the infusion bottle. The needle was passed

TABLE III—RESULTS OF EXPERIMENTS IMITATING INFUSION CONDITIONS

Organism	Infusion fluid	No. of organisms introduced into first litre bottle	Organisms per ml. after				
			0 hr.	1 day	2 days	3 days	4 days
From case 1	Physiological saline solution	1,500,000	1500	35,000	160,000	1,500,000	..
From case 1	Physiological saline solution	10	0	0	About 1	10	80
From case 2	Hartmann's solution with 5% dextrose	600,000	600	2500	5,000,000	Very large numbers	..
From case 2	Hartmann's solution with 5% dextrose	250	0	0	About 1	1000	..
From case 1	5% Dextrose	6000	6	0	0	0	..

number of principals increased by some 500 Fresh admissions to lists totalled 1566, of which 1177 were for replacement of doctors who had died or retired 781 doctors were admitted to partnerships in established practices, and, of these, 344 had served preliminary assistantships During the last three years rather less than one-fifth of the total of assistants have become partners, but the evidence suggests that this proportion is increasing as a result of the Danckwerts award At first sight these figures are encouraging, but several questions must be answered before the chances of the more recently qualified can be estimated We do not know, for instance, how many mature doctors, including senior registrars who have been unable to attain consultant status, are still trying to enter general practice, but the total is likely to increase in the coming months, as Dr FORRESTER and Dr WALTON make clear in a letter on p 793 Nor do we know how many replacements can be expected in future—the number was rather smaller last year than the year before An actuarial forecast would be helpful. The increasing rate of admission of assistants to partnerships is on the whole satisfactory, but the fall of 150 in their total suggests that its effect may be to improve the status of those already practising without increasing the opportunities of entry for younger men Certainly advertised assistantships, even in some of the less attractive areas, continue to draw an excessive number of applications The formation last year of over 300 new practices in under-doctored areas is welcome, but such expansion will obviously be limited, and there are already signs of a better distribution of doctors, the number with either very large or very small lists is tending to decrease At the top of the scale, last year there were 7397 practitioners with average lists of 2869, whereas the year before there were 7055 with average lists of 3009 At the other end of the scale, last year there were 1062 practitioners with average lists of 2010, as against 1075 with average lists of 1941 in the previous year

Recruitment to medicine is governed by the demand for doctors and the capacity of the medical schools After the late war the demand seemed to be inexhaustible and the numbers qualifying increased but the position has changed, and now the profession is probably becoming overcrowded The Medical Practices Committee emphasises the difficulties of attempting to predict future requirements of doctors in the present changing situation Nevertheless the attempt should be made The medical curriculum lasts more than five years, if the schools are accepting too many students they should know as soon as possible From the professional standpoint the health service ought to provide a reasonable chance of a permanent post, without undue competition, for a doctor as soon as he is experienced enough to fill it, too long in temporary or junior posts is not good for the doctor or for the service The status of principal should be generally attainable in general practice between the ages of 30 and 35, and that of consultant a year or two later Last year the average age of successful applicants in general practice was 36 This is better than the average of 38 in the previous year but there are still doctors over the age of 40 who are finding entry extremely difficult Oddly enough there are still too few applicants for junior posts as house officers, senior house officers and registrars in the peripheral hospitals This is partly due to an absolute shortage, but it also to some extent reflects unequal distribution The compulsory preregistration year in hospital may improve the supply of house officers, but it can hardly affect the slightly senior posts Doctors might be glad of a year or more as registrar in a peripheral hospital if their future seemed more assured than it is now, and if they were convinced that, when they applied for a post in general practice, registrar experience would be counted an added qualification and not, as FORRESTER and WALTON assert, "usually a positive disadvantage An improvement at the top would undoubtedly ease the situation lower down the ladder

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Annotations

MEASLES IN VIRGIN SOIL

MOST of us have heard of epidemics of measles which decimated the populations of remote islands or other *isolated communities from which the disease had been* absent for well over a generation There are records of very high mortality in such outbreaks among the native population of the Amazon (1749), Esthonia (1820), Hudson Bay Indians (1846), the Cape Hottentots (1852), Tasmania (1854), and Mauritius (1874) In Fiji in 1875 about 20,000 people—nearly 25% of the population—died of measles[1], and in the next outbreak 32 years later 6% of the population died In the Faeroe Islands, after a great epidemic in 1781 there was no measles until 1846 when about 6000 (78%) of the 7782 inhabitants contracted the disease, none of the 98 old persons who had had the disease in 1781 had a second attack

For the first time in medical history, measles gained a foothold in Southern Greenland in April, 1951[2] The source of infection was a young Greenlander, infected in Copenhagen, who, soon after landing in Greenland and just about the time of onset of symptoms, took part in a public dance attended by 200–300 people from all parts of the community This outbreak is certain to become a classic in medical history because of the extremely high attack-rate The number of persons who contracted typical measles within three months was 4221, a further 36 had less definite attacks 31 who had previously had measles in Denmark, and 27 treated prophylactically with convalescent serum or gamma globulin did not contract the disease In the Julianehåb district, to which the disease was localised, of the whole unprotected population of 4262 only 5 escaped the disease, this gives an attack rate of 999 per 1000—surely a record The mortality was much lower than might have been expected, probably owing to penicillin treatment of complications combined with the modification produced by sero prophylaxis of about 1000 people both of which measures were rapidly organised from Denmark Only 77 deaths were recorded—a rate of 18 per 1000

The incubation period was nearly always 13–14 days from rash to rash, but in 1 case it was certainly as long as 19 days, and in several it was only 6–10 days The course of the disease was remarkable only for two special features a very pronounced enanthem, usually hæmorrhagic of the mouth and palate present in 75% of the patients in the prodromal stage, and virtual absence of conjunctivitis, photophobia, and eye complications These may be related respectively to the Greenlanders' well known tendency to hæmorrhages and to the Northern climate The frequency of complications in a series of 1657 patients who were not treated prophylactically was 15% and of these complications 80%

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[1] [illegible] *Trans epidem Soc Lond* [illegible] 3 [illegible]

[2] Christensen, P E, Schmidt, H, J[illegible], Bang, H O, Andersen, V, Jordal, B *Acta med scand* 1953, 144, [illegible]

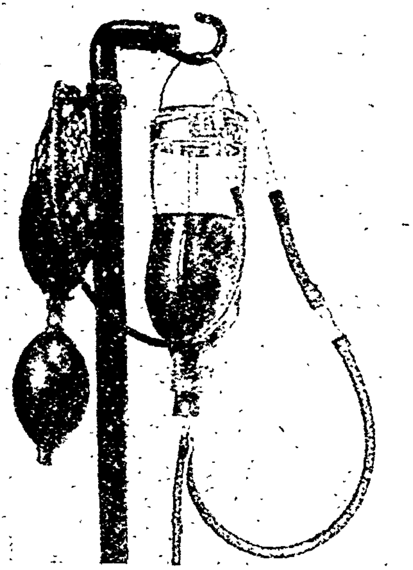
if the exposure was big enough, and if enough time and care were given to the operation, which should be as gentle and bloodless as it was courageous and ruthless.

Mr. Cooke mentioned the inflammatory factor in malignant disease—particularly of the colon. An "impossible" case might become a relatively easy problem after a short-circuit or colostomy. After a time most of the bulk and fixity of the mass might resolve, and the residual malignant mass could be dealt with by a reasonable operation. Re-exploration might then be well worth while.

New Inventions

AN AIR FILTER FOR PRESSURE TRANSFUSIONS

DURING investigation of cases of unexplained pyrexia following transfusion the possibility of introducing infection through the bellows used to apply air-pressure was studied. Though it is generally recognised that the use of positive air-pressure carries risks and requires direct medical supervision, we had not previously considered the hazard of infection. We have found that the bellows used for this purpose almost always become contaminated with small quantities of blood or other transfusion fluid which readily flows back through the air-intake tube of the standard giving set. The rubber bellows are difficult to sterilise and, being opaque, do not reveal the contamination which may exist inside them. Several such bellows after use were blown out over 6% agar plates, and in each case there was a heavy growth of bacteria, including *Pseudomonas pyocyanea* and gram-negative and gram-positive cocci.



To obviate the risk of infection of the transfusion fluid a simple cotton-wool filter was devised which consists of a glass U-tube containing a wad of dry cotton-wool in each arm. One arm is connected to the air-inlet tube of the giving set by about 18 in. of rubber tubing. A short length of glass tubing with a constriction is inserted in the rubber tubing about 3 in. from the U-tube to prevent the cotton-wool from being blown into the transfusion bottle. The U-tube hooks over the wire support of the bottle-holder, and the bellows are attached to the open end, the whole thus being conveniently supported without danger of kinking. The glass tubing and rubber tubing are cleaned after use, new pieces of cotton-wool are inserted, and the whole is sterilised at 5 lb. pressure for 15 minutes in a tin similar to that used for giving sets. In attaching the filter to the bottle it is important to hook the glass U-tube on to the support before attaching the rubber tubing. This prevents flow-back of the blood under gravity from the air-inlet tube of the giving set.

These filters have been tested with bellows known to be contaminated, and they prevent the passage of organisms; their regular use over the past year at this hospital has shown them to be convenient and acceptable in practice.

J. P. BULL
M.D. Camb.
L. HURST
F.I.M.L.T.

Medical Research Council Industrial
Injuries and Burns Research Unit,
Birmingham Accident Hospital

Reviews of Books

Influenza and Other Virus Infections of the Respiratory Tract

C. H. STUART-HARRIS, M.D. Lond., F.R.C.P., professor of medicine, University of Sheffield. London: Edward Arnold. 1953. Pp. 235. 30*s*.

IN the winter months the general practitioner spends much of his time in dealing with diseases of the respiratory tract, and particularly with the heterogeneous group of acute infections caused by filterable viruses. Professor Stuart-Harris has for many years been concerned with the delineation of clinical entities from the general run of "flu's" and "virus pneumonias," and, having graduated to a chair in clinical medicine via bacteriology and virology, he is well placed to consider these infections from both the clinical and the laboratory viewpoints. He has now condensed the results of many years' inquiries into a readable book which should commend itself to all who are interested in respiratory diseases. Influenza receives the most detailed treatment, but there are chapters on febrile catarrh, the common cold, atypical pneumonia, psittacosis and ornithosis, and Q fever. Each infection is considered in its clinical and epidemiological aspects along with descriptions of the pathology, laboratory diagnosis, and treatment. Throughout, Professor Stuart-Harris tries to avoid accepted textbook patterns of description and to write from his own experience, and the book contains much valuable and previously unpublished material. There are numerous X-ray films and photographs of histological material, and the text is well supplemented with figures and charts.

Biochemistry of Gastric Acid Secretion

EDWARD J. CONWAY, M.D., D SC., F.R.S., professor of biochemistry and pharmacology, University College, Dublin. Oxford: Blackwell Scientific Publications. 1953. Pp. 185. 47*s*. 6*d*.

Professor Conway's monograph on the mechanism of gastric acid secretion presupposes an intimate knowledge of the biochemistry of cellular secretion. It is thus of limited appeal; but it will be of particular interest to the biochemist and physiologist. Some of the reasoning is difficult to grasp at a first reading, and much of the subject matter is highly technical.

Dr. Conway draws an interesting parallel between the secretion of succinic acid by the yeast cell and the hydrochloric-acid secretion of the oxyntic cell of the gastric mucosa. The bulk of his monograph he has given over to a discussion of the redox-hydrogen ions, while under the heading of energetics he describes the energy changes involved in the redox cycle and the sources of energy consumed in cellular secretion and osmotic work. In a short final section he considers the significance of gastric urease in the human subject in relation to the neutralisation of gastric acidity and mucosal protection, and he gives an outline of the urea therapy for peptic ulceration. Unfortunately, he does not offer enough data about the 79 patients he has treated to allow the reader to judge of the value of the method.

Psychosomatic Medicine

Its Principles and Applications. FRANZ ALEXANDER, M.D., director, Chicago Institute for Psychoanalysis, clinical professor of psychiatry, University of Illinois. London: Allen & Unwin. 1952. Pp. 300. 21*s*.

Dr. Alexander has contributed much to the development of the psychosomatic approach, and his new book is a useful account of the underlying theory and practical therapeutic results in this field.

He describes the mechanistic "analytic" medical theories of the 19th century, which still exert undue—and largely unrecognised—influence. The new "synthetic" viewpoint first appears in the work of Kahlbaum, Wernicke, and Babinski and in the brilliant observations of Kraepelin. The discovery by Noguchi of the spirochæte in the brains of patients with general paralysis, and the results obtained by Horsley from thyroid transplantation in myxœdema, helped to convince clinicians that mind and body had mutual interactions; while in the study of the neuroses Freud's method of psycho-analysis, and his theory of ætiology, introduced scientific method to what had been a welter of unrelated observations. Members of the *Gestalt* school of psychology, is relatively acid, is less likely to support bacterial growth than normal saline or Hartmann's fluid with 5% glucose; but their finding is none the less important.

On page 775 Dr Bull and Mr Hurst report that they investigated cases of unexplained pyrexia after transfusion, and they give evidence that accidental infection is a possible hazard of transfusions assisted by air-pressure. Apparently the bellows of a pressure transfusion apparatus regularly become contaminated with small quantities of transfusion fluid, and this permits the growth of a variety of bacterial species including *Pseudomonas pyocyanea*. Bull and Hurst describe a simple device which prevents infection from this source by filtering the air from the bellows through a U-tube containing a wad of dry cotton-wool in each arm.

These different reports clearly emphasise that various forms of treatment as now administered in the wards of hospitals need to be carefully overhauled, because there is little doubt that some of them constitute potentially dangerous sources of infection. The first requirement of any treatment is that it should not do harm, and it is a grave reflection on all concerned when accidental infections in hospital cause avoidable suffering and even loss of life. Because of our increased control over many common infections there is a possible risk that we may grow forgetful and perhaps even contemptuous of bacteria.

DOCTOR AND CAMERA

PHOTOGRAPHY has been used in medicine for more than a century; but only in recent years have we begun to appreciate how much the camera can help us. An exhibition this month at the Royal Photographic Society's house in Kensington surveys the century's progress and makes it clear that this has been most rapid in the past fifteen years. For instance, close-up pictures of the eye, and colour photography of the living retina with snapshot exposures, have only been satisfactorily achieved since 1939. Techniques for endovesical and intraperitoneal photography are post-war developments, exemplified in a fine colour print of a nodule of regenerating tissue on the surface of a living syphilitic liver.

The main function of photography is simply to record—for example, the changing pattern of skin lesions, the repair of defects by plastic surgery, and the follow-up of a case. The exhibition includes a series of pictures showing a patient in 1905 before removal of his cerebellar tuberculoma, and as he is today, together with pictures of the pathological specimen and its histological section. There is also a panel of smallpox cases with views of the floating hulks on the Thames off Deptford which used to be an isolation hospital, which teaches a good deal of value in public health as well as illustrating a disease that is now uncommon. But photography is also an important research technique. Infra-red pictures will display the invisible subcutaneous venous network; and photogrammetry will record growth and physical type for somatotyping and other anthropometric studies.

As the techniques have grown so have the numbers of specialists, and now over 300 medical photographers belong to the Royal Photographic Society's medical group, which was founded in 1946. There are, however, still many hospitals and many doctors, even in research departments, who have no inkling of what the medical photographer can do to help them. The present excellent little exhibition is composed largely of portable panels, and could go on tour to medical schools. Perhaps the organisers will consider how they can circulate their show, if only in part. Photography is a part of the Science of Light, and should not be hidden under a bushel.

DESERTED CHILDREN IN FRANCE

IN France the task of saving and rearing children deserted by their parents, begun in the 17th century by St Vincent de Paul, has been faithfully pursued by later generations. His plan of placing the newly born with country foster-parents is still sound; and, though the infant mortality among these foundlings was at first very high, the centuries have seen a steady improvement. Marcel Lelong[1] notes that of 55,000 newborn children saved between 1790 and 1802, some 31,000 died. Up to 1862, when receiving centres were set up, children were still being left on the turntables set in monastery doors for the purpose. In 1874 medical supervision of foster children was started and in 1926, in the Département de la Seine, the *Pouponnière d'adoption*—giving the newly born residential care in a crèche—was established, working in conjunction with the centres for approved wet-nurses. In this department the neonatal mortality among children in the care of the Assistance Publique (A.P.) is now lower than the average for the country as a whole.

The numbers of deserted children coming under the care of the Seine A.P. have fallen considerably in the course of time (from 7676 in 1772, to 5026 in 1900, 3477 in 1920, and 758 in 1946); but a change—presenting serious problems—has taken place in the age range of children deserted. In 1900 more than half the children were under the age of 3 months, and two-thirds of them under the age of 2 years; in 1949 only about 5% were under 3 months, nearly half were over the age of 6 years, and some 15% over 14. Concurrently, the numbers of children confided temporarily to the care of the A.P. have risen steeply—from 3307 in 1880 to nearly 12,000 in 1952. This has been partly due to a humane interpretation of regulations: the A.P. will accept children brought in at any hour of the day or night. Not all of them come from the Seine area—some are from overseas, from distant or neighbouring departments, or from other European countries, and many of them are children of refugees or displaced persons passing through Paris. About 70% belong to normal families temporarily in difficulties and unable to look after them, and these children usually rejoin their parents within three weeks.

The decline in the numbers of babies under 3 months is said to be leading to a gradual disappearance of would-be adopters. Many of the older children have been profoundly affected by their experiences, which often include a broken home, immoral or delinquent parents, and sometimes a personal experience of sexual assault or incest. Small wonder that they are often abnormal—vagabonds, potential delinquents, or at the very least socially maladjusted. Children with such a background, as we know from our own experience, are not reclaimed in a moment; but many of them do respond to sympathetic handling in secure surroundings. But French children of this kind suffer a further devastating blow. As soon as the A.P. undertakes their permanent care, a process is started to secure their legal separation from their parents. Months pass before the judgment is given, and even when it has been passed the parents retain the right for three years to ask that it shall be reconsidered. The whole process is extremely painful and damaging to any child who is old enough to know he is being cast off or—as he more often imagines it—cut off by tyrannical authorities from parents who want to keep him. Moreover, he is thus artificially made into an orphan at an age when adoption can no longer be expected, and when readjustment is at best difficult to achieve. The older children rebel against the judgment and resent all attempts to place them with foster-parents. They remain a charge on society and ultimately a danger to

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[1] Bull. Acad. Méd. Paris, 1953, 137, 10.

"I dread the rustling of the grass"

WILLIAM WORDSWORTH

No sooner has the blossom languished and spring shed her coat of many colours than the tall grasses ripen. The air is again pollen-laden. To those who love the countryside these richly-clothed meadows are a joy: to sufferers from hay-fever they are merely the signal for a fresh period of acute discomfort. Yet there is a solution — BENADRYL, probably the most potent of all histamine antagonists, may be taken just before and during the pollen seasons and, in the majority of cases, provides effective relief.

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[1] *Bull. Acad. Med. Paris*, 1953, 137, 4

THE LANCET

LONDON: SATURDAY, APRIL 18, 1953

Poliomyelitis Vaccines

THERE have lately been important changes in our outlook on the pathogenesis of poliomyelitis, and in this issue Dr. MEENAN describes the basis for the modern concepts of this disease. Epidemiological investigations have established that the paralytic disease, on which attention had earlier been focused, is the exceptional rather than the general result of first contact between patient and virus. The virus is widely distributed throughout the world, and, curiously enough, the more widespread it is in a particular population the smaller the number of paralytic cases. This paradox is explained by the fact that if the first contact with the virus is in infancy paralytic disease is less likely than if the first infection is in adult life. In countries where the general standard of hygiene is poor, most first infections are in infancy, and the population has a high general level of immunity to the virus. In more civilised communities this first meeting with the virus is often postponed until the age at which paralytic disease is a more common result of infection, and, as MEENAN points out, it is we who, by altering our living conditions, have upset the happy balance between virus and man which had earlier prevailed.

We have also changed our ideas about the strict neurotropism of the virus. The strongest evidence that poliomyelitis viruses are not strictly neurotropic has been the discovery by ENDERS et al.[1] that the viruses can multiply in cultures of non-neural tissue maintained in vitro. This discovery opened out an enormous new field in which to study the growth habits of the virus and raised hopes of preparing practical vaccines. Moreover, it supported the view that in its pathogenesis poliomyelitis resembled other virus diseases much more closely than had hitherto been believed. The subsequent news from HORSTMANN [2] and BODIAN [3] that the virus entered the blood-stream in the early stages of experimental poliomyelitis fell on receptive ears. It is not yet clear whether this viræmia, which is believed to be present in human infection as well, is an accidental occurrence or a pointer to the all-important route by which the virus invades the central nervous system from its primary site of infection; but there is no doubt that opinion has swung over to the latter view. If poliomyelitis behaves like other virus diseases, it should be possible therefore to set up an antibody barrier to the spread of virus through the blood-stream and to prevent invasion of the central nervous system. And so a cheerful optimism has replaced the all-pervading pessimism about the chances of preventing paralytic poliomyelitis.

The first indication that these theoretical possibilities might work in practice came from a trial [4] in which it was shown that gamma-globulin given to large numbers of children caused a significant reduction in the prevalence of paralytic poliomyelitis. But active immunisation is obviously the only practical proposition, and here there are two clearly divided schools of thought. The first favours immunisation with live attenuated virus, and its members can cite smallpox, yellow fever, and more recently rabies, as strong arguments to support their view. The second and more cautious school prefers the use of inactivated vaccines whose safety, it is said, would outweigh the disadvantages of difficult and expensive production. Preliminary trials with inactivated vaccines were lately described by HOWE,[5] but these vaccines carry the risk of allergic encephalomyelitis arising from injections of nervous tissue. This danger can best be averted by growing the virus in vitro in non-neural tissues, and the results of trials with vaccines prepared in this way have now been reported. SALK [6] and his colleagues have taken advantage of some recent advances to prepare a vaccine which seems to have considerable promise. Poliomyelitis viruses of the three immunological types [7] were grown in vitro in cultures of monkey kidney and testis. (Monkey tissue was preferred to human because it was more readily available and because the virus of serum-hepatitis might be transmitted by human material.) The tissues were suspended in a chemically defined medium [8] in the absence of serum, amniotic fluid, or other foreign proteins; this medium has lately been shown [9] [10] to maintain the viability of the tissues and to support virus multiplication. Virus grown in these cultures was inactivated by careful treatment with formaldehyde, and it was then shown to be non-infective by intracerebral inoculation of monkeys. These vaccines were then given to 161 persons by one of two techniques: in one series of experiments the aqueous vaccine was inoculated intradermally; in a second series the vaccine was given intramuscularly in a water-in-mineral-oil emulsion, which has an adjuvant effect.[11] The results of these experiments were measured by antibody tests in tissue culture, comparing antibody levels of sera taken before and after vaccination. It is difficult at present to assess fully the value of these results, for although they are described at length, many of the experiments were still in progress at the time the report was written. It is clearly shown, however, that shortly after immunisation with a mixed adjuvant vaccine, containing the three antigenic types of virus, antibody was induced to all three types. Moreover, it seems that the vaccine mixed with adjuvant is, in some cases, a better antigen than the aqueous vaccine. A number of questions on the effect of the preliminary immune status of the subjects and on the duration of the

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[1] Enders, J. F., Weller, T. H., Robbins, F. C. *Science*, 1949, 109, 85.

[2] Horstmann, D. M. *Proc. Soc. exp. Biol., N.Y.* 1952, 79, 417.

[3] Bodian, D. *Amer. J. Hyg.* 1952, 55, 414.

[4] Hammon, W. M., Coriell, L. L., Wehrle, P. F., Klimt, C. R., Stokes, J. jun. *J. Amer. med. Ass.* 1952, 150, 757; see leading article, *Lancet*, 1952, ii, 970.

[5] Howe, H. A. *Amer. J. Hyg.* 1952, 56, 265.

[6] Salk, J. E. *J. Amer. med. Ass.* 1953, 151, 1081.

[7] Committee on Typing of the National Foundation for Infantile Paralysis. *Amer. J. Hyg.* 1951, 54, 191.

[8] Morgan, J. F., Morton, H. J., Parker, R. C. *Proc. Soc. exp. Biol., N.Y.* 1950, 73, 1.

[9] Franklin, A. E., Duncan, D., Wood, W., Rhodes, A. J. *Ibid*, 1952, 79, 715.

[10] Melnick, J. L., Riordan, J. T. *Ibid*, 81, 208.

[11] Freund, J. *Amer. J. clin. Path.* 1951, 21, 645.

the W R was negative in all cases Histoplasmin tests were also negative and so was the Kveim test in the three patients on whom it was performed All twenty patients were afebrile during the period of observation In four cases there was enlargement of the peripheral lymph-glands which subsided at the same time as that of the hilar glands Chaves and Abeles emphasise that the probability of spontaneous regression should be kept in mind when deciding what to do Irradiation is seldom justified until the diagnosis has been confirmed, and in particularly difficult cases where the lesion is unilateral, a thoracotomy may be necessary to identify an operable neoplasm It seems probable that many of the unexplained cases are the result of persistence of glandular enlargement due to a subclinical infection which has passed unnoticed

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THOUGH he had previously worked on goitre and cretinism, Sir Robert McCarrison's studies of nutritional disease may be said to have begun in early 1918, when he returned to India from active service and was posted to the Pasteur Institute Coonoor Built in 1906, for the production of anti rabies vaccine and the treatment of patients with rabies this institute is situated in the Blue Mountains amid magnificent scenery, and the climate is mild McCarrison occupied an empty room in which he started officially to study beriberi and though his work was twice stopped he twice managed to begin it again Fortunately in 1926 Lord Linlithgow's Royal Commission on Agriculture visited Coonoor, and with its backing he was able to build up the well known Nutrition Research Laboratories which he directed until he retired in 1935 His successor there was W R Aykroyd, now director of the Nutrition Division of the United Nations Food and Agriculture Organisation who held the appointment for ten years and Aykroyd in turn was succeeded by a biochemist V N Patwardhan under whom are clinical and pathological sections under the clinical scientists C Gopalan and V Ramalingaswami

Despite the ideal climate of Coonoor, the situation has had two serious disadvantages for the most important centre of nutritional research in India—it is relatively inaccessible and it has no immediate contact with clinical material Further, although the research laboratories took over the whole of the first floor of the Pasteur Institute and overflowed into a neighbouring jam factory they have had insufficient space The governing body of the Indian Council of Medical Research has accordingly decided that they should be transferred to Hyderabad, and on March 31 the health minister for India, Rajkumari Amrit Kaur, laid the foundation stone of the new buildings In her speech she spoke of the debt India owes McCarrison "India" she said "has particular reason to be proud of his achievements, for it was his foresight and, may I say, genius which made it possible to establish these Laboratories as an institution devoted entirely to the study of nutrition" She emphasised the need for pure nutritional research, and for bringing this into intimate contact with those advancing or practising clinical medicine In Hyderabad the Nutrition Research Laboratories will be closely associated with the hospital and the medical college

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[1] London Victor Gollancz 1953 Pp [illegible]

[1] See *Lancet* April 11 1953, pp 73[illegible] 749

THE LANCET AIR-MAIL EDITION

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demonstrated microscopically in vaginal smears. Many methods for collecting the material from the posterior fornix have been described: PAPANICOLAOU [2] used a curved glass pipette and rubber suction bulb; KRAUSHAAR et al.[3] recommended a damp standard cotton swab protected by a sheath of rubber tubing; and HYAMS [4] described an ingenious "direct contact smear technique." AYRE,[5] on the other hand, maintained that smears taken directly from the external os provided better material for the diagnosis of cervical carcinoma, and he designed a spatula [6] for collecting predesquamated cells from the squamocolumnar junction of the cervix. However the material is obtained, it is spread as a thick smear on a glass slide and immersed immediately in a fixative of equal parts of 95% alcohol and ether. Fixation takes only a few minutes, though the slide can be left in the fixative up to one week without harm. The slides are stained with PAPANICOLAOU's or SHORR's "differential stain." [7 8] But, though the taking of a vaginal smear may be simple enough, the interpretation of the microscopical appearances can be very difficult, even for those with considerable experience in normal and abnormal vaginal cytology. The appearances which suggest a diagnosis of malignancy are the same as those of individual cells in ordinary paraffin sections of malignant tissue. They include pleomorphism with bizarre cell shapes (the so-called tadpole cells), intranuclear changes (an irregular chromatin network and an increase in the chromatin content), variations in the size and shape of the nucleus, atypical mitoses, cells with multiple nucleoli, and excessive cornification. In addition there are the abundant leucocytes, histiocytes, and degenerated red cells characteristic of the infection that is so often present. A diagnosis of cancer can be made with greater confidence when groups of cells, rather than single cells only, are seen. PAPANICOLAOU et al.[9] recommended the following classification:

Class 1.—Abnormal or atypical cells absent.

Class 2.—Atypical cells present, but without abnormal features.

Class 3.—Cells with abnormal features present, but not pathognomonic.

Class 4.—Fair number of pathognomonic cells and cell clusters present.

Class 5.—Large number of conclusive cells and cell clusters present.

Thus, classes 1 and 2 are negative smears, class 3 is suspicious, and classes 4 and 5 are positive.

Much has been written during the past ten years about this method of detecting early carcinoma of the female genital tract, and many gynæcologists have welcomed the method with enthusiasm and advised its routine use. On the other hand, some doubt the accuracy and others the practicability of the procedure as a routine. The shortcomings of the method lie in its expense and in the tremendous time it takes—"some 500 hours of work necessary to reveal one carcinoma" [10]—as well as in the difficulty of securing staff who have sufficient experience of its use. Limitations such as these have restricted its use to the larger teaching centres where adequate funds and skilled staff are available. A further drawback is that at best the diagnosis can only be provisional; and the final answer depends on the examination of material obtained by cervical biopsy or by curettage. Clearly, the vaginal smear can never replace these orthodox biopsy methods. On the credit side, the best that can be said is that by a simple, painless, and harmless procedure an occasional case of clinically unsuspected cancer of the genital tract may be recognised and so treated in good time. Against this would have to be set the mental and physical trauma in borderline cases, eventually found to be free of cancer, during observation which may be prolonged and investigation which may well include cervical biopsy under anæsthesia. There is also the danger that extensive operations may be undertaken unnecessarily. Again, if cancer has been overlooked or develops later, a negative vaginal smear may perhaps give a false sense of security and delay treatment. A sense of proportion is clearly needed. In the years 1939–49, just over 400,000 women died of malignant disease in England and Wales, and of these deaths 48,000 were due to uterine cancer. In the same period, 81,000 women died of carcinoma of the breast, and nearly 27,000 of carcinoma of the rectum. These figures suggest that there is probably a stronger case for establishing routine examination of the breast and rectum in all gynæcological clinics; for in this way the gynæcologist may detect a symptomless cancer, and perhaps save a patient's life, more readily than he would by searching for an elusive cancer cell in vaginal smears.

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[2] Papanicolaou, G. N., Traut, H. F. *Amer. J. Obstet. Gynec.* 1941, 43, 193.
[3] Kraushaar, O. F., Bradbury, J. T., Brown, W. E. *Ibid*, 1949, 58, 447.
[4] Hyams, M. N., Hyams, R. G., Wainess, E. E. *Ibid*, 1950, 59, 445.
[5] Ayre, J. E. *Canad. med. Ass. J.* 1944, 51, 17.
[6] Ayre, J. E., *Amer. J. Obstet. Gynec.* 1947, 54, 363.
[7] Papanicolaou, G. N. *Science*, 1942, 95, 438.
[8] Shorr, E. *Ibid*, 1941, 94, 545.
[9] Papanicolaou, G. N., Traut, H. F., Marchetti, A. A. The Epithelia of Woman's Reproductive Organs. New York, 1948.
[10] Novak, E. *Amer. J. Obstet. Gynec.* 1949, 58, 851.

Too Many Doctors?

SOME time ago we reviewed the rate of entry into the profession and tried to estimate the number of permanent posts required for those qualifying.[1] Since the likely opportunities for consultants were known we were able, by an arbitrary calculation which we believed to be conservative, to show that in England and Wales about 700 openings were required each year in general practice. Some of those who qualify elsewhere in the United Kingdom settle in England and Wales; but for want of precise information these were excluded.

New figures for Scotland [2] fill in a little more of the picture. In Scotland between 550 and 600 doctors are qualifying each year, of whom at present about 230 can expect to find employment at home. These appointments are chiefly for replacement: the rate of expansion in general practice has not been rapid; in the two years up to July, 1952, principals increased by 37 and assistants by 23. A quarter of those attaining principal's posts are over 50 years of age; but calculations based on the ages of those now practising do not encourage hopes of a speedy increase in the openings. If a fair proportion of the 300 surplus Scottish graduates are to find employment as general practitioners in England and Wales, the total number of vacancies required will be about 1000, and even this may not be enough if the demand for British doctors overseas contracts further. The report of the Medical Practices Committee for 1951–52 gives an idea of the present position. During the year the

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[1] *Lancet*, 1951, ii, 331.
[2] *Hlth Bull., Edinb.* 1953, 11, 19.

the W.R. was negative in all cases. Histoplasmin tests were also negative, and so was the Kveim test in the three patients on whom it was performed. All twenty patients were afebrile during the period of observation. In four cases there was enlargement of the peripheral lymph-glands which subsided at the same time as that of the hilar glands. Chaves and Abeles emphasise that the probability of spontaneous regression should be kept in mind when deciding what to do. Irradiation is seldom justified until the diagnosis has been confirmed, and in particularly difficult cases where the lesion is unilateral a thoracotomy may be necessary to identify an operable neoplasm. It seems probable that many of the unexplained cases are the result of persistence of glandular enlargement due to a subclinical infection which has passed unnoticed.

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[1] London: Victor Gollancz. 1953. Pp. [illegible]

[1] See *Lancet*, April 11, 1953, pp. 748, 749.

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were pneumonias which occurred early, commonly in the prodromal stage or during the first two days of the rash. Otitis media accounted for only 10% of the complications—probably owing to the early use of penicillin for the treatment of pneumonia. An unusual, and quite the most serious, complication was circulatory failure. This appeared most usually in elderly patients and pregnant or puerperal women. It most often took the form of congestive heart-failure, and acute myocarditis was rare. It was thought to be the result of stress on a previously weakened myocardium, mainly in the elderly. Encephalitis was seen in 6 of this series of 1657 cases; and in 4 of these cases the patient died. This gives a rate of 1 case of encephalitis per 275 cases of measles, which is at least three to four times the highest rate previously recorded: and the fatality-rate also was very high. Postinfectious encephalitis, at least the post-vaccinal type, has been said to be rare in the tropics. Is it relatively common in the far North? Of the 26 women in this series who were known to be pregnant, half were delivered at term and half gave birth to premature infants or aborted. No congenital abnormalities were observed in any of the infants born of mothers who had contracted measles during pregnancy.

In this epidemic a very interesting relation was established between measles and tuberculosis. Practically every tuberculous person in the district must have contracted measles, and this very unusual happening seems to have brought an increase both of deaths from tuberculosis and of new cases. In one of the larger villages examination of 352 people immediately before and after the measles epidemic showed 19 new cases of tuberculosis (13 with positive sputum); and among 58 cases of tuberculosis recognised before the epidemic 9 patients died, and at the second examination 13 showed progression. This was clearly more than normal for the district and seems to justify the conclusion that measles reduces resistance to tuberculosis. It was also confirmed, in 51 cases tested, that tuberculin allergy was temporarily suspended during and after measles. The majority did not again become tuberculin-positive until 8–12 days after the rash cleared, and a few cases not until 30–35 days thereafter. Further, no less than 9 cases of postprimary erythema nodosum were observed within a month after the rash. This was thought to be due most probably to a mutation of the bacillus after the temporary suspension of tuberculin allergy.

THE CASE FOR GERIATRICS

TEN years ago the American Geriatrics Society held its first meeting, and this year sees the publication of the first number of its journal.[1] Interest in the welfare of the elderly is increasing rapidly, and the appearance of such a journal is welcome. Medicine in the elderly does not in fact differ noticeably from medicine in the middle-aged, and there are signs of reaction from the former despondent attitude towards the treatment of elderly patients.

It is useful to have a journal devoted entirely to geriatrics, for, as in all pioneer work, there is a tendency to lose sight of the advances, gained or promised, if no attempt is made to create some special interest in the subject. Although medically geriatrics is simply part of general medicine, administratively this work has to be established as a new field for special endeavour: such work as that described by Dr. Andrews and Dr. Wilson on p. 785 shows how much can be done in this way. Probably it is also true to say that much of the advantage to be gained from this approach to the treatment and prevention of disease among the elderly will be lost if in the initial stages these patients are treated and cared for by those whose real interest remains the care of younger persons; for, although it would be absurd to attempt any clear segregation of patients based on age alone, there are some elderly patients who, because of their social background, their general physical condition, or their disease, seem more suitable for the geriatric than for the general physician.

The first number of the *Journal of the American Geriatrics Society* lays emphasis on, among other things, the excellent response of elderly patients to surgery, and shows how, by means of early ambulation, improved methods of anæsthesia, and thorough preoperative investigation and treatment, age can be prevented from being any contra-indication to radical surgery. Such work strengthens the challenge of medicine to our society. Old age can be made active and healthy: what framework can be provided within which life will continue to have a meaning?

ACCIDENTAL INFECTIONS

THE patient's safeguard against accidental infection depends on the vigilance of his medical and nursing attendants, whose "aseptic conscience" may be developed in different degrees according to the nature of their normal work. Agar slopes and tubes of broth are designed to grow bacteria; therefore bacteriologists must either learn a strict aseptic ritual or change their job. The patient in a first-class operating-theatre is safe in the care of a staff well schooled in the practice of asepsis, and his tissues can deal with the few organisms that may be accidentally introduced no matter how carefully an operation is conducted. In the ward, however, the dangers of accidental infection are sometimes less keenly felt, and unexpected disaster may be the consequence. For example, Rabinowitz and Schiffrin[1] report a tragic series of infections caused by *Chromobacterium prodigiosum* (*Serratia marcescens*) in a children's ward of a Jerusalem hospital. The source of infection was apparently a bottle containing 5% glucose in normal saline, which had been used for intravenous treatment. The organism was first isolated in pure culture from two septic wounds. Next it was found as the cause of meningitis in a child, aged 4 months, who died. During the next 2 months the same organism was isolated from nine patients with various lesions involving the skin, meninges, ears, and joints. When the source of infection was traced, and the contaminated bottle discarded, the trouble ceased. The organism was sensitive only to chloramphenicol and aureomycin; and broth cultures killed mice, apparently by the action of a heat-stable endotoxin.

The report by Rabinowitz and Schiffrin confirms other evidence[2] that chromobacteria cannot be disregarded as potential pathogens, and it emphasises that the aseptic standards of the laboratory and operating-theatre must be applied with equal vigour in wards. It is clearly inadvisable, for example, to use the same bottle of glucose saline more than once; in the laboratory any container which has been opened only once, no matter with what care, is no longer accepted as sterile. The importance of applying this doctrine to ward practice is further underlined by the experience of Dr. Michaels and Dr. Ruebner, described on page 772 of this issue, who found that under favourable conditions coliform bacilli may grow quickly enough in some fluids to cause severe effects during intravenous infusion prolonged for more than one day. They suggest that if intravenous therapy is required for several days a new giving set should be used approximately every 24 hours: if the patient has few good veins, the original needle may be left in position. Admittedly, Michaels and Ruebner observed infection in only two cases during 2 years and they found that 5% glucose saline, because it

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[1] *Journal of the American Geriatrics Society.* Published bi-monthly by Williams & Wilkins Co., Baltimore. London agents: Baillière, Tindall, & Cox. 52s. per annum.

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[1] Rabinowitz, K., Schiffrin, R. *Acta. med. or., Jerusalem*, 1952, 11, 181.

[2] Annotation. *Lancet*, 1952, ii, 617.

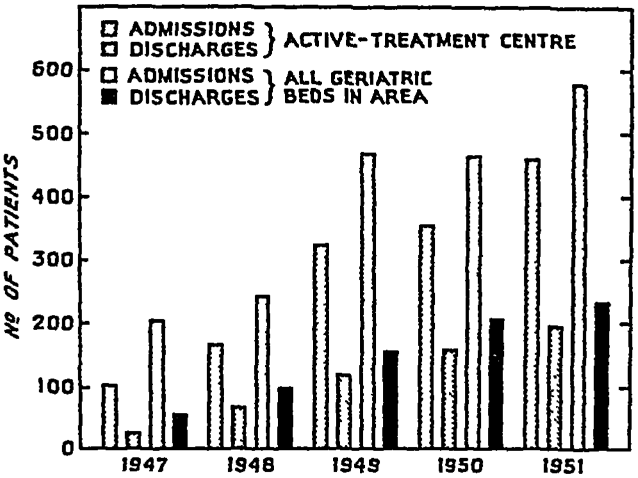

Fig. 1—Admissions and discharges.

the lines of a home, though with facilities for the nursing care of patients confined to bed.

THE ACTIVE TREATMENT CENTRE

A start was made on building up facilities in the active treatment centre in April, 1948. In the course of time the nursing staff was augmented, physiotherapy and occupational therapy departments were initiated, and an almoner was appointed. Radiological and laboratory facilities were made available at the adjacent general hospital, and close contact with the hospital specialist departments was established. As the resources of the geriatric unit improved, the rehabilitation of suitable inpatients was begun. This might mean either the mobilisation of a patient confined to bed for no adequate reason, or a long course of intensive remedial exercises to restore some degree of personal independence to an infirm patient. Considerable difficulty was experienced in returning patients to their homes or relatives when they became fit for discharge, especially when they had been in hospital for a long time. Arrangements had therefore to be made for transfer to welfare hostels of a much higher proportion of patients discharged during this early phase than was found to be necessary later.

TURNOVER IN GERIATRIC BEDS

Gradually, through the discharge of some of the original cases, through the deaths of others, and also through the transfer of suitable patients to the long-stay annexes, an increasing number of beds for new patients became available at the active-treatment centre, and the flow of admissions steadily accelerated. In 1947, before the inception of the geriatric service, some 200 new patients were admitted to these five hospitals, whereas in 1951 575 were admitted—that is, the rate had almost trebled (fig. 1). In recent months there have been indications that this rise in turnover has reached its peak, and that—with existing facilities and the type of patient being treated—no further considerable rise can be expected. It will be seen that not all patients were admitted to the active-treatment centre; about 20% went directly into long-stay beds. These were mainly patients who had been investigated in the wards of general hospitals, and who needed long-stay hospital care. Thus, the patient with inoperable malignant disease or the elderly patient with congestive heart-failure, who was not fit enough for a welfare hostel, are typical examples of this group.

The 575 admissions to 330 beds, in 1951, represents an average annual turnover of 1·7 patients per bed. There were, however, some "inherited" patients who had been in hospital for years and still occupied beds. 1 admitted in 1881 as a young mental defective is still in residence as an elderly dement over seventy years later. As this heritage diminishes in size, the average annual turnover will be in the region of 2 patients per bed.

DEMAND FOR ADMISSION TO GERIATRIC BEDS

Concurrently with this rise in the admission rate, there has been a still larger rise in the number of applications for beds—from 200 in 1947 to 780 in 1951 (fig. 2). This has meant a lengthening waiting-list, especially during recent months, when the rise in admission rate has been slowing down. In 1950, the average waiting time was 15·1 days, and in 1951 it was reduced to 11·6 days, but in the first six months of 1952 it rose to 23·5 days.

TABLE I—SOURCE OF ADMISSION

—	Home	Hostel	Hospital	Living alone
	%	%	%	%
Males	72·8	15·9	11·3	11·3
Females	83·6	6·4	10·0	25·3
Total	79·5	10·0	10·5	20·0

Some method of assessing patients for whom application was made soon became essential, in order that a true picture of the need for beds and of the relative urgency of individual cases might be obtained.

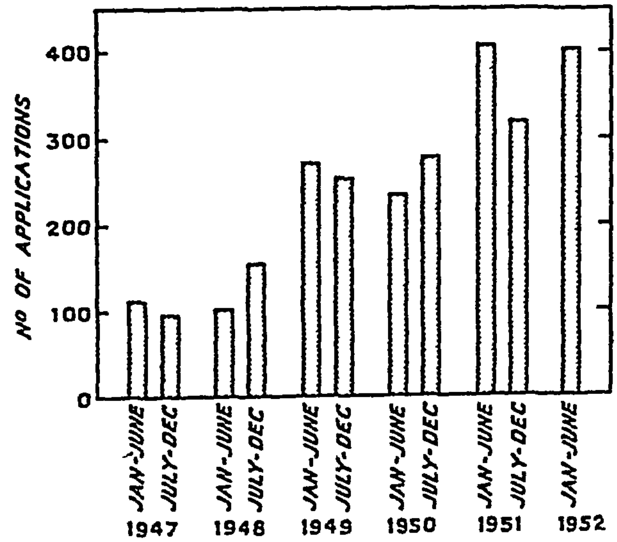

Fig. 2—Applications for admission to geriatric beds.

DOMICILIARY VISITING

Domiciliary visiting of patients awaiting admission has proved valuable. For some patients arrangements other than admission to hospital can be made: those who are suitable can go to a home for old people, run either by the local authority or by a voluntary body, or privately as a rest home. A few patients can be sent to the appropriate special departments for treatment as outpatients. Sometimes a patient can be adequately cared for at home or by relatives if the necessary social props—such as home helps—are provided.

In 1951, 355 patients were visited and 93 were removed from the waiting-list. These represented 12% of the 780 patients referred for admission during that year. For a further 12% a bed was not required when offered either because the patient did not want to enter hospital or because he had died before a bed became available.

REASONS FOR REFERENCE TO HOSPITAL

Analysis of the reasons why patients were referred to the geriatric service revealed a significant difference between this group of patients and those finding their way into general hospitals. Elderly patients in general hospitals were admitted because of [illegible] it, for they refuse to adjust to anything but their original milieu, to which they are always seeking to return. The younger ones form fantasies about their lost parents, and sooner or later develop such signs of instability as anxiety, truancy, aggressiveness, or antisocial behaviour of various kinds. On Jan. 1, 1951, there were 27,263 children in the care of the Seine A.P., of whom 12,591 were under tutelage and 14,772 under protection or confided to care—that is, still having a real or fictitious link with their parents.

It is interesting that in his proposals for relieving this general situation Lelong does not suggest any change in the law which requires this damaging severance of the parental tie. On the contrary, he favours the separation, though at a much earlier age. A child, he says, certainly needs a mother, but it does not particularly matter what mother he has; and to force a mother to take back a child whom she has abandoned, when she has neither the material goods nor the moral qualities to bring him up properly, is not a sound solution. He deprecates those social services which enable a French mother to retain her child while he is an infant, only to discard him when he is older. "Material aid to a mother is illusory when that mother is unfit to fulfil her rôle." This runs counter to current opinion in this country, where we are finding that even a feckless mother may contribute something to her child's development which a deputy, unless highly devoted, finds it hard to supply. Lelong's solution to the problem is an extension of the idea of family placement. He would have the children boarded out with foster-parents or in residential homes where family groups of children of various ages can live under the care of a house-mother. Children would be placed from disposal centres, and would attend clinics for medical supervision and (if necessary) child guidance; social workers would also visit the homes. The older children, he suggests, should live in a "children's village," specially built in the suburbs and consisting of a cluster of "family-group" residential homes, and equipped with its own school and school-teachers. This again runs counter to English experience: we find that children in such homes do best when their house is one of an ordinary row, and they go to the local school and join in the life of the neighbourhood. Separation from parents and segregation from ordinary families are ostracising techniques, designed—it almost seems—to make these deprived children feel acutely, and resent, their difference from ordinary children.

LATAH

THE study of such exotic mental abnormalities as latah and amok has hitherto been left mainly to physicians interested in tropical medicine, to general practitioners working in Eastern countries, and to anthropologists and other non-medical observers. Now a psychiatrist, Dr. P. M. Yap, lecturer in mental diseases at Hong-Kong University, has surveyed latah and related conditions.[1]

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All this is very difficult to place in any one psychiatric category. Yap attempts to group the obvious psychological release of the syndrome with the echo-symptoms and the shameless and coprolalic behaviour occasionally arising in women, apparently caused by organic deterioration. He seeks to relate latah to the culturally simple society in which the patients live; and he compares it with reflex-like fright reactions observed in German soldiers in the first world war. This is by far the most comprehensive account of latah, which, though a relatively harmless peculiarity of elderly women in remote societies, should arouse special interest since it seems to become rare with the intrusion of the Western mode of life.

ENLARGED HILAR GLANDS

WITH the introduction of mass miniature radiography, more cases of asymptomatic enlargement of the hilar glands are being discovered. The people affected are commonly young adults, and students and nurses are often among them. Enlarged hilar glands can usually be identified as smoothly rounded shadows projecting into the lung fields, causing enlargement of the normal hilar roots. Occasionally enlarged glands in the carina cause a backward displacement of the barium-filled œsophagus at this level. But it is sometimes hard to decide whether enlarged hilar shadows are due to dilatation of the pulmonary artery or to glandular enlargement. In these cases a single tomographic cut through the plane of the carina may show the glands situated in the bifurcation of the main bronchi and distinct from the pulmonary-artery shadows.

In generalised diseases of the lymphatic system, such as the leukæmias and Hodgkin's disease, the intrathoracic glands are sooner or later involved; indeed, the first symptoms may be caused by pressure of the glands on the bronchi. In Hodgkin's disease the mediastinal groups are not infrequently the first to be involved. As well as the part they play in the primary complex of tuberculosis, enlarged glands also appear in sarcoidosis and the pneumoconioses, and sometimes in atypical pneumonia and in lobar pneumonia in young children. And of course the segmental glands draining a peripheral carcinoma of the lung become enlarged by lymphatic spread. Involvement of the mediastinal glands may be seen in acute infections, such as glandular fever, german measles, and whooping-cough, and it can also occur in scarlet fever and systemic fungus infection. It is important to remember that the enlargement of the glands may persist for a considerable time after the infection has subsided.

When enlarged hilar glands are found by routine examination of a patient who has no symptoms, a thorough search may in the end show no definite evidence of the cause. Biopsy of suspicious superficial glands, however, may identify the disease; and blood-counts, the Wassermann and Mantoux reactions, and the histoplasmin and Kveim tests may also help. Bronchoscopy is often necessary to exclude carcinoma of the lung.

Chaves and Abeles[1] have now followed up for periods of from 1 to 9½ years twenty patients with asymptomatic enlargement of hilar glands for which no cause could be found. The enlargement subsided in every case, and the time it took to do so varied from 4 to 16 months. Only four of the patients had a positive Mantoux reaction, and in this group the glands took longer to subside than in other patients. The two patients with the greatest glandular enlargement had negative Mantoux reactions. Examination of the blood showed no abnormality, and discharge more rapidly than did the women The average turnover for each active-treatment bed was 6 patients per annum

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Of all patients admitted, 41 1% were discharged, the great majority to their homes or relatives, 31 7% died, and 21 5% required long stay hospital beds (table IV) There was a slightly higher discharge rate and an appreciably higher death-rate among the males than the females, with the result that the percentage of males needing long stay beds was only half the percentage of females Patients who were transferred to long-stay beds, about a fifth of all admissions, included not only those who needed continued nursing care but also the frail ambulant patients who had not become fit enough for a welfare hostel and those mentally infirm patients who although without serious behaviour disorders, remained unsuitable for such a hostel About 42% of these patients were confined to bed

We have not sufficient information as yet to state the average length of stay of a patient in a long stay annexe, but it seems likely that this will prove to be somewhere in the region of two or two and a half years

DISTRIBUTION OF BEDS

The ratio of male to female beds was 1 3, the ratio of the active treatment beds being 1 2 2, and of the long-stay beds 1 3 3 This preponderance of female beds is accounted for by the greater numbers of females requiring admission, the quicker turnover in male beds in the active treatment centre, and the smaller proportion of males eventually requiring long-stay beds The ratio of active treatment to long stay beds was 1 3 2

ESTIMATING REQUIREMENTS

It is possible from these figures to arrive at an estimate of the load which the geriatric hospital service of West Cornwall, or a similar area, with a population of 250,000, might be called upon to carry

In 1951, the number of applications was approximately 800, but about a quarter of these did not require admission, and the real demand was in the region of 600 Probably this figure would have been slightly greater had beds been immediately available on demand Of these patients almost 80% were admitted to the active-treatment centre As has been noted, however, the applications for hospital beds are still increasing It would, therefore, be wise to budget for, say, 1000 requests per annum—a 20% increase on 1951 figures It is not, of course, possible to say how much the load on these beds will increase in the future, but a demand rate of 1000 represents just over 2% *of the aged population*

As each active treatment bed can deal with 6 patients per annum, 100 beds are needed Of these, 31 should be for males, to provide a ratio of male to female beds of about 1 2 2 A small number of these beds (say 6) should be capable of being used for either sex in order to cope with transient fluctuations in demand The number of long stay beds required, being in a ratio of 3 2 1 to the acute beds is 320, of which 74 should be for males The total bed requirement for such a service is 420, of which 105 should be male beds This number of beds provides a ratio of 1 7 beds per 1000 population

WELFARE ACCOMMODATION

It is essential that hospital beds whether in the active treatment centre or in the annexes should not be blocked by patients who do not require hospital facilities

In West Cornwall there are at present 215 'part III accommodation' beds provided by the local authority These are mainly in the former workhouse blocks of the various institutions and are not the most suitable accommodation for old people Two hostels however, have been opened in recent years providing 39 beds In addition, there are 52 beds in three hostels including a home for the blind run by voluntary bodies and a smaller number of beds in privately run rest houses usually with 4 or 5 residents

Of the patients discharged from the geriatric unit during the period under review, about a third went to hostels or old people's homes more could have been discharged had the vacancies been available But the greatest need was for a more sheltered type of hostel for the frail old person, not in need of hospital care yet incapable of climbing flights of stairs—often difficult stone steps in the older institutions These perforce had to remain in a hospital bed

GENERAL HOSPITAL SERVICE

A survey carried out on April 2, 1950, showed the distribution of old people in the hospitals of West Cornwall on that day The hospitals in the area do not serve their own population exclusively there is some overlap with East Cornwall, now in the Plymouth area, from which the West Cornwall Mental Hospital still draws 18% of its admissions The outstanding fact which emerged from the analysis was the high proportion (41 8%) of hospital beds occupied by persons over 60 years of age

About 1 8% of the aged population were in hospital on the day the Census was taken, and of these 35 3% were in hospitals of the geriatric service, a further 17 8% were in general and cottage hospitals The high proportion of old people in the mental hospital (43 0%) is a measure of the increasing load of mental infirmity in old age which the community now carries It is probable that, as elsewhere, admission to mental hospital is often requested as a means of securing a bed, it has been found that, of 2991 patients aged 65 and over in mental hospitals in the South Western Region, 743 (24 8%) do not require mental hospital care but could be housed elsewhere if accommodation were provided

Analysis of the number of patients over 60 admitted in a year (1949) to hospital units of different types showed that 67 6% were admitted to general hospitals with specialist staff This high figure is of course related to the relatively short stay and rapid turnover in these units, the figures of 13 1% and 4 9% for the geriatric and mental hospital services respectively are associated with a much longer period of stay But in any case in 1949 the geriatric service was in its infancy The figure of 351 admissions in that year rose to 575 in 1951 and the percentage of admissions of all aged sick to hospitals of the geriatric service to 21 Of the 575, 70 (12%) were transfers from general and cottage hospitals Nevertheless, a very large amount of work is done for this age group in general and cottage hospitals, and effective cooperation has been achieved between them and the geriatric unit Regular visits to the unit are made by a consulting physician, an orthopædic surgeon, a dermatologist, an ophthalmic surgeon, and a psychiatrist A general surgeon and other consultants are readily available on call Conversely, the advice of the geriatrician is often sought by the general hospitals not only about the disposal, but about the treatment of geriatric patients in their wards Thus the geriatric unit has come to be regarded as an integral part of the area hospital service with the geriatrician a member of its staff committee and of the medical advisory committee of the West Cornwall area

There are no geriatric outpatient clinics in the area nor is it intended to provide these except on a limited scale Outpatient attendance by old people in rural areas often entails a long and exhausting day, particularly if X ray and other investigations are required Attendance for physiotherapy in winter may mean strain and exposure which outweigh any advantage to be gained from the treatment Outpatient clinics in all the main specialties are held in the cottage hospitals and the large general hospitals in the area and attendance at these involves less travelling At Truro and Redruth ov 18% of outpatients attending in one year were over 6 Nevertheless, the actual numbers of outpatient atte it, for they refuse to adjust to anything but their original milieu, to which they are always seeking to return. The younger ones form fantasies about their lost parents, and sooner or later develop such signs of instability as anxiety, truancy, aggressiveness, or antisocial behaviour of various kinds. On Jan. 1, 1951, there were 27,263 children in the care of the Seine A.P., of whom 12,591 were under tutelage and 14,772 under protection or confided to care—that is, still having a real or fictitious link with their parents.

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Public Health

The Nation's Health in 1951

In his report[1] for 1951 on the state of the public health in England and Wales, Sir John Charles, chief medical officer of the Ministry of Health, says · "We have . arrived at a time when the citizen himself must actively participate in the campaign for better health if further substantial progress is to be made" He points out that most of the improvement in public health over the past century has been achieved without the citizen having had to exert himself or put himself to any great inconvenience, for "a silent army of sanitary technicians has unobtrusively worked this miracle on his behalf" But now the era of sanitary engineering was giving place to that of personal hygiene when "each person must definitely contribute to the common weal"

VITAL STATISTICS

The fall in the birth-rate, which has been declining since 1947, continued the rate for 1951 was 15 5 per 1000 population The report says that the lack of progress in reducing the stillbirth-rate in the last two or three years must be regarded as disappointing and disturbing, particularly when compared with the rapid reduction achieved between 1936 and 1948 The stillbirth-rate rose from 22 7 per 1000 total births in 1950 to 23 0 in 1951 The infant-mortality rate increased very slightly from 29 6 per 1000 live births in 1950 to 29 7 in 1951

The total number of deaths was 549,380—an increase of 39,079 over 1950 Almost all the increase could be attributed directly or indirectly to the severe influenza epidemic during the early weeks of the year The crude death-rate of 12 5 per 1000 population was the highest for several years

COMMON CAUSES OF DEATH

The list of the *most important causes* of death during the year is headed by diseases of the circulatory system (35 9%), followed by cancer (15 7%), diseases of the respiratory system (11 7%), and vascular lesions affecting the central nervous system (12 5%)

Coronary Disease —Deaths attributed to coronary disease continued their 'alarming and perplexing increase, alarming because of the size of the increase perplexing because it had by no means been established that the increases arose solely from a changing fashion in certification though it was undoubtedly a factor of importance" There were 58 309 deaths from coronary disease in 1951, compared with 37,393 in 1947 Hypertension with heart-disease was also appearing more often on death certificates and almost 17,000 deaths were ascribed to this cause in 1951, as compared with 7750 in 1947

Cancer —The number of deaths from cancer and the crude death-rates have increased each year for the past eleven years In 1951 the total was 80,050, which was 810 more than in 1950 The increase in male deaths was again largely due to the deaths from primary neoplasms of the lung, trachea, and bronchus which were responsible for 25% of all male deaths from cancer

Tuberculosis —There was a further considerable decline in deaths from tuberculosis the total number from all forms of the disease was less than 14 000, giving a rate of 315 per million Of this total 12,000 were due to respiratory tuberculosis—2000 less than in 1950 Referring to the welcome increases in nursing staff and in the number of beds available for the treatment of tuberculosis and to the valuable work of mass miniature radiography units the chief medical officer concludes that "it is possible to register a qualified optimism with regard to tuberculosis the end of the battle may be in sight But there were still some unsolved problems calling for further investigation before the final attack was launched

INFECTIOUS DISEASES

Diphtheria, which caused only 33 deaths in 1951, was joining the rare causes of death, and the new low total (661) of notifications also illustrated the success of the immunisation campaign 1951 was the worst *measles* year since notifications were introduced in 1940 there were 616,192 notifications, with 317 deaths The infection was again mild, and "the fall in the case fatality rate continued" In contrast, *scarlet fever* notifications were the lowest on record For the second successive year *whooping-cough* was very prevalent and the total number of cases reported 169,411, was higher than ever before Deaths from whooping cough totalled 457

The number of deaths from *influenza* in the first quarter of the year was greater than in the same period in any of the preceding fourteen years It was estimated that 50,000 people died directly or indirectly as the result of influenza during January and February Influenza was the certified cause of 15,809 deaths—about 12,000 more than in 1950 Since 1918 the proportion of deaths at ages under 55 has gradually decreased in 1951 only 12% of those who died from influenza were under 55, while in 1918 no less than 80% were under that age For the first time in this country absence from work was used as a measure of the progress of an influenza epidemic The outbreak reached its peak in the third week of January when 438,150 people claimed sickness benefit

Dysentery behaved as inexplicably as ever There were 28,561 notifications, the highest number ever recorded and 71 deaths A special subcommittee of the Public Health Laboratory Service has been formed to study the subject Most cases were in outbreaks in day nurseries, residential nurseries, children's hospitals, mental hospitals, and day and residential schools The chief medical officer remarks "Were all meat consumed on the day it was cooked outbreaks in institutions or associated with catering establishments would very soon cease" For the first time since 1942 the number of *food-poisoning* incidents decreased, but "food poisoning, though less prevalent, was still sufficiently widespread to give rise to continued misgiving on our present standards of food hygiene"

There were fewer new cases of *syphilis* and *gonorrhœa* but, the report continues, "we must expect . the appearance of increased neuro and cardio-vascular syphilis consequent upon old and latent infections in fact, the larger numbers of women attending the clinics for the first time for neuro syphilis may represent the beginning of the new host of the afflicted ' Cardio vascular syphilis arising from war-time infection has not yet appeared, but there is little doubt that it will make its presence apparent in due course" Indeed the legacy from the last war was likely to be large, and an extension of routine blood testing would help to discover the thousands who must still be untreated in the late and latent stages of syphilis

NUTRITION

Since the late war, clinical surveys of the nutritional state of the population have shown an almost complete absence of definite evidence of malnutrition or undernutrition In order to provide evidence on which to base future comparisons and with which to detect small deviations, data have been collected from specified groups of children In 1951 observations were confined to boys aged 11 and 17 Boys from grammar schools were on the average taller and heavier than those from modern schools whatever the dietary pattern The factors responsible for this difference seemed to be associated with parental care, higher social group and perhaps parental intelligence Whatever the social class school and family size boys who shared beds were on the average lighter than those who did not and boys whose mothers went out to work were heavier than those whose mothers did not

ACCIDENTS IN THE HOME

Domestic accidents continued to take a heavy toll —between 5000 and 6000 deaths every year The

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[1] Report of Ministry of Health [illegible] Part II on the State of the Public Health [illegible] of the Chief Medical Officer for 1951 [illegible] Cmd [illegible] Pp 222 [illegible]

Special Articles

ORGANISATION OF A GERIATRIC SERVICE IN A RURAL AREA

C. T. ANDREWS
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CONSULTING PHYSICIAN

T. S. WILSON
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GERIATRICIAN

WEST CORNWALL GERIATRIC SERVICE

IN July, 1947, the Cornwall County Council invited one of us (C. T. A.) to carry out a survey of aged and chronic sick patients in the seven public-assistance institutions in the county. This paper gives an account of the development of the service which followed.

In the reorganisation which took place after July, 1948, the western part of the county became a "clinical area," with a population of 250,000 and a nearly complete hospital and specialist service. The geographical isolation of this area, bounded as it is on the north, west, and south by the sea, and on the east by Bodmin Moor, has afforded an opportunity to study the problems of providing a geriatric service for a predominantly rural area.

THE SURVEY

The object of the survey was to find out to what extent modern methods of treatment and rehabilitation would be likely to benefit these patients. It was hoped that a considerable proportion of patients might be restored to such a degree of activity as no longer to require nursing care.

The 454 hospital patients were housed in seven joint-user institutions located at Penzance, Helston, Redruth, St. Austell, Falmouth, Launceston, and Liskeard. Later, the units at Launceston and Liskeard were included in the Plymouth clinical area; which left five institutions, housing 303 patients and 190 "house" inmates, as the basis of the service in West Cornwall.

The buildings varied in quality from that at Madron, near Penzance, which had had press publicity ("Pull this workhouse down"), to units of fair quality containing hospital wards of 16–20 beds. In the main they were the same dull drab institutions found in other parts of the country.

There was no modern hospital unit among them, and sanitation was woefully inadequate: on the "house" side, earth-closets were still in use in some places. Heating was by coal fires, and windows were often small and high, which meant patients confined to bed could not see out. In one case, a single bath served 50 male patients. The walls were sometimes unplastered, and the colour scheme was uniformly sombre and depressing. New building, however, was in progress at Falmouth (16 beds) and Liskeard (14 beds).

Traditionally, each institution served its own area and accepted everything that came its way. Thus there were found in the same buildings, and often in the same wards, mental defectives and borderline and certifiable mental patients as well as the chronic sick patient suffering from congestive failure, chronic rheumatism, parkinsonism, or fractured neck of femur, and the occasional acute medical case.

The only medical attention was provided by a local general practitioner calling once or twice a week; he was a busy man and had no time to keep records. Patients were admitted at the request of their general practitioner through the agency of the relieving officer. No clinical details accompanied them, except a document that certified the need for admission. There was no almoner service: patients generally came for life, and the possibility of their return home was never envisaged, either by the relatives or doctor sending them or by the hospital staff receiving them.

Nursing was good in quality but numbers were short. In the seven institutions there were 7 State-registered nurses, including the matrons who were often called upon to deputise for absent staff. The ratio of nursing personnel and ward orderlies of all types to patients was 1 : 5. In the circumstances, it was amazing what good work was done: it was not unusual to find a unit of 50 patients without a bedsore, and moreover there was a bond of affection between staff and patients not always seen in hospitals caring for short-stay patients. But the evils resulting from nursing shortage were real. The bedfast patient was an easier problem to the nurse with her hands full than the frail ambulant patient. So all patients remained in bed; and the evils of the bedfast state were only too apparent in apathy, contractures, wasting, and incontinence. There was no occupational therapy or physiotherapy. The situation in Cornwall was thus no better but rather worse than that in the country as a whole.

A study of 1% sample tables from the 1951 Census shows that the population over 60 amounted in Cornwall to 19·5% of the total population as against only 15·8% for the whole of England and Wales. This higher proportion of the elderly is probably due rather to the large numbers of people who come to live in the county on retirement than to special longevity in the native Cornish. The figures have a practical significance in an area from which the private nursing home has almost entirely disappeared.

The buildings were surveyed with a view to deciding their possible use in an organised service, and the patients were individually examined and classified. The results of the classification were:

	No.
Elderly infirm	42
Acute sick	16
Chronic sick:	
(*a*) Remediable	114
(*b*) Irremediable	162
Psychiatric:	
(*a*) Requiring care in annexe	55
(*b*) Certifiable	8
Mental defectives	39
Blind and deaf	10
Others	8
Total chronic sick	454
Elderly fit patients not examined ("house" inmates)	268

The average age of the chronic sick was 71·2 years.

This investigation showed that we needed to provide both for the investigation, treatment, and rehabilitation of those patients classed as remediable who were already occupying hospital beds, and also for the reception, investigation and treatment of new patients. These were central and closely allied problems. We also needed more effective means of segregating elderly psychiatric patients and mental defectives.

OUTLINE OF THE SERVICE

It would obviously have been neither economical nor desirable to provide the full range of hospital facilities (such as X-ray and physiotherapy departments) in all the institutions. The principle of a central active-treatment unit, linked with a number of peripheral long-stay annexes, was accepted as the framework for the geriatric hospital service of the area.

Barncoose Hospital, close to Redruth General Hospital, and the most central of the five institutions, was chosen for development as the geriatric unit, while the other four institutions were to be long-stay annexes. Remediable patients in the peripheral hospitals were to be brought to the geriatric unit for treatment, being exchanged for patients for whom active treatment in the geriatric centre was no longer required. New admissions were to be taken into the central unit in the first instance, and only those patients who eventually required indefinite hospital care would be transferred to the annexes on completion of treatment. As far as possible, such patients would be sent to the annexes nearest their homes and friends.

The long-stay annexe was conceived as a permanent home, and its development was therefore to be along

In England Now

A Running Commentary by Peripatetic Correspondents

I WAS told that the Central Line was out of action, so I went on the other one as far as Stratford. Crashes never happen on the Underground, and even when I found that typical air of controlled excitement I thought it was due to an unusually complicated breakdown. The unused fire-hose running across the platform was a little surprising, but I thought it was just a precaution. Then coming down the passage as I went towards the exit was a bunch of nurses; they were carrying splints, and bandages in kidney dishes. And the place seemed full of policemen. At the exit there was a mass of press cameras, then I knew that something really had happened. Outside in the narrow street were packed the ambulances, and half a dozen red London Transport vans with notices on the front saying "Urgent," and fire-engines, and police cars. I went on my way, but as more ambulances arrived and joined the queue I wavered and finally went back to see if I could help. Down in the tunnel everybody seemed to be waiting, too—policemen and firemen with walkie-talkie sets and a couple of dozen men and women standing talking. The whole scene was lit brilliantly like a film set, and the quiet voices boomed and echoed. Railwaymen were bringing up cutting tools and cylinders. Somebody said "There's nothing to do. We can't get at them." So we went on waiting. It had happened an hour before, and many of the casualties had been got away but there was so little room to work. I waited in the tunnel until half a dozen doctors (I guessed they were housemen from the local hospital) came out from the train and went back to the surface. There were too many of us, so I went too. It was just like the blitz, with three or four independent services working with complete confidence and apparently nobody giving any orders. There were even the cups of tea. One feels such an amateur when the public services go into action like this.

* * *

Those who teach us, either in the lecture-theatre or by correspondence, often refer to the value of systematic reading, and it is hard to think of a phrase at once so impressive and so awe-inspiring. It conjures up a vision of the human mind as the prepared building site of a vast fabric of knowledge which is slowly but steadily built up over the years till it touches the skies. By systematic reading day by day we add fresh bricks to the growing pile. Everything not only falls firmly into place but stays there, so that in our later years we are, or ought to be, great towers of knowledge to which our juniors can turn whenever they find themselves perplexed. Unhappily it does not always turn out like that. Not all of us have the capacity to read systematically and, even if we have, there are constant interruptions. Memory, moreover, is a fickle jade and not a few of our carefully built-in bricks tumble out and lie scattered untidily among the foundations, which are themselves too often very dicky indeed. Sometimes the gaps remain merely as such; sometimes they become temporarily or even permanently filled up with inferior or shoddy material. Not uncommonly, if we are honest with ourselves, we are forced to admit that the almost completed structure bears less resemblance to a skyscraper than to an untidy ruin; indeed, viewing it objectively, we may legitimately wonder whether it is a structure at all—or ever was.

* * *

"Each to his art" is one of those workaday slogans so well suited to some aspects of the British temperament. The moment the hooter blows, however, it is remarkable to hear how abruptly the note changes to "hand me down my neighbour's tool." Out come the spanners, spades, scissors, palettes, penny-whistles, inkpots, fretsaws, and frying-pans according to taste, and our whole game-but-not-too-gifted nation surges forward on a formidable tide of creation. Not least enviable are members of the Medical Art Society[1] turning from patients to paint. No doubt a psychiatrist (if all they say of art-therapy is true) could detect the bedside form of these self-expressing doctors, distinguishing the physician from the surgeon (and gynæcologist from both), the voluble from the taciturn, the careful from the high-spirited, the mild from the mince-'em-up-alives. I shall not attempt this feat (though tempted), for doc should not eat doc. Let me stick rather to art criticism, which lies so strangely outside the laws of libel.

The medical artists seemed to be happiest among the water-colours, and so was I. A group of four hanging together—*Betteshanger Mine* by C. P. F. Boulden, *Looking South from Gogs Hills* by Henry Wilson, *Ramatuelle* by Edith Whetnall and *Poole Harbour* by Roland Rushton—were all worth looking into for a good long time. I also enjoyed the bold strokes of dark wood against snow in Rushton's *Rue Savoyarde*, and the almost poster gaiety of his *Hayes Common*. Eric Topham's *River Thurne* and Reginald T. Payne's red crayon *The Strand at Rye* both had quality, and I liked the long distances of land and sky in Charles Milner's *Vale of the White Horse*. G. Sparrow had amused himself with reproducing the spirit of eighteenth-century hunting prints in *Point-to-Point*, *the Paddock* and *Cowdray Point-to-Point*; he has the right flavour of caricature and a gay and easy line. But very few of the pictures in the water-colour room deserve to be ignored.

The oils show a lower general level of attainment and more of a scatter round the mean. Since I turn to any picture of a fair-ground as a heliotrope turns to the light, I found myself observing with pleasure the battered, coloured *Steam Engine* of R. A. Beaver, and afterwards with a sad nostalgia, his *The Old Music Hall* painted on a forlorn damp day at Hackney. Quite different from this close and lowering little scene are the wide expanses and pale colours of his *Brooklands*, and another change of light comes with a visit to Sir Philip Manson-Bahr's tropical island, where bold green palms enclose *The church, Rambi, Fiji*. B. E. Barsby-Smith has yet another quality of un-English light in *Dahok, Iraq*. Norman Ashton has done some elegant formal flowers, R. F. Jamieson some *White and Yellow Boats* that somehow lift the spirits, and R. W. M. Strain, in *The Harbour, St. Peter Port*, has been highly extravagant with his paint. H. Elliot Blake's *Palamos Harbour at Dawn*, where little yellow boats are waiting in the misty morning, will please all parties.

* * *

The doctors' Easter has come and gone. Before the holidays I had averaged 30 surgery consultations a day. I closed the surgery on Good Friday and opened again on Saturday. To my mild surprise I was not crowded out with the left-over Friday sufferers who had nursed their pains and licked their sores waiting for the Saturday. On the contrary it was easier than an ordinary Saturday. The sick seemed to have taken a new lease of health.

On Sunday and Monday I was closed, and on the Tuesday steeled myself to receive the accumulated battalions of 48-hours' untreated sick. But, apart from the regulars for their certificates and the medicines as before and an odd one or two sick of a surfeit, business was at a standstill. The chronics of Sunday, Monday, and Tuesday, with their pains here and their aches there and the twittery feelings in the pits of their stomachs, just did not turn up.

Why, one asks oneself, does Easter stay the march of disease, or has it a secret curative influence? Or is most of our daily sickness not really necessary? Will some psychologist kindly explain?

* * *

My fellow peripatetic (April 11, p. 712) will find the formula for Lockyer's pills in the *Dictionary of Practical Receipts* (1848):

Panacea of antimony 10 grains, white sugar candy 1 oz. Make the mass into 100 pills, of which 1, 2, or 3 taken at a time will act as a gentle emetic and aperient.

The Panacea of Antimony is made thus:—

Sulphuret of antimony [illegible] oz., nitre 10 oz., [illegible] 1 oz.; mix in fine powder [illegible] and keep in the fire [illegible] powder and wash it. [illegible] colour.

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[1] Whose annual exhibition is in progress until April 2[illegible], at Walker's Galleries, 118, New Bond Street, London, W.1. (Weekdays 10 A.M. to 5.30 P.M., Saturdays 10 A.M. to 1 P.M.)

for which they required treatment, and usually for that reason alone; whereas with nearly all the patients referred to geriatric hospitals the physical disability was complicated by a considerable social problem. Only a small number of patients were referred to the geriatric service for purely medical reasons, and these were almost always patients for whom physical rehabilitation was indicated. This social problem is emphasised by the high proportion (20·0%) of patients who lived alone (table I). It is significant that the percentage of women (25·3) in this category is more than double the percentage of men (11·3). When an old person living alone becomes ill, admission to hospital is almost inevitable, for the kindly neighbour is rarely willing, or indeed able, to look after him for long.

Disorders of behaviour placing an intolerable strain on the domestic structure also lead to admission: 19·0% were confused and irrational on admission, and 23·0% incontinent of urine or fæces. The social difficulties of these patients influenced both the effect of treatment and their disposal on discharge: it was often found that patients did not make the expected progress until the problem of their future had been solved.

TABLE II—AGE-DISTRIBUTION

—	Under 60	60–69	70–79	80–89	90 +	Total
	%	%	%	%	%	%
Males	5·3	18·0	48·9	26·3	1·5	100
Females ..	7·3	19·4	35·3	32·8	5·2	100
Both sexes ..	6·6	18·9	40·2	30·4	3·9	100

Between August, 1950, and June, 1951, 365 patients were admitted to the active-treatment centre, 133 (36·4%) being males and 232 (63·6%) females. The ratio of females to males was thus 1·7 : 1. Their age-distribution is shown in table II; most of them were between the ages of 70 and 90, with an average age of 76. The average age of the females was somewhat higher than that of the males—77 as against 74—and there were more females than males aged 80 or over.

CLINICAL GROUPING

Certain well-defined clinical entities appear to gravitate to geriatric beds, such as cases of stroke, arthritis, and other conditions requiring physical re-education and reablement. More than one disorder was an almost invariable finding. In the main, however, the patients were infirm old people with ill-defined senile disabilities complicated by unfavourable social circumstances, who required investigation and treatment of their physical complaints and a solution of their social problems. The following clinical conditions were found among them:

	No.	%
Hypertension	102	28·0
Congestive heart-failure	67	18·4
Coronary occlusion	16	4·4
Cerebrovascular accident	75	20·5
Senile dementia	47	13·0
Chronic bronchitis	7	1·9
Acute pulmonary inflammations	46	12·6
Neoplasm	27	7·4
Fractures	24	6·6
Advanced arthritis	18	4·9
Paget's disease	4	1·1
Pernicious anæmia	7	1·9
Other severe anæmias	13	3·6
Diabetes	18	4·9
Thyrotoxicosis	3	0·8
Myxœdema	2	0·5
Cholecystitis	6	1·6
Peptic ulceration	5	1·4
Ulcerative colitis	3	0·8

As might be expected, cardiovascular disorders formed a high proportion.

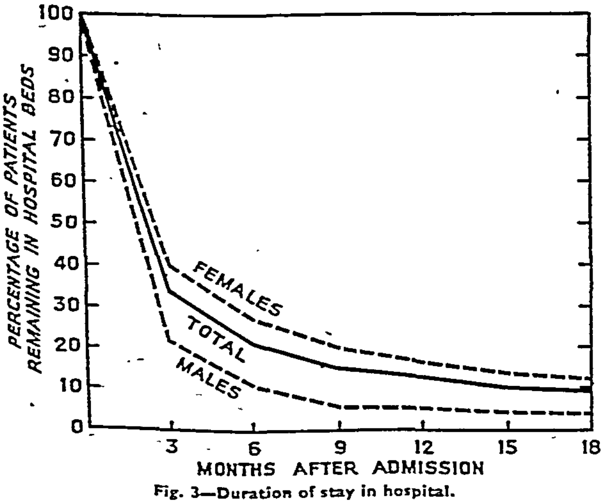

Fig. 3—Duration of stay in hospital.

TABLE III—DURATION OF STAY (WEEKS) IN ACTIVE-TREATMENT BEDS

—	Discharged	Died	All patients
Males	10·5	3·3	7·5
Females	13·5	3·6	9·9
Both sexes	12·2	3·5	9·0

Some 28·0% of the patients suffered from hypertension. A systolic blood-pressure of 190 mm. Hg or over, or a diastolic pressure of 120 mm. Hg or over, or both, were the criteria accepted for such a classification. The high proportion of patients (almost a fifth) who suffered from congestive heart-failure indicates the extent to which this clinical group—many of whom would formerly have been admitted to general hospitals—now tend to come into geriatric beds. The fact that 20% of the patients suffered from a cerebrovascular accident of more than minor degree and that over 10% had advanced arthritic conditions and fractures (usually fractures of the neck of femur) indicates that the rehabilitation load was considerable.

TABLE IV—FATE OF PATIENTS ON LEAVING ACTIVE-TREATMENT BEDS

—	Discharged	Died	Transferred to	
			Other hospitals	Long-stay beds
Males	42·9%	37·6%	6·0%	13·5%
Females	39·7%	28·4%	5·6%	26·3%
Both sexes ..	41·1%	31·7%	5·7%	21·5%

Acute pulmonary inflammations were present in a significant proportion. A neoplastic condition was detected in only 7%, the gastro-intestinal tract being the site of the neoplasm in almost half these cases. Anæmia of severe degree was present in about 5%; diabetes was the commonest endocrine disorder; and peptic ulceration was relatively uncommon.

Only a third of the patients occupied a bed for more than 3 months, and at the end of eighteen months only 12% of the patients still remained in hospital (fig. 3). There was a significant difference between the sexes, the percentage of males remaining at the end of each quarterly period being much less than that of the females. This greater rapidity of turnover in male beds is borne out by an analysis of the duration of stay of patients in active-treatment beds (table III). The average stay for all patients was just over two months. The men averaged only 7·5 weeks, however, as compared with 9·9 weeks for the women. This was due not only to the fact that the men who died did so after a slightly shorter stay in hospital than the women but also to the fact that those men who were eventually discharged became fit for

JUNIOR HOSPITAL STAFF

SIR,—If anything, Dr Gee, in his letter of April 4, understates the position If we are right in our interpretation of the signs, something like a breakdown in the junior staffing of regional-board hospitals appears to be imminent The result will be a catastrophic fall in the standards built up since 1948

In view of the muddle and inhumanity which have characterised the Ministry's handling of the senior-registrar problem, it is not surprising that it is already proving difficult to find suitable applicants for registrar appointments in peripheral hospitals

It appears to us that the main reason for this lamentable situation is that the Minister's main advisers have been from the teaching hospitals

A R KELSALL
Watford C W C KARRAN

TRICHOMONAS VAGINITIS

SIR,—A disease is important, apart from any clinical or pathological interest, if it is common, difficult to treat successfully, and a cause of much distress By these criteria trichomonas vaginitis is indeed important and needs every effort to prevent and cure it In addition it is a serious social disease by reason of its malign effect on married life Not only does the local pain and tenderness often prevent coitus until finally it is cured, but it *may even break up a marriage* Recently I have seen a young married couple, with one baby, tortured by the frustration of compulsory abstinence which has finally separated them, and most gynæcologists have seen similar domestic tragedies

You are right when you say (April 4) that it has been a neglected disease, though not by the immense amount of investigation of the parasite and attempts at treatment Trussel's monograph, giving some 1200 references, is evidence of the amount of attention devoted to this baffling infestation The neglect is in the day-to-day clinical management in outpatient clinics Vaginitis is regarded more as a nuisance than a serious affliction, and this often leads to perfunctory treatment

All the severe cases in which the vulva and vagina are too tender for any outpatient treatment, and all relapsing cases, should be admitted to hospital for thorough disinfestation under anæsthesia This must be followed by repeated visits to the outpatient department for further treatment through a speculum It is entirely useless to expect a cure by instructing the patient to insert a pessary each day She cannot place a pessary—many more than one are needed—in the fornices around the cervix where the parasite can maintain itself even though the lower vagina is bathed by the melted pessary

Mr McCullagh (April 4) is probably right when he incriminates the oval lavatory seat, though I believe he exaggerates its importance If it is the chief factor why do we so seldom see the disease in virgins, in children, and after the menopause? Occasionally cases arise in these groups, but relatively the number is very small compared with the incidence in married women

The interesting experiment described by Dr Lanceley and Dr McEntegart (April 4) *shows not only that the* male urethra can harbour *Trichomonas vaginalis* but also that two of their cases were infested *for some weeks*

My own view, after having considered and treated some hundreds of patients, is that the disease is chiefly communicated by coitus with an infested man

London W 1 ALICK BOURNE

THE GAP SEAT

SIR,—Mr McCullagh (April 4) exhorts medical practitioners to demand the introduction of the gap type of non-infecting lavatory seat in public lavatories

The reform he advocates is inadequate What is required is the abolition of the lavatory seat and the basin thereunder and their replacement by a squatting platform The obvious advantages are (*a*) the feet are the only part to have contact with the lavatory, (*b*) the lavatory can be cleansed with a water jet from a hose pipe, (*c*) the squatting position maintains better tone of the abdominal and perineal muscles, (*d*) "bearing down" does not induce inguinal hernia, and (*e*) evacuation is more effective For perfection water replaces toilet paper, and facilities for hand-washing will in any case be available

As many of us know, this is a matter in which the East can teach the West

J. H HUDSON
Dartford, Kent Medical Officer of Health

OSTEOPATHY

SIR—I, in turn, would like to correct any false impression created by Dr Turner's letter (March 28).

Dr Turner has obviously never watched Dr Cyriax dealing with a case of intervertebral-disc displacement His examination and diagnosis is made with great care and skill, and his treatment is carefully worked out according to the history and physical signs Manipulative treatment is only given in about half his cases But when given, it is not a method of "uncontrolled torsional forces" After each careful manœuvre the patient is re-examined and his condition assessed If there is an improvement the manœuvre is repeated, if not the next manœuvre is performed and the patient again re-examined

Dr Cyriax's results compare very favourably with any others I have practised his methods for nearly five years, and a failure to cure is exceptional I should like Dr Turner to hear the complimentary remarks by patients (*I am one of them*) treated by these methods.

Dr Turner's remark about "the process of reductio ad absurdum" is, in itself, absurd He implies that the osteopathic methods will reduce living tissue, whereas Dr Cyriax's can only reduce "dry friable matter" Again the answer is in the results

Hoddesdon, Herts R BARBOR

SIR,—Sir Charles Symonds in his very able article on cervical spondylosis (March 7) was obviously stressing the great need for adequate diagnosis This would seem to be a prerequisite for therapy of any kind, and if one teaches therapy to an auxiliary therapist for even x number of years, it will not increase his ability unless he is also taught pathology and the correct interpretation of the signs and symptoms of disease Physiotherapists are not taught thus

The osteopath is taught in this way He has to study the basic sciences and receives long tuition in the craft of manipulation—which is why he does apply manipulation with discretion

The argument will, of course, lead many once again to confuse osteopathy and manipulation These rather naive blessings upon, and acknowledgments of, the osteopath's skill ignore all question of the theory behind the physiological consequences of manipulation, assuming that the osteopath manipulates, as the orthopædist does, just plainly to mobilise, as though rigidity were in itself a bad thing and mobility the reverse Lack of mobility, spondylosis or any other outcome of morbidity is not the disease but its result, and manipulation applied to any such effects will do nothing to cure the disease although perhaps relieving it

The osteopath will apply manipulation on much more of a strategic basis, possibly leaving an area of spondylosis entirely alone, while convinced that his treatment to the spine in other areas can provoke physiological consequences beyond mere mobility and in the direction of reducing the process of disease from within

General Council and Register R F MILLER
of Osteopaths Ltd Registrar
[illegible] Buckingham Street London W C

dances are low when it is remembered that the aged in Cornwall constitute 19·5% of the total population, and when their high morbidity-rate is considered. They suggest that outpatient clinics are of limited value for this age-group, and seem to argue against the establishment of special outpatient geriatric clinics, at any rate in rural areas. In contrast, of 2609 recent domiciliary consultations in this region, 37·4% were made to patients over 60. The services of the geriatrician and his staff should be freely available for home visiting, not only in an advisory capacity, but for such simple investigations and treatment as are practicable in the home. The almoner can be particularly helpful in making arrangements for the care and disposal of the patient elsewhere than in hospital.

DOMICILIARY SERVICES

If Sheldon's figures for Wolverhampton [1] apply to the country as a whole, the great bulk of the load of infirmity in old age is being carried by the home. No comparable survey has been carried out in Cornwall but it may be useful to note, in passing, the various ageneies which help to give domiciliary service in this as in most other rural areas.

1. *The Family.*—Family ties are strong among the rural population and there is less tendency than in the cities for every member of the family to go out to work. The load is most often carried by a daughter when the mother is ill and by the wife when it is the husband.

2. *The Good Neighbour and Relatives.*—In such a rural area as this, the relatives often live in the same, or a neighbouring, village. Probably at least 80% of cases of infirmity in the home are cared for without recourse to professional nursing help.

3. *The district nurse*, 34% of whose patients in this area, according to a recent study, are aged 60 and over, pays 48·7% of her visits to members of this age-group.

4. *The health visitor* can help by providing assistance for patients awaiting admission, by preparing the way for discharge of patients in hospital, and by subsequently following them up. The nursing officers in charge of the five local health authority areas in West Cornwall pay regular visits to the active treatment centre, where they see patients from their own areas, and discuss any necessary arrangements with the hospital almoner.

5. *The home-help service*, provided by the local authority, is still in its infancy in West Cornwall. However, a good start has been made in organising part-time and "good neighbour" help in the villages. A woman who lives in the same village can be much more knowledgeable on the social problems of her aged patient and much more readily available for the large number of chores for which her services are required.

6. *The general practitioner* carries, and must continue to carry, the main responsibility for medical care in the home. He would benefit considerably by closer liaison with the geriatric service.

LIAISON

The need for liaison arises not only in the domiciliary service, though it is most obvious here because of the number of bodies concerned. Within the hospital service itself there is need for close coöperation, in view of the large amount of work undertaken for old people by nearly all specialties. Between the hospital authority and local authority, the need extends from the level of planning to the care and disposal of the individual patient. We have been fortunate in West Cornwall in having virtually only one hospital management committee and one local authority. We have also been fortunate in the favourable attitude of people and press, and in the ready help given by the Council of Social Service for Cornwall. Nevertheless, the lack of a body with statutory powers to coördinate the activities of all the various committees is sometimes apparent; and a joint planning committee, representing hospitals, general practitioners, local and welfare authorities, and voluntary bodies, is now projected.

SUMMARY

An account is given of the development of a geriatric service in a well-defined geographical, and predominantly rural, area with a population of 250,000.

The service was based on the existing public-assistance institutions, and now consists of a central active-treatment unit linked with peripheral long-stay annexes.

This arrangement made it possible to admit, in 1951, almost three times as many patients as were admitted to the same number of beds in 1948.

We estimate that, in an area like ours, about 1·7 geriatric beds are needed per 1000 of population. In West Cornwall this figure represents 9 beds per 1000 of the population over the age of 60; but the age-structure of the population varies from area to area.

The ratio of long-stay to active-treatment beds should be in the region of 3·2 : 1, and the ratio of male to female beds 1 : 3.

The need for homes and hostels for discharged patients is emphasised.

The part played by the general and special hospitals is illustrated by the fact that, on a given day, 1·8% of the aged population were in hospital, 0·7% in hospitals of the geriatric service, and 1·1% in general and special hospitals. Beds occupied by patients over 60 accounted for 41·8% of the total.

The limitation of the general outpatient services is discussed and the importance of the domiciliary services emphasised. In this area, with 19·5% of old people, the proportion of outpatient attendances in the over-60 group was 18·5%; and 37·4% of those needing domiciliary consultations were in this group.

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[1] Sheldon, J. H. The Social Medicine of Old Age. London, 1948.

SCOTTISH REGIONAL HOSPITAL BOARDS

THE Secretary of State for Scotland has made the following appointments to the five Scottish boards. Out of 27 appointments, 18 are reappointments of retiring members. Those now appointed will hold office until March 31, 1956. The names of doctors are shown in bold type:

NORTHERN REGION

Reappointed: Miss M. B. Clyne, S.R.N.; Rev. Father Neil MacKellaig; G. Ralph; J. South.

New member: Rev. A. Gemmell, F.PH.S.

NORTH-EASTERN REGION

Reappointed: D. Cochran, LL.B.; Provost H. J. Milne, M.C.; R. Ollason; Mrs. J. Wolrige-Gordon.

New members: R. Esslemont; Miss Bell Jobson (till March 31, 1955).

EASTERN REGION

Reappointed: W. I. Brown, J.P.; Prof. **W. L. Burgess**, F.R.C.P.E.; Miss M. C. Cameron, S.R.N.; Councillor J. R. Christie.

New member: **J. C. Anderson**, M.B.

SOUTH-EASTERN REGION

Reappointed: **W. Boyd**, M.B.; Councillor R. Burnside, J.P.; Bailie D. R. Matheson, LL.B.

New member: **G. J. Summers**, M.B; two vacancies.

WESTERN REGION

Reappointed: **T. Anderson**, F.R.F.P.S.; **P. K. McCowan**, F.R.C.P., J.P.; J. Stewart, J.P.

New members: **R. S. Barclay**, F.R.C.S.E.; D. Burns; W. H. Dunlop, C.A.; P. R. Jacobs; A. M. Robertson, J.P.; **J. Bruce Dewar**, F.R.C.O.G., J.P. (till March 31, 1954).

The Secretary of State has made a slight reduction in the size of the boards; the number of members (excluding the chairman) is now as follows: Northern region 16, Northern-Eastern region 18, Eastern region 18, South-Eastern region 23, Western region 29.

words, we earned about 6 units a day! But a good deal of the unofficial work we did laid the foundations of modern routine. Lastly, we refused to "accept" any published *technique*, "standard" or "pirate," until we had given it a thorough trial.

I venture to suggest that were it possible for analysts in hospital laboratories to adopt these principles, results in trials such as that reported by Dr Wootton and Professor King would be closer.

Chichester, Sussex G. A. HARRISON

DISORDERS OF MOTILITY OF THE SMALL BOWEL

SIR,—Mr MacPhee's article (April 4) was of especial interest to us as a similar case to that described by him was seen at this hospital in November, 1952. In this case treatment relieved the patient's symptoms.

The patient, a man aged 62, had a partial gastrectomy in 1942 for a duodenal ulcer, and after this operation he always had loose pale motions. In January, 1952, he began to have persistent central abdominal pain unrelieved by food or alkalis. There was nausea but no vomiting, some regurgitation and eructation of a foul-tasting gas. Diarrhœa—consisting of 4–5 soft putty-coloured stools daily—was constantly present. The patient had lost about 2 stone in weight from the onset of the symptoms, had gradually become dyspnœic on exertion, and had had swelling of the ankles for 3 weeks. He further complained of a sore tongue and of cracks at the angles of his mouth.

A gastrocolic fistula was suspected, giving rise to anæmia, hypoproteinæmia, and riboflavine deficiency.

A barium meal and barium enema excluded the presence of a gastrocolic or jejunocolic fistula. Passage through the small intestine was rapid, the barium reaching the transverse colon in 2 hours; segmentation of the barium in the small gut was seen. The hæmoglobin was 50%, red blood cells 2,000,000 per c.mm., colour index 1·2. Sternal marrow showed active erythrogenesis in excess of normal; megaloblasts predominated among the red-cell precursors. Stool examination revealed no pathogenic organisms, but undigested meat fibres were present. Charcoal and gentian violet given orally were present in the stools in 3–4 hours.

Treatment was carried out as follows: the hypoproteinæmia was corrected by a high-protein diet, the anæmia by a blood-transfusion, vitamin B_{12} injections and iron by mouth, which resulted in a good reticulocyte response; the diarrhœa was treated with codeine phosphate and folic acid, and the ariboflavinosis with injections of vitamin-B complex ('Becosym').

During the next 3 weeks the diarrhœa lessened but was not completely controlled; the hæmoglobin rose to 70%; the œdema disappeared and the cheilosis improved slowly; but the patient remained depressed and still complained of abdominal discomfort and regurgitation.

It was thought that the pancreatic enzymes were unable to act, owing to the contents of the stomach passing rapidly into the small bowel; and pancreatin and sodium bicarbonate were added to the treatment. The patient's condition improved immediately. The pain ceased and there was no further regurgitation. The stools became formed, the hæmoglobin rose further, and the patient gained weight. On leaving hospital 2 months after admission his general health was satisfactory.

It therefore appears that in some people an inherent weakness of the small bowel, when thrown into prominence by subtotal gastrectomy and then giving rise to a clinical picture akin to that of gastrocolic fistula, can be corrected by suitable medical treatment.

Wanstead Hospital,
London, E.11.

ERIC FRANKEL
J. LEWIS MOORE

SIR,—Mr MacPhee has drawn attention to the "much neglected field of small bowel function," and articles such as his may well herald an increased interest in the small intestine. May I suggest that in future studies details of the barium preparation should always be given. My colleagues, Dr J. M. French[1] and Prof. A. C. Frazer, have shown that the so-called deficiency pattern is really a property of the barium rather than the gut, for barium sulphate flocculates when mixed with mucus, and this accounts for the segmentation seen on radiography—an outline that bears little or no relation to the contour of the bowel wall itself. When a non-flocculating barium suspension is used in such cases, the bowel is usually dilated, so that the appearance of spasm is probably an artefact.

In our studies on the sprue syndrome, we use routine barium sulphate initially, as the flocculation pattern is a useful diagnostic guide to the presence of a fat-absorption defect. A non-flocculating barium is, however, essential to outline the intestinal wall and to obtain a mucosal pattern; otherwise such conditions as jejunitis may easily be missed.

Birmingham. C. F. HAWKINS

PITUITARY-THYROID RELATIONS

SIR,—In a recent annotation (Feb. 28) you consider the thyroid-pituitary relationship in Graves's disease and mention a paper from this laboratory.[1] The results of present work, though incomplete, may thus be of interest.

Briefly the argument advanced by us against the pituitary having any part in the production of Graves's disease included the demonstration that the actively hyperthyroid gland responded to small doses of exogenous thyrotropin and could not be suppressed by the administration of large doses of desiccated thyroid. You point out the weaknesses inherent in the use of whole thyroid and cite the experiments of Morgans et al.[2] with sodium *l*-thyroxine, which gave results comparable to those with the whole gland. These two experiments, however, leave unsettled the possibility that insufficient hormone was administered to suppress the pituitary.

EFFECT OF TRIIODOTHYRONINE FOR 7 DAYS IN GRAVES'S DISEASE AND IN EUTHYROID SUBJECTS

Patient	Daily dose	Serum protein-bound iodine (µg. per 100 ml.)		Radio-iodine uptake (%)	
		Initial	After treatment	Initial	After treatment
S. I.	1 mg.	11 2	12 3	71	74
N. S.	2 mg.	11 0	11 2	77	[illegible]
R. F.	"	17 2	17 8	73	67
S. I.	"	9 4	11 6	64	[illegible]
P. M.	"	11 2		49	[illegible]
S. I.		13 0	11 7	96	[illegible]
V. V.	"	10 5		67	62
		Control			
P. M.	70 µg.	3 9	4 3	29	[illegible]
I. H.	100 µg.	4 8	[illegible]	33	[illegible]
H. H.	70 µg.	3 8	2 4	21	[illegible]
N. M.		4 1	2 1	20	[illegible]
N. H.		4 6	4 6	33	[illegible]
I. S.	"	4 6	4 6	30	4
		Non-toxic diffuse goitre			
M. M.	2 mg.	4 0	[illegible]	[illegible]	15

This possibility has been under investigation in this laboratory. Triiodothyronine has been given in large dosage to patients with active hyperthyroidism. This agent, isolated by Gross and Pitt-Rivers,[3] is more potent and acts more rapidly than thyroxine. The daily dosage in our experiments—2 mg. daily—is roughly equivalent to 8 mg. sodium *l*-thyroxine or 2·4 g. desiccated thyroid daily. Alarming exacerbations of disease resulted during the week of administration, and in the one patient in whom the basal metabolic rate was repeatedly estimated this rose from +27% to +67%.

The pituitary and hence thyroid was not significantly depressed by these large doses of triiodothyronine (see accompanying table). This tends to rule out the same age-groups were particularly affected; about 20% of the fatalities occurred in children under five years of age and about 60% in people over sixty-five. More children under fifteen died from accidental causes in their homes than were killed on the roads: and between the ages of one and five a fatal home accident was still one of the commonest causes of death.

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[1] French, J. M. In Modern Trends in Gastro-enterology. Edited by F. Avery Jones. London, 1952, chap. 21.

[1] Werner, S. C., Hamilton, H., Nemeth, M. *J. clin. Endocrin.* 1952, 12, [illegible]

[2] Morgans, M. E., Oldham, K. K., Trotter, W. R. *J. Endocrin.* [illegible]

[3] Gross, J., Pitt-Rivers, R. *Lancet*, [illegible]

Smallpox

Another 2 cases of smallpox have been reported from Lancashire and the West Riding during the week ending at noon on April 14. The total number of cases is now 23; and 1 of the new patients, a boy, aged 8, living in Leeds, has died, bringing the total of deaths to 5. The boy, who was unvaccinated, fell ill on April 6. A rash which appeared on April 8 was diagnosed as measles. He was admitted to hospital on April 11 and vaccinated, but he died on April 14. A confident clinical diagnosis of hæmorrhagic smallpox awaits laboratory confirmation. The source of infection has not yet been traced. This is the first case in Leeds during the outbreak. The second patient, a 17-year-old girl in Oldham, had already been in quarantine as a contact and had been vaccinated on March 20. She became ill on March 29, and this illness has now been confirmed as modified smallpox. In Todmorden, where workers at a cotton mill were the first to be infected, Dr. J. Lyons, medical officer of health, said[1] on April 13 that all contacts were out of quarantine in the area and the town might be regarded as free from the disease. Quarantine restrictions were lifted at Halifax General Hospital on April 13 after the 2 remaining suspects had been found to be free from infection.

Diphtheria

Last year there were only 31 deaths from diphtheria in England and Wales, the lowest figure ever recorded. This compares with 2480 deaths in 1940 when the national immunisation campaign opened. But in telling local health authorities of the publicity material available for this year's campaign, the Minister of Health, Mr. Iain MacLeod, stresses that the complete elimination of the disease depends upon the maintenance of an adequate level of immunisation. Sustained publicity by local authorities is essential if parents are to be helped to realise that diphtheria is still a deadly threat. The target for this year is the immunisation of 500,000 children under the age of one.

Metropolitan Water Board Jubilee

After the disastrous cholera epidemic of 1854, routine chemical examination of London's water-supply was introduced in 1858, and in 1871 the position of Government water examiner was established by statute. From about 1882 onwards the isolation and examination of bacteria provided a much more delicate test for assessing pollution or establishing purity; and in 1885 routine bacteriological examinations of the Metropolitan water-supply were started. Then, in April, 1903, fifty years ago, the Metropolitan Water Board held its first meeting in the council chamber of the Privy Council in Downing Street.

Today the board supplies approximately 320,000,000 gallons of water to a population, in round figures, of 6,500,000—one-seventh of the total population of Great Britain. The rivers Thames and Lee provide most of this water, but storage reservoirs are necessary to meet users' needs to the full in a period of drought. Much work is being done to raise output, increase efficiency, and secure economy, and to ensure that methods of waste detection and suppression and of water examination and treatment are of the highest standard. A large filtration and pumping station, with a capacity of 90,000,000 gallons daily, is being built in the Thames valley at a cost of over £4,000,000; and a 75-inch main to carry raw water from the Thames to the Lee valley is being planned. A Government white-paper of 1944 stated: "Not so many years ago it was thought in responsible quarters that London would have to abandon the use of the Thames and the Lee, but today 90% of London's water—bacteriologically one of the purest in the world—comes from these two rivers."

Although the increase in urbanisation and pumping has made it necessary to chlorinate all water from wells, in only a few cases is filtration required. But the river-supplied water, polluted by domestic sewage, trade waste, and plant life, needs elaborate methods of purification. After storage in the large reservoirs, all river supplies are filtered. The ordinary slow sand filtration, first used by the Chelsea Waterworks Co. in 1829, was replaced in 1923 by rapid primary filtration, which removes the larger suspended matter before the water is passed to the slow secondary filters. The board now uses nearly 200 slow sand filter beds, 100 primary filters, and 12 mechanical filters. The ultimate guarantee of purity is conferred by chlorination. Chlorination was first used in the early years of this century; and in 1921 the board began chlorinating filtered river water before it was passed into supply. After 1936 all water was treated by the ammonia-chlorine process, and since 1948 the latter process has been replaced by superchlorination, which has improved the physical quality of the water and its bacterial purity more than any other measure since the introduction of sand filtration.

The board's water examination department at New River Head is divided into three sections: the biological section concentrates on the conditions of the reservoirs and rivers and their treatment; the bacteriological section is concerned with the improvement in the bacterial quality of the water as it passes through the various stages of purification and with the safety of the final water for domestic consumption; and the chemical section deals with chemical treatment and with the examination of the chemical and physical quality of the water, including clarity, colour, and taste. During 1952 the total number of samples collected for all purposes exceeded 93,000.

Improved Physique of Glasgow Children

In his report on the medical inspection and treatment of school-children in Glasgow during the year ended July 31, 1952, Dr. James Ewan, principal medical officer of the education health service of Glasgow, refers to the gratifying results of routine inspection. Fewer children were found to be abnormal; 42·8% of all the pupils examined were recorded as having no defect of any kind—the highest proportion since the establishment of routine medical inspection of school-children in Glasgow in 1909. Moreover, of those children who were found to be abnormal, fewer than ever before had the less remediable type of condition. Average measurements also showed improvement, and only the weights of the 5-year-olds (particularly the girls) failed to conform to pattern. For example, in 1952 13-year-old boys were on the average 0·62 in. taller and 1·65 lb. heavier than boys of the same age in 1945; and for girls the corresponding increases were 0·32 in. and 1·75 lb. During these 7 years, the average measurements for 9-year-old boys rose by 0·56 in. and 1·02 lb., and for girls of the same age by 0·42 in. and 1·08 lb. Defective vision was also less common, and the proportion (14%) of children whose sight was below normal was less than in any previous year except 1949.

Infectious Diseases in England and Wales

Disease	Week ended March			
	7	14	21	28
Diphtheria	22	31	20	20
Dysentery	289	362	433	463
Encephalitis:				
Infective	3	2	5	2
Postinfectious	5	3	1	4
	183	94	47	60
	27,638	26,924	27,227	25,793
	35	45	49	44
Ophthalmia neonatorum	42	35	39	39
Paratyphoid fever	6	6	2	5
Pneumonia, primary or influenzal	1301	1099	1045	1069
Poliomyelitis:				
Paralytic	12	15	20	42
Non-paralytic	5	2	6	4
Puerperal pyrexia	265	220	256	241
Scarlet fever	1534	1675	1625	1739
Smallpox	—	1	7	6
Typhoid fever	6	1	3	2
Whooping-cough	2758	3072	3104	3202

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[1] *Times*, April 14, 1953.

or conversely above 32°C the blood-flow may show a continued increase without a rise in surface-temperature

I also agree with Dr McPherson that the temperature changes recorded on exposure to room-temperature in the patients with diabetic neuropathy were so small as to be insignificant But then, of course, this was interpreted as indicating no change in the state of peripheral vasoconstriction or vasodilatation

Diabetic Clinic
King s College Hospital
London S E 5

M Mencer Martin

THE PROBLEM OF PEPTIC ULCERATION

Sir,—In his letter of April 4, Mr Downie invites opinions on the treatment of high gastric ulcers In 1933 I devised (as I thought) the operation of gastrectomy below the ulcer,[1] which I now know should, by priority, be attributed to Madlener It is not often necessary but produces excellent results, and I have found no reason to regret it Of course carcinomatous ulceration must be excluded today with greater certainty than was necessary twenty years ago, because of the increased possibility of its resection It is also necessary nowadays to think about the possibility of diaphragmatic herniation and retraction of the cardia, both of which may be associated with high gastric ulcer This last combination, however, is also probably best treated by gastrectomy below the ulcer

Department of Surgery,
University of Liverpool

Charles Wells

SCHOOL ORTHOPÆDIC CLINICS

Sir,—I found the special article on school orthopædic clinics by Mr Hulbert (March 14) of great interest

As a result of a certain amount of experience obtained in work in school clinics, I came to the conclusion that minor degrees of symmetrical knock-knees in children were normal and, as Mr Hulbert points out, subject to spontaneous cure

I claim no originality for the following explanation, although I have not seen it mentioned before If it is assumed that the external angle between the femur and the tibia when fully extended, remains constant during growth, it stands to reason that as the neck of the femur grows and as the distance from the acetabulum to the midline increases, so the lower end of the tibia tends to approach the midline Counteracting this tendency is the natural growth in length of the shaft of the femur, but if this increase in length is proportionately less than the increase in distance from the midline to the great trochanter then the apparent knock knees disappear

London, W 1

R J Gourlay

VITAMIN E AND INTERMITTENT CLAUDICATION

Sir,—Dr Hamilton and his colleagues (April 11) have misread my letter. I did not criticise them for trying to prove a null hypothesis but for drawing the invalid conclusion "that vitamin E is of no value in the treatment of intermittent claudication" I cannot accept "condensation" as an excuse for an invalid conclusion brevity should be no hindrance to precision

If as they say, they were really trying to prove the null hypothesis (that vitamin E has no more effect on intermittent claudication than an inert substance), then the "double blind" principle is useless This principle may protect the investigator against his prejudice in favour of a treatment and any consequent suggestions, but if the observer is prejudiced against a treatment or is attempting to prove that a drug is useless, it will not protect him against suggesting to the patients that both the drug and the control substance are without benefit

It would be interesting to know if the arachis oil used as a control substance by Dr Hamilton and his colleagues contained any vitamin E

Flimwell near Wadhurst
Sussex

Geoffrey E Loxton

PHARMACEUTICAL ADVERTISEMENTS

Sir,—It is a pity that the activities of the pharm ceutical firms in this country should be represented b such extreme views—the diatribe of Dr Elek (March 2 on the one hand and the robust and somewhat ove simplified defence by Sir Reginald Watson Jon (April 11) on the other

A large number of reputable firms undoubtedly do ex who bestow large sums of money from their resource without stipulation, and with the sole object of promotin altruistic research In so far as their income is quit often derived, to an appreciable extent, from sal under the National Health Service, this is perhap after all, a commendable form of long term nationa reinvestment We must admit, however, that there ar many other firms, not so "reputable," who are apparentl engaged, not in furthering knowledge or welfare as such but simply in exploiting the discoveries and technique of others, camouflaging otherwise standard product with new names and elegant packages, and pressing them upon the profession with the most persuasive of overture

To attempt to curb such machinations by the impo tion of further restrictive statutes is clearly undesirabl Is it, therefore, quite impossible for the manufacturers and traders' associations to implement a more determined policy by which these renegades might be induced t follow a more ethical course ?

I write, Sir, not with any authority from my medica school (lest Sir Reginald should tweak me !), but simpl as an individual who is interested in this topic

London S E 1

Roy Goulding

TREATMENT OF ADVANCED MALIGNANT DISEASE WITH RADIOTHERAPY AND A C T.H

Sir,—The letter from Mr MacGregor and Dr Lewi (April 4) prompts us to send you the following report

Our experiments on animals, performed in collaboration with Mr D E A Jones, principal physicist at the Mount Vernon Hospital, suggest that there may be some advantage in the use of cortisone or A C T H during the course of deep radiation therapy

In view of these experiments, A C T H was given to two patients with carcinoma of the bronchus who, whilst they were undergoing radical deep X ray treatment,* had developed radiation sickness Both patients showed a dramatic improvement within 48 hours Symptoms of radiation sickness had appeared early in one of these cases and became sufficiently severe to necessitate suspension of treatment with A C T H, not only did systemic symptoms disappear but dysphagia, which had previously been severe, was greatly relieved This patient completed his radical course without further trouble

In four other cases A C T H was given throughout a radical course of radiotherapy and was continued for 2 weeks after the completion of X ray treatment These patients developed no symptoms of radiation sickness, and in three cases marked clinical improvement was observed during the course of treatment

The first patient was having attacks of auricular fibrillation and invasion of the pericardium was suspected This was confirmed during a subsequent attempt at pneumonectomy The patient, however, has remained reasonably well 6 months later The second case proceeded to pneumonectomy the resected specimen showed minimal damage to irradiated normal lung tissue and microscopy revealed islets of tumour tissue which was probably not viable This patient developed a fistula and the postoperative course was complicated by secondary infection, resulting in fatal hæmorrhage from the pulmonary artery

Secondary infection also supervened in the third and fourth cases One patient died from *Pseudomonas pyocyanea* infection and this proved to be resistant to all antibiotics except polymyxin which was unsuccessful in controlling the

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[1] Brit med J 1933 i [illegible]

* Carried out in collaboration with Dr L G [illegible] Mount Ver Hospital Northwood Middlesex

Letters to the Editor

THE SENIOR REGISTRAR

SIR,—At this critical period in the affairs of many senior registrars we should appreciate an opportunity to state the views of the registrars' group of the British Medical Association.

In April, 1952, we put to the Joint Committee our opinion that within a year there would be a serious crisis because, for the first time since the start of the National Health Service, large numbers of senior registrars would reach the end of their four-year tenure. A review carried out by us this month reveals the following facts :

1. In 17 of the 20 regions there are at least 279 senior registrars whose appointments are due to be terminated shortly as they are in their fourth or subsequent years. Figures for the remaining regions, including a considerable number of teaching hospitals, are not yet available ; but it is clear that the over-all total will be considerably more. The great majority of these senior registrars are employed in general medicine or surgery.

2. A survey of the advertisement columns of the medical journals has shown that during 1952 only 25 consultant posts in general medicine and 28 in general surgery were advertised ; these figures do not include the 6 posts in medicine and 5 in surgery created in late 1952 by the North-West Metropolitan Regional Board in an endeavour to solve the senior-registrar problem in their region.

We have never held the view that all senior registrars should eventually obtain consultant posts ; on the contrary, in all discussions we have agreed that competition is essential to ensure a high-quality consultant service. On the other hand it is surely reasonable to suggest that the wastage at senior-registrar level should be no more than about 25%—an ideal which should be fulfilled when the senior-registrar establishment is eventually scaled down to the agreed level so as to be related to future consultant vacancies. Last year, however, in one region between 50 and 70 well-qualified surgeons applied for each general surgical post advertised. This situation bears no relation to the fair competition we have envisaged ; it is the direct outcome of post-war expansion, for which the Ministry must bear responsibility. It is the present generation of senior registrars for whose welfare we are particularly concerned ; this is a special, non-recurring problem which needs special and immediate measures for its solution.

The following suggestions of the Registrars' Group council have been received sympathetically by the Joint Committee.

1. *The consultant service can still be expanded to the benefit of the National Health Service.*

Although the Ministry of Health have admitted their error in announcing abruptly a "freezing" of hospital establishments,[1] it is clear that they would not welcome a general expansion of the consultant service. However senior registrars are at present doing important work ; they are not just supernumerary trainees, and when establishments are cut their work will still have to be done. Consultants will be needed to replace them, and it is surely better to foresee the need and to create additional posts while the present senior registrars are available to fill them. We must point again to the action of the North-West Metropolitan Regional Board which appears to us an important contribution.

2. *The run-down to the agreed senior-registrar establishment should be slow.*

This would allow a gradual but parallel increase in the consultant service, as suggested above. We have agreed that a reduction in establishment is necessary to prevent the present problem from continuing indefinitely, but we feel that no senior-registrar appointment should be terminated before the end of the normal four-year term. It will still be possible to reduce the establishment when posts are vacated voluntarily or when the holders of posts no longer "established" reach the end of their fourth year. It is hoped that the suggestions in the next paragraph will enable suitable individuals in the latter category to continue a specialist career in another post.

3. *Any senior registrar reaching the end of his normal tenure should be allowed and encouraged to apply in open competition for his own post or for other posts in the same grade and specialty, either in his own region or elsewhere.*

It has been suggested that any senior registrar who fails to obtain a consultant post before the end of his four years in office is unlikely to be successful and that prolongation of tenure would only postpone the final disappointment. With this we would agree *in normal times* ; but, as we have mentioned, present conditions are far from normal. It is also admitted that there may be some senior registrars who for one reason or another are unlikely to attain consultant status. We believe that the method outlined above is the most equitable way of solving the present dilemma. A full selection committee is given the onus of deciding whether a man is likely to become a consultant ; if so, they will reappoint him, and if he is not reappointed it will be clear that he would be unwise to continue further. A senior registrar whose post is discontinued owing to a reduction in establishment would be able to apply for posts in the same specialty elsewhere. This plan would ensure that good potential consultants are not lost to the service purely owing to passage of time. Registrars (intermediate grade) might criticise this plan as lessening their chance of promotion. They would, of course, be eligible to compete with senior registrars for the vacant posts ; furthermore it has been agreed that there need be no limit on the duration of registrar (intermediate grade) appointments. This objection also loses substance as the shortage of registrars in the intermediate grade increases, and it is becoming difficult even to fill certain senior-registrar posts. Indeed, we would suggest that unless the Ministry encourage reapplication by senior registrars the shortage of suitable applicants will increase. We appreciate that it may be necessary to place some time-limit (say two years) on the tenure when a man is reappointed to his own post.

4. *Entry into general practice should be made easier for the ex-registrar.*

This is an immensely complicated subject. We have been pressing its importance for over three years, as there is no doubt that registrar experience is usually a positive disadvantage when application is made for a position in general practice. It is now clear that this is the main reason for the increasing shortage of junior medical staff in many hospitals. It seems to us that the manifold problems involved remain unsolved because of the sharp division that has been created between the hospital and general-practitioner services ; there appears to be no mechanism within the Ministry or even within the B.M.A. for discussing it, let alone for taking action.

The Joint Committee have been negotiating registrar affairs with the Ministry of Health for a long time ; but although the Ministry have said that they are considering the problem sympathetically, there is no indication that they realise its urgency or that they are taking steps to solve it. The figures given in this letter have been forwarded to the Joint Committee in the hope that they will be able to persuade the Ministry that the problem not only is serious but also can be solved.

R. M. FORRESTER
Late chairman.
JOHN N. WALTON
Chairman,
Registrars' Group, B.M.A.

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[1] *Brit. med. J.* Jan. 24, 1953, suppl. p. 23.

no member of the court had ever heard of objection being taken to such a question It was one which could properly be asked If it were held inadmissible, great difficulty might be introduced and perhaps in many cases great injustice to an innocent prisoner The appeal was dismissed

A Coroner Complains

Members of the medical profession hardly need to be reminded that coroners enjoy an independent jurisdiction to which respect may be paid and, moreover, that anything like lax certification will hardly escape comment at an inquest At a recent inquest[1] there was evidence that a woman, aged 71, had been taken to hospital because a bone had stuck in her throat At the hospital a surgeon examined her throat through a tube, he told the coroner that he saw no bone, "only a greyish black mass covered with blood" On a warning from the anæsthetist the operation was discontinued, the patient was taken back to the ward and placed in an oxygen tent Further examination was made by radiography, but the patient's condition deteriorated and death occurred two days after admission to hospital The Home Office pathologist who conducted the necropsy stated that death was due to a left pyopneumothorax caused by a wound leading from the œsophagus into the left pleural cavity

The coroner, who announced a verdict of death by misadventure, complained that the two doctors concerned had been less than cooperative One of them had made difficulties when asked for a statement, the other had wanted to send the coroner's court a statement in lieu of attendance, since he was going on holiday Worst of all, a certificate of death from natural causes had been signed, when, as the coroner observed, the history of a bone stuck in the throat should have suggested the possibility of accidental death The coroner was fully justified in pointing out that regional hospital boards, and local authorities' functions in no way affected his jurisdiction If he was asking more of the doctors than his legal authority allowed only in the High Court could his procedure be challenged

Parliament

QUESTION TIME

Flour Improvers

Viscount HINCHINGBROOKE asked the Minister of Food whether he was aware of fresh evidence that consumption of wheat flour treated with nitrogen trichloride (agene) or chlorine dioxide produces eczema and mental disturbance in allergically responsive persons, and what steps he was taking to make chemically untreated flour or bread available to such persons and to those who prefer it —Major GWILYM LLOYD GEORGE I assume that my hon friend is referring to a recently published article in a medical journal reporting a single case of allergic response to flour treated with agene or chlorine dioxide I am assured that flour which has not been treated with either of these improvers and bread made from such flour, will as hitherto be available on special request

Mr BERESFORD CRADDOCK Will the Minister not agree that bread made from wholemeal flour is much higher in nutritional value than bread made from white flour? If so, will he be good enough to inform the public widely of the beneficial effects of such flour?—Major LLOYD GEORGE I think the public have a very good idea The public also have a very keen desire to have white bread

Dr BARNETT STROSS Although the Minister has been informed that up to now there has been one single case of allergy to nitrogen trichloride has he also noted that it is expected that further cases will be found showing similar reactions? Does he not think that as we have been campaigning since 1926 to get rid of nitrogen trichloride as an improver we might have something better at long last?—Major LLOYD GEORGE This matter has been subject to careful examination for a considerable time I am very much alive to it I hope we may have an alternative which is neither of the present substance

Mr R R STOKES Is not a return to white flour much more the desire of the millers than of the general public? Why does the Minister's Department consider that it is better for people to get the right vitamins through the digestive organs of animals than from whole wheat meal?—Major LLOYD GEORGE I am not sure that I altogether accept the remark of the right hon Member about the miller because after all it is in the long run the consumer who decides what he or she should eat

Obituary

ALEXANDER MILES

M D, LL D Edin, F R C S E

Mr Alexander Miles, consulting surgeon to the Edinburgh Royal Infirmary, and the oldest resident fellow of the Royal College of Surgeons of Edinburgh, died on April 9 He had spent his whole life in Edinburgh and even at the age of 87 was still in contact with academic and medical work in the city

Born in Leith, he graduated M B at the University of Edinburgh in 1888 and in 1890 he became F R C S E The following year he was awarded the gold medal for his M D thesis and was appointed to the Syme surgical fellowship Later he became clinical tutor to A G Miller in the Edinburgh Royal Infirmary, and in 1898 he was appointed assistant surgeon He held also the post of surgeon in Leith Hospital and, following the useful and almost invariable custom in Edinburgh at that time he lectured on surgery and operative surgery in the extramural school In 1909 he was made full surgeon to the Infirmary, and he held wards for the statutory fifteen years Thereafter he was chairman of the Astley-Ainslie Rehabilitation Hospital in Edinburgh, and he carried this duty into the era of the National Health Service

After he had retired from surgical practice, he found time for much useful administrative work He served the Royal College of Surgeons of Edinburgh as secretary treasurer, and president and for fifteen years he was its representative on the General Medical Council For many years he was a member of the university court and curator of patronage, and the university conferred on him the honorary degree of LL D in 1925

The first of his important books appeared in 1904 when he collaborated with Alexis Thomson in the publication of their *Manual of Surgery*, which became immediately one of the most popular textbooks with students and graduates Forty six years later, in 1950, he was joint editor with Sir James Learmonth of the lastest edition of the volume on *Operative Surgery* His other publications included a history of prominent past surgeons of the Edinburgh school He contributed many papers to the medical journals and for a time he was editor of the *Edinburgh Medical Journal*

W J S writes "Slim in figure, Miles gave an immediate impression of quickness and alertness of body and mind, which he amply justified As a surgeon he was characterised, especially in abdominal operations by great rapidity without sacrifice of accuracy or care and he was an excellent clinical teacher with always a large following of students He was till recently so interested in the Edinburgh medical school that despite his age his death leaves a blank in the school especially of course among the older members who had been his colleagues "

Mr Miles married Miss Helen Greig, of Leith, who survives him with a daughter

RALPH PATERSON SMITH

M D Glasg D P H

Dr Paterson Smith, director of pathology at the Newcastle General Hospital, and formerly professor of pathology and bacteriology at Dalhousie University Nova Scotia, died at his home in Newcastle upon Tyne on April 7 at the age of 57

He was born in Greenock and was educated at Greenock Academy and the University of Glasgow where he graduated M B with honours in 1918 Soon afterwards he joined the R A M C and became assistant pathologist to the 4th Indian General Hospital After demobilisation he spent a short time in general practice but in 1922 he

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[1] Peterborough Standard March 27 1953

Letters to the Editor

THE SENIOR REGISTRAR

SIR,—At this critical period in the affairs of many senior registrars we should appreciate an opportunity to state the views of the registrars' group of the British Medical Association.

In April, 1952, we put to the Joint Committee our opinion that within a year there would be a serious crisis because, for the first time since the start of the National Health Service, large numbers of senior registrars would reach the end of their four-year tenure. A review carried out by us this month reveals the following facts:

1. In 17 of the 20 regions there are at least 279 senior registrars whose appointments are due to be terminated shortly as they are in their fourth or subsequent years. Figures for the remaining regions, including a considerable number of teaching hospitals, are not yet available; but it is clear that the over-all total will be considerably more. The great majority of these senior registrars are employed in general medicine or surgery.
2. A survey of the advertisement columns of the medical journals has shown that during 1952 only 25 consultant posts in general medicine and 28 in general surgery were advertised: these figures do not include the 6 posts in medicine and 5 in surgery created in late 1952 by the North-West Metropolitan Regional Board in an endeavour to solve the senior-registrar problem in their region.

We have never held the view that all senior registrars should eventually obtain consultant posts; on the contrary, in all discussions we have agreed that competition is essential to ensure a high-quality consultant service. On the other hand it is surely reasonable to suggest that the wastage at senior-registrar level should be no more than about 25%—an ideal which should be fulfilled when the senior-registrar establishment is eventually scaled down to the agreed level so as to be related to future consultant vacancies. Last year, however, in one region between 50 and 70 well-qualified surgeons applied for each general surgical post advertised. This situation bears no relation to the fair competition we have envisaged; it is the direct outcome of post-war expansion, for which the Ministry must bear responsibility. It is the present generation of senior registrars for whose welfare we are particularly concerned; this is a special, non-recurring problem which needs special and immediate measures for its solution.

The following suggestions of the Registrars' Group council have been received sympathetically by the Joint Committee:

1. *The consultant service can still be expanded to the benefit of the National Health Service.*

Although the Ministry of Health have admitted their error in announcing abruptly a "freezing" of hospital establishments,[1] it is clear that they would not welcome a general expansion of the consultant service. However senior registrars are at present doing important work; they are not just supernumerary trainees, and when establishments are cut their work will still have to be done. Consultants will be needed to replace them, and it is surely better to foresee the need and to create additional posts while the present senior registrars are available to fill them. We must point again to the action of the North-West Metropolitan Regional Board which appears to us an important contribution.

2. *The run-down to the agreed senior-registrar establishment should be slow.*

This would allow a gradual but parallel increase in the consultant service, as suggested above. We have agreed that a reduction in establishment is necessary to prevent the present problem from continuing indefinitely, but we feel that no senior-registrar appointment should be terminated before the end of the normal four-year term. It will still be possible to reduce the establishment when posts are vacated voluntarily or when the holders of posts no longer "established" reach the end of their fourth year. It is hoped that the suggestions in the next paragraph will enable suitable individuals in the latter category to continue a specialist career in another post.

3. *Any senior registrar reaching the end of his normal tenure should be allowed and encouraged to apply in open competition for his own post or for other posts in the same grade and specialty, either in his own region or elsewhere.*

It has been suggested that any senior registrar who fails to obtain a consultant post before the end of his four years in office is unlikely to be successful and that prolongation of tenure would only postpone the final disappointment. With this we would agree *in normal times*; but, as we have mentioned, present conditions are far from normal. It is also admitted that there may be some senior registrars who for one reason or another are unlikely to attain consultant status. We believe that the method outlined above is the most equitable way of solving the present dilemma. A full selection committee is given the onus of deciding whether a man is likely to become a consultant; if so, they will reappoint him, and if he is not reappointed it will be clear that he would be unwise to continue further. A senior registrar whose post is discontinued owing to a reduction in establishment would be able to apply for posts in the same specialty elsewhere. This plan would ensure that good potential consultants are not lost to the service purely owing to passage of time. Registrars (intermediate grade) might criticise this plan as lessening their chance of promotion. They would, of course, be eligible to compete with senior registrars for the vacant posts; furthermore it has been agreed that there need be no limit on the duration of registrar (intermediate grade) appointments. This objection also loses substance as the shortage of registrars in the intermediate grade increases, and it is becoming difficult even to fill certain senior-registrar posts. Indeed, we would suggest that unless the Ministry encourage reapplication by senior registrars the shortage of suitable applicants will increase. We appreciate that it may be necessary to place some time-limit (say two years) on the tenure when a man is reappointed to his own post.

4. *Entry into general practice should be made easier for the ex-registrar.*

This is an immensely complicated subject. We have been pressing its importance for over three years, as there is no doubt that registrar experience is usually a positive disadvantage when application is made for a position in general practice. It is now clear that this is the main reason for the increasing shortage of junior medical staff in many hospitals. It seems to us that the manifold problems involved remain unsolved because of the sharp division that has been created between the hospital and general-practitioner services; there appears to be no mechanism within the Ministry or even within the B.M.A. for discussing it, let alone for taking action.

The Joint Committee have been negotiating registrar affairs with the Ministry of Health for a long time; but although the Ministry have said that they are considering the problem sympathetically, there is no indication that they realise its urgency or that they are taking steps to solve it. The figures given in this letter have been forwarded to the Joint Committee in the hope that they will be able to persuade the Ministry that the problem not only is serious but also can be solved.

R. M. FORRESTER
Late chairman.
JOHN N. WALTON
Chairman,
Registrars' Group, B.M.A.

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[1] Brit. med. J. Jan. 24, 1953, suppl. p. 23.

Notes and News

HEALTH EDUCATION

IN London during the past week the World Health Organisation has been holding a regional conference on health education Attended by experts from the United Kingdom and 18 countries of Western Europe, its object has been to bring together " for mutual discussion medical administrators and persons actively engaged in health education work with the primary objective of, first, identifying the constituents of a total programme of health education of the public and, second, of planning toward expansion of health education within countries and the European region as a whole " The joint chairmen have been Dr J M Mackintosh, professor of public health at the London School of Hygiene and Tropical Medicine, and Dr Eugène Aujaleu, director of the department of social hygiene in the French ministry of public health and population On April 11 the meeting was opened by Dr N D Begg director of the W H O regional office for Europe, and the delegates were welcomed by Sir John Charles, chief medical officer, Ministry of Health, and by Professor Mackintosh who gave an introductory address Mr Iain Macleod the Minister of Health, met the delegates on April 13 The leaders of discussions were Dr John Burton, medical director of the Central Council for Health Education, Prof Pierre Delore of Lyons, Frau Magda Telber, and Prof Jaap Koekebakker, and visits were paid by delegates to hospitals, clinics, and exhibitions in London The proceedings of the conference were private

On the eve of the conference the Central Council for Health Education gave a reception at B M A House

SCOTTISH N.H S COSTS

IN Scotland the total hospital expenditure for the year ended March 31 1952, was £31 424 354, and for the executive councils £16,572 122 The report of the Comptroller and Auditor-General [1] records that examinations were undertaken at 25 hospitals where costs were high compared with the national average, and at a further 17 hospitals where " housekeeping " costs seemed high Some of the high costs were due to circumstances outside the control of the regional board, or had to be interpreted carefully in the light of variations in the volume of service provided and the general movement of prices, but it was thought that such special inquiries were nevertheless worth while Special emphasis was placed on the cost of heating which in some war time hospitals built in dispersed blocks was equivalent to £120 a year per occupied bed, but plans were already under way which would reduce this cost by a third

The pharmaceutical services for Scotland accounted for an expenditure of £5 472 758 A total of 151 000 prescription forms (1 3% of the total) were scrutinised for evidence of extravagance, but only 22 reports on prescribing of various doctors were referred for inquiry and only 2 fines were ultimately imposed In addition, the Drugs Accounts Committee, who price the prescriptions, referred back 213 individual prescriptions Of these, 89 were thought to be excessive and 4 fines were imposed

LIVING WITH TUBERCULOSIS

INSTEAD of recording that the tuberculous are constitutionally timorous, aggressive, hysteric, schizoid, obsessional, psychopathic, and whatnot (with appropriate percentages), Dr Wilmer [2] propounds that they are normal men and women who in their pretuberculous days had found life a mixed blessing but had made an average sort of adjustment to it Then the catastrophe of tuberculosis with all its implications and repercussions suddenly *befalls them* *How*, he asks, can they be helped to stand up to this additional burden ? And he makes a gallant attempt to answer this question

Just as in a sanatorium there is a basic physiological régime of abundant food fresh air, and long rest-hours, so has he set out to devise a basic psychological régime to which all patients may similarly be exposed His new patients having been given two or three weeks in which to settle down and get over their initial *bewilderment* are then gathered together in a group and given informal little talks about adjusting to tuberculosis and to sanatorium life, after which, free floating discussions are encouraged Later in the course of treatment patients with similar cultural backgrounds are invited to form discussion groups which meet from time to time and are led, if necessary, throu deeper psychiatric waters This pattern of psychother peutic action is thus partly prophylactic and partly fir aid (The occasional patient who needs more intensi personal treatment is spotted all the quicker) It is offere not as a panacea, but merely as a suggested line of action be modified according to circumstances

The three informal lectures on " Adjusting to Tuberculosis, written as they were for American patients in Americ institutions, cannot be expected to travel well Great stre is laid on the folly of patients who discharge themselve prematurely (the irregular discharge rate in the United State is higher than 50%) but this warning is, so far, less necessa in this country The sputum positive patient's infectivity played down in Great Britain, is rubbed in vigorously in th U S A (witness the habit of mask wearing among all wh come in contact with the patient—except his visitor On the other hand, the possibility that tuberculosis coul ever prove anything more than a tiresome interlude, let alor a fatal disease, to any member of his audience, is implicitl denied by Dr Wilmer (" You are bound to get well in time he seems to say, inviting, surely, the rejoinder, 'Oh yeah What about Joe who was in the next bed ? ") It seems al that the American patient does not mind being urged t enlighten his visitors about tuberculosis, and is willing on h discharge to engage in propaganda against the disease Nevertheless, in spite of these transatlantic differences i approach and emphasis, the basic idea of these talks i excellent Of his ballad, " This is Your World," some 60 lines of dialogue in vers libre between the wise doctor and th patient in varying moods, it is hard to express an opinion When read aloud by two intelligent actors to a *musica* accompaniment, it may register more than it does in col print Rather more fun is promised by the performance o his sixteen inconclusive charades, in which childhood episodes are enacted by patients, who have to improvise their lines and round off the dramatic situation when the script gives out

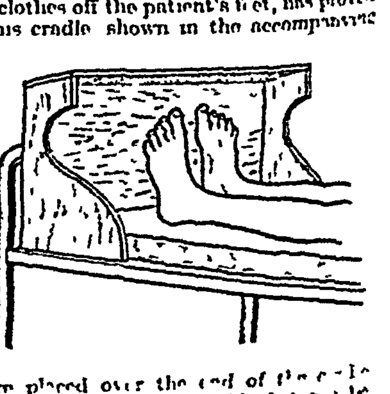
The book is certainly one that all sanatorium superintendents should borrow, in view of the price, and ponder

A BURNS UNIT AT GUY'S

THE Ministry of Health lately suggested that the training of surgeons should include more experience in the treatment of burns, and this was one of the reasons why a new children's burns unit has been established at Guy's Hospital [1] The unit has 12 beds—4 at Guy's for the primary treatment of severe burns, and 8 at the nearby Evelina Hospital, to which cases will be transferred for reparative surgery The Evelina beds will be part of the reconstructive and plastic unit which is already dealing with congenital deformities Mr Patrick Clarkson, who directs the burns unit, and Mr Rex Lawr , senior surgeon at the Evelina, will be in joint charge of reparative treatment and aftercare

WOOD BED-CRADLE

AT Nottingham General Hospital a wood bed cradle designed by the senior nursing staff with the aim of taking the weight of the bed clothes off the patient's feet, has proved very satisfactory This cradle shown in the accompanying figure is easy and inexpensive to make, it is put together with brass screws so that it can be easily washed and when not in use it can be clamped under the bed in a steel frame The foot of the mattress fits inside the cradle and is thus fixed so that " creeping " is prevented The sheet and blankets are placed over the end of the cradle and tucked in. If necessary an additional blanket can be placed across the end of the bed for extra warmth.



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[1] National Health Service (Scotland) Acts 1947 to 1951 Accounts 1951 1952 H M Stationery Office Pp 27 1s 6d

[2] This is Your World By Harold A Wilmer M D consultant in psychiatry San Mateo (Calif) Tuberculosis Sanatorium Springfield Ill Charles C Thomas Oxford Blackwell Scientific Publications 19[illegible] Pp [illegible] [illegible]

[1] *Guy's Hosp Gaz* March [illegible], 1953 p [illegible]

SITTING DOWN TO SURGERY

SIR,—I read with particular interest Mr. Sacks's article (April 4), having already heard the details of his method, applied to biliary surgery, from his anæsthetist colleague, Dr. N. C. Smiedt. The method is so simple that I have used it routinely in the past twelve months, at first standing on the left of the patient, but latterly sitting on an ordinary theatre stool.

The gall-bladder delivers readily through the right upper paramedian incision as soon as a little air is introduced above the liver. All the biliary organs become so superficial that the whole operation only requires short-handled instruments. Only one assistant is needed, and he has to do a minimum of retraction.

The gall-bladder can be removed almost bloodlessly by the method Mr. Sacks describes, which also makes it easy to raise the peritoneal flaps required for reperitonealising the gall-bladder bed. The cystic artery can be identified and ligated in continuity, before dividing it where it reaches the gall-bladder. One can then proceed to expose the junction of the cystic and common bile-duct and common hepatic duct.

I would confirm all that Mr. Sacks claims for his approach in cholecystectomy and choledochostomy, and would suggest that the method is well worth while even if the surgeon prefers to stand—as do certain artists, with the conviction that no worth-while painting was ever produced sitting on a stool.

I would stress particularly the ease in exposing and exploring the common bile-duct. The fingers can readily palpate the whole duct. The passage of a Bakes dilator along the duct (by the right hand) is readily controlled by the left fingers and thumb, which gently support the descending portion of the duodenum and easily palpate the dilator as it emerges through the ampulla. Should a transduodenal approach be necessary the position would be eminently suitable for it.

If from the preliminary exploration of the abdomen it appears that appendicectomy is also advisable, this is more easily done through the upper right paramedian incision in the position described, than with the patient lying flat and the surgeon on the right.

I have not yet tried the position for gastrectomy. Whilst realising the easy access to the duodenum and distal half of the stomach, I would have thought that (from its position under the left ribs) the approach to the proximal half of the stomach, and for that matter to the upper descending colon and splenic flexure, would be easier from the right side as is customary, perhaps with the aid of a sandbag under the left half of the chest.

Guildford, Surrey.   H. A. C. CHALMERS.

REMEDY FOR ANÆMIA

SIR,—I agree with Dr. George Discombe, in his letter of April 11, that the introduction of unnecessary, high-priced, polypharmaceutical mixtures encourages waste of public money, but I do not agree that the proper use of the preparation he mentions, which contains the principal known hæmopoietic substances, is either unnecessary or wasteful. Ideally, a specific nutritional deficiency should be treated with a specific nutriment, but it is rare to meet with a deficiency of one factor without depletion of others. This is particularly true in the common anæmias, since foods low in iron are for the most part low in folic acid and vitamin B_{12}. For example, Litwins and Greenwald[1] have obtained a more rapid response in hypochromic anæmia when liver extract was added to iron therapy. Smith[2] has also presented evidence of the existence in liver of still other factors than folic acid and vitamin B_{12} which account in part for its efficacy, which makes desirable the inclusion of liver fraction in therapeutic preparations.

As Dr. Discombe says, "no-one can exaggerate the importance of diagnosis in anæmia," nor can one underestimate its treatment. The use of a preparation that combines the principal substances known to be involved in hæmopoiesis would seem to be a reasonable therapeutic measure.

Bush House, Aldwych, London, W.C.2.   A. T. MENNIE.

THE FEVER NURSE

SIR,—In your leading article of April 4 you affirm your support for the present age-limit of 18 years for entrants to the nursing profession. Under the system of training in this country, where the student nurse leads an arduous and often dangerous life, lowering the age-limit would certainly be a retrograde step.

One aspect of the Russian method of training nurses, which I saw on a recent visit to Soviet hospitals and nurse-training schools, particularly impressed me. The girls begin their training *at 15 years of age and complete* a 3-year course before sitting the final examination at 18. During this period of training nurses are not allowed to work on the wards, but receive practical instruction under the supervision of their tutors, who accompany them to various hospitals in the locality. Up to 3 hours a day is spent on practical instruction. Only after passing the final examination is the nurse permitted to work on the hospital wards; and, as a result of recent directives from the ministry of health, only doctors and qualified nurses may treat patients.

London, N.10.   JOHN PREWETT.

INACCURACY IN THE LABORATORY

SIR,—The causes of the errors to which you refer in your leading article (March 7) are numerous. In addition to those mentioned two are of great importance: the calibration of glassware, especially pipettes, and the quality of the chemicals, which are purchased from several sources.

In the early days, when chemical pathologists were struggling for recognition, it was possible to set and maintain a high standard of accuracy in technique. Thus, in the first two posts I held there was time to check, and when necessary correct, the graduation of every pipette. Indeed, it was a rule that no pipette should be used until it had been checked and marked with a writing diamond. As the years passed and the work increased without a corresponding increase in staff, more and more glassware was bought—and broken—and it became impossible to check everything. Also it became increasingly difficult to teach the technicians how to do the checking. When there was only a single assistant one was able, if he stayed for several years, to impart to him virtually all one's technical knowledge. Inevitably those days have passed. Considering the pressure of work today, I marvel that the results are as good as they are.

The time factor is equally important in the testing of chemicals. In the "early days" it used to be our rule that no results should be reported until we had (*a*) mastered the technique, (*b*) made satisfactory "recovery experiments," and (*c*) established our own normal range by analysing our own bloods and those of our friends who would allow us to bleed them. Often this led to questioning the purity of the chemicals we bought. Sometimes we purified them ourselves, sometimes we enlisted the help of the firm from whom the purchase was made, and sometimes we substituted the product of another firm. If none of these expedients succeeded we refused to use the method. I estimate that for every "unit" of time nowadays allowed for a result reported, we used to spend additional time equivalent to 6 to 10 units in preparation, checking, and experimenting, for the first one or two years in which a particular method was employed. In other

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1. Litwins, J., Greenwald, L. *Bull. N.Y. med. Coll.* 1950, 13, 116.
2. Smith, E. L. *J. Pharm., Lond.* 1950, 11, 409.

Lind Bicentenary

In honour of the bicentenary of the publication of James Lind's *Treatise on the Scurvy*, the Nutrition Society is holding a conference at Edinburgh on Friday and Saturday, May 22 and 23 During the conference Surgeon Vice Admiral Sir Sheldon Dudley, F R S, will give an address on Lind, and Prof V P Sydenstricker will speak on the Impact of Vitamin Research on the Practice of Medicine Further particulars may be had from Dr C P Stewart, the department of clinical chemistry, clinical laboratory, Royal Infirmary, Edinburgh

Courses for Matrons of Homes for Old

The National Old People's Welfare Committee will hold a four month training course, beginning in October, for women wishing to take up work as matrons or assistant matrons of homes for old people The course will include six weeks' theoretical training at a centre in London four weeks' practical training in the geriatric units of London hospitals, and six weeks practical training in old people's homes Further particulars may be had from the committee, 26, Bedford Square W C 1

Medical Research in Liberia

A broad international programme of research into problems of tropical medicine and health is to be initiated immediately in Liberia, West Africa, by the Liberian Institute of the American Foundation for Tropical Medicine Dr Edward I Salisbury, president of the institute, has announced that the institute is also to provide for the education of physicians in the treatment and control of tropical diseases "Today," he declared, "graduates seeking opportunities for field work are limited almost entirely to the few large companies operating in the tropics which maintain medical departments"

Clergy and Doctors

A meeting for clergy and doctors in the Rural Deanery of Caterham is to be held on Tuesday, May 19, at 8 30 P M, in the clubroom adjoining St Andrew's Church, Coulsdon, when the Rev F. S Sinker, M B, will speak on Coöperation between Clergy and Doctors Further particulars may be had from Dr J B Gurney Smith (Royal Earlswood Institution, Redhill, Surrey), treasurer of the Union of St Luke for Communicant Anglican Doctors, or from Dr R H Hardy (1, Rolle Villas, Exmouth, South Devon) secretary of the union, who will also supply details about the union to those interested

Prizes for Medical Films

In the second competition organised by La Presse Médicale for medico surgical films, the first prize (frs 50,000) was awarded to J Frederic and R Robineaux (Paris) for their film "Cytophysiologie des phagocytes", two second prizes (frs 25,000) were awarded to M Dargent (Lyons) *for the film* 'Resection du maxillaire supérieur," and to Hofmann-Saguez (Paris) for the film 'Laryngectomie reconstitutive" Awards (frs 10 000) were also made to Lapeyssonnie (Corps de Santé colonial) for the film "La lèpre", to Baron (Paris) and Fowler (New York) *for the film* "Vertiges et lentilles prismatiques", to J Demirleau (Tunis) for the film "Traitement chirurgical des kystes hydatiques du poumon par la kystectomie", and to J T Rice Edwards (Newport, Mon) for the film "Resection of the œsophagus"

Medical Art Society

After the opening of this society's annual exhibition in London last Monday members and their guests dined together at the Café Royal Mr Bernard Adams, R P, proposing The Society, provided professional encouragement and cheerfulness Sir Philip Manson-Bahr, the president, spoke favourably of other guests and benefactors including Mr Phillip Lambe Mr Adrian Beach Mr J L Naimaster of Walkers Galleries and especially Dr A M Rackow, the hon secretary Replying for The Guests Lord Moran admitted that soon after qualifying he had forsaken medicine for a year spent among the art galleries of Italy He could not understand why men of business or affairs should grudge the 40 sittings—a mere two or three days—that would give them their one chance of posthumous fame

The society, which was founded in 1935 and now has about 130 members holds meetings monthly in the winter These include criticism by professional artists demonstrations of techniques in various media, and discussions The present exhibition, which is briefly reviewed on p 792, remains open till April 25 The hon secretary may be addressed at Flat 4 11 Hornton Street London W 8

Food and the Future

The fourth meeting in the series on this subject, which the food group of the nutrition panel of the Society of Chemical Industry is holding, will take place at the Chemical Society's rooms, Burlington House Piccadilly, London, W 1, on Wednesday, April 22, at 6 15 P M Mr W F J Cuthbertson, F R I C, and Mr P N Williams, F R I C, will speak on Synthetic Food Potentialities, and Mr Norman Wright, D SC, will summarise the whole series

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CORRIGENDUM *Tracing the Staphylococcus*—In the third paragraph of our annotation last week (p 734) the sentence beginning in line 11 should read "In the mothers of these infants the prevalence was higher than the adult normal level (40–60%) only in the first 2 months after delivery, ."

Lord Boyd Orr, F R S former director-general of the United Nations Food and Agriculture Organisation arrived in Karachi on April 12, to become chairman of the newly formed Pakistan 'grow more food" emergency committee

Dr C H Andrewes, F R S, Prof L P Garrod, and Prof Robert Cruickshank are to attend the third Middle East Medical Symposium at the American University of Beirut from April 17 to 19 as delegates of the United Kingdom They will also give lectures in the Near East on behalf of the British Council

Under the chairmanship of Prof Arvid Wallgren (Stockholm) a W H O team of experts is visiting Indonesia The team includes Prof E W H Cruickshank, Prof M L Rosenheim Prof R I Macintosh, and Prof Alan Stevenson

A low sodium milk powder is shortly to be marketed by Trufood Ltd In a note on April 4 (p 703) we drew attention to low sodium foods manufactured in the U S A

Diary of the Week

APRIL 19 TO 25

Tuesday, 21st

ROYAL COLLEGE OF SURGEONS *Lincoln's Inn Fields, W C 2*
3 45 P M Dr B E Heard Structure of Tumour Cells (Erasmus Wilson demonstration)

SOCIETY FOR THE STUDY OF ADDICTION
8 P M (11 Chandos Street W 1) Dr W R Bett Vincent van Gogh—Artist and Addict

Wednesday, 22nd

ROYAL COLLEGE OF SURGEONS
5 30 P M Mr Arthur Jacobs Enterocolic Anastomosis

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
5 P M *Section of Endocrinology* Prof G W Pickering Bilateral Adrenalectomy for Hypertension Dr R G Sprague Cushing's Syndrome

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28 Portland Place W 1
3 30 P M Dr W Bentley Purchase Experiences at the Bar and as a London Coroner

HARVEIAN SOCIETY OF LONDON, 11 Chandos Street W 1
8 15 P M Dr John Hawksley Prof Montague Maizels [illegible]

NORTH WESTERN TUBERCULOSIS SOCIETY
3 30 P M (Aintree Hospital, Liverpool 9) Dr W S [illegible] Bronchiectasis

Thursday, 23rd

ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P M Sir Francis Fraser Privileges of a Learned [illegible]

ST GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Corner S W 1
5 P M Dr Desmond Curran Psychiatry demonstration

HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place, Edinburgh) Dr A Rae Gilchrist Coronary Sclerosis

UNIVERSITY OF ST ANDREWS
5 P M (Medical School, Small's Wynd Dundee) Mr P Maller Treatment of Peptic Ulceration

Friday, 24th

ROYAL SOCIETY OF MEDICINE
8 15 P M *Section of Obstetrics and Gynaecology* Mr [illegible] Norbury Mr T W Riches Mr D H MacLeod [illegible] of Intestine and Renal Tract Resembling Disease of Female Genital Tract

BRITISH ASSOCIATION OF PLASTIC SURGEONS
11 30 A M (Royal College of Surgeons) Mr J P Reidy [illegible] F W Peet Prof T P Kilner Corrective Plastic [illegible]

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray's Inn Road W C 1
5 30 P M Mr S [illegible] Otitis Externa

MEDICAL SOCIETY FOR STUDY OF VENEREAL DISEASES 11 Chandos Street W 1
8 P M Dr C S Nicol Dr D G ff Edward [illegible] pneumonia-like Organisms in Genital Infections

Saturday, 25th

UNIVERSITY OF CAMBRIDGE
11 30 A M (Addenbrooke's Hospital) [illegible] Vascular Disease

view that the pituitary causes Graves's disease because it behaves like a thermostat set for an abnormally high level. The other possibility—namely, that the pituitary is unable to respond to thyroid hormone—was shown to be very unlikely in our original paper.[1]

One minor mis-statement in your editorial might stand correction. This laboratory has been well aware that repeated test doses of I^{131} in Graves's disease may by themselves influence the course of the disease.[4] No dose in excess of 40 μc. was used in the original work or in these later studies.

This work was aided by a grant from the Division of Research Grants, U.S Public Health Service, National Institutes of Health. Triiodothyronine was obtained through the courtesy of Smith, Kline, and French Co.

Columbia University, College of Physicians and Surgeons; and Presbyterian Hospital, New York.
SIDNEY C. WERNER
HOWARD HAMILTON.

HOSPITAL COSTING

SIR,—In your annotation of March 28 the need for the measurement of quality as well as quantity is very rightly stressed. Costing analysis on a departmental basis would at least indicate the services which a hospital provides, and would show the presence or absence of the many medical diagnostic or therapeutic aids. It would not show the quality of the work done in each department, and this can only be assessed by personal examination by those with the necessary experience and knowledge. Costing analysis can never be regarded as a cure for waste and inefficiency, but only as a guide to diagnosis. When comparisons are made on a departmental basis, many of the differences arising through individual hospital circumstances can be eliminated; and when information on departmental cost is available for a whole region, variation much below or above the mean would point to the necessity for an examination of standard. Cost analysis should point to too cheap as well as too extravagant a service.

The plea for simplification is one of importance. It may be found, however, that a financial comparison of the cost of salaries and wages is simpler than one of numbers only. Numbers of staff as such are useless if some of the staff are whole-time and some are part-time, and further calculations have to be made to show total staff on a whole-time basis; by using the cost of payments to the staff as the basis for comparison this result is automatically provided. Moreover, if a comparison is needed of the use of varying grades of staff in individual hospitals, the financial aspect has to be taken into account.

Oxford.
D. M. LIVOCK.

COMPLICATION OF CAUDAL BLOCK

SIR,—Dr. Humphries's letter (April 4) about the development of high spinal analgesia following the aspiration of cerebrospinal fluid from a needle introduced into the caudal canal, prompts me to quote something I wrote in 1944.[5]

> "Once pierced, the dura must be considered able to admit any quantity of fluid introduced into the epidural space, thereby producing spinal analgesia. In one such case the writer proceeded cautiously and produced spinal analgesia up to a height of D8, with as low a volume as 11 c.c. metycaine 1%—even after the needle had been withdrawn half an inch and a further aspiration test had proved negative. Had the large dose required for caudal analgesia been injected disaster might well have supervened."

Dr. Humphries is to be congratulated upon reintroducing Silvester's method of artificial respiration. Passive movements of limb muscles have been shown to stimulate the respiratory centre by bombarding it with proprioceptor (afferent) impulses which originate in receptors in mammalian muscles. Silvester's method, which employs passive movements of the arms, is, therefore, theoretically the best method of artificial respiration. Intravenous adrenaline is the best way of combating circulatory failure in these cases—1 ml. of a 1 in 1000 solution injected very slowly in acute cases, and a 1 in 250,000 drip in circumstances where circulatory depression is less sudden in onset.

King's College Hospital,
London, S.E.5.
A. H. GALLEY.

INVOLVEMENT OF AUTONOMIC NERVE-FIBRES IN DIABETIC NEUROPATHY

SIR,—Dr. McPherson (March 28) calls attention to the limitations of surface-temperature recordings as an index of blood-flow in an extremity.

We would agree with him that only under the strict conditions mentioned by Fetcher et al.[1] does the surface temperature correspond well with the blood-flow. This does not mean, however, that measurements made under other conditions are of no value. Indeed, Fetcher et al. state elsewhere[2] that if only gross changes in blood-flow are to be measured then lower heat-loss rates than the 240 kg. cal./hr./m.^{2} mentioned by Dr. McPherson may be adequate. It is clear, therefore, that Dr. Martin's results (March 21) are not invalidated by Dr. McPherson's considerations. The majority of the surface-temperature changes in the foot recorded by Dr. Martin are certainly sufficient to constitute a satisfactory indication of change in blood-flow.

Lewis, in the sentence presumably referred to, wrote: "Perhaps the most reliable method of gauging the state of the blood flow to a resting limb *clinically* is to estimate its surface temperature" [our italics]. The venous occlusion plethysmograph, with which he obtained results embodied in many of his papers, he regarded as too cumbersome to employ in the routine work of the clinic.[3] The same objection was made to the calorimeter, although, as Cooper et al.[4] recently showed, this method will follow large changes in blood-flow with considerable accuracy.

It is possible that the heat-flow meter described by Hatfield,[5] while of comparable simplicity, may be more reliable than the thermocouple for clinical assessment of blood-flow in an extremity. Most workers would agree, of course, that estimations of blood-flow calculated from surface-temperature and heat-loss, singly or together, are less accurate than measurements of actual flow.

Division of Human Physiology,
M.R.C. Laboratories,
Holly Hill, London, N.W.3.
M. J. ALLWOOD
H. S. BURRY
Satra fellows.

SIR,—I agree with Dr. McPherson that measurements of total blood-flow by means of a plethysmograph would have been of great value in my investigation of vasomotor tone in diabetic neuropathy, but unfortunately I had no plethysmograph at my disposal.

I should like to point out, however, that the changes in skin-temperature that were recorded were never supposed to be true indices of total blood-flow or even accurate estimations of skin-flow, as it is well known that there is no linear relationship between blood-flow and surface-temperature. In the investigation reported (March 21) changes in skin-temperature were simply reported as an indication of vasomotor activity—i.e., of the presence of vasoconstriction (about 20°C) or vasodilatation (above 32°C)—and even the workers quoted by Dr. McPherson do not deny the reliability of thermocouples for this purpose. As far as my conclusions are concerned, it appears to be immaterial whether below 20°C the blood-flow may be reduced further without a corresponding drop in the skin-temperature,

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[4] Werner, S. C., Hamilton, H., Nemeth, M. *J. clin. Endocrin.* 1952, 12, 1349.
[5] Galley, A. H. *Proc. R. Soc. Med.* 1944, 37, 680.

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[1] Fetcher, E. S., Hall, J. F., Shaub, H. G. U.S. Air Force Memorandum, March, 1949.
[2] *Science*, 1949, 110, 422.
[3] Lewis, T. Vascular Disorders of the Limb. London, 1946.
[4] Cooper, K. E., Cross, K. W., Greenfield, A. D. M., Hamilton, D. McK., Scarborough, H. *Clin. Sci.* 1949, 8, 217.
[5] Hatfield, H. S. *J. Physiol.* 1949, 111, 10P.

capillaries in the choroid plexus and the pressure of the ventricular fluid produces a fluid in Donnan equilibrium with the blood This theory has been discussed by Mestrezat and F Fremont-Smith. Mestrezat showed that a collodion sac left in the peritoneal cavity gradually comes to contain a fluid with a composition similar to that of the C.S F.

Donnan's equilibrium is reached when two solutions are separated by a membrane with very small stomata, allowing diffusion of the smaller but not of the larger molecules The smaller molecules migrate to the side of the lower osmotic pressure, until the osmotic pressure is equal on both sides of the membrane Thus if there is blood on one side and distilled water on the other, after a time there will be more sodium chloride in the water than in the blood-serum but much less protein However, Donnan's law does not hold exactly for the C.S.F For instance, the alkalinity of the C S.F is somewhat lower than that of the blood Magnesium is present in higher concentration and sugar in lower concentration, in the C.S F. than in blood-serum Moreover, the C.S.F. changes considerably in constitution during its migration from the ventricles to the subarachnoid space of the lumbar region

It is true that spinal fluid is produced below the level of complete occlusion of the spinal canal (for instance, by spinal tumour), but this fluid has a composition very different from that of the normal C.S.F., as Nonne and Froin have shown Electrophoresis of the C.S.F permits refined analysis of its components, and shows that it contains the same proteins as blood, but in different proportions—the globulins being rather scarce in the normal C.S.F There is also a special component, consisting of very small albumin molecules, which appears as a precursor during electrophoresis, examples of which have been collected by my assistant, Dr J Steger.

We use strips of paper for electrophoresis. We stain the proteins and measure the intensity of the stain photoelectrically This method has shown that the small albumin molecule is almost absent in the blood serum though relatively concentrated in the ventricular fluid It diminishes by degrees during the migration of the fluid to the cisternæ and to the lumbar region.

This molecule is completely absent from the thick yellow fluid below a complete spinal blockage of the subarachnoid space. It is also absent from the fluid of gliomatous cysts, which seems to indicate that it is not produced by the glia. So this small-molecule albumin seems to be further evidence for a specific function of the choroid plexus

Lina Stern and others have believed the C S.F to have a nutritional function for the nervous system They assumed that all substances passing from the blood to the brain must pass the C.S.F barrier *This brings us to* the perivascular spaces, first discovered in pathological conditions by Virchow and Robin These aroused the special interest of Cushing who always thought that they acted like a lymphatic space, evacuating waste-products from the nerve cells into the subarachnoid space Cushing induced me to investigate these perivascular spaces, and with Percival Bailey I spent a considerable time in studying them. We found that they exist only round the larger vessels of the brain, round the capillaries there is only a little connective tissue In certain pathological conditions—e g inflammation and œdema—perivascular spaces can be demonstrated round the smaller vessels In certain types of meningitis like that caused by torula the fungus invades the perivascular spaces, which distend enormously, but we have not found in these conditions any perivascular space round the capillaries, nor are they visible in cases of tumour sealing the subarachnoid space. All this proves that there cannot be very much fluid discharged from the perivascular spaces into the subarachnoid space

Folders and Arrowood have shown the enormo importance for the C.S F. of the osmotic pressure of t blood; and Weed used this method to investigate t fluid transport in the perivascular spaces He was al to show that only by increasing the osmotic pressure the blood to a high level could C S.F be forced from t subarachnoid space into the perivascular spaces

We used this method to study experimentally the chan of the perivascular sheaths in animals injecting a hyperto solution of saline into one carotid and a hypotonic solut into the other The animal was killed by adding formalin the solutions and the skull was opened immediately and t brain studied We found that on the side of the hypoto solution the brain was swollen the subarachnoid spaces emp the perivascular spaces collapsed, but the spaces arou the pia described by His, were dilated In contrast, on t side of the hypertonic fluid the vessels were dilated, the su arachnoid spaces and the perivascular spaces were dilate and the tissue of the brain was shrunk But nowhere d we find any spaces round the capillaries

It thus seems unlikely that there is any circulation spinal fluid accompanying arteries which are breakin up into the capillaries or leaking alongside the veins i the subarachnoid spaces, as has been assumed by som authors without experimental proof The substance exchanged between the brain tissue and the vessels pa only through the vessel wall and the surrounding gli tissue

Still, a good deal of exchange is possible between th C S.F and the nervous system though it is not by wa of the perivascular spaces It takes place simply b diffusion

One can show this experimentally by introducing a Bi schowsky solution into the subarachnoid spaces The silve penetrates into the depth of the brain, precipitating in parall Liesegang layers. The importance of diffusion has also bee shown by the experiments of Goldman and Spath, wh injected trypan-blue into the subarachnoid spaces This dy spreads diffusely through the nervous system, and though i certainly accumulates in macrophages round the vessels, th is merely the result of active phagocytosis We were ab to demonstrate this by putting glass capillaries filled wi trypan-blue into the brain This time the dye escaped fro the opening of the capillary the surrounding tissue wa stained, and macrophages transported the dye to the vess in the neighbourhood

What is the volume of spinal fluid produced in a day and absorbed in a day? Flexner and Winter found that cats with an average weight of 3 kg and a brain weight of 22 g would produce about 12 ml of spinal fluid a day Haug and Haug stated that man needs from 3 to 6½ hours in order to produce 40–65 ml of spinal fluid In three-quarters of an hour, 10 ml of spinal fluid is produced Similar results were obtained by Riser and Massermann in France If a needle is left in the subarachnoid space for some hours 3–5 ml of spinal fluid is produced hourly The absorption of the spinal fluid has been studied by Falkenheim and Naunyn who injected normal saline under different pressures They were able to show that the speed of absorption depends on the fluid pressure Fog Rasch and Stuerup got the same results with experiments on animals Folders and Arrowood who studied this question in human beings, found that up to 2000 ml of fluid at a pressure of 50 cm of water can be injected in twenty four hours into the subarachnoid space

Woodehoff and I have tried to develop a clinical test based on these experiments We measured the spinal pressure of a patient lying quietly on his side As soon as his spinal fluid pressure was constant we removed 5 ml by puncturing the rubber tube connecting the needle with the manometer We observed the drop of pressure and waited until it had risen to the original level Using this method we found that 5 ml is usually replaced within twenty minutes In a second experiment we injected 5 ml of spinal fluid slowly into the rubber tube The spinal fluid pressure rose and we again waited until it had dropped to the original level This infection. The fourth patient was found at necropsy to have widespread secondaries in the pancreas and liver, but the immediate cause of death was pneumonitis due in part to *Staphylococcus aureus*, resistant to all antibiotics except penicillin, which had no clinical effect even in enormous doses.

It is common experience that latent infection may be exacerbated in patients undergoing treatment by these hormones for any condition, and, in the animal experiments referred to above, the animals submitted to radiation and cortisone injections suffered much more seriously from secondary infection than the control animals without cortisone. It is felt that A.C.T.H. was in part responsible for the infection which supervened in two of the above patients. In order to avoid this known complication of prolonged hormone therapy, the period of A.C.T.H. administration was covered by injections of streptomycin twice weekly and penicillin daily. It is probable that this prolonged prophylactic course of antibiotics was unhelpful and even predisposed to the development of resistant organisms.

Investigations are proceeding to evaluate the possible use of A.C.T.H. in combination with radiotherapy in the treatment of carcinoma of the lung, but it is obvious that the risk of so treating a lung which may well be heavily infected at the start of treatment must receive very serious consideration. These cases and further animal experiments will be reported more fully in a later communication.

Harefield Hospital, Middlesex. L. E. HOUGHTON.
Middlesex Hospital, London, W.1. J. B. WALTER.

RENAL DUCTS OF BELLINI

SIR,—Dr. Duran-Jorda states, in his article last week, that he is sceptical of accepting the existence of openings of the ducts of Bellini, and is considering the possibility that in the normal kidney the urine is dialysed through a pelvic epithelium and not excreted by the ducts of Bellini into the renal pelvis. The views of other histologists on this should prove interesting.

It is quite easy to make a cast of the ducts of Bellini in man by injecting 'Neoprene' (latex) up the ureter, thus proving irrefutably that openings of the ducts into the calyses do exist. The ducts of Bellini are also demonstrated from time to time in retrograde pyelograms—the phenomenon of pyelotubular back-flow. Pyelotubular back-flow, though not as common as pyelovenous back-flow, is well known to urologists and radiologists. When it occurs, it clearly demonstrates the continuity of the ducts of Bellini with the renal calyces.

Photographs of pyelotubular back-flow, and of a neoprene cast of a kidney showing tufts of pyelotubular back-flow into the ducts of Bellini, are included in an article by me on pyelorenal back-flow.[1] These should give Dr. Duran-Jorda some proof that, whatever the state in the newborn, openings of the ducts of Bellini into the renal calyces certainly do exist in the adult.

Edinburgh. JAMES A. ROSS.

KERNICTERUS

SIR,—Dr. Govan and Dr. Scott (March 28) ascribe kernicterus to brain lesions from anoxia at the time of birth. Another explanation seems possible to me.

Kernicterus usually makes its appearance a few days after birth, and might be due to the withdrawal of an inhibiting or neutralising substance or substances present in utero but unavailable to the infant after birth. This substance might originate in the placenta, and by its presence prevent kernicterus in the unborn infant. The withdrawal of this factor after birth might permit the development of kernicterus within a few days.

On this hypothesis placental extract was administered to a group of infants with hæmolytic disease by intramuscular injection of 1 ml. morning and evening from birth to five or six days of age—that is, until the danger period for the development of kernicterus was probably over. The results were as follows:

Group	*Transfusions*		*Kernicterus*	
	Exchange	*Simple*	*No. of cases*	*Incidence (%)*
Control (48 cases)	13	35	8	16·66
Treated (57 cases)	35	22	1	1·07

While these results would appear to warrant further investigation, they may be fortuitous or related to the somewhat higher rate of exchange transfusion in the treated than in the control group. This investigation continues, but meanwhile it would be interesting to have the opinions of other workers in this field.

National Maternity Hospital, Dublin. COLMAN M. SAUNDERS
Director of Pædiatrics.

HUGH OWEN THOMAS

SIR,—I am writing a new Life of Hugh Owen Thomas, together with a revised edition of his collected works. Any assistance in this task would be welcomed; in particular, I am anxious to have access to previously unpublished material. Letters or documents relating to any aspect of Thomas's private or professional life, or to the history of the family, will be carefully handled and returned to the owners as soon as possible.

10, Harley Street, London, W.1. DAVID LE VAY.

A LONG-ACTING LOCAL ANÆSTHETIC

MR J. I. M. JONES, D.SC., writes from the research department of Crookes Laboratories Ltd.: "Your annotation of March 28 implies that 'Efocaine' remains stable for about three months. This view is evidently based on the paper by Ansbro and his colleagues to which you refer. Later results show that for practical purposes the preparation is stable for an indefinite period."

Medicine and the Law

A Doctor's Cross-examination

APPEALS from convictions for murder are often brought with insubstantial prospect of success. The recent appeal in R. *v.* Holmes[1]; was based on a complaint that a question to a medical witness was wrongly allowed. The appellant, after making what his own counsel described as a savage and frenzied attack on his landlady, went to the police and said he wanted to give himself up for murder; he wrote out a detailed account of his actions. At the trial a doctor, called by the defence, was asked in cross-examination whether, in his opinion, such conduct, immediately after the murder, would indicate that Holmes knew that what he was doing was unlawful—i.e., wrong in law, within the meaning of the McNaughten rules. The witness answered "Yes." Counsel cited judicial dicta to the effect that medical opinion must never usurp the function of the jury in finding the facts; the witness, he contended, could not be asked what was in the accused person's mind when the homicidal assault was committed. The question and answer were inadmissible.

The Lord Chief Justice interrupted counsel's argument with the suggestion that the appeal seemed to raise a merely academic question. The doctors on both sides now agreed that Holmes was certifiably insane; he would be dealt with under the Trial of Lunatics Act, 1883, and kept in custody during Her Majesty's pleasure. Counsel replied that a long line of authorities laid it down that medical men, however eminent, could not be allowed to take on the functions of a jury by giving an opinion on the question which the jury had to answer.

The Lord Chief Justice observed that, whatever fine distinctions had been drawn in some of the cases cited, the blood circulation Within certain limits the air-bubble within the cranial cavity will behave as if there were no skull around it Observations on a patient with a rather large hydrocephalus taught us that he felt comfortable only at a certain atmospheric pressure level He would develop a headache as soon as the pressure rose above this level or as soon as it dropped below it One instance caused a relative hypertension of this air bubble, the other a relative hypotension In fact this was the first observation we made of the clinical effects of a hypotension, and it led later to our becoming interested in aliquorrhœa

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[1] Ross, J. A. *Brit. J. Urol.* 1952, 24, 27.

[1] *Times*, March 31.

Another factor which causes an increase in the C S F is lack of oxygen (e g, at high altitudes) Forbes and Wolff have already reported such increases in animals It can be abolished immediately by the breathing of oxygen These effects of high altitude on the brain are important when people with wounds of the head are transported by air Before the second world war, French army physicians observed large prolapses of the brain in soldiers who had been wounded in Morocco and transported to France by air We now know the explanation the brain is blown out of the skull, partly through lack of oxygen, and partly because air has entered the ventricles and is expanding in the high altitude These factors must be taken into consideration when people with wounds of the brain are transported by air The danger can be avoided if the patient is transported in a pressurised cabin, or if the air is carefully removed from his ventricles before transportation, and he breathes oxygen during the flight

THE PIA-ARACHNOID

In discussing the physiology and pathology of the C S F circulation we cannot ignore the pathology of the membranes lining the subarachnoid space Even the normal membranes behave neither like rubber nor like glass they are semipermeable and allow of diffusion of proteins and other substances from the blood and the brain There are many conditions in which this diffusion is enormously increased—particularly in all cases of true inflammation Here the spinal fluid assumes a composition which resembles that of the blood serum There are several other conditions in which there is no leucocytic exudation—for instance in what Roessle and Eppinger would call serous inflammation, and what Schuermann called dysoria Dysoria means that the stomata of the vessels are too wide, and so too much protein is able to leave the vascular channels I believe that we need not bother to decide whether dysoria really means the beginning of an inflammation or not It is more interesting to know in which conditions we find dysoria, and what are its consequences

The oldest known example of dysoria is the dysfunction of the meninges which causes the enormous increase of proteins in the spinal fluid below a spinal tumour and in its vicinity The fact that even the spinal fluid above a tumour has a raised protein content shows that obstruction of flow cannot be the only cause Guillain and Barré have shown that the composition of the spinal fluid in polyneuritis is very similar to that below an obstruction Here again we have dysoria as one of the most important parts of the syndrome Another syndrome in which dysoria evidently plays a role is aliquorrhœa What spinal fluid we are able to draw off in aliquorrhœa is high in proteins This is due to the greater difference in pressure between the blood circulation and the spinal-fluid spaces, which causes engorgement of the vessels and hence widening of their endothelial stomata We have observed a fourth condition associated with dysoria—namely a chronic change following a mild meningitis

A patient had been wounded in the right temporal lobe by a shell fragment For some time he had been suffering from a small abscess of the temporal lobe which drained well and which was cured (as necropsy later proved) During his surgical treatment signs of meningitis developed which were controlled by intensive peroral sulphonamide treatment As the raised cell count in his spinal fluid fell, he began to complain about terrible pains in his legs and back Lumbar puncture showed that the proteins in the C S F increased from week to week, while the Queckenstedt test showed no blocking We even tested the patency of the spinal fluid system by introducing a small air-bubble which passed into the ventricles without difficulty Finally lumbar puncture drained some fluid which immediately clotted in the tube Further lumbar punctures did not produce any more fluid Eventually the patient developed flaccid paralysis and segmental sensory disturbances of his legs, indicating a cauda equina lesion He acquired pressure sores and urinary infection, and died from septicæmia Necropsy revealed that the spinal fluid in the C S F spaces had clotted just as it had done in the tube Cauda equina and spinal cord were wrapped in a gelatinous mass which was in the process of organisation by fibroblasts

I believe that this process of colloid exudation followed by fibroblastic organisation is very common, many instances of increased protein in the spinal fluid after lesions of the brain or inflammation of the meninges may be associated with it Of course the enormous rise of protein content can only happen when large areas of the meninges show such a pathological change But localised changes of this kind may be the cause of the adhesion and fibroblastic organisation which go under such different names in neurology as arachnoiditis adhesiva circumscripta, arachnoiditis serosa cystica, pachymeningitis, and dural hygroma I propose that we should regard all these disorders as meningopathies and distinguish them from the recognised inflammatory disorders which are accompanied by leucocytic infiltration

* * *

The facts discussed here have been collected and contributed by great physicians of all nations Knowledge of these disturbances is indispensable for the clinician, yet there are still many riddles to be solved, and we of the older generation have left enough for the younger ones to do

EFFECT OF ISONIAZID ON TUBERCULOUS LESIONS OF THE KIDNEYS

JOHN C DICK
M D Glasg, F R F P S

GLASGOW UNIVERSITY LECTURER IN PATHOLOGY AT STOBHILL HOSPITAL, SENIOR PATHOLOGIST, GLASGOW NORTHERN GROUP OF HOSPITALS

THE use of isoniazid in the treatment of tuberculosis has produced some contradictory results The first intimations of its clinical effects (Robitzek and Selikoff 1952, Monaldi 1952, Klee 1952, Morland 1952, Sita Lumsden 1952, Bartley 1952, and others) were full of hope in view of its dramatic results after even a short period of treatment The preliminary report of the M R C Tuberculosis Chemotherapy Trials Committee (Medical Research Council 1952) showed that, after a 3-month course of treatment in pulmonary tuberculosis the results with isoniazid were comparable to those with streptomycin and *p* aminosalicylic acid (P A S) showing greater gain in weight and general condition, though slightly less effect in reducing fever and erythrocyte sedimentation rate (E S R), and in sputum conversion and radiographic improvement, but a warning was given that drug resistant tubercle bacilli appeared quickly (as had already been found in vitro) On similar lines Joiner et al (1932) found that isoniazid alone had a beneficial effect in some cases of pulmonary tuberculosis in the first 3–6 weeks, but thereafter the improvement was not maintained, and ultimately deterioration ensued associated with the excretion of resistant strains of tubercle bacilli, whereas isoniazid combined with strep took his D.P.H., and while holding a Medical Research Council appointment carried out an investigation into enteric carriers. The following year he became demonstrator in pathology at Durham University, and assistant pathologist in the Royal Victoria Infirmary, Newcastle.

In 1927, at the age of 32, he went to Dalhousie University as professor of pathology and bacteriology and provincial pathologist for Nova Scotia. In the following year he was awarded his M.D. with honours and also the Bellahouston gold medal. During his years in Canada his advice was widely sought on medicolegal problems in all the Maritime Provinces. He was a founder fellow of the College of American Pathologists; and examiner in pathology to the Dominion Medical Council of Canada and the Canadian College of Physicians and Surgeons. Apart from his abiding interest in medicolegal pathology, he was for many years a member of the American Association of Geographic Pathology and he was also a member of the International Association for Dental Research. Three years ago he returned to this country as consultant pathologist to the Newcastle General Hospital, and he administered his department with his customary energy and enthusiasm until his death.

A colleague writes: "Paterson Smith was an excellent teacher, and his students often had the highest average standing in pathology examinations, in which they had to compete with men from all other Canadian universities. As a man he was courteous and unselfish; he was endowed with an enormous fund of energy which was evident to all those who visited his department. His careful work in various branches of pathology was published in a series of admirable papers, and his writings were not without influence on the medical teaching of his day. His introduction of the term 'lobular hyperplasia' into the classification of diseases of the breast did much to dispel confusion."

Dr. Paterson Smith leaves a widow and five sons, one of whom is a medical student at Durham University.

EDWARD SCOTT WORTHINGTON

K.C.V.O., C.B., C.M.G., C.I.E., M.D. Toronto

Sir Edward Worthington, formerly an assistant director-general of Army Medical Services, and physician to the late Duke of Connaught, died in London on April 5, at the age of 76.

He received his medical education at Trinity University, Toronto, and he held the degree of M.D. Toronto. In 1899, after coming to this country, he took the Conjoint qualification and in the following year he joined the R.A.M.C. He served in the South African war from 1899 to 1902. He was appointed medical officer on the staff of the Duke of Connaught for the opening of the Union of South Africa Parliament in 1910, and he was again M.O. to the Duke of Connaught while he was governor-general of Canada from 1911 to 1914. He was knighted in 1913.

For his services in France from 1914 till 1916 he was mentioned in despatches and "brought to notice for valuable services rendered." He also received the brevet of colonel, the American Distinguished Service Medal, the Order of Leopold (4th class), and the Belgian Croix de Guerre. He was appointed C.M.G. in 1915. In 1917 he rejoined the staff of the Duke of Connaught, and in 1918 he was appointed C.B., and the following year created K.C.V.O. He was with the Duke at the opening of the Princes' Council in India in 1920, and in 1921 he was appointed C.I.E. Sir Edward was deputy assistant director-general and assistant director-general at the War Office from 1917 to 1922. He was appointed K.H.P. in 1922 and he retired in 1926.

EUGEN POLLAK

M.D. Vienna

Dr. Pollak's death on April 9 will be keenly felt by his colleagues in Manchester, his adopted city, where he had lived since 1939 and where he was university lecturer in neuropathology. He was one of that small band, the really widely informed and accomplished neuropathologists. At the Neurological Institute in Vienna he had been a pupil of Marburg, Obersteiner, and Erdheim, as well as of Wagner-Jauregg, who had first encouraged him in neurology. He had a large number of important papers to his credit chiefly about the degenerative and chronic infections of the nervous system.

Dr. Pollak came from a Vienna that had already lost the glitter, the panache of the royalist times which he had known, but still was magnetic in a medical sense. Everybody went to Vienna sooner or later to listen to one authority or other. There was no branch of medicine that the Viennese school had not richly adorned. The pilgrimage was made the more attractive by the charm of the surroundings as well as the good humour and tolerance of the Austrian character. Dr. Pollak himself had good humour in abundance, a remarkable memory, and a wide and, what is more, a critical knowledge of the medical personalities of Central Europe. Toleration he kept within bounds. He was unable to speak of the Vienna of the last war without rancour, since he was ashamed of the way that so many of his countrymen had succumbed to the Nazi influence. He was deeply grieved by the murder during the war of his sister to whom he was so devoted. He was therefore insulted rather than flattered when offered the directorship of his old laboratory four or five years ago.

He was a lonely figure in many ways, proud and reticent about himself, but as fine an example as one could have of a courageous man of principle, the victim of political misconduct and worse. But this was not all. Until his illness he was always excellent company, and he was a wit whose comments on medical or world affairs were always eagerly listened to by his friends in the university. Moreover he was deeply interested in music and, as an ardent admirer of the Vienna Philharmonic Orchestra and the friend of musicians, he had much to tell that was refreshing and original. In the old days before the first world war Manchester had had a liberal-minded German colony of cultured business men who were responsible for a great deal of that city's supposed addiction to the arts as well as to the mechanical crafts. Pollak would have been instantly at home with them, they had the same wide interests, the same artistic passions. That colony of course has long been gone, but Pollak rekindled memories of those times.

I have spoken mainly of Pollak as a man whose company I and many others will sorely miss. He wrote very little after he came to England, preferring to accumulate material and make histological preparations in a way few, if any, could surpass. But then, before he had time to put together the fruits of his labours, illness took hold of him. We shall long remember his witty personality, his intelligence, his courage, his honesty, his independence.

Mrs. Pollak died young. He is survived by a married daughter in Vancouver, B.C.

G. J.

Appointments

BELL, W. J., M.B. Edin., M.R.C.P.E., D.P.H.: physician (S.H.M.O.), pneumoconiosis and tuberculosis, Bangor Hospital, Broxburn.

FURNIVAL, J. T., M.R.C.S., D.M.R.D.: consultant radiologist, S. Shields, S.E. Northumberland, and Wansbeck H.M.C. groups.

HOFFMAN, EUGENE, M.D. Prague, F.R.C.S.: consultant thoracic surgeon, Newcastle regional thoracic service.

SMITH, W. H., M.B. Lond., D.M.R.D.: consultant radiologist, Plymouth clinical area.

East Anglian Regional Hospital Board:

DAS, J. B., M.B. Madras: surgical registrar, E. Suffolk and Ipswich Hospital.

MCCARTHY, AGNES, M.B. Lond., D.A.: anæsthetic registrar, Peterborough Memorial Hospital.

MCCONNELL, JOAN, B.A., M.B. Camb.: registrar in psychiatry, St. Andrew's Mental Hospital.

MONRO, R. S., B.A., M.B. Camb., F.R.C.S.: consultant surgeon, Ipswich hospital group.

Appointed Factory Doctors:

CLARKE, R. W., M.B.E., L.R.C.P.: Rushden, Northamptonshire.

RILEY, E. F., M.B. Birm.: [illegible] shire.

SIM, C. G., M.A., M.B. Durh.: [illegible] erland.

STEWART, D. L., M.B. Aberd. [illegible]

The Hospital for Sick Children, Great Ormond Street, London:

HOYTE, F. C., M.B. Lond.: house-surgeon, orthopædic and plastic departments.

LUDER, JOSEPH, M.D. Lond., M.R.C.P., D.C.H.: medical registrar and pathologist.

PALLOT, DOREEN, M.B. Lond., D.A.: junior resident anæsthetist.

RICHARDSON, F. L., M.B. Birm.: house-physician.

SIMPKISS, M. J., M.B. Birm.: asst. medical registrar.

Western Regional Hospital Board, Scotland:

BROWN, R. C., M.B. Glasg., D.A.: asst. anæsthetist, Western Infirmary, Glasgow.

GERRARD, BARBARA, M.B. Lond., D.A.: asst. anæsthetist, Victoria Infirmary and Hairmyres Hospital, E. Kilbride.

SNODGRASS, MARJORY, M.B. Glasg., F.R.F.P.S., D.O.M.S.: asst. ophthalmologist, Glasgow Eye Infirmary.

nothing like this appearance round the lesions was found Further, no such appearance was present in specimens from cases after treatment with streptomycin either alone or combined with P A S

Microscopic Lesions

AFTER LESS THAN A MONTH'S TREATMENT WITH ISONIAZID AND NO PREVIOUS CHEMOTHERAPY (CASES 1–4)

In the kidneys from these cases the edges of the cavities showed appearances quite distinct from those of corresponding stages of tuberculous granulation tissue in specimens from untreated cases In the latter the acute stage showed a fairly broad reactive zone at the caseating edge, in which the kidney tissue was infiltrated with lymphocytes and epithelioid cells, with or without giant-cell follicles, and in which the interstitial tissue was undergoing early caseation and the parenchymatous elements were becoming disorganised and necrotic the whole process was avascular

In specimens after treatment with isoniazid (figs 6 and 7) the reactive zone was much narrower and more definite, there was much less cellular reaction, both epithelioid cells and lymphocytes being relatively scanty, the interstitial tissue was not caseating but showed vacuoles near the caseated edge, while the remainder looked healthy, though œdematous, and contained numerous small blood-vessels, newly formed and intensely congested, and the tubules were no longer necrotic or broken up but well formed right up to the caseated edge, with their epithelial cells clear and distinct Thus, not only had the caseating process stopped but the surrounding tissue was reacting strongly and even causing absorption of some of the caseated material

In somewhat more chronic areas of the granulation tissue (fig 8) there was the usual palisading of epithelioid cells, but in place of formation of fibrous tissue and thickening of the edge of the cavity there was a looseness in which epithelioid cells were more indefinite than usual, the interstitial tissue was œdematous and vacuolated, and fibrous tissue was completely absent Occasionally there were thinning and absorption of old caseous material near the margin (fig 9), and young blood-vessels were found, often running close to the caseous area (figs 8 and 9) In densely fibrosed parts of the cavity walls (fig 10) epithelioid cells again showed palisading at the edges, with lack of collagen and with vacuolation in the caseation, suggesting absorption of the necrotic material—i e, almost a reversal of the process by which it was formed The dense fibrous tissue was broken up and traversed by newly formed capillary blood-vessels

Similar abnormalities in the tuberculous lesions were found in the mucosa of calyx, pelvis, and ureter Thus there appeared to be a cessation of activity in acute caseation, with vacuolation in its deep layer (fig 11), accompanied by vascularity of the mucosa and reduplication of epithelium in nearby tubules In older lesions the main features were œdema and vacuolation in place of fibrosis between the palisaded epithelioid cells, and vascularity deep to the edge of the granulation tissue (cf figs 8 and 10)

Apart from the "open" tuberculous lesions—i e, those in cavity, calyx, pelvis, &c, leading to bacilluria and causing changes in the pyelogram—the other small and large lesions scattered throughout the parenchyma showed slight but definite changes from those in specimens from controls and untreated cases The individual epithelioid follicles (fig 12) were numerous and "loose," the epithelioid cells showed no tendency to orient themselves, nor was there any fibrous tissue in or surrounding the follicle, even though fibrosis and round celled infiltration were conspicuous in the surrounding

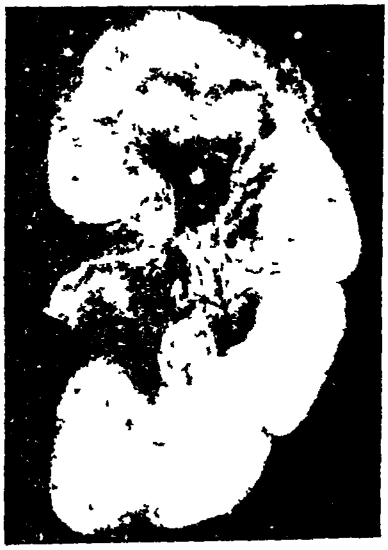

Fig 4 (case 6)—After 3 months treatment with isoniazid extensive ulcerocavernous tuberculosis of upper pole with congestion calyces and ureters with nodules of tuberculosis congestion and large areas of hæmorrhage and a few isolated follicles with surrounding congestion spreading down into middle zone (× 3/5)

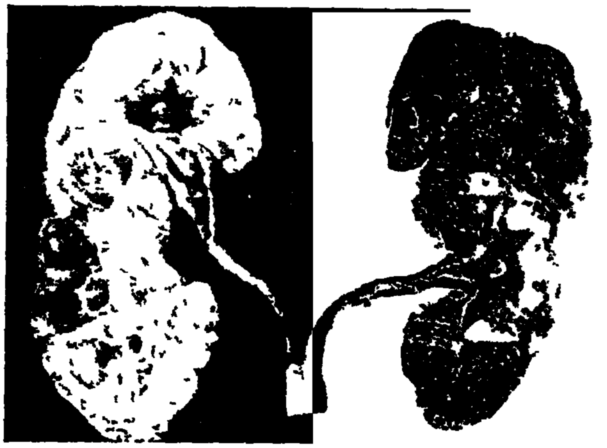

Fig 5 (case 8)—After 48 days treatment with isoniazid, kidney with double ureter Recent irregular ulcerocavernous lesion at upper pole with congestion and hæmorrhages, also in ureter from this pole, and extensive diffuse disease in parenchyma round it, and middle-zone and lower-pole lesions, drained by lower ureter, more chronic, with slight patchy congestion (× 4/5)

LEGENDS TO ILLUSTRATIONS

Fig 6 (case 1)—Edge of acute cavity showing prominent tubules in very vascular œdematous granulation tissue leading to narrow line of poorly defined epithelioid cells, beyond which is caseated material, edge of which shows fissures and a few vacuoles between epithelioid cells, but no fibrosis (× 100)

Fig 7 (case 1)—Edge of cavity, not quite so acute as fig 6, showing tubules and granulation tissue as before Broader line of epithelioid cells still no spread of caseation or fibrosis, but more vacuolation between cells (× 100)

Fig 8 (case 2)—Edge of more chronic cavity Zone of epithelioid cells fairly broad but with vacuolation between and no fibrosis interrupted by ingrowth of group of capillaries Instead of layer of fibrosis outside there is infiltration of lymphocytes and young capillaries no fibrosis in parenchyma beyond (× 100)

Fig 9 (case 1)—Edge of chronic cavity below, with old caseation at top Across centre there is a zone of lightening of caseation near epithelioid zone which is composed of indefinite cells, shows no fibrosis and is being infiltrated by young capillaries from below (× 100)

Fig 10 (case 4)—Edge of densely fibrosed cavity The fibrosis has lost its orientation by being infiltrated with young capillaries and by superficial layer losing its collagen to form indefinite epithelioid cells caseation beyond is showing vacuolation (× 100)

Fig 11 (case 1)—Mucosa of calyx showing increased vascularity and prominent tubules with epithelioid cells, vacuolation, and indefinite caseation at surface (× 100)

Fig 12 (case 4)—Isolated tubercle in kidney parenchyma. Epithelioid and giant cells very ill defined and no fibrosis within or immediately round follicle (× 100)

Fig 13 (case 4)—In the centre there is an indefinite area of eosinophilic material extensively infiltrated by young congested capillaries —probably an absorbed follicle (× 100) prevent draughts. The cradle does not interfere with the patient using a bed-table. The chairman of the hospital writes that many patients who have been in bed for a long time have been grateful for having their feet free. "The medical staff," he adds, "find these cradles an excellent elbow-rest when stopping to talk to a patient. In fact, some ward sisters call them 'doctors' detainers.'"

Any hospital management committee that is interested can obtain a sketch showing dimensions and details of construction from the Secretary, Nottingham no. 1 Hospital Management Committee, *c/o* the General Hospital, Nottingham.

THE MEDICAL DIRECTORY

THE names of untraceable medical practitioners, mainly with overseas qualifications, having been omitted, *The Medical Directory 1953*[1] contains 3116 fewer names and 97 fewer pages than it did last year. There are no new features, and the price remains the same.

TO COMPLETE THE SET

THE Harveian Librarian of the Royal College of Physicians of London (Prof. E. C. Dodds, F.R.S.) is seeking a copy of the Harveian oration for 1849, which is the only volume missing from the college's set of these lectures. The following particulars of the oration are given in the catalogue of the Army Medical Library:

> BADELEY (Joh. Carr.) Oratio ex Harveii Instituto in ædibus Collegii Regalis Medicorum habita pridie calend. Julii, A.D. 1849. 20pp. 8°. London: J. Churchill, 1849.

Professor Dodds asks anyone who can help him in the quest to write to him at the college, Pall Mall East, S.W.1.

University of Liverpool

At recent examinations the following were successful:

Ph.D. in the Faculty of Medicine.—E. S. Jones.

M.B., Ch.B., final examination, part II.—J. D. Agnew, J. A. Barlow, A. G. Bowers, M. J. A. Britten, N. T. Burnett, B. J. Charlick, R. W. Coffee, J. S. Comaish, J. R. Cope, G. W. Danger, K. S. Davies, R. J. G. Downie, Florence M. Duckenfield, D. P. Duffield, T. R. Evans, R. Finn, J. G. Foley, D. Gardner, Anne M. Godfrey, D. H. Goldsmith, Mary Gregson, Patricia O. Grundy, W. B. Hanley, P. A. Harrison, J. W. Hill, H. B. Hilton, E. J. M. Hopkins, C. L. Imison, R. A. Johnson, P. L. Jones, P. King, J. B. Laine, V. Leach, C. L. Levene, G. Lloyd, B. A. Lowe, Joan K. McCann, Anne D. Micah, J. B. Middleton, J. M. Nichols, F. T. O'Brien, B. J. O'Dow
S. S. Rubenstein, M.
T. F. Shelley, Mary E.
D. A. Thomas, R. S. T
W. P. Walsh, P. K. W
G. H. Worsley, I. Wort.

University of Aberdeen

On April 2, the following degrees were conferred:

M.D.—Joan M. Burrell, with commendation; R. N. Johnston, S. J. H. Miller.

M.B., Ch.B.—J. W. Davidson, Marion E. Mackay, C. G. Clark, W. D. Wilson, with commendation; J. B. O. Armstrong, R. A. Browne, C. I. T.
ald, Annabelle M.
Duguid, Mary E.
Graham Findlay,
J. A. Fowler, C.
Garson, G. M. Gill,
A. J. Gray, Eliz
ck, Wilma E. M.
Hoyte, A. G. Iron
n, A. A. Lawrence,
James Lawrence,
dingham, Douglas
Leslie, R. D. Little, I. M. Lowit, Robert Lynch, A. P. McBain,
A. M. McConachie,
Macleod, Joseph Main,
Helen M. Maitland,
M. J. Mitchell, P.
Mowat, J. H. Pal
R. D. Richmond,
Robson, Lydia J.
Simpson, A. J. Smith, R. W. G. Stewart
Swapp, P. G. Todd, A. H. Wade, G. W.
Jane M. Wiseman, J. R. Wood, M. B. Yorston.

University of Glasgow

Mr. W. A. Mackey has been appointed to the St. Mungo chair of surgery (Royal Infirmary) in succession to Prof. J. A. G. Burton, who retires at the end of the session.

Mr. Mackey graduated M.B. with honours at the University of Glasgow in 1927 when he was awarded the Brunton prize as the most distinguished graduate in medicine of his year. For three years he acted as assistant in pathology under Sir Robert Muir, F.R.S., and later he became an assistant
under Prof. Archibald Young. With
surgery he spent a year in the United
F.R.F.P.S. and the following year F.R.C.S.E.
late war Mr. Mackey was in command o
university O.T.C., and during the war he
lieut.-colonel in charge of the surgical divisions of various hospitals in Europe and the Middle East. On his return from war service he became assistant in surgery under Prof. C. F. W. Illingworth, and last year he was appointed a surgeon in charge of wards at the Southern General Hospital, Glasgow. Mr. Mackey is a member of the council of the Association of Surgeons of Great Britain and Ireland, a member of the International Surgical Society, and a founder member of the European Society of Angeiology. He has published papers on the surgical treatment of arterial hypertension and of Banti's syndrome.

Royal College of Surgeons of England

At a meeting of the council held on April 9, with Sir Cecil Wakeley, the president, in the chair, Prof. Reynaldo dos Santos of Lisbon was admitted to the honorary fellowship. The following were elected to the fellowship without examination as being medical practitioners of at least 20 years' standing: Mr. W. E. Tucker (Bermuda), Prof. F. Davies (Sheffield), Mr. J. Dobson (Wigan), Mr. R. Scot Skirving (Sydney), Mr A. E. Coates (Melbourne).

The Jacksonian prize for 1952 was awarded to Mr. John Borrie, and a certificate of honourable mention was awarded to Mr. Rodney Smith. The council selected the following as the subject for the Jacksonian prize for 1954: Melanomas and Melanosis.

Diplomas were granted jointly with the Royal College of Physicians to the following:

D. Phys. Med.—L. S. Bain, E. E. Bullock, A. B. Coyer, J. A. Joyce, Stephen Mattingly, A. P. H. Randle, Dorothy J. Roth, R. A. Shaddick, G. O. Storey.

D.O.—Judith MacA. Brown, Rahmat Ullah Chowdhary, Khurshed Jehangir Dastur, J. M. Heaton, Savitri Itchhaporia, B. R. Jones, Mary A. C. Jones, A. T. Karsgaard, Mithlesh Kumar Mehra, John Moss, Mohamed Nawaz, C. I. Phillips, Ahmad Samad, Jagjit Singh, J. R. van der Merwe, B. I. Williams, Thomas Wilson.

D.T.M. & H.—Imteyazuddin Ahmad, Anwar-ul-Islam, Timothy Awuku-Asabre, Abdu Rasaki Oladeinde Bakare, S. A. Biggart, E. B. Bright, G. H. Burgess, Carmel Cachia, J. E. Cranswick, R. A. Davis, Silas Rofine Amu De
C. H. Gurd, Shiekh Mohammed
Hendow, C. S. Heymann, Jasmine
W. N. Laing, A. R. T. Lundie, A. D.
Supperamaniam Madesan, M. C.
Dattatraya Ramadwar, Saville Pau
H. G. Skinner, G. J. Stott, Glad
Vethanayagam, Shyamlal Vyas, M.
Ross Woodward.

D.L.O.—P. J. Damato.

D.I.H.—P. H. Nash.

D.M.R.T.—R. Finney.

Royal College of Physicians of London

Prof. R. A. McCance, F.R.S., will deliver the Humphry Davy Rolleston lectures at the college, Pall Mall East, S.W.1, on Tuesday and Thursday, May 5 and 7, at 5 P.M. The subject of the lectures is Overnutrition and Undernutrition.

Sanderson-Wells Lecture

Prof. E. C. Dodds, F.R.S., will deliver this lecture on May 20, at 4.30 P.M., at the Middlesex Hospital, London, W.1. The title of the lecture will be Chemicals and Food, A Reconsideration.

Society of Chiropodists

The annual convention of this society will be held in London from May 7 to 9. Further particulars may be had from the secretary of the society, 21, Cavendish Square, W.1.

Society of Chemical Industry

At a meeting of the crop-protection panel of the agriculture group, to be held at the Chemical Society, Burlington House, London, W.1, on April 20, at 5.30 P.M., Mr. J. R. Booer, PH.D., will discuss Organo-mercurial Fungicides.

British Association

The annual meeting of the association will be held this year in Liverpool from Sept. 2 to 9 under the presidency of Sir Edward Appleton, F.R.S.

Convalescence for the Elderly

Seapark House, Greenisland, co. Antrim, was opened on April 10 by Mr. Iain Macleod, Minister of Health for England and Wales, as a convalescent home for elderly patients discharged from geriatric units who no longer need hospital care but are not yet fit to look after themselves in their own homes or in residential homes. The house was bought and equipped with money allocated from a gift of £1 million to the people of Britain from the people of South Africa. It belongs to the National Corporation for the Care of Old People, and is the fourth of its sort—the other three are at Englefield Green, Stanmore, and Glasgow. The new home will be maintained jointly by the Northern Ireland Hospitals Authority and by welfare authorities.

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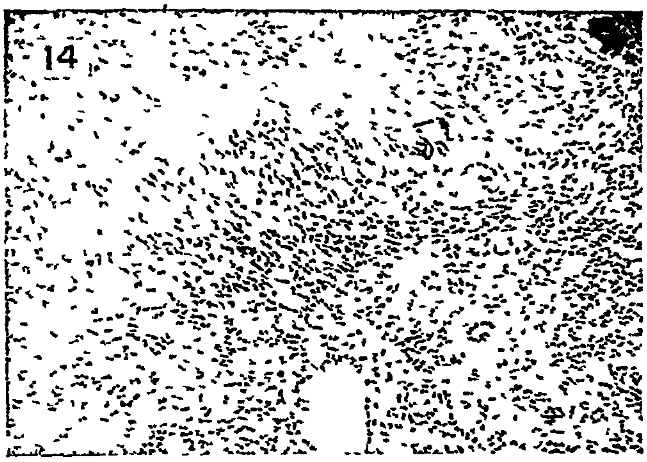
[1] London: J. & A. Churchill. 1953. Pp. 2727. £3 12s.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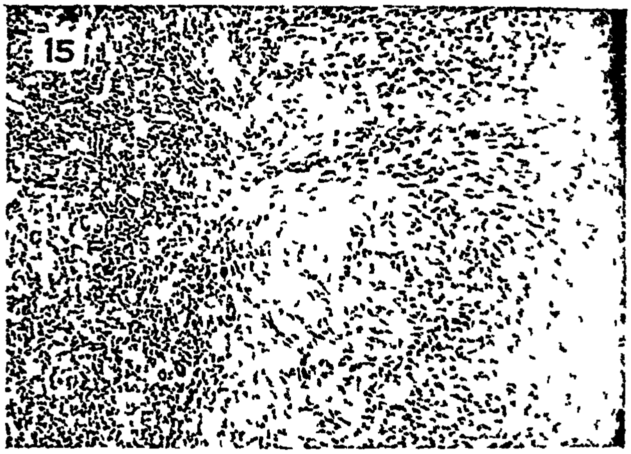
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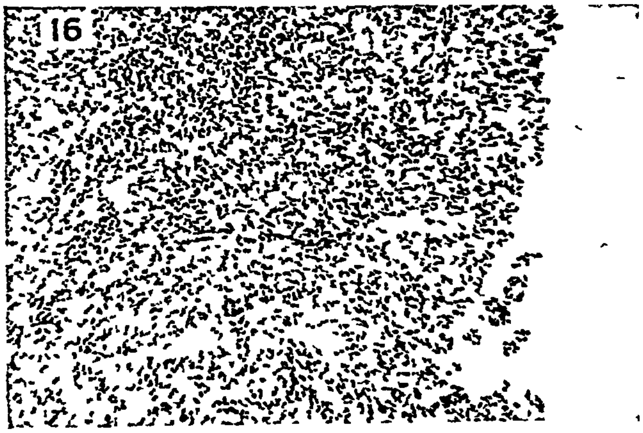
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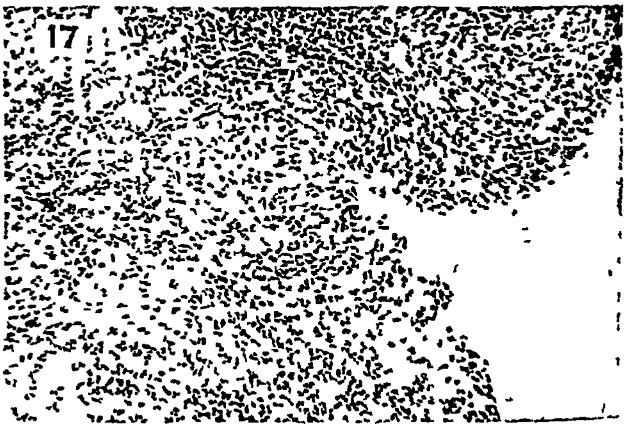
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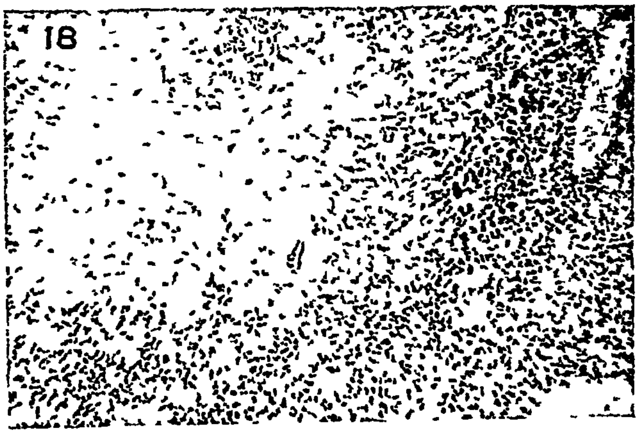
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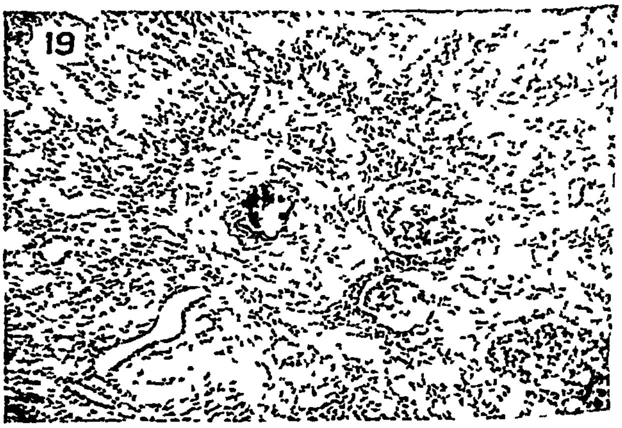
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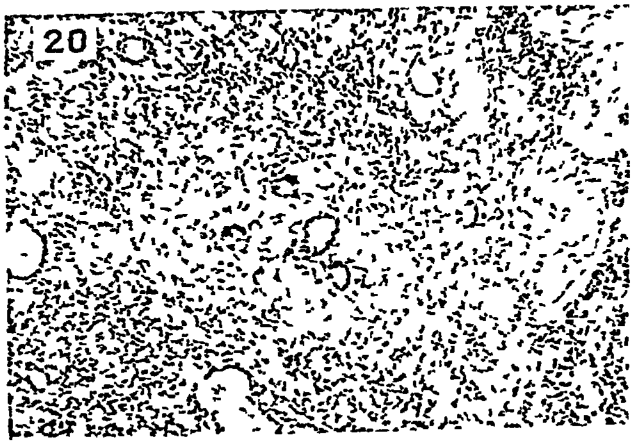
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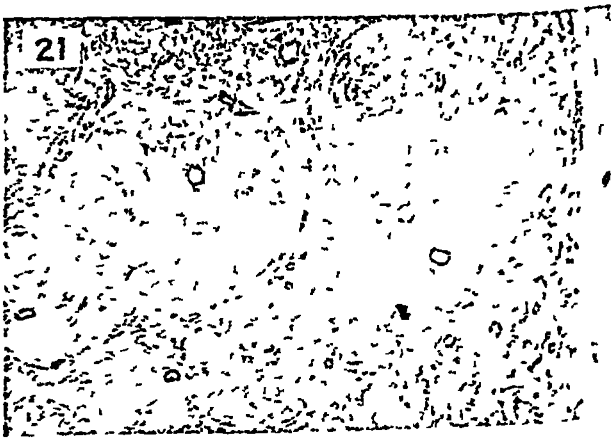
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NORMAL AND PATHOLOGICAL PHYSIOLOGY OF THE CEREBROSPINAL FLUID CIRCULATION *

GEORGES SCHALTENBRAND
M.D.

PROFESSOR OF NEUROLOGY OF THE UNIVERSITY OF WUERZBURG, GERMANY

FOR millions of years the nervous system of the vertebrates has been irrigated by the cerebrospinal fluid. Probably the C.S.F. took the place of the water of the ocean in which the first living beings originated. But whereas the blood has been known since remote antiquity, Galen, in the second century after Christ, said that the cavities of the brain are inhabited by a gas-like *spiritus animalis*, and this opinion survived until modern times. Varolio, in 1591, was the first to describe a fluid in these spaces, but his statements were not believed; and even Albert von Haller and Romberg (1820) held that during life the cavities of the brain are filled not by fluid but by a humid gas. It was François Magendie who, at the beginning of the last century, convinced his contemporaries of the existence of the C.S.F. The circulation of the blood was discovered by William Harvey in 1628, but only during the last forty years has the circulation of the C.S.F. been gradually brought to light by the wonderful researches of Quincke and of Cushing, and his pupils Dandy and Weed. It was Cushing who, in his Cameron lecture, first spoke of the "third circulation."

DEVELOPMENT

The C.S.F. system, like the lymphatic system, forms a short circuit between the arterial and the venous circulations.

To understand the C.S.F. system we must start with its ontogenesis and phylogenesis. The entire nervous system develops from an ectodermal groove which closes itself to a tube and sinks below the surface of the body. The interior of this tube is the *Anlage* of our ventricular system. The tube is sealed at both ends but the dorsal wall of the medullary tube, in the cephalic part, gets thinner in several places. The surrounding meningeal tissue increases in vascularity in these places and pushes the membrane-like thin part of the medullary tube into the ventricles. This is the beginning of the choroid plexus. During the further development of the brain the plexus carefully follows the changes in its shape. The roof-plate of the fourth ventricle forms membranous sacs which extend around the cerebellum and the brain-stem; from these derive the fluid spaces in the leptomeninges, which in adult mammals surround the entire nervous system. These fluid spaces lie between a double connective-tissue sheet—the pia mater, which is, as it were, soldered to the nervous system, and the arachnoid, which is in direct contact with the dura mater everywhere. The external C.S.F. communicates with the internal C.S.F. via the foramen of Magendie and the foramina of Luschka of the fourth ventricle. A third foramen, the foramen of Elze, has recently been discovered in the roof plate of the fourth ventricle in some individuals.

This macro-anatomy was elucidated by the classical investigations of Key and Retzius in the last century. These workers emphasised the connection of the C.S.F. with the venous system by way of the arachnoid villi, the largest of which are known as pacchionian granulations. Arachnoid villi can be found around the entire nervous system in the neighbourhood of the veins, and are especially numerous along the sinus longitudinalis. The arachnoid villi consist of very soft connective tissue which can easily be distinguished from the dense dural tissue. Only a very thin endothelial layer separates them from the blood in the veins. Some of them seem to end near a complicated system of tubes running parallel to the sinus and ending in it. This tubular system evidently contains not blood but C.S.F.; and if the dura is scratched in this region during an operation, spinal fluid will leak out.

The most important organ in the ventricles is clearly the choroid plexus. It is an extension of the meninges, covered by a single layer of cuboid epithelial cells. These have the typical structure of glandular cells, with many mitochondria, big Golgi bodies, small vacuoles, large nuclei, and one or more nucleoli. They also have cilia, producing a *bordure en brosse*. Under the microscope one can see how the living cell occasionally extends through the *bordure en brosse* fingerlike processes which seem to evacuate their contents into the surrounding fluid. Lack of oxygen causes the cells to disintegrate very rapidly into a foamy structure, when they produce a picture which—most likely erroneously—has been taken as evidence of secretory function. The choroid plexus is innervated by a dense network of nerves as has been demonstrated by Stoehr and Clarke.

CIRCULATION OF C.S.F.

Quincke, the inventor of lumbar puncture, first assumed that there was a C.S.F. circulation from the ventricles into the subarachnoid spaces, and his theory was proved by the studies of Cushing, Dandy, Weed, and Wegefarth.

Dandy produced artificial hydrocephalus by blocking the escape channels of the C.S.F. Weed injected an isotonic solution of iron ammonium citrate and iron potassium cyanide into the subarachnoid spaces, killing the animals several hours later by injecting formalin and hydrochloride acid into the arteries. Prussian-blue formed wherever Weed's fluid had penetrated, and could be seen in microscopical sections, both in the villi and the venous system, as well as in the sheaths of the cranial and spinal nerves. The circulatory flow of the C.S.F. was demonstrated with X ray in the living organism by Wustmann, who injected 'Diodrast' into the subarachnoid spaces of animals.

There is a strong suspicion that the choroid plexus plays an essential part in the production of the C.S.F. If the plexus is exposed by operation in the ventricles of an animal one can observe under the binocular microscope the formation of fluid lakes around this organ. Putnam and I were able to show that fluorescein, injected into the veins, leaves the choroid plexus in the form of thick green clouds. But we also observed that green colour leaked out from all the vessels of the subarachnoid space. There is a possibility that the ependyma, too, participates in the formation of C.S.F., for we find C.S.F. in the embryonic ventricles before the choroid plexus has formed.

Some authors have held that the choroid plexus has an absorptive function; and in fact Askanazy found iron in the epithelium after hæmorrhage into the ventricular system. The conditions are easily reproduced experimentally. Moreover, fat and lipoids are increased in the cells of the choroid plexus after the injection of erythrocytes into the ventricles. Ma Wen Chao, Chen Ju Lin, and myself were able to prove that this is a non-specific response of the plexus, similar to an inflammatory response. Any injection into the C.S.F. (for instance, of air or trypan-blue) will cause the same changes—swelling of the connective tissue, and increase of the lipoids and of neutral fat in the epithelial cells. These changes persist for several days.

FORMATION AND CONSTITUTION

There are two theories about the production of C.S.F.—the theory of secretion and the theory of ultrafiltration. According to the theory of ultrafiltration, or dialysis, the production of the C.S.F. is a physical phenomenon in which the difference between the pressure in the which were undergoing disintegration and were surrounded by intensely congested and dilated blood-vessels, while the tubular epithelium in the neighbourhood was often reduplicated and apparently rejuvenating

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* Lecture delivered at the National Hospital, Queen Square, London, on Oct. 31, 1952.

Apart possibly from the fibrosed caseous lesions in case 7, the previous shortened courses of therapy with streptomycin + P A S left no histological changes in the tuberculous lesions The other changes present were all referable to the immediately preceding isoniazid therapy

In case 9, after 180 g of streptomycin $1^{1}/_{2}$–2 years previously, most of the cavity walls (and these formed by far the greatest amount of kidney tissue still remaining in both organs) showed reactivated but modified acute caseation, as in cases 5 and 6 (cf fig 14) Interest was focused more, however, on parts which had been densely fibrosed by the previous streptomycin therapy Fig 26 shows such a part caseated material intermingled with a few red blood-cells lay on a densely fibrosed wall, but there were no signs of reawakened tuberculous activity at the margin, the fibrosis, however, seemed to be softening, a tubule showed more active epithelium than was found in post-streptomycin fibrosis and was apparently pushing its way through, and several minute blood-vessels, surrounded by slight round-cell infiltration, were found Among the isolated lesions scattered throughout the parenchyma small loose epithelioid follicles (fig 12) were present, sometimes embedded in areas of chronic pyelonephritis, and were surrounded by numerous young blood-vessels and occasionally by frank hæmorrhage Of the lesions fibrosed by the previous courses of streptomycin the collagen had become homogenised (fig 27) and invaded by numerous congested blood-vessels, and tubules were prominent A variation is shown in fig 28, where there was a small hæmorrhage in the centre of a homogeneous focus, with numerous capillaries and slight surrounding infiltration A further stage of absorption in a smaller lesion is shown in fig 29

Secondary Infection

Only two of the nine specimens of kidney showed no evidence of secondary pyogenic infection This is in keeping with the previous finding (Dick 1953) that the great majority of "surgical" tuberculous kidneys show evidence of secondary pyogenic infection by the time of operation Even in connection with one of the uninfected kidneys the ureter showed subacute and chronic pyogenic inflammation In four of the specimens there were both acute and chronic stages of pyogenic infection, and in the other three there were only scattered foci of chronic pyogenic inflammation, these last three were from patients who had received the full 3-month course of isoniazid The fact that acute pyogenic infection was present in four specimens from patients under treatment with isoniazid confirmed that on some pyogenic organisms isoniazid did not exert an antibacterial effect

Care was taken throughout this investigation to ensure that changes due to these secondary infections were not attributed to the isoniazid, this was especially important as regards the increased vascularity, but it is believed that the fields chosen for the illustrations do show that there is a great increase in vascularity quite apart from any possible mild pyogenic inflammation in these areas Also, the renal changes due to isoniazid were found just as clearly in specimens with no secondary pyogenic changes

Discussion

The effects of isoniazid on the tuberculous lesions in human kidneys consisted of an extraordinary series of changes involving absorption of caseation, vascularisation of the edges of lesions, inactivation of epithelioid cells, and complete lack of surrounding fibrosis, forming a process quite unlike the natural defensive mechanism of the untreated host to tuberculous invasion Although the specimens examined were few, the extent of cavity walls and the number of lesions studied were very large The main changes were so consistent that it seemed reasonable to accept these changes as the fundamental effects of the isoniazid treatment Further details of any or all of the changes may still await discovery in different tissues of the body Here each of these changes is considered as regards not only the renal lesion but also its importance in the treatment of tuberculosis in general

ABSORPTION OF CASEATION

Though the absorption of caseation is the first effect of isoniazid chosen for discussion, the clinical evidence of very rapid subjective improvement in the patient and the regular fall in temperature indicate that the drug has a very early and effective action in checking the toxæmia by direct action against the tubercle bacilli (as has been shown in vitro)

This absorption is shown in acute lesions in figs 6, 11, 16, and 22 For its accomplishment it depends on the other features, especially the increased vascularity and lack of fibrosis at the margins of the lesions In open lesions, however, *the full effect of isoniazid appeared* to diminish after long-continued administration of isoniazid alone (fig 14, and cases 5, 6, 8, and 9) In the more chronic lesions, there is definite evidence of its beginning after a month's treatment with the drug, in figs 8 and 9, and absorption of the homogeneous material into which fibrous tissue can be converted by the action of isoniazid is found after longer administration (figs 18 and 27–29) Clinical corroboration of this is provided in pulmonary cases by the diminution in volume of sputum The volume of necrotic material being absorbed and the time the patient takes for this process may be the determining factors in the fall or lack of fall in the E S R, a feature which has varied considerably in clinical reports

This effect of isoniazid is obviously of great importance and places the drug in the forefront of those effective against tuberculosis From the evidence of these kidneys the absorption was optimal from the 2nd to 4th week of treatment in acute lesions and appeared to continue throughout the course in chronic lesions Complete absorption of lesions is the aim of all treatment, and isoniazid gives great promise of accomplishing this in recent acute lesions

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LEGENDS TO ILLUSTRATIONS

Fig 22 (case 7)—Wall of small cavity at tip of calyx, showing regenerating epithelium, under which is one indefinite epithelioid follicle becoming absorbed No fibrosis (× 100)

Fig 23 (case 7)—Epithelioid follicle, possibly with some central caseation becoming vacuolated, with no evidence of fibrosis, and with rejuvenating kidney tubules round it. (× 100)

Fig 24 (case 7)—Several fibrosed epithelioid follicles, becoming vacuolated and infiltrated with round cells centrally and peripherally This is not the picture of renewed tuberculous activity nor of normal process of fibrosis but appears to be an early stage of absorption (× 100)

Fig 25 (case 8)—A follicle, near a calyx with poorly formed epithelioid cells, central vacuolation and a ring of intensely congested capillaries. Epithelium in neighbouring tubules shows some reduplication. (× 100)

Fig 26 (case 9)—A cavity wall with dense old fibrosis (partly due to previous streptomycin and P.A.S) but now showing some loosening with young capillaries and a tubule pushing through *There is no evidence of tuberculous activity* (× 100)

Fig 27 (case 9)—An old densely fibrosed lesion with fibrosis hyalinised but now being broken up and infiltrated by congested blood vessels (× 100)

Fig 28 (case 9)—Another hyalinised old lesion with hæmorrhage and vacuolation centrally, and congestion and round-cell infiltration round it. (× 100)

Fig 29 (case 9)—Small old hyalinised lesion with no epithelioid cells slight central vacuolation and congestion and round-cell infiltration round it. (× 100)

happened in about twelve minutes. Reimers has confirmed our results, which indicate that the daily production of C.S.F. is some 100–250 ml.

EXCESS AND DEFICIENCY

I have already mentioned the changes in the rate of production mechanically produced by alteration of the osmotic pressure of the blood. But the clinician knows conditions in which the rate of production of the C.S.F. is changed because of other factors. Quincke has described symptoms caused by abnormal production of C.S.F.: headache and choked disc developed, and Quincke called this condition meningitis serosa. Unfortunately this term is now being used by many writers for inflammatory conditions, and therefore I propose for the non-inflammatory type the name *liquorrhœa*. This condition can imitate a tumour; it is often secondary to a focal infection: Molhant and McAlpine found it after infections of the nasal sinuses, and Symonds saw it after otitis. Liquorrhœa can also be caused reflexly by lumbar puncture, or by concussion of the brain. In these cases we sometimes find the proteins in the lumbar fluid diminished so that it resembles ventricular fluid in its composition.

Aliquorrhœa is the opposite to liquorrhœa. Here the production of spinal fluid ceases. This has been discussed in the French literature for twenty years under the name of hypotension of the spinal fluid, or ventricular collapse. The clinical symptoms have a remarkable resemblance to those of increased C.S.F. pressure. The patient complains of severe headache, and we find retraction of the neck, slowing of the pulse-rate, nausea, dizziness, and buzzing in the ears. One is inclined to think of increased intracranial pressure, but the optic discs are not choked and the patient complains of increased headache when he tries to sit up or to stand up. Lumbar puncture is dry: we do not get a drop of spinal fluid. After removing the needle's pilot, we even hear a noise because air is aspired into the subarachnoid spaces. Only by aspiration do we succeed in getting a few drops of yellowish spinal fluid. Its protein content is increased. All the disagreeable symptoms disappear immediately when we fill up the subarachnoid space carefully and slowly with warm Ringer solution until a normal pressure has been reached. This helps for a day or two, but then the old symptoms return and we sometimes have to give repeated injections before they finally go. Repeated lumbar punctures show nicely how the pressure gradually increases and the composition of the spinal fluid gradually becomes normal.

I have seen aliquorrhœa develop spontaneously in young women. There are some similarities with acute anuria in nephritis, and I believe that there is a reversible disturbance of the function of the choroid plexus, possibly of vasomotor origin. In other cases the diminution of C.S.F. pressure is probably due to a general dehydration. This type of aliquorrhœa can be regarded as an aspect of osmotic change. We often see aliquorrhœa as a result of lumbar puncture; it seems as if the diminution of C.S.F. pressure is too strong a stimulus for the choroid plexus, and causes a sudden stop of spinal fluid production. Leriche, Mahoudeau, and Vincent have described aliquorrhœa after head injuries and operations on the brain. In some of these cases there must be an additional cause—namely, atrophy of the choroid plexus. This is particularly true in old cases of hydrocephalus due to obliteration of the fourth ventricle by tumour. When the tumour is removed the choroid plexus is unable to resume normal activity. It is my opinion that aliquorrhœa is one—if not the most important—cause of pachymeningitis hæmorrhagica, chronic subdural hæmatoma, and even of cerebral hæmorrhage. The reduced volume of C.S.F. must be compensated by abnormal engorgement of the vascular system; and, when the vessels are diseased or otherwise damaged, this causes hæmorrhage. Old people, especially, are disposed to such accidents because in old age, as Zalka has shown, the choroid plexus atrophies. In operations for subdural hæmatoma it is striking to see how deeply the brain is sunk into the cranial cavity, showing no tendency to expand after the evacuation of the blood-clot. Only when the ventricular system is filled with saline solution does the brain resume its normal shape.

ABSORPTION

Are there any disturbances of absorption of the spinal fluid? So far no facts are known suggesting any nervous regulation of absorption. It seems that the absorption largely depends on the pressure of the spinal fluid; and of course the size of the stomata leading into veins and lymphatic channels is of importance. Increased absorption follows many conditions with increased C.S.F. pressure, particularly meningitis. Some results of meningitis are apt to interfere with absorption, particularly obliteration of the channels leading into the blood and lymphatic system, occasioned by the particular composition of the spinal fluid. Not only corpuscular elements but also colloidal clots are liable to obliterate these stomata. In addition, all spinal fluids with a high protein content have a higher viscosity than normal spinal fluid, and so have less tendency to be absorbed. A similar effect is caused by hæmorrhages into the subarachnoid space. High viscosity may also be responsible for the surprising observation that at levels below spinal tumours absorption is practically zero. The same holds true for the polyneuritis of Guillain and Barré: in this condition a somewhat reduced absorption of spinal fluid is associated with increased C.S.F. pressure, and this may be due to the high protein content of the spinal fluid, which resembles the spinal fluid below a tumour.

In 1783 the Scots anatomist Alexander Monro, of Edinburgh, published a paper on the structure and function of the nervous system in which he pointed out that the skull and bony spinal canal are a rigid container; in consequence he believed that the blood content of the brain would always be the same. George Kellie, an English physician, supported Monro's assumption on the strength of necropsy findings on hanged and frozen people. But both these authors ignored the rôle of the spinal fluid. Cushing took this into consideration and gave a new formula to the Monro-Kellie doctrine as we may fairly call it. He said that the sum of the volume of the brain plus the volume of the spinal fluid and the volume of the blood within the skull must be constant. Increase of the volume of one of these must automatically cause reduction of the volume of one or both of the others. As the spinal fluid can escape to some extent into the spinal canal, some change in the blood volume of the brain is possible; and since we know that the width of the arteries and capillaries of the brain depends on nerve impulses, there is not much left of the original Monro-Kellie doctrine by Cushing's modification. The possibility of compensation through escape of the spinal fluid, however, holds true only for small and rapid changes in the volume of the brain. Slower and bigger changes must be compensated for by increased or diminished production or absorption of spinal fluid.

The Monro-Kellie theory can be well studied by introducing a fourth substance into the C.S.F.—namely air, which can be seen on X-ray examination.

We have made studies on these lines in a pressure chamber, in order to find a method of improving the absorption of air after encephalography. We were able to prove that once there is an air-bubble in the ventricles its size depends on pressure in the external atmosphere. The influence of the atmospheric pressure in the interior of the cranial cavity is exerted through

VASCULARISATION OF EDGES OF LESIONS

One of the features of untreated tuberculous lesions is the lack of blood-vessels within the lesion itself and their comparative scarcity in the immediate vicinity The action of the tubercle bacillus seems to be almost specifically directed against them Thus, when numerous young blood-vessels appear round a tuberculous lesion and infiltrate into the very substance of the lesion, it can be interpreted as a sign that the tuberculosis is no longer active and healing is taking place Young blood vessels in a congested state are shown especially in figs 6, 14, 16–18, 25, and 27 (mostly after the full 3 months' treatment) but were found in all the lesions They may be accompanied by minute hæmorrhages into the surrounding tissues or occasionally by macroscopic hæmorrhages into or around the lesions These hæmorrhages into small regressing follicles were reported by Berblinger (1952) in his necropsy findings in a case of pulmonary tuberculosis after 45 days' treatment with isoniazid No such increased vascularity is found after treatment with streptomycin alone or with streptomycin and P A S This vascularity with occasional hæmorrhages also seems to occur in pulmonary cases under treatment with isoniazid as evinced by the occurrence of hæmoptysis (Borthwick 1952) It provides the mechanism for absorption of the caseation and the homogenised material from old fibrosis Further, it occurs to a lesser extent in old fibrous lesions (figs 10 and 26), and if this aspect of the action of isoniazid can be developed it may provide a means of attacking organisms embedded in chronic lesions, though it cannot hope to lead to complete physical cure of such lesions

Though this feature of the action of isoniazid is almost entirely beneficial, three dangers must be pointed out (1) if the organisms become resistant to isoniazid, vascularisation may open up surrounding tissues, causing local extension of the lesion, (2) some organisms may possibly enter the blood-stream and be disseminated throughout the body (especially back to the lungs) and cause reinfection by resistant strains, and (3) vascularisation may increase the size of a lesion and possibly bring on unexpected symptoms—e g, in meningitis fits may be caused by a tuberculoma in the brain It may be possible to minimise this risk by giving a short course of streptomycin and P A S before administering isoniazid This vascularity may be the cause of the primary exacerbation of symptoms mentioned by Bartley (1952)

INACTIVATION OF EPITHELIOID CELLS AND LACK OF FIBROSIS

In the great majority of untreated tuberculous lesions epithelioid cells play a most important rôle (Cameron 1952) They are present, often in a most characteristic palisaded arrangement (Marshall 1953), round the edges of all but the most acute and very chronic caseated lesions, and they are the principal cells scattered throughout the so called "epithelioid" lesions, in each case being very closely associated with the development of fibrosis in and round the lesion as it becomes more chronic, or softening into caseation if it becomes more acute Though the appearance of epithelioid cells and the development of fibrosis in and round the tuberculous lesions are due to separate constituents of the tubercle bacilli (Blacklock 1951, Cameron 1952) it is too early to differentiate the effects of isoniazid on these processes and for the present they will be discussed together The most important effect of streptomycin with or without P A S (in addition to checking the spread of acute caseation) was an intensification of the fibrosis both throughout and round all the tuberculous lesions

Isoniazid does not further this natural defence reaction, it even puts this whole process out of action apparently by liquidating so far as it can the epithelioid cells Where the acute caseating process was stopped abruptly (figs 6 and 11), there was no zone of epithelioid cells, or, where caseation had been not quite so acute (fig 7), the cells were few and even more indefinite than usual, and no fibrosis was found Where a more chronic area of caseation already had established a well palisaded row of epithelioid cells, the zone was much looser and vacuolated, the cells were more indistinct, and no collagen was seen (fig 8) the fibrosis which normally would be developing deep to the epithelioid zone was completely absent In still more chronic lesions (fig 9) absorption of caseation near the epithelioid zone was found and the epithelioid and fibrous zones again showed loss of collagen, very indistinct epithelioid cells and infiltration by young capillaries In a still denser fibrous wall (fig 10) there were breaking up of the fibrosis by young capillaries, vacuolation towards the caseated surface, and the apparent conversion of the fibrous tissue cells into an irregular layer of indistinct epithelioid cells —a complete reversal of the normal tuberculous process Even where the process of fibrosis had been consolidated previously by streptomycin (fig 26), isoniazid appeared to be having some effect in vascularising and softening the fibrosis

This effect of isoniazid has been dealt with in considerable detail as regards cavity walls because of the far-reaching implications involved, if this is the true interpretation of the histological appearances The *British Medical Journal* (1952) suggested that a satisfactory drug for the treatment of tuberculosis should be able, among other properties, to vascularise chronic fibrous tissue and to enable the chemotherapeutic action to reach bacilli deeply embedded in old lesions Isoniazid appears to have considerable possibilities in this direction

Isoniazid has the same effect in causing disintegration of the epithelioid cells and preventing the development of fibrosis in isolated parenchymatous "epithelioid" lesions (figs 22–25) Where the lesion had already fibrosed completely, a most unexpected series of events took place the fibrous tissue became converted to an eosinophilic and very finely granular or almost homogeneous substance (fig 29), which became surrounded by large congested blood-vessels (figs 18 and 27), with some round cell infiltration, sometimes showing a small central hæmorrhage (figs 18 and 28), and became gradually absorbed (fig 13) No epithelioid cells appeared throughout the whole process

There has been considerable difficulty in fitting the radiological appearance to the clinical in patients under treatment with isoniazid The realisation of this lack of fibrosis, even absorption of fibrous tissue, in the healing of tuberculous lesions after treatment with isoniazid suggests that reassessment of the criteria of radiological improvement may be required

Another important consideration arising from this effect on fibrosis applies to the treatment of tuberculous meningitis Isoniazid may prove to be the drug required to cause absorption of the exudate rather than fibrosis and thus to prevent the development of hydrocephalus

RESISTANCE TO ISONIAZID

In a few highly selected cases the proportion in which the tubercle bacilli develop resistance to isoniazid would be misleading A true indication of the number of cases under treatment with isoniazid alone which developed drug-resistant bacilli could be reached only by a large scale investigation as in the M R C's second interim report on pulmonary cases (Medical Research Council 1953) and from this it emerged that the figure was 35% after 3 months' treatment This seems to explain the regressive histological appearances in the open lesions in cases 5, 6 8, and 9 and indicates most emphatically that isoniazid should not be used by itself for longer than 6 weeks But longer treatment is required for the satisfactory effects in isolated lesions Fortunately, the same M R C report showed that the development of tomycin gave continued improvement. Further, in a trial of isoniazid in renal tuberculosis, Borthwick (1952) requested permission to stop treating the cases with isoniazid alone, because the clinical results were disappointing.

The results in laboratory animals are also somewhat equivocal.

In mice Bernstein et al. (1952) reported that isoniazid was far superior to streptomycin or to P.A.S. in preventing infection, even when treatment was delayed after inoculation. In guinea-pigs and rabbits, however, Steenken and Wolinsky (1952) found that, though isoniazid very successfully suppressed experimental tuberculosis, the infection was not eliminated. In intra-corneal tuberculosis of mice Knox et al. (1952) found that isoniazid controlled the development of infection, but that, when isoniazid was withdrawn after 4 weeks, typical lesions developed. Goulding and Robson (1952) confirmed this and showed that streptomycin and isoniazid given together controlled the disease much more distinctly, whereas in rabbits isoniazid alone had a greater suppressive action than had streptomycin.

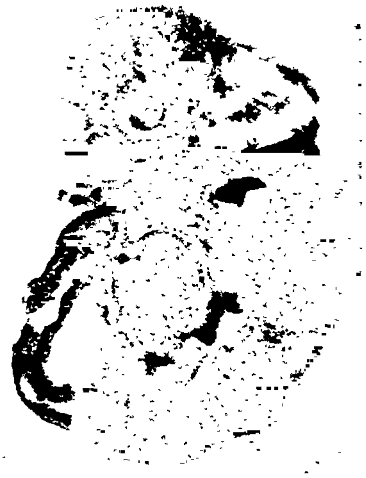


Fig. 1 (untreated case)—Small kidney with large ulcerocavernous lesion in lower part of upper pole, showing irregular ulceration round tips of other calyces; small nodules of tuberculosis in pelvic and ureteric mucosæ; and collections of white nodules in bands across medulla and cortex in middle zone and lower pole. ($\times {}^{2}/_{3}$)

A further development is the study of the action of isoniazid on tubercle bacilli and macrophages in tissue culture.

Suter (1952) and Mackaness and Smith (1952) have shown that, even with fully bacteriostatic concentrations of both streptomycin and isoniazid, the intracellular bacilli remained viable for at least seven days, though isoniazid was equally active against intracellular bacilli and those in liquid medium.

These animal and in-vitro experiments, however, do not explain the complexities of the clinical findings.

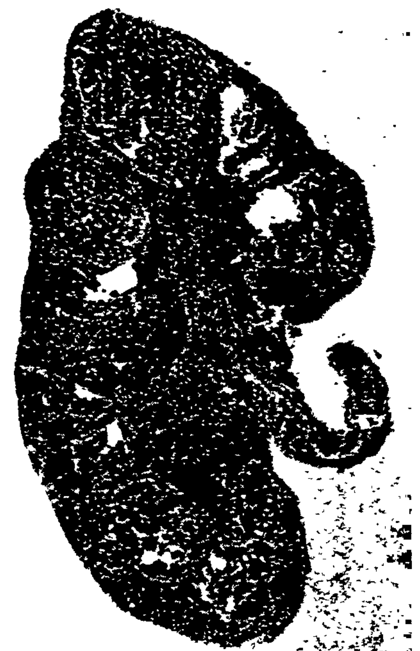


Fig. 2 (untreated case)—Considerably enlarged kidney showing ulcerocavernous lesions in all areas, largest in upper pole, smallest in middle zone; and lining of cavities consisting of hard cracked greyish-white caseated material with irregular white tuberculous granulation tissue round it. ($\times {}^{2}/_{3}$)

In this paper I report observations on the effects of isoniazid on tuberculous lesions in the kidneys of patients treated with isoniazid alone before nephrectomy. These effects, I believe, not only explain the paradoxical clinical findings but also help to show what part isoniazid can be expected to play in the treatment of tuberculosis in general.

Material

Kidneys were obtained from nine patients under treatment with isoniazid alone as part of the M.R.C. trial of isoniazid in genito-urinary tuberculosis at Robroyston Hospital, Glasgow. In seven of the cases nephrectomy was indicated, as in routine genito-urinary practice, by the extent of the tuberculous lesions in kidney and bladder: the period of isoniazid treatment before operation was less than 1 month in four cases, 6 weeks in two, and 3 months in one. In one case nephrectomy was necessitated by deterioration of the patient's condition and by extension of originally minor tuberculous lesions, as shown by pyelography, after 3 months' treatment with isoniazid; and in the ninth case the patient died from uræmia after 3 months' treatment with isoniazid. Three of the patients had received previous treatment, mostly with streptomycin plus P.A.S. The relevant details of the nine cases are given in the appendix.

Suitable control material was already available from examination of specimens in the previous streptomycin trial (Dick 1953), and the lesions were also compared with those after streptomycin alone and after streptomycin plus P.A.S. The control series, now totalling forty specimens from patients who had received, at the time of nephrectomy, no specific drug therapy, showed numerous examples of every variety of tuberculous lesion at all stages, in the naturally occurring state.

Macroscopic Lesions

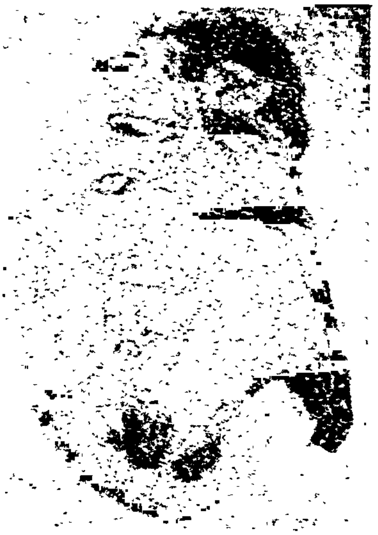


Fig. 3 (case 3)—After 23 days' treatment with isoniazzid, kidney with ulcerocavernous lesion forming "cyst" at upper pole, showing intense congestion round tuberculous lesion, fairly sharply demarcated from rest of organ. ($\times {}^{2}/_{3}$)

Specimens from patients who had been treated with isoniazid, like specimens from untreated patients (figs. 1 and 2), showed all degrees of tuberculous lesions ranging from very small ulcers at the tip of one or more calyces, through fairly large ulcerocavernous lesions involving a small or a large part of a zone or a pole (the commonest stage), to extensive lesions involving all the calyces and leaving a thin rind of kidney tissue.

To the naked eye the lesions in the specimens after treatment with isoniazid showed a degree of congestion most unusual in tuberculous lesions. In addition, frank hæmorrhages were found either in the cavity (fig. 3), in the cortex and under the capsule (fig. 4), or under the mucosa of the calyx or pelvis (see especially the upper pole in fig. 5). Some congestion in the calyx and pelvic mucosa was found in several of the untreated specimens owing to secondary pyogenic infection, but

TABLE I—RESULTS OF DIAGNOSTIC TESTS BEFORE TREATMENT

—	Histology positive	Chronic endometritis	Histology negative
Guineapig test positive	26	3	8
Guineapig test negative	4 (2 not done)	-	

Culture was positive in 6 cases

A clinical trial of isoniazid in female genital tuberculosis was started in Newcastle upon Tyne, 43 patients with tuberculous endometritis and 3 with tuberculous cervicitis being chosen In 17 of these patients adnexal masses were palpable on pelvic examination, in none was there any gross disturbance of general health

DIAGNOSIS

The diagnosis was confirmed in all the cases by curettage in the premenstrual phase immediately before treatment The tissue obtained was examined histologically, by guineapig test, and by direct culture on Lowenstein Jensen (L J) medium The results are shown in table I

The guineapig test was positive in 37 patients, 29 patients showed typical histological evidence of the lesion in the endometrium, and 3 others showed a chronic cellular reaction, suggestive but not typical of tuberculosis Of the 14 patients in whom histological evidence of the lesion was lacking, a microscopical diagnosis of typical endometritis had already been made in 5 at a previous examination In the remainder further sections were cut from the paraffin blocks, and in this way definite microscopical evidence of tuberculous endometritis was found in another 3 patients Histological evidence of the lesion was seen therefore in 37 patients altogether

A direct culture of *Mycobacterium tuberculosis* was obtained from the endometrium in 6 cases In all of these the biological test and histological diagnosis were also positive, suggesting that a direct culture is obtained only in the presence of heavy infection of the endometrium

SENSITIVITY OF TUBERCLE BACILLI TO ISONIAZID AND STREPTOMYCIN

In 20 of the cases in which the biological test was positive the spleen of the guineapig was cultured on L-J medium In all the primary cultures the growth was luxuriant and characteristic of the human type of *Myco tuberculosis* Tests for isoniazid and streptomycin sensitivity were carried out The method of testing for isoniazid sensitivity used in the M R C investigation (Medical Research Council 1952) was followed Isoniazid was incorporated into L-J medium to give concentrations of 0, 0 2, 1, 5, 10, and 50 µg per ml The cultures were compared after two weeks and four weeks with a culture of H37RV inoculated on a similar series of L J slopes, and in all the cases the growth was inhibited at a concentration of 0 2 µg per ml, whereas the controls showed a confluent growth Cultures from only 4 of the 11 patients selected for combined therapy with isoniazid and streptomycin were available for sensitivity tests with streptomycin, and all of them showed inhibition of growth in Dubos medium at a concentration of 0 125 µg per ml The standard strain H37RV was inhibited at a concentration of streptomycin of 0 25 µg per ml

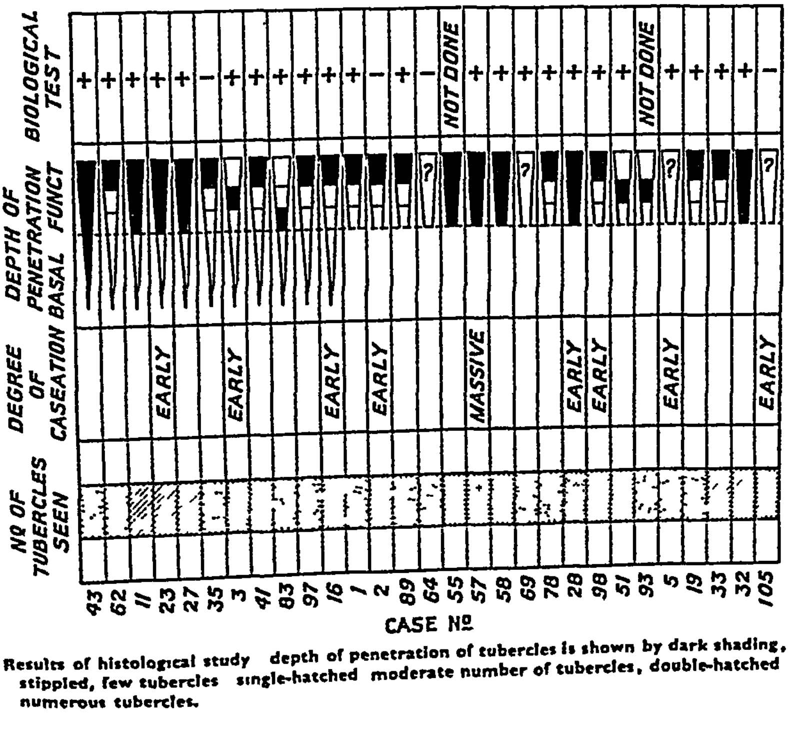
HISTOLOGICAL STUDY

Because it was suspected that the heaviness of the infection, the presence of caseation in the lesion, and the depth to which infection penetrates the endometrium may influence the response of female genital tuberculosis to treatment with antibiotics, a further detailed histological study was made of those 29 sections in which microscopical evidence of tuberculous endometritis had been immediately apparent In this study the degree in which these three factors were present was assessed in each case

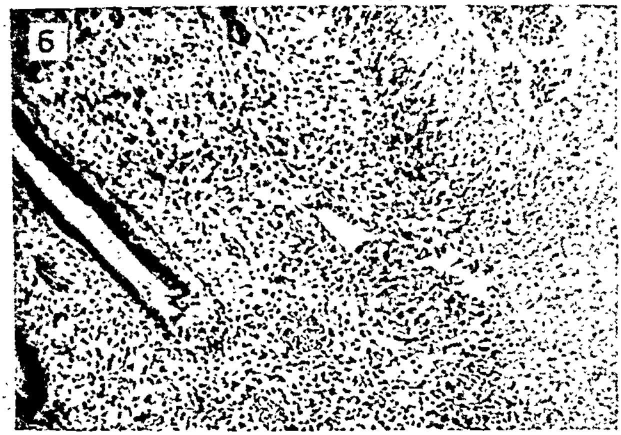
The heaviness of infection was roughly estimated by counting the number of tubercles seen during a complete search of each section These were classified as few, moderate in number, or numerous and confluent The amount of caseation present was classified either as nil, early, moderate, or massive The depth to which the lesion penetrated the tissue was also assessed, particular note being made of the presence or absence of tubercles *in the basal layers of the endometrium* In several cases the basal endometrium was difficult to identify with certainty, and, except in those sections in which a portion of myometrium had been included in the field, or in which a vertical section had been cut through the tissues, showing the lumina of the endometrial glands at all levels, it was impossible to distinguish basal endometrium from non-functioning superficial endometrium

The results of this histological study are shown in the accompanying figure In 11 cases basal endometrium was identified, in only 1 case was there evidence of tuberculosis at this depth, and then only one tubercle was seen In the remaining 10 cases the lesion was confined to the functional layer of the endometrium which is shed with each menstruation In 13 cases only a few tubercles (from one to six) were found in the endometrium, in 10 cases a moderate number were present, and 6 cases showed *a numerous confluent distribution* of tubercles throughout the section Caseation was absent in 20 cases, and in the remaining 9 cases only early caseation was present, except 1 case in which massive caseation was present There seemed to be no relation between the number of tubercles present and the degree of caseation, suggesting that all these lesions were of recent contemporary origin

In the 3 cases with tuberculous cervicitis the diagnosis was made on histological



Results of histological study depth of penetration of tubercles is shown by dark shading, stippled, few tubercles single-hatched moderate number of tubercles, double-hatched numerous tubercles.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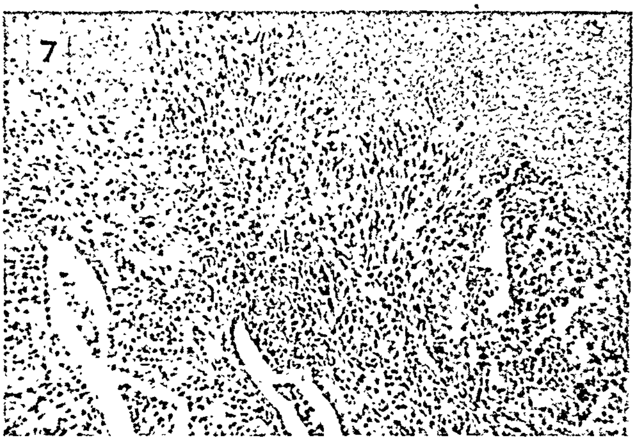
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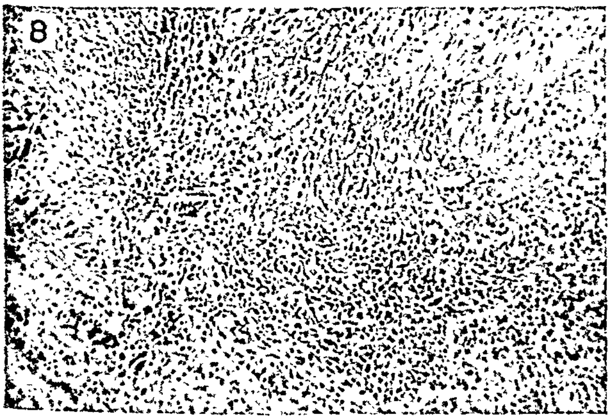
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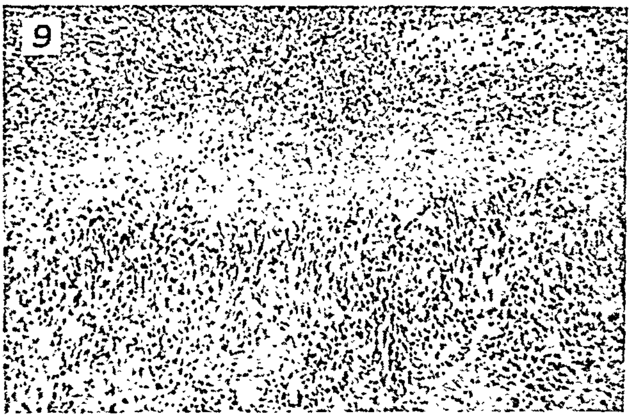
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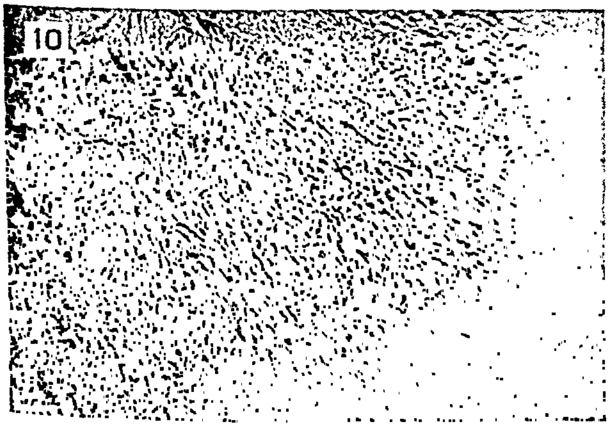
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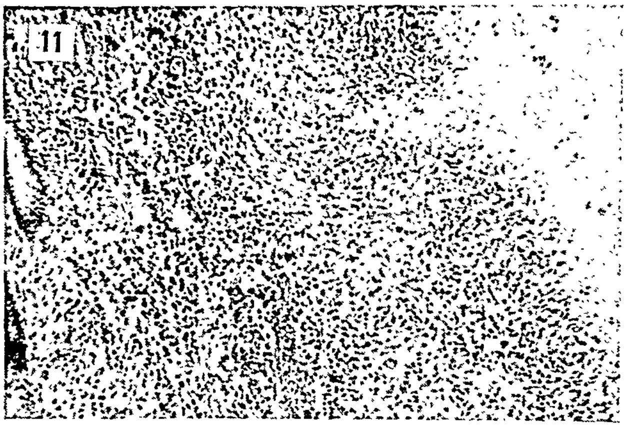
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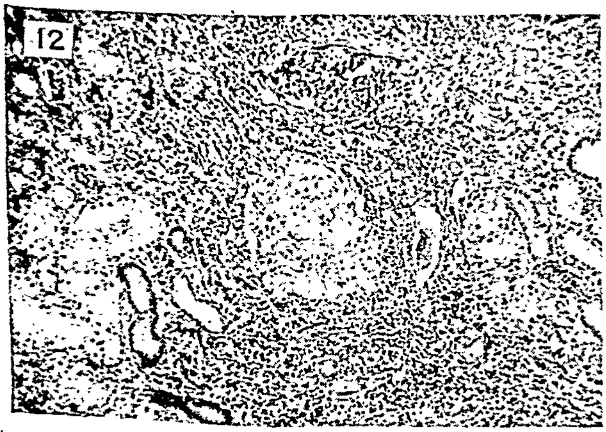
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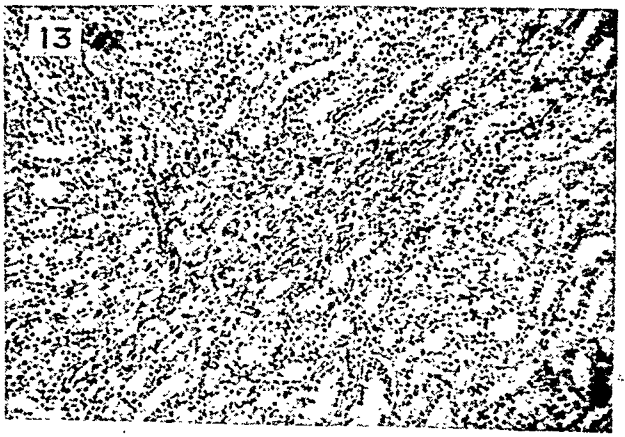
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The reason for this reappearance of tubercles in the endometrium is obscure There seem to be three possible explanations

(1) An active tuberculous focus persists in a fallopian tube in spite of antibiotic therapy, and this is responsible for reinfection of the temporarily cured endometrium

(2) Tubercle bacilli persist in an inhibited state in the endometrium, where after a time they become reactivated and give rise once again to histological response in the tissues in this event one has to suppose that the bacilli remain in the basal layer of the endometrium, for they would otherwise be shed during menstruation in the intervening period

(3) The endometrial lesion is periodically renewed by an intermittent tuberculous bacillæmia which arises from an active tuberculous focus in a remote situation in the body (Haines 1951)

(1) As regards reinfection from a persisting tuberculous focus in the fallopian tube, it is clearly impracticable to obtain a biopsy from the fallopian tube both before and after treatment with antibiotic agents Apart from clinical appraisal of the alteration in size of adnexal masses, and changes in the clinical condition of the patient while under treatment, it is seldom possible to assess the effect of antibiotic therapy on a lesion in this situation

Hence very little is known about the response of tuberculous salpingitis to antibiotics O'Driscoll (1951) has reported a patient who received 135 g of streptomycin and underwent surgery towards the end of the course, a persisting active tuberculous lesion was found in a fallopian tube

Florey (1952) has emphasised the relevance of the cytological pattern of the tubercle to its response to treatment with antibiotics He has pointed out that chemotherapeutic agents introduced by the systemic route must not only be transported to the site of the disease but must also be able to penetrate the avascular caseous area surrounding the lesion, the wall of the giant cell, and the waxy outer envelope of the tubercle bacillus P A S has no intracellular action, while streptomycin has only a limited action within the cell The activity of isoniazid, owing to the smallness of its molecule, is as great inside as outside the cell The unique absence of caseation from the lesion in tuberculous endometritis, in which respect it differs from tuberculosis in every other part of the body, and the invariable presence of caseation in tuberculous salpingitis, lead one to expect the lesion in the endometrium to respond more readily to antibiotic therapy than the lesion in the fallopian tube Reinfection of a temporarily cured endometrium from a persisting focus in the tube therefore seems to be likely

(2) As regards the persistence of tubercle bacilli in the basal endometrium, Ryden (1950) reports that tubercles can be found in the basal endometrium in all cases in which a careful search has been made This is contrary to the classical description of the histology of tuberculous endometritis by Schroder (1921), in which the lesion was shown characteristically to be confined to the superficial layers, a concept confirmed later by many pathologists including Delarue and Bergerot-Blondel (1949) and also by the present findings (see figure) It therefore seems unlikely that infection can persist in the basal endometrium unless we postulate that tubercle bacilli may ordinarily be present in the basal layer without giving rise to any histological response in this situation

(3) As regards periodical renewal of the endometrial lesion by intermittent tuberculous bacillæmia, in a survey of a large series of cases with pelvic tuberculosis to which reference was made by one of us at the Congress of Obstetrics and Gynæcology at Leeds (Smith 1952) we have shown that tuberculous infection is disseminated to the genital tract early in the postprimary phase of the general infection of the body by the tubercle bacillus These findings are inconsistent with the concept of periodical renewal of the lesion in the endometrium by intermittent bacillæmia throughout life, derived from an active tuberculous focus elsewhere in the body

We want to emphasise that this is only a preliminary report on the initial response of tuberculous endometritis and tuberculous cervicitis to treatment with isoniazid We propose to repeat all these investigations on these patients in a year, by which time the comparative effectiveness of isoniazid used alone with that of isoniazid used in combination with other antibiotics may have become apparent The significance of the cytological factors assessed histologically in the present series may also be apparent by that time We do not claim that the response which followed treatment with these drugs is in any way permanent, but that it is nevertheless of therapeutic value is proved by the fact that one of these patients has already become pregnant

SUMMARY

The effect of isoniazid on pelvic tuberculosis has been assessed in 43 patients with tuberculous endometritis and 3 with tuberculous cervicitis

The patients were divided into two groups, of which one received isoniazid only and the other isoniazid, streptomycin, and P A S

All the cases were confirmed by histological, biologica or cultural examination All the cultures that were obtained were of the human strain of tubercle bacillus

Only 2 patients with tuberculous endometritis and 1 with tuberculous cervicitis did not respond to treatment, 40 showed no evidence of infection after treatment, and 1 became pregnant

Since endometrial lesions often reappear twelve months or more after treatment with streptomycin, these *apparent cures cannot be regarded as permanent* Relapse after treatment may be due to persistence of the lesion in the fallopian tubes, where caseation, insulating the bacillus from the action of the antibiotic, is usually present Ryden's (1950) findings of persistent tubercles in the basal endometrium have not been confirmed in the present study

We have also shown that tuberculous dissemination occurs during the early postprimary phase of gener infection of the body by the tubercle bacillus, a vie inconsistent with Haines's (1951) concept of periodic renewal of the endometrial lesion by bacillæmia fro remote foci

We wish to thank Dr B E Tomlinson, who supplied th histological reports for this study Our thanks are al extended to Messrs Roche Products, who provided th 'Rimifon' (isonicotinyl hydrazide) used in this clinic trial

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The volume of basic knowledge which must be mastere by the medical students of today is far greater than eve before And yet we are now urged to teach students l about the science of medicine and more about the practica aspects of home care and office practice Why, may I ask should the undergraduate curriculum be any different for a general practitioner than for a neurosurgeon ? *Do they no both have to know a maximum of medical science* ? — W BARRY WOOD, jun, M D *J Lab clin Med* 1953, 41, parenchyma. Another feature, seen in the medulla of these specimens, was the numerous irregular or rounded areas of eosinophilic material between the tubules, infiltrated and surrounded by numerous congested capillaries (fig. 13). From intermediate stages throughout these specimens it was concluded that this appearance sometimes represented a late stage in the disappearance of a tuberculous follicle which was being absorbed, although similar appearances were found in non-tuberculous healing lesions.

AFTER THREE MONTHS' TREATMENT WITH ISONIAZID AND NO PREVIOUS CHEMOTHERAPY (CASES 5 AND 6)

In the specimens from these cases there was a sharp distinction in appearances between lesions in the cavities, calyx, and pelvis, and in the isolated follicles in the renal parenchyma. The recent open lesions showed a diminution of the good effect seen in the cases treated for a month or less, though there were still modifications from the appearances in untreated cases. The zone of reaction in the cavity wall (fig. 14) was broader than in figs. 6 and 7, though still not nearly so broad as in an untreated cavity. There was still minute vacuolation of the caseation in parts, as if some absorption was taking place, but in other parts there appeared to be direct extension of the caseation into the surrounding tissues. The vascularity was still prominent and, if anything, increased. The greatest change, however, was in the increased cellular reaction: epithelioid cells were prominent, with slight fibrosis between them; a few giant cells had developed at the caseating margin; and there was a slight increase in lymphocytic infiltration.

In older parts of cavity walls with dense fibrosis (fig. 15) caseation appeared to spread into the fibrosis, which softened before it; and, although there was no clear zone of epithelioid cells, there were considerable round-cell infiltration and vascularity beyond the advancing caseation.

Towards the calyx, at the neck of the cavity, a vascular granulation tissue showed signs of reactivating tuberculosis: the superficial layer (fig. 16) showed epithelioid cells lining the lumen, more active in appearance than the vacuolated caseation in fig. 11; and elsewhere active epithelioid follicles from deeper in the submucosa (fig. 17) were ulcerating to the surface. In addition to the renewed activity of tuberculous lesions, the vascularity and lack of fibrosis were prominent features in this site.

LEGENDS TO ILLUSTRATIONS

Fig. 14 (case 5)—Renewed acute caseation in edge of cavity. Part of the picture shows epithelioid cells with vacuolation of caseation between them, and other parts show no barrier at all, the caseation extending directly into vascular granulation tissue. (× 100.)

Fig. 15 (case 5)—Renewed caseation in chronic cavity. The caseation extends directly, with few epithelioid cells, into fibrous wall. (× 100.)

Fig. 16 (case 6)—Vascular granulation tissue at neck of cavity with margin of poorly formed epithelioid cells. (× 100.)

Fig. 17 (case 6)—Epithelioid follicle, in vascular granulation tissue wall, rupturing to surface. (× 100.)

Fig. 18 (case 6)—An old follicle, the fibrosis of which has become converted to almost homogeneous eosinophilic material, with hæmorrhage into it and numerous congested capillaries surrounding it to absorb it. (× 100.)

Fig. 19 (case 5)—An old follicle, with giant cell round concentric laminated body: there are loose cells round but no dense fibrosis. (× 100.)

Fig. 20 (case 6)—A giant cell and epithelioid follicle showing no evidence of fibrosis. (× 100.)

Fig. 21 (case 6)—Aggregation of fibrosed epithelioid follicles with prominent tubules in and round them. Follicle nearest surface shows loss of fibrosis with recent caseation centrally and no clear demarcation from kidney parenchyma—a recently spreading lesion. (× 50.)

Thus, in these open-cavity lesions the early beneficial effects of isoniazid had been partially lost after 3 months' treatment. As regards the isolated tuberculous lesions (small and large) scattered throughout the renal parenchyma, the changes were much greater after 3 months' treatment than after less than 1 month's treatment, and were far different from those found in controls.

In two-thirds of the untreated specimens small and acutely caseating follicles were present, causing active destruction of the kidney tissues. All of them showed epithelioid follicles with or without central caseation and with either early or well-marked surrounding fibrosis, which had in some cases penetrated diffusely into the surrounding parenchyma.

In specimens after treatment with isoniazid, however, small caseating follicles seemed inactive, as if all the elements so characteristic of tuberculous lesions were melting into a homogeneous fibrinous matrix (fig. 18), which was then becoming vascularised by numerous congested capillaries, and there were often small central hæmorrhages, ultimately becoming absorbed, the later stages of small recent lesions of this kind having been found earlier (fig. 13). Even old fibrosed lesions with concentric laminated bodies showed a loosening of the fibrosis (fig. 19). Individual epithelioid follicles, too, showed œdema and loss of fibrous tissue (fig. 20) both throughout the lesion and round it. If there had been old fibrosis round it, this was now much less compact, and the collagen was disappearing. This loss of compact fibrosis round old epithelioid lesions even permitted breaking out of fresh caseation in larger lesions (fig. 21). Another feature noticed in these lesions was the prominence and apparent rejuvenation of tubules round the lesions (fig. 21).

AFTER ISONIAZID TREATMENT FOLLOWING PREVIOUS CHEMOTHERAPY (CASES 7–9)

The effects on the histological lesions in renal tuberculosis of streptomycin alone and of streptomycin and P.A.S. have been described already (Dick 1953).

To summarise, a 3-month course of streptomycin alone checked acute caseation, encouraged considerable fibrosis along the edges of chronic caseating cavities, and caused a dense fibrous reaction round all the isolated lesions scattered throughout the renal parenchyma. When streptomycin-resistant strains of the tubercle bacillus became predominant, the beneficial effect of the fibrosis was nullified by renewed caseation, especially in the mucosa of calyx and pelvis. Streptomycin and P.A.S. caused an even greater fibrosis round all tuberculous lesions, and no lesions still actively caseating were found after a 3-month course of these drugs combined.

In the present series cases 7 and 8 had received about a month's treatment with streptomycin and P.A.S. followed by 6 weeks' isoniazid treatment before nephrectomy, yet their lesions were completely different histologically. In case 7, a boy aged 7 years, the tuberculous lesions were all becoming inactive. There were three small cavities at the tip of one calyx, all showing fresh growth of epithelium on the surface (fig. 22), with a few small absorbing follicles scattered under it. Scattered caseous lesions in the parenchyma were still well fibrosed. The numerous epithelioid follicles were loose, vacuolated, infiltrated with lymphocytes (figs. 23 and 24), and gave little evidence of tuberculous activity. The isoniazid appeared to be controlling the infection. Case 8 was of peculiar interest because there were two ureters, one draining the upper pole and the other the mid-zone and lower pole, but both drainage areas showed extensive tuberculous lesions (fig. 5). In these lesions there were extensive areas of modified caseation, as in fig. 14, with no evidence of fibrosis in some cavities while others showed patchy fibrosis. Thus the isoniazid was not controlling the infection in the open lesions. That it was having some effect in the isolated lesions was shown by the appearance of some epithelioid follicles (fig. 25) thromboplastin suspension. The mixture is placed in a water-bath at 37°C for 5 minutes, 0.2 ml. 0.33% calcium chloride solution is added, and the time required for clotting is measured.

A correlation graph is prepared from dilutions of normal plasma. The clotting-time of 1:10 dilution of normal plasma in barbitone buffer is regarded as equivalent to 100% prothrombin activity. Higher dilutions of the normal plasma are made with a barbitone buffer containing 30 mg. potassium oxalate in 100 ml. solution.

The accompanying figure shows the distribution of results by Quick's and Owren's methods of determining prothrombin activity in 80 cases where tromexan was given in varying amounts. Statistical analysis of the figures does not reveal any significant difference between the two sets of observations. In the therapeutic range of activity—i.e., 10–25% of prothrombin activity—there were 37 results by one method and 39 by the other. The only pronounced difference between two groups of results was at 15–20% and 20–25% of prothrombin activity. In our opinion this is immaterial. The experiment also provides evidence that factor V is not affected by the administration of tromexan.

In view of our experimental results, we believe that it is unnecessary to add a sample of factor V to every routine prothrombin test, and that Owren's one-stage prothrombin test has no practical advantage over that of Quick's. Owren's method may have certain definite advantages from the research point of view.

A typical series of results is shown in table I. The clotting-time of normal plasma by the modified Quick method using thromboplastin (Geigy) is 15.6–18.2 seconds. The addition of factor V does not shorten the clotting-time significantly; when factor VII is added there is a distinct shortening of the clotting-time which tends to approach the optimum clotting-time of 12–15 seconds (Biggs et al. 1953). Further work on this aspect of blood coagulation will be described in a later communication.

TABLE I—CLOTTING-TIME (SEC.) OF NORMAL PLASMAS WITHOUT AND WITH THE ADDITION OF FACTOR V OR FACTOR VII

Normal plasma	Normal plasma with factor V added	Normal plasma with factor VII added
18.2		
17.0	16.0	12.5
16.8	14.0	13.5
16.4		
17.8		
18.2	18.0	16.2
15.6		
16.4	15.8	15.0
16.0		
17.6	16.4	14.4

PROTHROMBIN TIME OF TROMEXAN-TREATED PLASMA WITH ADDED FACTOR V AND FACTOR VII

Specimens of plasma were obtained from patients receiving tromexan. Clotting-times were estimated by the method of Quick, modified as above and also by the addition of one other reagent. Thus 0.2 ml. factor-VII preparation or 0.2 ml. factor-V preparation, or in the control 0.2 ml. of normal saline, was added to 0.2 ml. plasma, 0.2 ml. thromboplastin suspension, and 0.2 ml. calcium chloride solution, and the time taken for the mixture to clot determined in a water-bath at 37°C.

The results of this experiment are shown in table II. The addition of plasma containing factor V did not make any significant difference to the clotting-times. Addition of serum samples containing factor VII shortened the clotting-times in every case, and statistical analyses of the two groups show that the result is highly significant.

TABLE II—EFFECT OF FACTOR VII ON THE CLOTTING-TIME (SEC.) OF TROMEXAN-TREATED PLASMA

No.	T.P. + T. + Ca + saline	T.P. + T. + Ca + F.V.	T.P. + T. + Ca + F.VII
1	27		15
2	42	41.5	22
3	46	48	14.4
4	47	49	22
5	29	26	16
6	31	30	18
7	20	21	15
8	34		19
9	25.6	27	19.5
10	32	32.5	18
11	22		15
12	30		17
13	47		20
14	29		21
15	42	43	18
16	38	40	17
17	51	50	23
18	29	30	15
19	26	27	17
20	48	49	21
21	33	32	21
22	31	32	18
23	31	30	15
24	6[illegible]	67	27
25	30		16
26	33	36	17
27	29	31	19
28	48		15
29	13		15
30	34	35	15
31	40		15
32	28		14

T.P. = Tromexan-treated plasma. F.V. = Factor V.
T. = Thromboplastin. F.VII = Factor VII. Ca = Calcium.

Several of the clotting-times when factor VII is added are in the region of 14 seconds, which is shorter than the clotting-time, measured by the modified Quick method, *of normal plasma using thromboplastin (Geigy)* (table II).

It is evident therefore that the addition of serum containing factor VII will greatly shorten the clotting-times of tromexan-treated plasma. The only adequate explanation for our findings is that the prothrombin of tromexan-treated plasma is still present but its conversion to thrombin is delayed because of a deficiency of factor VII. Owen and Bollman (1948) and Koller et al. (1951) describe similar findings for dicoumarol-treated plasma.

DISCUSSION

Until 1943 it was generally believed that the low clotting power of blood in dicoumarol poisoning and in vitamin-K deficiency was due to a fall in prothrombin content. It was believed that even in the presence of an abundant supply of thromboplastin and calcium ions thrombin was formed in insufficient amounts to ensure proper conversion of fibrinogen to fibrin. The work of Quick, Owren, and others suggests that what is estimated as "prothrombin" may in fact be a complex of two or more substances.

We have prepared by Owren's method plasma and serum samples which contain factor V and factor VII, the latter being free from prothrombin. When the factor-V preparation is added to tromexan-treated plasma the clotting-time is not shortened; this finding agrees with those from experiments with dicoumarol-treated plasma and suggests that factor V is little, if at all, affected by tromexan.

We have also reported evidence that factor VII, which is present in plasma and serum (Koller et al. 1951, Biggs and Macfarlane 1953a and b), accelerates the clotting of tromexan-treated plasma and that this defect results from the administration of tromexan. This evidence as to the mode of action of tromexan agrees with that of Owren (1950) and Owen et al. (1951), who studied dicoumarol-treated plasma. Owen et al. state:

The rate with which prothrombin converts to thrombin would seem to be a function of these accessory factors

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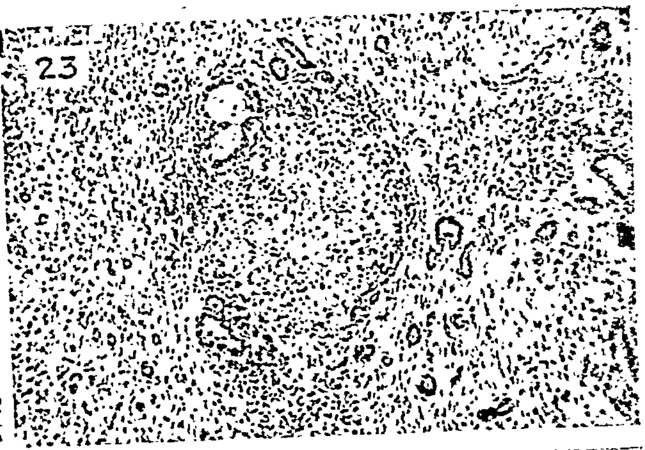
23



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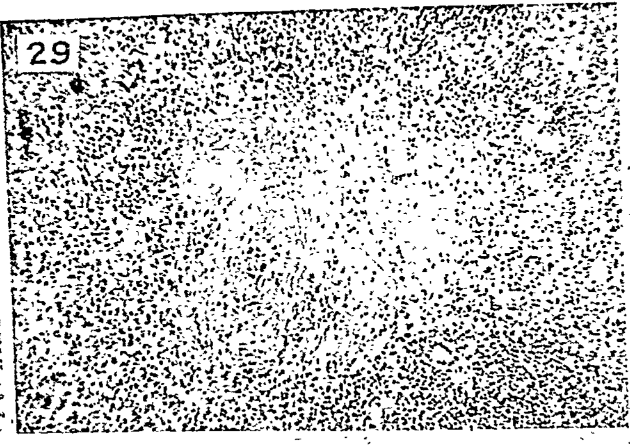

TABLE II—EFFECTS OF ADDITION OF DILUTIONS OF PATIENT'S PLASMA ON CLOTTING TIME OF HÆMOPHILIC BLOOD AND OF DILUTIONS OF HÆMOPHILIC PLASMA ON PATIENT'S BLOOD

Hæmophilic blood (ml)	1 0	1 0	1 0	1 0
Patient's plasma (ml)	0 1			
Patient's plasma dil 1 10 (ml)		0 1		
Patient's plasma dil 1 100 (ml)			0 1	
Clotting time (min)	13	16	24	300
Patient's blood (ml)	1 0	1 0	1 0	< 1 0
Hæmophilic plasma (ml)	0 1			
Hæmophilic plasma dil 1 10 (ml)		0 1		
Hæmophilic plasma dil 1 100 (ml)			0 1	
Clotting time (min)	12	14	26	360
Patient's blood (ml)	1 0	1 0	1 0	1 0
Normal plasma (ml)	0 1			
Normal plasma dil 1 10 (ml)		0 1		
Normal plasma dil 1 100 (ml)			0 1	
Clotting time (min)	13	17	24	360

(2) The plasma of a hæmophiliac in the same dilutions caused the same reduction of the coagulation time in our patient as normal plasma did

(3) Intravenous injection of fraction I of Cohn (Cohn et al 1944) (carrier of the antihæmophilic factor=A H F) did not reduce the coagulation-time in our patient, whereas transfusion of normal plasma did so—e g , from 5 hours to 22 minutes after an hour

(4) In vitro the A H F did not reduce the coagulation time in our patient

(5) The fraction active in hæmophilia (Bendien and van Creveld 1937) which can be precipitated by adding 1/10 *N* acetic acid to tenfold diluted fresh plasma till the pH is 5 4 had no influence on the prolonged coagulation time in our patient However, after precipitation of this fraction, the supernatant fluid did promote coagulation

The boy did not have hypoprothrombinæmia, because .

(1) His prothrombin time (Quick) was normal This fact also indicated that a deficiency of one of the factors active in the conversion of prothrombin into thrombin in the presence of thromboplastin and calcium was highly improbable (see below)

(2) The prothrombin content, determined by the two stage method, was also normal

The boy had not got parahæmophilia, because the prolonged prothrombin-time of normal stored plasma, which does not contain plasma Ac-globulin [=proaccelerin (Owren 1952)=labile factor (Quick 1943, 1947)=factor V (Owren 1947)], could be reduced to normal by the addition of small quantities of our patient's fresh plasma Moreover the quantitative determination of plasma Ac-globulin in the plasma of our patient by the method of Ware and Seegers (1948) gave a normal value

We still had to examine the concentration of proconvertin (Owren 1951) in the plasma of our patient In this connection we had to keep in mind that some cases of hæmorrhagic diathesis have been described where a deficiency of an unknown coagulation factor was found Clinically this disease may resemble parahæmophilia and hæmophilia Such cases have been described by Koller et al (1951), Alexander et al (1948), Alexander (1952), Owren (1951, 1952), and Beaumont and Bernard (1952) In those cases the plasma is deficient in a factor which differs from plasma Ac globulin but which is also necessary for the normal conversion of prothrombin into thrombin This factor is present in a rather inactive form in plasma and in an active form in serum Alexander et al have named the rather inactive form S P C A precursor, and the active form S P C A , Owren calls them respectively proconvertin and convertin , and Koller calls the active form factor VII

Biggs et al (1952) assume that the factor lacking in Christmas disease is probably identical with Koller's factor VII but differs from it in other ways Both factors are present in the serum in a stable form, and both can be adsorbed by asbestos (Seitz filter), barium sulphate, and aluminium hydroxide The difference between them is that the Christmas factor is necessary for the formation of thromboplastin, whereas factor VII is required for the conversion of prothrombin into thrombin Hence both factors should be active at different stages of coagulation

The determination of proconvertin in the plasma of our patient according to Owren's method gave a value which was 60% of normal This proved with certainty that the hæmorrhagic diathesis of our patient was not caused by a *hypoproconvertinæmia* (*Alexander* et al found only 3%, and the coagulation-time and prothrombin consumption at coagulation were only slightly abnormal)

Other arguments against the diagnosis of hypoproconvertinæmia were

(1) The addition of a very small quantity of thromboplastin to our patient's blood greatly reduced the coagulation time (as in hæmophilia) This does not happen in hypoproconvertinæmia and in parahæmophilia

(2) The prothrombin time of our patient, determined by the one stage method, was normal

So we must conclude, as did Aggeler et al (1952), Schulman and Smith (1952), and Biggs et al (1952), that there was a *deficiency of a thromboplastin component* which differs from the thromboplastin component absent in hæmophilia (A H F) Further, by the thromboplastin generation method recommended by Biggs et al we could demonstrate in our case an inability to form *blood-thromboplastin*

We have previously reported (van Creveld and Paulssen 1952) the isolation from normal thrombocytes of factor 3, which is necessary for the formation of thromboplastin in the blood At that time the Christmas factor was still unknown, and we concluded from our investigation that factor 3 and A H F cooperated to form thromboplastin In the light of the present findings it may be concluded that A H F , Christmas factor, and factor 3 together form thromboplastin

Transfusions of blood and plasma have a favourable effect on the clotting-time in Christmas disease In our patient the effect of such a transfusion lasted longer than in hæmophilia Therefore it is very likely that after *transfusion the Christmas factor disappears* less quickly from the blood than does the antihæmophilic factor in hæmophilia

SUMMARY

A case is described which clinically resembled hæmophilia, except that the antihæmophilic factor was present in the plasma, and another coagulation factor was lacking

The disease belongs to the group of cases included under the name of Christmas disease

In the differential diagnosis emphasis is laid on the difference from the hæmorrhagic diathesis due to a deficiency of a prothrombin conversion factor, called proconvertin (Owren) and S P C A precursor (Alexander)

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sistant strains could be diminished very considerably y combining isoniazid therapy with streptomycin herapy. It remains to be seen how this combination ill affect the histological changes caused by each drug eparately; and, if the results are satisfactory, it will e some years before suitable material will be available or examination. It does appear, from the cases in this eries previously treated with streptomycin, that the eneficial effects of isoniazid will take full effect. It hould be pointed out, however, that after treatment vith combinations of drugs the changes in the histological icture may be so altered or even cleared up that a etrospective diagnosis of tuberculosis by biopsy or ecropsy may be almost impossible. Thus, in future it vill be even more essential than before to establish the liagnosis firmly before treatment is begun.

Summary

Changes are described in tuberculous lesions in kidneys from nine patients who had been treated with isoniazid alone: four of the patients had been treated for less than a month, two for about 6 weeks, and three for 3 months. Three of the patients had received previous chemotherapy.

The macroscopic changes were congestion and hæmorrhages in relation to the tuberculous lesions.

The microscopic changes were absorption of recent caseation, vascularisation of all stages of tuberculous lesions, including the dense fibrosis round old lesions, and prevention of fibrosis in and round the lesions.

Open lesions showed the optimal effect after a month's treatment, and regression was taking place after 3 months' treatment; isolated lesions, however, showed more satisfactory effect after the 3-month course.

Some implications of these changes in the tuberculous lesions are discussed as regards the treatment of tuberculosis in general.

With the knowledge of the changes effected in the histological lesions of tuberculosis by the various chemotherapeutic agents, further emphasis is provided, in addition to the clinical findings, that none should be used alone. The various combinations and succession of combinations can be based on rational principles.

I am deeply indebted to Dr. M. A. Foulis, physician-superintendent, Mr. A. Jacobs, consultant urologist, Mr. W. Borthwick, urological surgeon, and Drs. W. G. Wimsett, P. Macpherson, and A. Drimmie, of Robroyston Hospital, for their clinical coöperation: to my colleagues in the department of pathology, Stobhill Hospital, for their helpfulness and criticism: and to Mr. Ian Mackie and Mrs. C. Neilson for their photographic and secretarial assistance respectively.

Appendix

Case 1.—Man, aged 26. Bilateral renal tuberculosis requiring nephrectomy on the worse side. This was done 16 days after the start of isoniazid treatment.

Case 2.—Woman, aged 28. Diffuse disease of the right kidney with involvement of the ureter and bladder. Nephrectomy was done after 18 days' treatment with isoniazid.

Case 3.—Man, aged 46. Unilateral renal tuberculosis with cystitis. After 23 days' isoniazid treatment, nephrectomy was done (fig. 3).

Case 4.—Girl, aged 17. Unilateral renal tuberculosis with involvement of ureter and bladder. After 29 days' isoniazid treatment, nephrectomy and partial ureterectomy were done.

Case 5.—Man, aged 23. Showed cavitation at the lower pole of one kidney and was adjudged suitable for partial nephrectomy. A full 3-month course of isoniazid was given in preparation for this. At operation, however, the ureter was found to be dilated, and nephrectomy was performed.

Case 6.—Woman, aged 22. Presented with a small unilateral lesion and no cystitis. Treatment with isoniazid was pursued for 3 months but the lesion appreciably worsened and cystitis developed, so that nephrectomy was required (fig. 4).

Case 7.—Boy, aged 7. 2 years previously, pain in one loin and colicky pains at times in the line of the ureter on that side. In March, 1952, he had epididymitis, and examination revealed renal tuberculosis. He was treated first with streptomycin 1 g. every third day and P.A.S. for 6 weeks, and then with isoniazid for 6 weeks before nephrectomy.

Case 8.—Man, aged 30. In 1948 he received 90 g. of streptomycin for trochanteric disease: urinary symptoms started in December, 1951. In April, 1952, he received streptomycin 1 g. daily plus P.A.S. for 21 days. In July a full course of isoniazid was started and nephrectomy was done after 6 weeks of the course (fig. 5).

Case 9.—Woman, aged 39, with advanced bilateral renal tuberculosis. During a previous admission (October, 1950–June, 1951), she had received a course of 90 g. of streptomycin followed by another course of streptomycin 90 g. plus P.A.S. In April, 1952, her urine was positive to tubercle bacilli. She died from uræmia after 3 months' treatment with isoniazid. The left kidney was a small sac, the wall 0·5 cm. thick, filled with caseous white debris, and the ureter was kinked at the pelvic brim. The right kidney was large and slightly hydronephrotic, with congested cortex and with tubercles in the papillæ, and the ureter was somewhat dilated.

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ISONIAZID IN THE TREATMENT OF FEMALE GENITAL TUBERCULOSIS

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In recent years there has been a great increase in the number of cases of female genital tuberculosis diagnosed in the latent stage, largely through the medium of infertility clinics. These patients formerly received no active treatment, but the advent of streptomycin and *p*-aminosalicylic acid (P.A.S.) led to attempts by many workers (Schaupp 1949, Delarue and Bergerot-Blondel 1949, Ryden 1950, Stallworthy 1950, Sutherland 1952) to eradicate the disease completely with these drugs, even to the extent of permitting pregnancy. So far results have been disappointing; even though the preliminary response appeared favourable, there was evident a very strong tendency towards the reappearance of tuberculous follicles in the endometrium even six months or more after apparent cure. Intra-uterine pregnancy in an established case of pelvic tuberculosis has been reported only very rarely (Rabau 1952, Stallworthy 1952).

œsophagus in the region of the tracheal bifurcation In other films of this area mucosal ridges are seen which show a lateral twisting from their normal longitudinal course

COMMENT

The presumed arrangement of the great vessels in this case is shown in fig 2 Obliteration of the anterior loop of the arterial vessel by side-to side digital pressure in the region marked with an X led to disappearance of both femoral pulses, both radial pulses, and the right carotid pulse Fig 3 represents the probable pattern of persistence of arterial vessels in the primitive formation (Congdon 1922)

Our patient has been under observation periodically for the past sixteen years There has been no great change in the cervical aortic knuckle, and his symptoms have never been severe He is regular in attendance at his work and has had no serious illnesses The presence of the large double arterial trunk in the confined space of the thoracic inlet does not seem to have given rise to any ill effects should it do so, a case may be made for enlarging the space by removal of the first rib on the right side

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A CASE OF POLYORCHIDISM

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Polyorchidism is a surgical curiosity, and the number of published cases is small Lowsley and Porras (1951) found 18 authentic cases and added 1 of their own The differential diagnosis is from a spermatocele and from a hydrocele of the cord, and the diagnosis is usually established at operation

Embryology—The testis arises from the medial side of the urogenital ridge, whereas the epididymis and vas deferens are derived from the mesonephric ducts The müllerian duct disappears in the male, except when the upper end may persist as the appendix testis of Morgagni The lower end, by fusion with the opposite side, forms the prostatic utricle As the testis descends, new seminiferous tubules are formed caudally, while the cephalad ones degenerate If the anterior seminiferous tubules persist, an extra testis may develop with a common vas deferens and epididymis

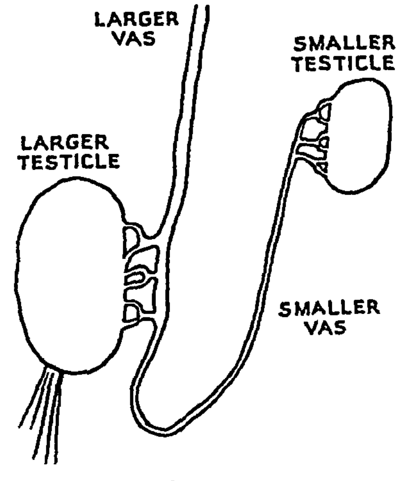

Fig 1—How the two testicles lay in the left side of the scrotum

Case record—A young man, aged 19, was admitted to hospital with a history that seven hours previously he had suddenly developed a painful swelling in the left groin and had vomited once There was a tense tender irreducible swelling in the left groin, and a diagnosis of strangulated left inguinal hernia was made

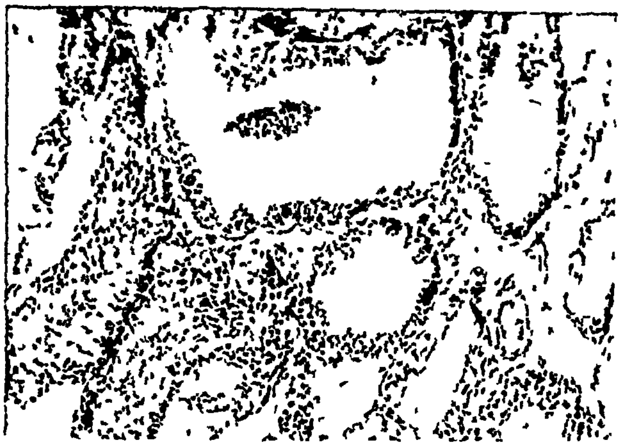

Fig 2—Biopsy specimen of larger testicle (× 85)

The swelling was explored through an inguinal incision After exposure of the cord what was thought to be a hernial sac was incised, clear fluid escaping This proved to be a hydrocele containing two distinct swellings, both of which appeared to be testicles The hernial sac was found just above the hydrocele, it was opened, viable bowel was returned to the abdomen, and the sac was transfixed and excised The vas was traced from the internal ring to the lower testicle, and a smaller vas was found which was traced from it to the smaller and upper testicle (fig 1) A piece of tissue was removed from each for biopsy As each swelling was incised, the typical spongy yellow appearance of testicular tissue was seen While the two left sided testicles were palpated an independent observer was able to palpate a normal testicle in the right side of the scrotum After the biopsy the wound was closed in layers

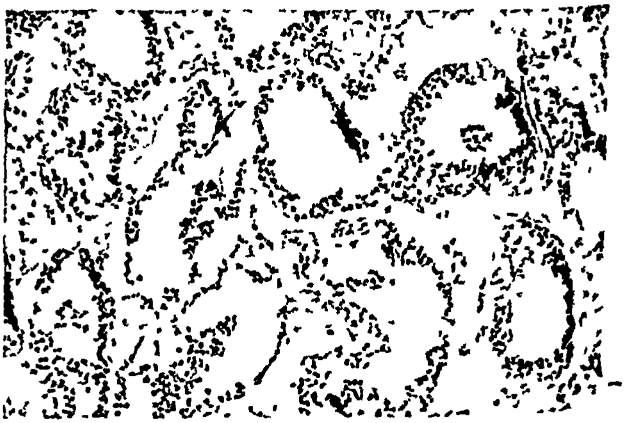

Fig 3—Biopsy specimen of smaller testicle (× 85)

The patient made an uninterrupted recovery, and some weeks later all three testicles were easily palpated the upper one on the left side lying in a high scrotal position

Biopsy Reports—The biopsy specimens were both composed of testicular tissue In neither was there any spermatogenesis, but proliferation of the spermatogonia was well marked (figs 2 and 3)

I wish to thank Mr J E Schofield under whose care the patient was admitted, for permission to publish and Mr R Thexton, H D D , L D S , for the drawing

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examination and confirmed by biological test. In 2 of these cases the lesion was a frank fungating growth on the portio vaginalis; in the 3rd case the cervix appeared healthy on inspection, but tuberculous endocervicitis was found on biopsy. Massive caseation was present in one of these lesions.

TREATMENT

All the patients were treated with isoniazid (' Rimifon,' Roche) 150 mg. daily for sixteen weeks. 11 patients were also given streptomycin 1 g. daily and P.A.S. 15 g. daily in addition to isoniazid during the last eight weeks of the course. These drugs were added because, during the conduct of this trial, the reports of Joiner et al. (1952) and the Medical Research Council (1952) showed that the development of isoniazid resistance could be postponed or averted by using these drugs together.

TABLE II—RESPONSE TO THERAPY

—	Histology positive	Chronic endometritis	Histology negative
Guineapig test positive	..	..	1
Guineapig test negative	1	..	40

Culture was negative in all the cases. One patient was pregnant.

The patients were seen at intervals throughout treatment. At each visit the central nervous system was examined completely, the blood-pressure was estimated, the patients were weighed, the hæmoglobin was estimated, and total and differential white-cell counts were made. No side-effects from isoniazid were noted in any of these patients, and none of the aforementioned tests showed any deviation from normal. Only 4 patients gained more than 4 lb in weight, and none developed abnormal appetite. A patient who received streptomycin and P.A.S. in addition to isoniazid developed a rash on her chest and complained of feeling weak; streptomycin therapy was therefore discontinued after 30 g. had been given.

RESPONSE TO THERAPY

Response to treatment was assessed in 42 cases by repeating full-scale curettage in the premenstrual phase within six weeks of finishing treatment. The results of this investigation are shown in table II.

2 patients with tuberculous endometritis did not respond to treatment. In 1 of them histological evidence of the lesion persisted, although the biological test and direct culture, both of which had been positive before treatment, had now become normal. This case is of interest because it was the only one in which massive caseation had been seen in the endometrium on histological study. In the second case which failed to respond the biological test remained positive, although histological evidence of the lesion had disappeared. Tests for isoniazid sensitivity were made on the culture obtained from the spleen of the guineapig in this case; and the organism was found to be still sensitive to isoniazid.

Of the 3 patients with tuberculous cervicitis 1 did not respond; this also was the only case in which massive caseation had been present in the cervical lesion before treatment.

40 cases of tuberculous endometritis and 2 of tuberculous cervicitis were apparently cured, no evidence of tuberculosis being found either on histological examination, biological examination, or by direct culture. No significant alteration in the size of the pelvic masses was noted in any of these cases.

1 other patient was not curetted, because she became pregnant while under treatment. Only 2 other cases of pregnancy in patients with tuberculous endometritis have been published (Stallworthy 1952, Rabau 1952). In Rabau's patient the original diagnosis had rested upon a positive biological test, although histological evidence of tuberculosis was absent; the patient aborted in the third month of pregnancy. In the present case, the diagnosis was also made on the result of one biological test, no evidence of the lesion having been found on histological examination, although curettage was repeated twice during the three months preceding treatment. The patient was treated with isoniazid, streptomycin, and P.A.S. and became pregnant while receiving these drugs; she is now six months pregnant, and the Hogben test is positive. Her treatment is being maintained throughout pregnancy to prevent a relapse in her condition.

DISCUSSION

We are sceptical about the permanence of these apparent cures. This scepticism is founded upon the disappointing end-results which have followed the treatment of tuberculous endometritis with streptomycin and P.A.S. at the Newcastle General Hospital during the past three years. In most cases treated in this way, although all trace of the lesion disappears shortly after treatment, relapse occurs after an interval of twelve months or so. In table III are shown the end-results of antibiotic therapy in all the cases treated in this way at Newcastle during the past three years. The dosage used was admittedly small in comparison with that recently advocated by Sutherland (1952); but the tendency for the condition to relapse after treatment is demonstrated.

TABLE III—END-RESULTS AFTER STREPTOMYCIN THERAPY

Case no.	Laboratory Diagnosis	Treatment	Follow-up curettage				Final outcome
			0–6 mos.	6–12 mos.	12–18 mos.	1½–2 yr.	
3	Histology +ve Guineapig test +ve	Streptomycin 40 g.	..	..	..	H. +	Lesion still present 19 mos. after treatment
11	Histology +ve	Streptomycin 40 g.	H. + G.P. −	..	..	H. + G.P. +	Relapse after 19 mos.
8	Histology +ve Guineapig test +ve Culture +ve	Streptomycin 23 g. P.A.S. 168 g.	H. −	..	H. − G.P. +	..	Relapse after 14 mos. ..
10	Histology +ve Guineapig test +ve	Streptomycin 28 g.	H. − G.P. −	H. − G.P. −	..	H. − G.P. +	Relapse after 15 mos.
47	Histology +ve	Streptomycin 50 g.	..	..	..	H. + G.P. +	Lesion present 2 years after treatment
39	Histology +ve Guineapig test −ve	Streptomycin 40 g.	H. − G.P. −	H. − G.P. +	..	..	No lesion 1 year after treatment
78	Histology +ve Guineapig test +ve	Streptomycin 23 g. P.A.S. 280 g.	H. + G.P. +	..	..	..	Lesion present 3 mos. after treatment
73	Histology +ve Guineapig test +ve	Streptomycin 45 g. P.A.S. 230 g.	H. − G.P. −	..	..	..	No lesion 3 mos. after treatment
71	Histology −ve Guineapig test +ve	Streptomycin 40 g. P.A.S. 1080 g.	H. − G.P. −	..	..	..	No lesion 3 mos. after treatment
62	Chronic endometritis Guineapig test +ve	Streptomycin 46 g. P.A.S. 1080 g.	..	..	H. + G.P. +	..	Lesion present 18 mos. after treatment
..							

to nephrosis In both of them the œdema subsided rapidly

This result may be explained by the effect of choline on the liver or on the phosphatide tricomplex in the cells, according to the theory of Bungenberg de Jong (1949)

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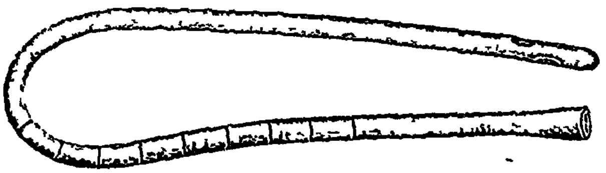
New Inventions

THE USE OF A GRADUATED CATHETER IN RETROPUBIC PROSTATECTOMY

DURING retropubic prostatectomy the urethral catheter is inserted before the prostatic capsule is closed This enables the surgeon to place the catheter in the bladder under direct vision However, at the end of the operation, when the surgeon proceeds to fix the catheter with strapping or by some other means, it may have altered position

I believe a simple method of overcoming this difficulty is to use a graduated catheter This is a Harris catheter 14 in long Starting at 8 in from the tip, it is graduated in half-inch and inch divisions The marks indicating inches form a complete ring round the catheter, the half-inches being denoted by half-rings



When the catheter is inserted during the operation, the body of the penis is stretched fully over it, and the mark opposite the external urinary meatus is noted After the operation the catheter is fixed at this reading This has been found at St Peter's Hospital to be on an average about 11 in

An additional advantage of a graduated catheter is seen postoperatively The nurses are informed of the correct reading If the catheter is not draining satisfactorily, a glance at the graduations will show whether it is in the correct position in the bladder

The catheter illustrated is made by the Genito-Urinary Company, 28A, Devonshire Street, London, W 1

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"There is a sense in which the present is an age of which a characteristic is its failure to understand the status of its own abstractions, and this perhaps is the inevitable fruit of the divorce of natural science from metaphysics, to have achieved which was the empty triumph of the nineteenth century Thus those who are outright opponents of the notion that there must be an immaterial element in the human person have, for the most part, no language in common with those who think otherwise For the problem involved is essentially metaphysical and for the materialist metaphysics are sour grapes —Dr F M R WALSHE, F R S, *Brain*, 1953, 76, 1

Medical Societies

ROYAL SOCIETY OF MEDICINE

Psychiatry in General Practice

THE psychiatric section of the society met on April 1 under the chairmanship of Dr W S MACLAY, preside of the section, to discuss Psychiatry in General Practic

Dr JOHN FRY gave an account of his experience the psychiatric problems in 1951 and 1952 in a suburb middle class practice of about 4500 patients In 195 out of 14,602 attendances 1379 were for psychiatr disorders, in 1952, of 14,821 attendances 1422 we psychiatric Patients receiving treatment for psychiatr illness out of the total population of his practice were in 1951, 502 out of 4406, and in 1952, 570 out of 470 From both these angles, psychiatric cases figured about 10% of his work, but the average attendances a psychiatric patient were 5 per annum, compared wi the non-psychiatric patient's average of 3

He had found that psychiatric illness was the third mo prevalent form of illness, exceeded only by respirator and gastro-intestinal diseases

Women psychiatric patients outnumbered men b 5 to 2, whereas in other types of illness the sexes we nearly equally represented As regards age, th attendance rates for psychiatric illness rose sharply i the 40–60 age group, this was almost entirely due t psychiatric illness among women in the involutiona period

The ways in which the psychiatric patient presented himself varied There was the tonic seeker, for whom the prescribing of a placebo was a poor policy, neither saving the doctor's time nor benefiting the patient in the long run In this group the possibility of early tuberculosis, thyrotoxicosis, or new growth should be kept in mind There was the patient who came with organic symptoms, for whom the best treatment was a thorough clinical examination followed by explanation and reassurance Dr Fry emphasised the importance of patients referred to a psychiatric outpatient department receiving a thorough physical examination, for often such patients returned to their own doctor complaining that they had not been properly examined

In his own practice there were some 40 incurable neurotics, who attended his surgery about three times as often as other patients He referred about 8% of his psychiatric cases to hospital—a proportion comparable to the 10% referred by Watts[1] He thought that the general practitioner should treat the majority of his psychiatric patients, just as he should his obstetric cases, but should be aware of his limitations and not treat severe depression, psychopathy, or psychos Students should be taught more about the minor psychoneurotic conditions which they would encounter in general practice

Dr DENIS LEIGH said that at the Maudsley Hospital his unit was keeping a record of how the general practitioners referred patients to the hospital, and the recent figures agreed fairly closely with those given by Blacker[2] In 1950, for example, 696 doctors referred 1731 patients, 80% of the doctors and 86% of the patients were from the London area, 20% of the doctors and 14% of the patients from the country or abroad Taking the 1460 doctors practising in the south east and south west postal districts of London, it was found that 27% referred all the London patients, the remaining 73% referring none Of the 398 doctors in these two districts who referred patients, 168 referred 1 in the year, 170 referred 2–5, 43 referred 6–10, and 17 referred more than 10

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[1] Watts C A H Watts B M Psychiatry in General Practice London 1952

[2] Blacker, C P Neurosis and the Mental Health Services London 1946

MODE OF ACTION OF TROMEXAN

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IT is now established that in the treatment of thrombo-embolic phenomena 'Tromexan' (ethyl biscoumacetate, bis 3-3'-(4 oxycoumarinyl) ethyl acetate) is as effective as, and less dangerous than, dicoumarol, over which it has two advantages. First, its action in reducing prothrombin activity is much quicker (18–48 hours, compared with 48–72 hours). Secondly, because of its more rapid destruction and excretion by the body, prothrombin activity and complications can be better controlled by varying the oral dosage. When the drug is discontinued prothrombin activity will increase sufficiently in 8–12 hours to control bleeding (Stirling and Hunter 1951).

The original studies of the effect of dicoumarol in man (Butt et al. 1941) showed a gradual fall of prothrombin activity in 48–72 hours. This suggests that dicoumarol might act by preventing the production of prothrombin by the liver, and that the delay of 48 hours is accounted for by the consumption of prothrombin already formed. In our early work with tromexan we noted the now well recognised rapid fall of prothrombin activity. In some of our experimental studies initial dosage of 1800 mg. brought about low levels of prothrombin activity in 9–12 hours. Two possibilities suggested themselves: either the life of prothrombin was much shorter than was originally thought, or tromexan acted mainly not on prothrombin but on some accelerator factor, interference with which caused the one-stage prothrombin test to give low estimates of prothrombin activity.

By different methods Owren (1944 and 1949) and Quick (1943) arrived at the conclusion that normal plasma contained a prothrombin accelerator which disappeared from stored plasma. The existence of this prothrombin accelerator—pro-accelerin (Owren 1949), prothrombin accelerator (Fantl and Nance 1946), factor V (Owren 1947)—is now accepted, and in this paper it is termed factor V. Warner et al. (1939a and b) have suggested that there was another prothrombin accelerator which is stable—co-thromboplastin (Mann and Hurn 1951), S.P.C.A. (Alexander et al. 1949), proconvertin (Owren 1947), factor VII (Koller et al. 1951), and in this paper it is referred to as factor VII. Owren (1950) and Koller et al. (1951) found that during dicoumarol therapy the concentration of factor V is practically unaltered but that prothrombin and also, more notably, factor VII are decreased.

Owren (1949) has also suggested that the one-stage Quick (1935) method of estimating prothrombin-time and the two-stage method of Warner et al. (1936) can be improved by the addition of factor V to the clotting system. Owren claims that this method gives an exact quantitative estimation of prothrombin regardless of the amount of factor V present.

We here set out information concerning: (1) the practical merits of Owren's and Quick's methods of determining prothrombin, using tromexan-treated plasma; and (2) the effect of factor V and factor VII on the clotting-times of tromexan-treated plasma.

PREPARATIONS

The term "tromexan-treated plasma" is used for plasma taken from a patient to whom tromexan has been administered. The addition of tromexan to plasma in vitro is without effect on coagulation.

Factor V (*Owren and Aas 1951*).—This is prepared from ox-plasma. Nine volumes of ox blood are mixed with one volume 2·5% (*w/v*) solution of potassium oxalate monohydrate. After being spun, the plasma is first clarified by passing it through an 18% asbestos filter-pad, and then it is passed through a filter-pad containing 50% asbestos, which Owren states will adsorb prothrombin and factor VII but allow the passage of factor V. The filtrate is neutralised to pH 7·3 by *N*/2 HCl, and then stored in small glass tubes at below −10°C.

Factor VII (*Owren and Aas 1951*).—Stored human serum is used as a source of this factor. A small amount of thromboplastin (3 ml. to 100 ml. blood) is added to normal human blood immediately after withdrawal, and the mixture is stirred. Prothrombin disappears almost completely in 30 minutes, and any remaining factor V disappears after storage for a week.

Thromboplastin.—A commercial preparation of rabbit brain is used—'Thrombokinase' (Geigy). One tablet (10 mg.) is crushed in a small test-tube and mixed with 2·5 ml. of normal saline. The suspension is warmed in a water-bath at 37°C for 10 minutes and is then ready for use.

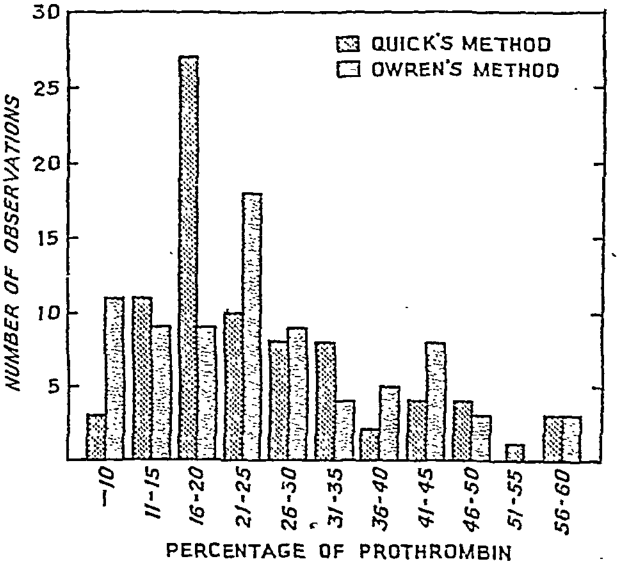
Barbitone Buffer Solution (*Owren 1949*).—This solution is prepared by adding 430 ml. *N*/10 HCl and 5·67 g. NaCl to 570 ml. 0·10 *M* sodium diethyl barbiturate and diluting the mixture with an equal volume of 0·9% NaCl solution.

METHODS OF PROTHROMBIN ESTIMATION

(1) *Modified Quick's Method.*—A mixture of 0·2 ml. plasma and 0·2 ml. thromboplastin suspension is incubated in a water-bath at 37°C for 5 minutes. Then 0·2 ml. 0·2% calcium chloride solution is added and the time required for clotting is measured.

The percentage prothrombin activity can be estimated for each plasma by the use of a correlation graph which is prepared from the average result obtained by estimating the clotting of at least ten dilutions of normal plasma.

(2) *Owren's Method.*—The plasma to be tested is obtained from oxalated blood by centrifuging, and is then diluted with the barbitone buffer solution to give 1 : 10 dilution of plasma. A small sample, 0·2 ml., is mixed with 0·2 ml. factor-V preparation and 0·2 ml.



Results of prothrombin tests by Quick's method and by Owren's method in 80 samples of tromexanised plasma.

capacity of the upper intestine is normal In the sprue syndrome, however, the intraluminar phase of fat absorption is normal and the defect is secondary to depression of the absorptive capacity of the upper small intestine[3] This can be demonstrated by estimating glucose and urea absorption, using the intraduodenal drip method, and by differential radiography, using flocculable and non flocculable barium sulphate It is confirmed by the fact that fat absorption becomes normal after the removal of wheat gluten from the diet of children with cœliac disease The subsequent administration of gluten causes return of the absorptive defect[4]

Osteomalacia in Steatorrhœa

Dr. Paul Fourman (Oxford) said that in this country osteomalacia is seen most often in patients with steatorrhœa The patients complain of pain and they may suffer spontaneous fractures Radiographs usually show generalised rarefaction of the bones, pseudo fractures may occur In blood taken from the fasting patient the serum phosphate is low, the phosphatase is raised, and the serum calcium is usually low The deficiency of calcium in these patients is the result of excessive fæcal loss Dr Fourman has found that vitamin D in a dose of 10,000 units daily by mouth does not improve the absorption of calcium Vitamin D given in the same dose parenterally, or in a dose of 50,000 units by mouth, improves the absorption of calcium if the calcium intake is high It does not improve absorption if the intake of calcium is only moderate, unless the excretion of fat in the fæces is at the same time reduced by reducing the fat in the diet With parenteral vitamin D and large doses of calcium by mouth these patients are cured of their osteomalacia, but the amount of calcium that they retain is small and the cure is slow These facts are explained as follows In patients with osteomalacia secondary to steatorrhœa there is a failure to absorb vitamin D The resulting deficiency of vitamin D is partly responsible for a failure to absorb calcium In addition there is a failure to absorb calcium because calcium may combine with unabsorbed fat in the intestine to form soaps Lastly, when these two faults are overcome it is seen that calcium is also directly involved in the absorption defect of steatorrhœa.

Interference between Antibiotics

Dr S D Elek and Dr Pamela Jewell said that it has been known for some time that the bactericidal action of pairs of antibiotics may be greater or less than that of each drug alone Conventional methods for studying the problem are however, laborious Dr Elek and Dr Jewell described a simple method for investigating the lethal effects of antibiotics and for demonstrating any interaction between one antibiotic and another This is an adaptation of a technique used by Lederberg and Lederberg for studies on bacterial genetics, it is applied as an extension of a sensitivity test in common use, and is simple enough to be included in the work of a routine laboratory

A sensitivity plate (Fairbrother and Martyn 1951) is incubated overnight A wooden block covered with sterile velvet is pressed on its surface and then pressed on a sterile plate In this way a constant proportion of any viable organisms is transferred free of antibiotic The number of colonies appearing after incubation of the second or replica plate reveals the proportion of organisms surviving the action of each drug

To detect antagonism two discs, each containing a different antibiotic are superimposed on the primary plate The lethal effect of the combination is compared with that of each drug alone To [illegible] discs are placed 1–2 cm apart and in the zon[illegible] have been exposed to the action of both dru[illegible] number of survivors is seen

Three pairs of antibiotics were tested by this method against 65 strains of common pathogens, including ten strains of enterococci from cases of endocarditis It was found that penicillin and aureomycin together showed either antagonism or no interaction, a combination of penicillin and chloramphenicol gave similar results Streptomycin and chloramphenicol, on the other hand, showed either synergism or no interaction In this way, for a newly isolated organism it may be said that the first two combinations are likely to be antagonistic while the third is likely to be synergistic Further work is required to assess the clinical importance of findings obtained by this simple method

Microculture of Mycobacterium Tuberculosis

Dr H M Rice and Dr F C Rowan (Nottingham) observed that a modification of Pryce's[5] microculture method for detecting *Mycobacterium tuberculosis*, applicable to concentrates of urine, pus, &c, as well as to sputum, gives a high proportion of positive cultures in 2–5 days Sensitivity tests can in many cases be reported in 5 days The method has been used with streptomycin, P A S, and isoniazid Löwenstein Jensen cultures are always made from the same material, so that nothing is lost if the micro method fails If it succeeds much time is saved The method is not laborious and requires no special apparatus 50% lysed horse blood has proved the best medium The use of pancreatin as a concentrating agent has led to more rapid and profuse growth on Löwenstein Jensen medium, compared with Petroff's method Often it has succeeded where Petroff's method has failed 8% hydrochloric acid is used to kill contaminants

Isoniazid Sensitivity of Tubercle Bacilli

Dr D A Mitchison said that strains of tubercle bacilli can be tested for isoniazid sensitivity by three methods

1 The *direct test*, in which sputum concentrate is placed on Löwenstein slopes containing a range of drug concentrations This technique is only possible where numerous bacilli are present and may waste medium

2 The *indirect test*, in which growth from a primary culture on drug free medium is inoculated on to a similar series of slopes

3 The *subculture test*, in which subcultures are made in Dubos medium and tested in this medium This method yields false results since highly resistant strains fail to grow or only grow slowly in Dubos medium

The indirect test, which Dr Mitchison recommended, should be carried out with an approximately standardised inoculum from young primary cultures, and the results should be read after 4 weeks The technique is still not satisfactory since repeat tests yield gross discrepancies in about a third of resistant strains A medium more satisfactory than Löwenstein's is required for the growth of resistant strains

Sensitive strains are inhibited by 0 2 µg isoniazid per ml in Löwenstein medium, though a few colonies may grow in this and higher concentrations Strains growing on 1 µg per ml are likely to be resistant since animals infected with such strains do not respond to treatment with a higher dosage of isoniazid than is used in man Since strains with a higher degree of resistance appear avirulent in guineapigs, the results of tests on strains isolated via guineapigs cannot be considered reliable

Culture of Tubercle Bacilli and Sensitivity Tests

Dr W K Taylor (Godalming) said that in routine work concentration methods are valuable, but with watery sputa it is much more satisfactory to pick out purulent fragments Oxalic acid may affect acid fastness Papain is a valuable liquefying agent, and its addition should be followed by that of 5% oxalic acid This is the most useful disinfectant, no neutralisation, and only one centrifugation, is necessary Flotation methods are efficient but tedious, possibly dangerous to staff, and generally unsuitable for subsequent culture In a small series, about 25% of the negative smears from tuberculous patients gave a positive result with ligroin flotation The increase of sensitivity tests is making great demands on incubator capacity, but this difficulty can be overcome to some extent by using a four bottle technique with 0, 1 [illegible] and 100 µg streptomycin per ml in Dubos medium in screw cap bijou bottles This gives three degrees of resistance—slight, clinical, and marked—which simplifies interpretation of reports

Acute Hæmorrhagic Leuco-encephalitis

Prof T Crawford said that hæmorrhagic leuco encephalitis was first recognised in 1940 by Weston Hurst in Adelaide, and only seven examples have been recorded Three typical examples have, however, been seen at St George's Hospital London, in a two year period The condition occurs chiefly in males in the third and fourth decades There is often a prodromal upper respiratory infection, followed, perhaps after a brief recovery, by the neurological stage which is fatal within a few days The cerebrospinal fluid shows an increased cell count of up to three or four hundred per c mm—principally polymorphs—and there is a polymorph leucocytosis in the blood The naked eye lesions consist of petechial hæmorrhages limited to the white matter and usually maximal in one or both cerebral hemispheres They extend down a variable distance and may involve cerebellum and pons The most affected parts are œdematous and discoloured Microscopically the white matter shows ball and ring hæmorrhages, serous and cellular exudate, rich in polymorphs, fibrin impregnation in and around the vessel walls, and fibrin exclusively, for when normal plasma was mixed with purified prothrombin in various proportions, the conversion rate was independent of the prothrombin concentrations, but paralleled directly the concentrations of the accessory factors."

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[3] Frazer A C Trans R Soc trop Med Hyg 1952 46, 576

[4] Anderson C M Frazer A C French J M Gerrard J W Sammons H G Smellie J M Lancet 1952, i 836

[5] Pryce D M J Path Bact 1941 53 327

The majority of workers in this field would at the present time accept the view that the various factors mentioned are prothrombin accelerators. Biggs and Macfarlane (1953a and b) and Biggs et al. (1953), however, have recently reported very good evidence suggesting that five factors are concerned in thromboplastin generation—the platelets, factor v, factor vii, antihæmophilic globulin, and the Christmas factor (Biggs et al. 1952). They suggest that brain thromboplastin, whether it be derived from animal or human source, is not really thromboplastin at all but is a mixture of antihæmophilic globulin, platelet factor, and the Christmas factor. Thromboplastin preparations, therefore, such as we have used in this study do not contain complete thromboplastin but are deficient in both factor v and factor vii. It is only on the addition of these factors that thromboplastin formation proceeds, and this reaction takes a short but definite time—10–12 seconds. The use of brain thromboplastin reveals factor-v and factor-vii deficiency as well as prothrombin deficiency. Thus thromboplastin generation does not take place quickly in tromexan-treated plasma because of deficiency of factor vii. There is also evidence (Koller et al. 1951, Owren and Aas 1951, Biggs and Macfarlane 1953a and b) that prothrombin is reduced in amount by the administration of dicoumarol or tromexan; but this reduction is neither so rapid nor so great as that of factor vii, particularly with tromexan.

SUMMARY

Evidence is described which supports the view that tromexan acts on the mechanism of blood coagulation similarly to dicoumarol, and that its action is principally on factor vii.

A comparison of Quick's and Owren's methods of estimating "prothrombin" indicates that Quick's one-stage method is suitable for routine use.

Reference is made to recent views on thromboplastin generation.

We are grateful to Dr. Ann C. Donald for assistance in carrying out a number of estimations and to Mr. E. A. Asher, of Pharmaceutical Laboratories Geigy Ltd., for supplies of thromboplastin. Part of the expenses of the research were defrayed by a grant from Pharmaceutical Laboratories Geigy Ltd., Manchester.

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HÆMORRHAGIC DIATHESIS DUE TO ABSENCE OF CHRISTMAS FACTOR*

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LATELY some cases have been reported of a hæmorrhagic diathesis which clinically resembled hæmophilia but in which there was no deficiency of the antihæmophilic factor or any coagulation factor previously recognised. This condition has been attributed to the absence of another coagulation factor recently discovered in the plasma. The disease has been described by Aggeler et al. (1952), Schulman and Smith (1952), Biggs et al. (1952), and Poole (1953), and the familial hæmorrhagic disorder described by Koller et al. (1950) is probably the same. Biggs et al. (1952) named the condition Christmas disease after their first patient and described seven cases.

We report here a case of Christmas disease which illustrates the difference between it and another hæmorrhagic diathesis (hypoproconvertinæmia) which has also been recently described for the first time.

THE CASE AND THE DIAGNOSIS

A boy, aged 10 years, the only child of healthy parents, showed the first signs of a hæmorrhagic diathesis after an injury at the age of 15 months. Before this trauma, however, his parents had noticed that he was easily bruised.

This first hæmorrhage due to trauma was followed by many severe ones, especially in midsummer and midwinter. The hæmorrhages, especially from the nose, often began and stopped suddenly. Not rarely a hæmorrhage occurred some time after a preceding hæmorrhage had apparently stopped. The patient had also repeated hæmorrhages into the joints (ankles and knees), but there was no ankylosis of these joints or restriction of their function, such as develops in hæmophilia. Dr. G. J. van Lookeren Campagne, who sent us this patient, had many years ago found a prolonged coagulation-time and had diagnosed hæmophilia. No hæmorrhagic diathesis could be traced in the family.

When admitted to the Children's Clinic the boy had (table I) a much prolonged coagulation-time of the venous blood; normal values for bleeding-time, blood-clot retraction, fibrinogen content, and thrombocyte-count; normal capillary resistance; and insufficient consumption of prothrombin on coagulation.

TABLE I—RESULTS IN DIFFERENT DETERMINATIONS IN BLOOD

—	Patient	Normal values
Clotting-time	Several hours	10–14 min.
Bleeding-time (min.)	2–5	2–5
Clot retraction	Normal	—
Fibrinogen	Normal	—
Number of platelets	Normal	—
Capillary fragility	Normal	—
Residual prothrombin in serum (units per ml.)	220	<10
Prothrombin-time (Quick) ..	13 sec.	13 sec.
Prothrombin in plasma (units per ml.)	340	275–350
Plasma Ac-globulin (units per ml.)	15	13–17
Proconvertin	60 % of normal	—
Anticoagulant	Absent	

The boy was not (we concluded) suffering from hæmophilia, because:

(1) His plasma in various dilutions (table II) exerted a normal coagulation-promoting activity on the blood of a known hæmophiliac with a greatly prolonged coagulation-time.

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* This work was supported by a grant from the Nederlandse Organisatie voor toegepast Natuurwetenschappelijk Onderzoek (Dutch Organisation for Applied Scientific Research).

Mrs Klein's theory by some psycho-analysts in this country and the United States

Mrs Riviere, who edits it, writes an introduction which aims to rebut the objections made with varying force by Edward Glover, Sylvia Payne, Edward Bibring, and other psycho-analytic critics (who are, however, hardly mentioned by name) The contributors to the volume, who are, or were, strong supporters of the Kleinian theory, speak not only for themselves and a few contemporaries but also for a large proportion of the younger psycho analysts trained in London during the last twenty years The views put forward are technical and recondite, especially in the passages describing destructive and other fantasies which babies are supposed to entertain during the first few months of life Few who are not psycho analysts or "analysands" are likely to read the book with understanding and appreciation

Scope and Interpretation of the Commoner Biochemical Tests

South African Institute for Medical Research Johannesburg 1952 Pp 120 10*s* 6*d*

To many doctors the interpretation of biochemical tests is a continual difficulty while there are a number of larger works (e g , Peters and van Slyke) dealing with interpretation in detail, there is no simple book giving interpretation for general physicians and students This small volume from the biochemical department of the South African Institute for Medical Research is a worthy effort to fill the gap, at a very reasonable price

After a very brief introduction emphasising the important concept of a "normal range" rather than a normal value, it describes, under headings arranged alphabetically, the normal values for various blood constituents, and the changes which may be expected in disease, followed by sections on cerebrospinal fluid, fæces, gastric analysis, urine, liver and kidney function tests, and water and electrolyte balance Finally, there is an 18 page summary of normal values and the principal variations in disease, and an adequate index

The various paragraphs give clear information to a doctor who wants a simple explanation of what a result signifies, and usually the information given is fully adequate but the alphabetical arrangement does produce difficulty at times and leads to such subjects as Calcium, Phosphorus, and Phosphatase being widely separated, so that a rather long table giving the calcium, phosphorus, and phosphatase figures together is needed to correlate the findings In a future edition, it might be better to confine the alphabetical order to the summary and arrange the matter in the body of the book more systematically

The amount of space given to gastric analysis compared with that for water and salt metabolism seems disproportionate in 1953, and in the latter section, though "milli equivalents" are briefly mentioned, all other figures given are in volumes or milligrammes Surely at the present time milli equivalents should be used in the text and not merely put in as an academic curiosity

In the short chapter on liver function, it would probably be preferable if fewer tests were discussed more critically and in greater detail It is only too easy to get lost in a multiplicity of tests

Vitamins and Hormones

Advances in Research and Applications Vol 10 Editors ROBERT S HARRIS, professor of biochemistry of nutrition Massachusetts Institute of Technology , G F MARRIAN, F R S , professor of medical chemistry, University of Edinburgh , KENNETH V THIMANN professor of plant physiology, Harvard University New York Academic Press London Academic Books 1952 Pp 421 64*s*

WHEN a periodical of this kind has been running for ten years and the editors can say that it "continues to meet with acceptance and almost complete absence of adverse comment" there is little doubt that it has made a niche for itself

Volume 10, they remark is concerned with hormones rather than with vitamins but most of the articles seem to deal pre eminently with nutrition Thus Eric K Cruickshank, writing on dietary neuropathies, deals with beriberi, the painful feet syndrome Wernicke s encephalopathy , and other allied diseases—all good reading for clinical men Albert E Sobel discusses the absorption and transport of the fat soluble vitamins and Ernest Beerstecher the nutrition of the crustacea, of which very little seems to be known Other articles with a general bearing on nutrition cover the pituitary experimental glycosuria, the influence of the corticoid hormones on enzymes concerned with carbohydrate metabolism, steroids and tissue oxidation, and hormone assays in obstetrics and gynæcology The authors form an international coterie, for three hail from Switzerland, one from Jamaica, two from Scotland, and the remainder from the United States

Scientific Study of Personality

H J EYSENCK, PH.D London Routledge & Kegan *Paul 1952 Pp 320 30s*

THIS work bears constant witness to its twofold origin it is rigorous in method and thought because it comes from a department of psychology with a strong statistical bias , and, since Dr Eysenck is reader in psychology in the Institute of Psychiatry at the Maudsley Hospital, the investigations are everywhere indebted to the clinical material, stimulation, and validating judgments which such a medical centre affords Dr Eysenck's aim has been to discover the main measurable features of personality and to define them by means of quantitative experimental procedures, leaving no room for ambiguity His previous book, *Dimensions of Personality*, had the same aim but did not range so widely through normal and abnormal subjects, juveniles and adults He has organised a large programme of research, consistently related to his aim , and the results are woven, with those of other psychologists working in the same institute, into an intricate yet distinct and coherent pattern In many passages the exposition is provocative, and to some readers provoking, but in a field of knowledge dappled and sometimes wholly darkened by clouds of vagueness and compromising evasion, it is refreshing to have an author's standpoint and intention made quite plain It is likely that the findings reported here will contribute to a more constant diagnostic classification of mental disorder, and a more exact description of personality than we have now but even if this should prove an over-hopeful view, the argument developed in the book will undoubtedly serve to clarify some obscure stretches in our understanding of personality and mental illness, and the methods it describes will have a continuing part in further research

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The Suprarenal Cortex (London Butterworth 1953 Pp 232 42*s*) —Edited by Prof J M Yoffey, the proceedings of the fifth symposium of the Colston Research Society, held in the University of Bristol in 1952, now appear as a handsom book A report of the occasion appeared in our columns at the time Research workers and others interested in this subject will be glad to have the material contributed on that occasion so conveniently under their thumbs

Useful Drugs (15th ed Philadelphia and London J B Lippincott 1952 Pp 262 20*s*) —From time to time the American Medical Association's Council on Pharmacy and Chemistry skims the cream from *New and Nonofficial Remedies* whips it up with the more popular ingredients of the *U S Pharmacopeia* and *National Formulary*, and produces this palatable mixture It is a carefully selected list of "essential drugs, with brief discussions of their actions, uses, and dosage" Some of the drugs used for diagnostic tests, such as congo red and bromsulphthalein, are hard to accept as essential, but in general the blend is admirable Some readers may regret the absence of terramycin

Recent Advances in Obstetrics and Gynæcology (8th ed London J & A Churchill 1953 Pp 339 27*s* 6*d*) —In nearly thirty years this book has gone through eight editions and one reprint, all under the authorship of Mr Aleck Bourne and Mr Leslie Williams Its value, apparent from the outset, has increased with each successive issue Five chapters of the 7th edition have been dropped and new chapters on Hypertension and Pregnancy, Functional Uterine Hæmorrhage, and Intravascular Thrombosis have been added Extensive revision in some of the remaining chapters has brought them up to date The authors have always displayed a shrewd judgment of those subjects which deserve their attention In addition they not only present an accurate account of all recent work but they are able by their own knowledge and experience, to add valuable criticism and advice To all who practise obstetrics the new edition will be just as welcome as its predecessors have been—and it is unnecessary to say more

THE CERVICAL AORTIC KNUCKLE WHICH RESEMBLES AN ANEURYSM

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AN aortic arch may be present in the supraclavicular region and clinically resemble an aneurysm of the subclavian, carotid, or innominate arteries. In mistake for such it may be ligated with fatal results, as has probably been done on several occasions (Beavan and Fatti 1947). This accident nearly happened in the following case, but fortunately our suspicions were aroused and later strengthened by the late C. M. West, then professor of anatomy at the Welsh National School of Medicine, whom we invited to see the patient and who was present at the operation and suggested that the large pulsating vessel was a high aortic arch.

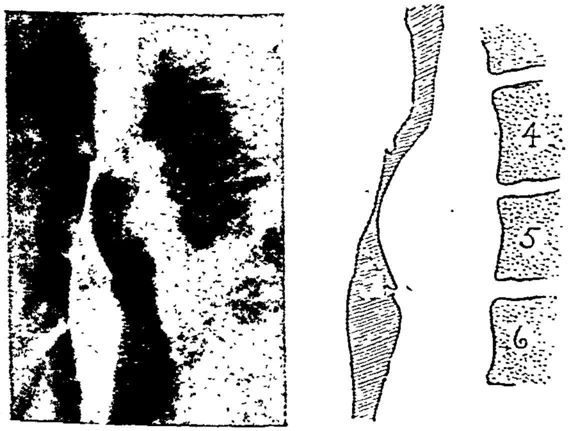

Fig. 1—Left anterior oblique view, after barium swallow, of concavity produced by aorta passing behind œsophagus at level of 4th and 5th thoracic vertebræ.

CASE-RECORD

In September, 1937, a boy, aged 5 years, was investigated in the children's department of the Cardiff Royal Infirmary (Dr. A. G. Watkins). A pulsating swelling in the lower part of the right side of the neck had been noticed three years previously and had not altered appreciably during that time. His mother described him as "very delicate and catches cold easily; is not lively and always wants to rest; his lips go blue at times and he becomes short of breath on walking to school." Past illnesses were scarlet fever, diphtheria, and measles. There was an oval tumour, measuring 1½ in. in its longest axis, in the region of the right common carotid artery; it exhibited an expansile pulsation with a palpable thrill and a bruit on auscultation. The right radial pulse was normal. On the left side axillary pulsations were faintly perceptible, but no pulsations were felt in the brachial, radial, or ulnar arteries. The blood-pressure was 95/64 mm. Hg in the right arm and could not be measured in the left. A murmur heard over the swelling was propagated to the base of the heart. Heart sounds were otherwise normal, and the heart was not enlarged. The pulses in the femoral arteries were palpable and equal on both sides. Electrocardiograms showed normal tracings, and radiography showed minimal cardiac enlargement with slight widening of the upper mediastinal shadow.

First Operation

In August, 1939, he was readmitted with dyspnœa and cyanosis on exertion, and diplopia of two years' duration. The pulses in the arteries of the upper limbs were unchanged, and the blood-pressure on the right side was 95/65 mm. Hg. On Aug. 9, under general anæsthesia, the swelling was exposed through a transverse incision in the lower part of the right side of the neck. The jugular vein was seen to be greatly enlarged and lying to the outer side of a grossly enlarged arterial trunk which was in the position of the common carotid artery; there was no arteriovenous communication. The arterial trunk extended to the hyoid bone, where it formed acutely an anteroposterior arch, with its afferent loop lying slightly internal to its efferent loop. From the apex of the arch the internal and external carotid arteries had their origin. A nerve descending from high in the neck was an external relation of the arch and was thought to be either the right superior laryngeal nerve or the right vagus, but it was considered inadvisable to dissect any further to establish its identity, and the wound was closed.

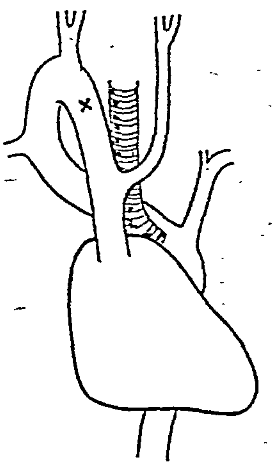

Fig. 2—Suggested disposition of great vessels: lateral pressure at X abolished both femoral pulses, both radial pulses, and right carotid pulse.

Second Operation

In January, 1940, the deep cervical fascia overlying the prominent vessel was reinforced with donor fascia in the form of mattress sutures, the free ends of the fascia being sutured diagonally over the surface. At this operation it was noted that compression of the vessel stopped the femoral pulses.

Further Investigations

In May, 1950, the patient was readmitted having fainted twice while at work as a fish-fryer and having had headaches on reading for any length of time. The cervical swelling was now about 3 in. long and 1½ in. wide. The trachea was displaced to the left of the midline. Pulsation in the left radial artery was present but considerably weaker than on the right side. Blood-pressure in the right arm was 112/86 mm. Hg, in the left arm 92/84. There was no evidence of cardiac enlargement. The right palpebral fissure was narrower than the left. There was no difference in the skin-temperature in the right and left sides of the face, and power in the arms was equal.

On June 2, 1950, 20 ml. of 35% diodone was injected into the prominent cervical vessel. Pain was felt by the patient in both arms simultaneously and in the head. Dispersion of the radio-opaque substance was too rapid, however, to enable any definite conclusions to be drawn from the X-ray exposures. Electro-encephalography showed scattered low-voltage theta waves in all the leads, intermingled with alpha rhythm, but hyperventilation had not much effect on the record, which was considered to be outside the normal range. For the first time a temperature difference was noticed, the right hand being 5 degrees warmer than the left.

Radiography after barium had been swallowed showed a smooth constant concavity in the œsophageal outline at the level of the 4th and 5th thoracic vertebræ (fig. 1). We presume that this appearance is due to the aorta passing behind the

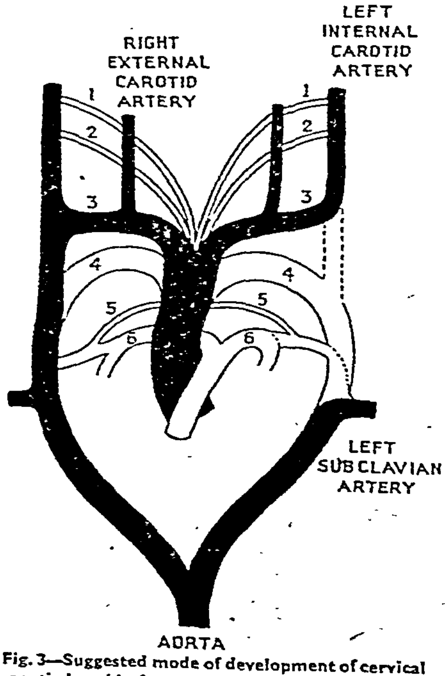

Fig. 3—Suggested mode of development of cervical aortic knuckle from primitive vascular pattern.

and thereby they expose a fiction which has sustained the opponents of analgesia since the days of SIMPSON The old saying that "after all they forget the whole thing" contains a germ of truth which relates only to the quality and perhaps the full intensity of pain Recollected pain can seldom be described, for it cannot be recalled in the sensorium as can visual or auditory images, and at a second or later labour women are sometimes heard to say "I remembered that it was bad last time, now I remember how awful it was" FREEDMAN's paper also underlines the fact that childbirth is especially remembered as an important event, though this memory, which is the pivot to less important ones, may be distorted by self-justification and by later experience

The patients studied by the Yale workers were all participating in the Newhaven "natural childbirth" programme[23] "Natural childbirth" is an attractive but misleading title, for the main aim of the Newhaven and similar schemes—for example, that of Prof W C W NIXON at University College Hospital, London—is to make delivery as easy and tolerable as possible within the limits of safe analgesia Much skill is required to ensure really effective analgesia in labour this cannot always be provided in hospital, let alone in the home These schemes, though differing in detail, consist essentially of two parts first, a psychophysical preparation for childbirth, and secondly, a labour-ward technique The first part is directed at giving the woman confidence in her own powers—the sort of self-confidence that was signally lacking in the days when society and the medical profession kept her in ignorance Thus lectures on various aspects of normal childbirth are combined with a small amount of physical training The lectures cover the development of the child, the process of birth, breast-feeding, and baby-craft The physical training, carefully dovetailed with the lectures, consists in postural adjustment to the strains of pregnancy, relaxation, and breathing exercises With the exercises evolved by the late HELEN HEARDMAN[24] the woman also learns pelvic rocking, and accustoms herself to the lithotomy position She should also get to know the hospital and its staff and familiarise herself with the analgesic apparatus NIXON[25] thinks that as regards labour the most important part of the programme is the labour-ward technique In the labour ward the woman is encouraged to rely on her own powers, by making use of the things she has learnt, and she is never left alone—thus averting an experience that has frightened many Like any other prophylaxis this programme does not deal with established disease As MANDY et al[26] rightly point out, the seriously disturbed woman needs treatment as well as 'natural childbirth' sexual disturbances, for example, which are widespread in our population and can have important sequelæ in labour[27–29] are not dealt with in the classes

Most of the critics of 'natural childbirth' programmes tend to assess their value purely in terms of the effect of the classes on the course of labour[26 30], and commonly they judge this only in terms of mechanical factors, ignoring emotional factors Perhaps this is partly the fault of some who, writing on the physiotherapeutic aspects, seem to have concentrated on statistics covering mechanical factors, in an attempt to appeal to the "obstetrician-in-the-street" There has been far too little research into emotional aspects and psychophysical mechanisms, and virtually no research into either the need for antenatal classes or their effects WOODWARD,[31] however, has inquired into the attitudes of 100 pregnant women who were attending antenatal clinics but not classes in natural childbirth She found that in the life of a woman loneliness and apprehension were ordinarily at their peak from the fourth month of her first pregnancy, when she leaves work and faces a lonely existence, a lower income, and the unknown terrors of confinement WOODWARD's findings would lead one to suppose that women who have attended classes would come to labour better prepared after a happier and less tense pregnancy

Regimentation of the patient and dependence by her on an authoritative figure has long been the basis of conventional maternity obstetric practice[27], but it has no place in natural childbirth The divergence between the two systems is evident at every medical discussion of the subject[30] "Natural childbirth" programmes represent one of the first attempts to practise a preventive medicine that recognises the unity of body and mind, by combining health education, group discussion, participation, and psychological techniques This promising approach, which GRANTLY DICK READ[32] has done much to promote, has captured the attention of the public, and is thus being given a fair chance to develop, and authority, which is playing its traditional rôle, is failing to put the clock back

Blood-clotting

AT last year's International Conference of Hæmatology, held in Argentina, the research-workers on blood clotting held a separate meeting to discuss their difficulties Such a meeting was necessary because progress towards a better understanding of blood clotting and its disorders was becoming obscured by a fog of nomenclature, everybody seemed to have their own name for the various "factors" concerned in clotting, and new ones were being added before the old ones were properly understood Some efforts towards resolving the confusion have now been made, and it is clear that the factors are nothing like so numerous as the literature might suggest The fifth conference on blood-clotting held by the Josiah Macy, Jr, Foundation in New York set up a committee which has published[33] a list of synonyms for the so called prothrombin accelerators—factor V of Owren and factor VII of Koller STEFANINI,[34] in a review of present ideas, has compiled a more comprehensive list He points out that most workers at present agree that blood-coagulation has three stages (1) activation of thromboplastin, (2) conversion of prothrombin to

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[23] Thoms H Training for Childbirth New York 1950
[24] Heardman H The Way to Natural Childbirth Edinburgh 1948
[25] Nixon W C W Personal communication
[26] Mandy A J, Mandy T E, Farkas R, Scher E Psychosom Med 1952 14 431
[27] Tylden E Lancet 1952 i 231
[28] O'Neill D Postgrad med J 1950 26 64 Ibid 1951 27 468
[29] Tylden E Nursing Times, Feb 17 1951
[30] Proc R Soc Med 1950 43 [illegible]
[31] Woodward L British Association Belfast 1952 Section J
[32] Read G D Natural Childbirth London 1933 Lancet 1949 i 721
[33] Alexander B, Flynn J E, Mann F D, Owren P A, Seegers W H Trans 5th Conf on Blood Clotting Josiah Macy Jr Foundation 1952 p 3[illegible]9
[34] Stefanini M Amer J Med 1953 14 64

Preliminary Communication

EFFECT OF CHOLINE ON CERTAIN FORMS OF ŒDEMA

THE theory of Starling (1896) and Schade (1935) states that transudation of tissue fluid is due mainly to variations of hydrostatic and colloid osmotic pressure. In those conditions of disordered physiology which give rise to œdema not all the observed facts can be explained by this theory. Thus Govaerts (1947) proved that a certain relation exists between the colloid osmotic pressure and the albumin/globulin ratio in cardiac or nephrotic œdema, but he did not find it in hunger œdema. Sinclair (1947) could not demonstrate a significant difference in plasma-protein level between hunger patients with and without œdema; and Keys (1947, 1950), using Tiselius's electrophoretic method, observed no difference in serum-protein fractions in these patients. On the other hand, some patients with very low plasma-protein levels have no œdema.

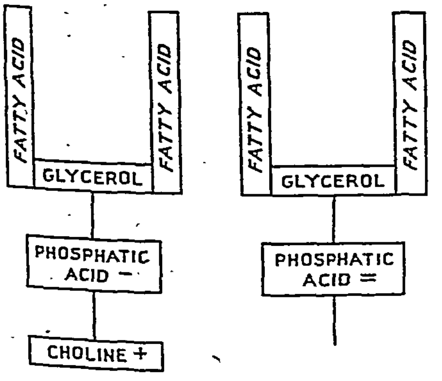
We have recently seen a woman, aged 39, with anorexia nervosa, who was much underweight (height 5 ft. 6 in., weight 6 st. 2 lb.) and had a very pronounced hypoalbuminæmia (total protein 4·86 g. per 100 ml.; albumin/globulin ratio 1·0, phospholipid 10 mg. per 100 ml.). Heart, blood-pressure, and circulation-time were normal. There was not a trace of œdema, which (according to Starling's theory) she should have had.

BIOCHEMICAL CHANGES IN CASE 2

Date	Total lipid (mg. per 100 ml.)	Phospholipid (mg. per 100 ml.)	Serum-albumin (method of Majoor) (g. per litre)	Flocculation test* (ml.)	Urinary protein (g. per litre)	Œdema
April 17, 1950	1150	7·8	21	0·6	36	+ + + +
April 18, 1951	1100	8·1	23	0·5	31	+ + + +
May 21, 1951	Choline therapy 6 g. daily started					
June 10, 1951	1000	12·4	22	0·9	22	+ +
Oct. 30, 1951	750	14·1	27	0·5	2·5	–
Feb. 20, 1952	630	12·6	37	1·4	2	–

* A flocculation test with $HgCl_2$ solution, expressed in ml. necessary to produce flocculation. Normal is 2 ml., corresponding to a normal albumin/gamma-globulin ratio.

However, during the famine period in Western Holland in the late war it was found that, although certain hunger patients with œdema had hardly any other biochemical abnormality, they did have a low blood level of lipid phosphorus (Neumann 1946). This was also observed by Feigl in 1917 during the first world war (Feigl 1920). In both periods the daily rations contained only small amounts of methionine, choline, and lecithin, owing to the lack of certain foods—e.g., bacon (Maase and Zondek 1920), soya, meat, and butter (Gounelle 1947). All of these foods are rich in phosphatides, and we know that methionine is transformed to choline in the body. It may well be that choline is an essential factor in hunger œdema; so we tried the effect of it in some cases of œdema.



PHOSPHATIDE PHOSPHATID ACID

Fig. 1—Relation of phosphatide to phosphatid acid.

CASE-RECORDS

Case 1.—A man, aged 70, with hunger œdema, had gone without meat, butter, eggs, milk and cheese for months and had slowly developed œdema. Physical examination revealed no abnormality. His heart, blood-pressure, and circulation-time were normal. Liver function was almost normal, but the serum-albumin level was low, 2·8 g. per 100 ml., with gamma-globulin 2·7 g. per 100 ml. The serum-lipid phosphorus level was 8·1 mg. per 100 ml. (total lipid 530 mg. per 100 ml.). We therefore gave him 3 g. of choline chloride daily by mouth, and his œdema entirely disappeared in fourteen days. There was no change in his serum-protein during this period.

Case 2.—A bricklayer, aged 54, who developed œdema had severe albuminuria (22 g. per litre). The urinary sediment contained a few leucocytes and casts. The heart and blood-pressure were normal. The basal metabolic rate was −7%; urea clearance was 76%; a phenolsulphonphthalein test gave 71%; urine sp. gr. 1·021. The serum-protein level was very low—4·1 g. per 100 ml. (albumin 2·1 g., gamma-globulin 2·0 g.). The diagnosis of nephrotic syndrome was clear. Treatment with a high-protein diet, protein hydrolysate, and blood-transfusions failed to arrest the steady increase in œdema. His weight went up from 67 to 90 kg. (10 st. 7 lb. to 14 st. 2 lb.). Neither thyroxine nor testosterone injections had any effect. The serum-lipid level rose to 1170 mg. per 100 ml., and the serum-cholesterol to 355 mg. Lipid phosphorus decreased (7·8 mg. per 100 ml.) and we therefore again tried choline therapy. On this treatment, although the serum-albumin level remained low, and in spite of loss of protein in the urine, the total serum-lipid level fell, the serum-lipid phosphorus rose, and œdema disappeared. After the disappearance of the œdema the protein loss in the urine became negligible, with a corresponding increase in the serum-albumin (see table). Phenolsulphonphthalein test and urea clearance were 70% and 43% at the beginning of therapy and at the end of it 50% and 50% respectively.

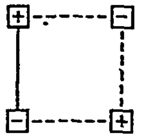


Fig. 2—Tricomplex of Bungenberg de Jong (1949).

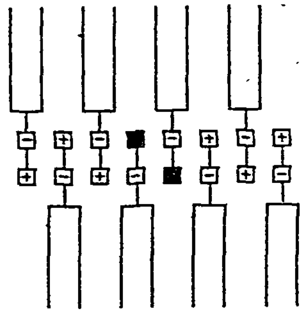


Fig. 3—Model of cell membrane (Bungenberg de Jong 1949).

DISCUSSION

The disappearance of œdema in these two cases might be explained as follows.

Choline is a lipotropic factor beneficial to liver function. Deficiency of choline may lead to a qualitative change in serum albumin, producing œdema. Suggestive evidence of this has been collected by Williams (1951), though it must be admitted that œdema seldom occurs in other cases of liver injury in which the serum-protein levels are low. Alexander and Engel (1953) found that choline prevented œdema in rats fed on low-protein diets, and that lack of choline led to fatty and cirrhotic livers, with the appearance of œdema.

According to Bungenberg de Jong (1949) the cellular wall contains a tricomplex of phosphatide (ampho-ion), phosphatid acid (negatively charged ion), and an exchangeable positively charged ion—e.g., Ca^{++}. Now the phosphatid acid is phosphatide which has lost its choline group, and the availability of choline will effect the ratio between phosphatide and phosphatid acid, and therefore the permeability of the cell membrane (figs. 1, 2, and 3)—e.g., of the cells of the capillary endothelium.

The effect of choline on cardiac œdema is still under investigation.

SUMMARY

The effect of choline chloride has been observed in two cases of œdema, one due to starvation and the other has also drawn attention This condition appeared clinically to be classical hæmophilia, but the missing factor proved to be not the antihæmophilic globulin of plasma but a serum factor, possibly identical with the "plasma thromboplastic component" described by some American workers[42,43] And this week Professor **VAN CREVELD** and Dr **PAULSSEN** describe another example of this condition **BIGGS** et al called the disease by the name of their first patient, which happened to be Christmas, and the factor was called the Christmas factor **BIGGS** and **DOUGLAS** found that plasma adsorbed with alumina still contained antihæmophilic globulin in addition to factor V, and normal serum contained Christmas factor in addition to factor VII These four factors together with a fifth—blood platelets—react together in the presence of calcium salts to form a labile thromboplastin Deficiency of any of these factors produces a coagulation defect that gives an abnormal result with thrombin-generation tests, and is reflected clinically in a hæmorrhagic syndrome

For thromboplastin-generation tests a mixture of alumina plasma, platelet suspension, and diluted normal serum is used to provide the five factors When calcium chloride is added, clotting is initiated As with the other tests, specimens are removed at intervals, and this time they are added to a recalcified platelet-free "substrate normal plasma", and from the clotting-time of this mixture a quantitative estimate of the thromboplastin formed can be made In hæmophilia a mixture of the patient's alumina plasma with normal platelets and serum shows in this way grossly defective thromboplastin generation, but in Christmas disease a similar mixture gives normal results If a mixture of normal alumina plasma and platelets and patient's serum is used, it is Christmas disease and not hæmophilia that gives the defective thromboplastin generation **BIGGS** and **DOUGLAS** were able to test a patient with abnormal giant platelets (thrombo asthenia), and this patient's platelets, mixed with normal alumina plasma and normal serum, gave abnormal results in this test The test therefore makes a clear-cut differentiation between classical hæmophilia and Christmas disease it will detect hæmophilia in patients who are so mildly affected that the whole-blood clotting-time and the prothrombin-consumption tests are normal It is unfortunately complicated, demanding much careful preparation of test materials and quite unusually complicated laboratory gymnastics during its performance For example, at one stage the technician has two graduated Pasteur pipettes each containing 0 1 ml of test solutions, and he must discharge them simultaneously into a tube containing 0 1 ml of substrate, start a stopwatch at the same time, and observe a clotting reaction that may be complete in 10 seconds Such tests are not likely to be popular, even in research laboratories, and are much too time consuming for routine use So it is fortunate that for most cases the tests at present in daily use will suffice The use of the Quick one-stage clotting test (the doubts about the "prothrombin" it measures have we suppose, made "prothrombin-time" out of order) is still the best way of controlling the factor-VII deficiency caused by anticoagulants Most cases of hæmophilia can be detected by a combination of the whole blood or recalcified-plasma clotting-time and the prothrombin consumption test The only therapeutic importance of the distinction between classical hæmophilia and Christmas disease is that hæmophilia must be treated with blood or plasma not more than one day old whereas serum can be used for Christmas disease The mild form of hæmophilia described by **GRAHAM** et al[44] in 14 members of a single family is due to deficiency and not complete absence of the antihæmophilic globulin It is clear that the identification of cases of hæmorrhagic disease that do not conform to the commoner syndromes must be left to the few special centres where the more complicated investigations are in regular use In no field does attention to technical minutiæ count for more, and it is waste of time to carry out occasional tests of this type Research centres will now have, in the thrombin generation test, a not too complicated tool for objective assessment of proposed remedies for hæmophilia

The story of coagulation continues to be unfolded at a brisk pace, which makes the attempt that is now being made to control nomenclature all the more necessary To many of those who are grappling with the latest chapters, uninformative eponyms, however seasonable, are less welcome than a definitive title and another trap to be avoided lies in the use of a name that has already been given to another condition For instance, **HOUGIE**[45] has lately used the name "pseudohæmophilia" to describe a syndrome due to a circulating anticoagulant, but this name has already been in use for some years to describe a hereditary capillary abnormality, also known as constitutional thrombopathy or von Willebrand's syndrome It would be a pity if the editing of this complicated but important story was offset by the reintroduction of disguised or equivocal characters

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Annotations

TREATMENT OF HYPERTENSION

THERE is no satisfactory treatment for essential hypertension, and none can be expected until more is known of the mechanism of raised peripheral resistance At present we wring what we can from a wide range of remedies Sympathectomy has passed through many vicissitudes, from enthusiastic reception to denial that it significantly benefits any form of hypertension[47] Now, however, its place has become stabilised Thorpe et al[48] reviewed 500 cases of bilateral thoracolumbar sympathectomy and found statistically significant benefit in "group 4" (papillœdema) cases only Morrissey et al,[49] who have reviewed 122 cases, take a rather less pessimistic view, and are prepared to recommend it to patients with disabling symptoms such as severe headache, without advanced retinal changes They emphasise, however, that in malignant hypertension a trial must first be made of 2–3 months' complete rest and adequate treatment with hypotensive drugs They note that symptoms—for example, headache—may be substantially relieved by sympathectomy even if this fails to lower blood pressure Possibly in adopting sustained lowering of blood pressure as the sole criterion of efficacy, we are taking too narrow a

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42 Schulman I, Smith C H *Blood* 1952 7 794
43 Aggeler P M, White, S G, Glendening M B *Page E W* Leake, T B Bates G *Proc Soc exp Biol* N Y 1952 79 692
44 Graham J B McLendon W W Brinkhous K M *Amer J med Sci* 1953 225 46
45 Hougie C *J clin Path* 1953 6 70
46 Platt R Stanbury S W *Lancet* 1951 i 651
47 Thorpe J J Welch W J Poindexter C A *Amer J Med* 1950 9 500
48 Morrissey, D M, Brookes V S Cooke W T *Lancet* Feb 1953 p 403

Since he had begun doing domiciliary visits, the number of doctors referring only 1 patient had fallen, and the number of those referring 2–5 had risen. He felt that the domiciliary visit offered the hospital consultant an invaluable opportunity for learning about the psychiatric problems of the general practitioner and for seeing the patient against his home background.[3] He had now made contact with all the doctors in the area who referred their patients.

Referrals came under five headings: depressions, neuroses, organic cases, marital problems, and social problems. He felt that general practitioners should be taught to diagnose the depressed patient earlier. There was difficulty in selecting the neurotic case to be referred to the consultant, who should bear in mind that the general practitioner usually sent this patient along for treatment, not just for another opinion. He did not think that the general practitioner should undertake systematic psychotherapy. Many of the chronic neurotics and the organic cases were referred because they were a nuisance to the busy practitioner. Social-problem cases were better dealt with at hospital where the psychiatric team, including the psychiatric social worker, were more qualified to advise on the facilities. Most patients with marital difficulties should be referred to a solicitor rather than to the psychiatric consultant, for few of them could be helped. He thought that psychiatric diagnostic terms were too complicated for the general practitioner, and that a committee of consultants and practitioners should draw up a simpler list. The psychiatrist embarking on domiciliary visits should be well qualified in general medicine and fully abreast of modern knowledge. He thought that students should be taught more of the simple neuroses. A large number of psychiatric cases went unrecognised in general practice because of the practitioner's ignorance of, or his prejudice against, the psychiatrist and the psychoneurotic patient.

Dr. C. A. H. WATTS said that his figures agreed largely with those of Dr. Fry, although people in his practice were not quite so neurotic. He thought that 50% of the neurotics were treatable by the practitioner, and disagreed with Dr. Leigh about the practitioner not being fit to undertake simple psychotherapy. He himself referred about 10% of his psychiatric patients to a consultant—an average of 15 cases per annum. If Dr. Fry's figures for a 4500 practice with about 500 psychiatric cases were representative of the whole country, this would give a total of 5 million cases; and it was obviously impossible for the psychiatric services to cope with this number.

Dr. GERALD GARMANY thought that the Geneva nomenclature was quite clear and no more complicated than that of the blood disorders or orthopædics. He disagreed, like Dr. Watts, about Dr. Leigh's exclusion of the marital cases, many of which benefited by coming under the attention of the hospital psychiatric team.

Dr. SAWLE THOMAS thought that the difference between the hospital-trained psychiatrist and the practitioner was that the former was more interested in diagnosis and the latter wanted something done for his patient. He had done about 130 domiciliary visits in 1952; about 30% of the patients had been depressives, and another 30% schizophrenics, who were much rarer in Dr. Denis Leigh's figures.

Dr. E. M. DIMOCK said that a family practice had taught him the importance of attention to the organic side of illness. When the doctor had satisfied the patient on this score, the patient was much more amenable to discussion of the emotional factors in his illness. He thought that the domiciliary visit could be of great help to the practitioner, who should be present at the interview. Dr. Dimock thought that most psychiatrists knew far too little about preventive psychiatry, and deplored their tendency, when patients were referred to them, to stir up a lot of mud which, very often, they were unable to settle again.

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[3] Leigh, D. *Lancet*, 1952, i, 915.

ASSOCIATION OF CLINICAL PATHOLOGISTS

THIS association met in Exeter on March 26–28. The following are brief summaries of some of the papers.

Effect of Benemid on Uric-acid Excretion

Dr. E. N. ALLOTT said that in the treatment of gout there are two problems: (1) the relief of acute gouty pain, and (2) the prevention of accumulation of uric acid and formation of tophi. 'Benemid,' which was devised to diminish urinary penicillin output by blocking tubular excretion, increases uric-acid output by blocking tubular reabsorption. Normally the increased excretion after benemid may cease after a few days, but in the gouty individual the rise may persist for many weeks. The increased excretion, with prompt fall in blood-uric-acid level has no effect on acute gouty pain. There is, however, some evidence from American experience that prolonged use of benemid may reduce the frequency of gouty attacks. There is no evidence of any permanent renal change after long use of the drug.

Creatine Examinations in Muscle Disorders

Dr. J. N. CUMINGS described creatine metabolic experiments in 67 cases of muscle disorder—myotonia, myasthenia, myopathy, neuronopathy, dermatomyositis, or porphyrinuria. Urinary creatine, creatinine, and guanidoacetic acid were estimated daily, and blood-levels before and after a creatine-tolerance test were also estimated. Normal results were obtained in myotonic patients and in some cases of myasthenia. Grossly diminished tolerance to ingested creatine was found in generalised myopathy, but not in any other disease except in old cases of myotonia with pronounced atrophy. Guanidoacetic acid was unaltered in all conditions except porphyrinuria, in which there was a considerable diminution which, on recovery from the paralysis, changed to a distinct excess.

Idiopathic Renal Acidosis

Dr. W. W. PAYNE remarked that a child with infantile renal acidosis typically presents with a history of normal birth and progress until the age of 4–6 months. Then there develop anorexia, vomiting, and constipation with failure to gain weight. The infant is irritable but hypotonic; there is wasting and dehydration; and fæcal masses are felt in the abdomen. The urine is alkaline; a trace of albumin and a few white blood-cells are present; and often a slight growth of *Bacterium coli* or proteus is obtained. The plasma-chloride is raised above 115 m.eq., and the bicarbonate is lowered below 18 m.eq. With good nursing the dehydration may be corrected, but the other symptoms persist; and a further blood examination after rehydration still shows a lowered bicarbonate but not always a raised chloride. Despite the acidosis the urine is persistently neutral or alkaline. With no treatment there is usually a steady deterioration, but occasionally after a few difficult weeks the infant will recover without treatment. The effect of giving sufficient alkali by mouth to correct the acidosis is striking: the anorexia and vomiting cease, the temper improves, and the weight begins to increase. In 13 out of 35 cases careful radiographic examination of the abdomen showed shadows in the renal areas suggesting calcium deposition. The diagnosis rests on the initial clinical picture, a persistent reduction of the plasma-bicarbonate, and an alkaline urine. No other condition (except forced hyperventilation) will produce an alkaline urine with acidosis. In all uncomplicated cases the final outcome has been complete return to normal after treatment for 2–30 months.

Physiology of Fat Metabolism

Prof. A. C. FRAZER (Birmingham) said that fat absorption in man is most satisfactorily assessed by the daily-fatty-acid-balance method.[1] The intraluminar phase can be directly studied by intubation. With pancreatic-enzyme deficiency intraluminar emulsification does not occur, particulate absorption is impossible, and the chylomicrograph is flat. Intraduodenal injection of finely dispersed emulsion causes a normal chylomicrographic peak,[2] provided that the absorptive prescribing For example, five days' treatment may be completed with 1 million units of crystalline penicillin at a cost of 2*s* 7*d* , whereas five days' treatment with 15 mg of aureomycin per kg body-weight per day will cost about 30*s*

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[1] Van de Kamer, J. H., Huinink, H. ten B., Weyers, H. A. *J. biol. Chem.* 1949, 177, 347.

[2] Frazer, A. C. Third European Congress of Gastroenterology. 1952; p. 60.

The Bristol Hospitals' booklet gives admirably clear summaries of the preparations, uses, modes of administration, and cost of each drug together with schemes of dosage for adults and children It also gives separate accounts of the local and systemic treatment of burns and of the use of antibiotics to prevent infection in head injuries and in patients in coma The booklet ends with a valuable section on how to take various specimens for the laboratory and a warning on the danger of infection during prolonged intravenous treatment Altogether, it may be warmly commended for its sound common sense

CIRCUMCISION OF THE NEWBORN

CIRCUMCISION is most commonly carried out during the first few months of life, but many pædiatricians delay the operation until soon after the age of 2 years [1] If it is deferred until the child is over 5 years of age, then its protective value against penile cancer seems to be lost [2] Miller and Snyder,[3] who have studied 1480 males circumcised at birth, find that operation at this early age carries no extra risk This is undoubtedly a convenient time for the physician, who "finishes his episiotomy, walks across the hall and circumcises the infant, and is finished with the whole business" The risk of infection is small, for at such a time the infant bears few bacteria, and, with a skilled operator, hæmorrhage is rare Apparently no anæsthetic is needed It might seem that immediate circumcision would enhance the infant's normal early loss of weight, but when these infants left hospital, after an average stay of 5 days, their weight compared well with that of controls, and 98% were gaining weight.

If there is to be circumcision, it is probably best done early, but perhaps operation on the neonate is less likely to become a usual method here than in the U S A , where a higher proportion of women are delivered in hospital

ELEPHANTIASIS NOSTRAS

ELEPHANTIASIS nostras is a most incapacitating condition, known also as Milroy's disease, Meige's disease, and congenital or familial lymphœdema Because of the clinical similarity, the range of lymphatic tissue involved, and the general resemblance of the deformities produced, it has been much confused with the filarial elephantiasis so common in Polynesia, South China, and indeed throughout the tropics, but, whereas in filarial elephantiasis the part played by the adult filaria parasites in the genesis of chronic lymph stasis is pretty well understood, very little is known about the condition of the lymphatic vessels in elephantiasis nostras What is certain is that the disease may be either hereditary or sporadic that it is commonest in females, that it becomes evident about puberty, and that it is extremely chronic and always permanent The swelling usually affects the lower limbs and it is usually circumscribed, in such a way that sometimes the foot escapes—a peculiarity not seen in the filarial disease The œdema gradually subsides to some extent at night-time The orderly progress of the elephantiasis is interspersed by febrile periods, with lymphangitis causing an increase in the swelling As a rule sepsis is a serious complication, and deaths from cardiac failure are not uncommon

Prof *Aldo Castellani*[4] now describes anew this condition as he has observed it in this country and in Portugal He lays emphasis upon the attacks of lymphangitis with high fever and red erysipelas like patches on the skin In these attacks the inguinal glands are generally enlarged and painful, and the skin, which is at first smooth, becomes raised in bosses to form the verrucose variety (elephantiasis nostras verrucosa) Castellani thinks that after some years the bouts of fever cease altogether, and it should perhaps be noted that other observers do not all agree that febrile attacks and lymphangitis are essential features of the condition According to Castellani the scrotum may be affected, and also occasionally the face and lips On symptoms and signs alone, it is, as he says, impossible to differentiate between elephantiasis nostras and filarial elephantiasis, but pathological evidence of the latter may be provided by eosinophilia and sometimes by the presence of microfilariæ in the blood, while in doubtful cases, the intradermal filarial test may be helpful

There seems to be general agreement that the acute phases of elephantiasis nostras are produced by the entrance of streptococci through the skin, or in cracks between the toes as in tinea pedis Castellani, however, believes that the responsible organism is the *Micrococcus* (*Coccobacillus*) *metamyceticus* which he first described in 1933 and 1934, and which was isolated from the inguinal glands in a case of non-tropical elephantiasis When first isolated the organism is a gram negative coccus with definite biochemical reactions, and Castellani holds that a vaccine made from this organism has shown curative value Neither sulphonamides nor penicillin have any effect, but he repeats his opinion that injections of fibrolysin (Merck) in doses of 2–4 ml into the gluteal region three times weekly for two to three months will bring about great improvement, though this does not last The pattern of the pathological changes is described by Castellani as follows first, bacterial invasion of lymphatic vessels and glands, secondly, œdema due to pathological changes caused by the micro-organisms, and, finally, lymphatic hyperplasia affecting the skin and subcutaneous tissues Lymph stasis alone does not suffice to produce elephantiasis, but the lymph, which contains protein in excess, becomes an excellent medium for fibroblasts and micrococci The histological changes of the skin in elephantiasis are great thickening of the dermal and subdermal tissues, close approximation of the nuclei in the malpighian layer, increase in the number of lymph spaces, dilated venules, and thickened arterioles and fibrosis

Although Professor Castellani has made out a good case for his opinions, it must be admitted that much further detailed investigation of the pathology of elephantiasis nostras will be necessary before the exact mode of production of this mysterious lymph stasis can be satisfactorily explained

BRONCHOSCOPY IN TUBERCULOSIS

BRONCHOSCOPY, like oth[illegible] subject to errors of observation and [illegible] chance of error is probably greater with bronchoscopy than with radiography of the chest, since the bronchi are seen by only one observer for a short time and the appearances are not photographically recorded An investigation initiated by the research committee of the British Tuberculosis Association, although not designed for this purpose, suggests that different observers differ considerably in their assessment of bronchoscopic appearances [1]

Six surgeons at six hospitals bronchoscoped a number of patients with pulmonary tuberculosis, each patient was examined by one surgeon only Of altogether 3[illegible] patients 34% were reported to have abnormal broncho[illegible] scopic appearances, but the proportion of abnormal

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[1] Higgins T T *In* Garrod Batten and Thursfield's Diseases of Children Edited by D Paterson and A A Moncrieff London 1949 vol 2

[2] Gairdner D *Brit med J* 1949 ii 1433

[3] Miller R L Snyder D C *Amer J Obstet Gynec* 1953 65 1

[4] Reprint from the *Imprensa Médica* Lisbon 1952

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[1] *Tubercle* 1953, 34 74

plugging of the capillaries. Areas of demyelination and neurofibrillar destruction occur in the hæmorrhagic lesions and around many venules, and there is widespread microglial proliferation. Comparison of the lesions with polyarteritis nodosa and postinfectious encephalitis and with experimentally produced hypersensitivity suggests that the disease results from acquired sensitivity of the white matter to a circulating antigen.

Transfusion Errors

Dr. G. H. Tovey (Bristol) described an analysis of 24 transfusion accidents reported from hospitals receiving blood from the South West Regional Transfusion Centre over a three-year period, during which about 40,000 transfusions were administered. The accident-rate was, therefore, 1 per 1660 transfusions; 5 (21%) of the accidents were fatal. In 5 cases (21%) the cause was ABO incompatibility from misgrouping of the recipient and failure or omission of the direct-matching test. Such errors arose mainly because of "short-cuts" in technique. 3 of the accidents (12%) occurred because Rh-negative recipients were incorrectly typed as Rh-positive; in 2 of these cases anti-D was present in the recipient's serum, but D-positive blood appeared to be compatible in 1 case in a capillary matching test, and in the other because the antibody showed a marked prozone effect with albumin-suspended red cells. Failure to detect incompatibility from irregular agglutinins other than anti-D caused 5 of the accidents (21%), the antibodies being anti-Kell, anti-c (2 cases), anti-e, and anti-M. The commonest mistake was the use of a saline-slide technique in direct-matching. 2 accidents, both fatal, resulted from faulty storage. The largest single cause of error, accounting for 9 of the 24 cases, was the transfusion of blood intended for another patient through failure to check carefully the labelling on the blood bottle. Accidents from this cause might be fewer if a coloured group-report were attached to the patient's case-history sheet and each bottle carefully checked against this report before transfusion.

Phthalylsulphacetamide

Dr. W. P. Foster and Dr. K. B. Rogers (Birmingham) said that phthalylsulphacetamide had been described as an ideal sulphonamide for treating intestinal infections and for reducing the bacterial content of the gut before operation. The drug was taken by two ambulant healthy adults in a dosage of 0·3 g. per kg. body-weight per day for 5 days. Within 2 days both had diarrhœa and abdominal discomfort due to excessive bowel movements. By the 5th day both had severe tenesmus and proctitis. The fæcal organisms did not apparently diminish, nor did any organisms disappear during this trial. A carefully conducted blind trial, on student volunteers, produced the same set of unpleasant reactions, which were so severe that the students' work and social activities were interrupted; there was no evidence of any reduction or alteration in their fæcal bacteria. Blood-levels were low in the students, but when the first two subjects took the same course, except for an initial dose of 10 g. instead of 3 g., on the fourth day, there was an average blood-level of 10·9 mg. per 100 ml. A very few cases of *Bact. coli* type 0·111 B4 infantile gastro-enteritis were treated with the drug, without clinical improvement or loss of the organisms. One carrier of *Shigella sonnei* and one of *Salmonella paratyphi-B* were treated without success.

Reviews of Books

Clinical Approach to Fevers

C. J. McSweeney, M.D., F.R.C.P.I., D.P.H., medical superintendent, Fever Hospital, Dublin. London: J. & A. Churchill. 1953. Pp. 146. 10*s.* 6*d.*

Dr. McSweeney records here the course of lectures which he gives to postgraduate students. The presentation is quite different from that of most textbooks on fevers: diseases are not treated systematically, but by considering certain leading symptoms and signs such as sore throat, croup, continued fever, rashes of various kinds, cough, paralysis, and diarrhœa in infancy. There are, in addition, short chapters on the more obvious aspects of virus infections, on general and specific treatment, and on the prevention and control of the common infectious diseases. This is the type of teaching usually given on ward rounds. It is in no way exhaustive or systematic, it takes little account of views other than the author's, and it gives no references or supporting data.

Infectious diseases are notoriously variable from time to time and place to place. Today, when they are often spoken of as if they were dying out, it is interesting to learn that measles in Eire in 1952 was more virulent than at any time within living memory, and that acute infantile gastro-enteritis came like a new disease to Dublin in 1941, causing upwards of 1000 deaths in the city every year during the late war, and remaining severe to this day. In view of this it is disappointing to get no information on the serological variants of *Bacterium coli* as a causal factor in this disease, and no mention of the place of antibiotics in the treatment.

There are a number of surprising statements. Appendicectomy performed during the prodromal stage of fevers is by no means unknown, but Dr. McSweeney has apparently seen "scores of appendicectomised enterics." He still regards sulphanilamide (hardly ever used elsewhere) as the remedy of choice for all hæmolytic streptococcal conditions, including sore throat (in which the evidence of its value is now considered very doubtful). He seems to advocate routine enemas on alternate days for fevers, a practice that has been discarded in most fever hospitals. He is certain that chloramphenicol is a specific remedy for, or outstandingly successful in, virus pneumonia, infective mononucleosis, infective hepatitis, and lymphocytic meningitis. He thinks that *every child under 5 years of age* should be given gamma-globulin within 4 days of exposure to measles (is this possible or even desirable?), that infantile vaccination is unnecessary, and that the original streptomycin used for tuberculous meningitis *invariably* provoked deafness.

There is much that is valuable in this book, but some of the dogma may be misleading.

Ocular Surgery

H. Arruga, M.D. Translated from the Third Spanish Edition by Michael J. Hogan, M.D., and Luis E. Chaparro, M.D. Barcelona: Salvat Editores, S.A. New York: McGraw-Hill. 1952. Pp. 936. 306*s.*

For many years now, ophthalmic surgeons from all over the world have made the pilgrimage to Barcelona, to see the clinic and admire the operative skill of Count Arruga. During the Spanish Civil War, when he had to leave the country, his skill was demonstrated in many lands, and as a result of requests from many quarters he put his surgical experience into a book, now brought up to date in its third Spanish edition.

Though Arruga's name is perhaps more widely known than that of any other ophthalmic surgeon, he has no hospital appointment and only thirteen beds in a private clinic. He believes, like Kocher of Berne, that a few patients thoroughly studied are more instructive to the surgeon than many times that number seen less often. His maxims have always been simplicity, neatness, and a careful study of every patient, and this volume reflects them. Nothing in it is unpractical, nothing unproven in use, nothing fanciful, and the whole is presented with style and finish. In each chapter Arruga first gives his own operations and predilections, then the operations of other leading ophthalmic surgeons, where these differ from his own, and finally, the newest thoughts on the subject culled from journals and society proceedings. As an exposition of modern technique in ophthalmic surgery this book is unequalled and seems likely to remain so.

Developments in Psycho-Analysis

Melanie Klein, Paula Heimann, Susan Isaacs, Joan Riviere. Toronto: Published for the Institute of Psychoanalysis by Clarke, Irwin & Co. London: Hogarth Press. 1952. Pp. 368. 30*s.*

During Freud's lifetime a number of adherents, who developed views which he considered irreconcilable with the basic principles of psycho-analysis, were extruded or withdrew to found schools of their own. This did not happen to Melanie Klein, but her theories are sufficiently divergent, if not schismatic, to have raised vehement questions about her orthodoxy (it is difficult to avoid using religious terms and analogies in this context). Here is a dignified rejoinder to the attacks made upon wrong times, being perhaps at their nadir during critical discussions Playing at home may be as important an advantage in this field as on others

THE SOCIAL ANIMAL

THE neurotic is isolated from the community, to which he cannot adjust Dr Maxwell Jones has tried the effect of giving him a hair of the dog that bit him, by guiding and absorbing him into another social community—that of the hospital Doctors, nurses, and patients provide between them a social unit with a therapeutic power comparable to that of a united family, or of the esprit de corps of other groups

In a new book[1] Dr Maxwell Jones describes three experiments on these lines First he treated soldiers suffering from "effort syndrome," in an emergency hospital during the war Here he mainly developed the educational approach, teaching patients the mental mechanisms of their symptoms , and he found that explanations were readily accepted when they had the weight of group acceptance behind them The second experiment was with "psychodrama," which gave patients the chance to act out their difficulties or to see them re enacted by others These two methods he afterwards modified for the rehabilitation of repatriated prisoners of-war who were having difficulty in readjusting to civilian life His most important and most lasting experiment, however, described in detail, was the establishment of the industrial neurosis unit at Belmont Hospital, Sutton Here he has treated patients of a very different type (though the difference is perhaps not made clear enough to the reader)—to wit, unemployed neurotics of long standing, often considered unemployable by the authorities, patients with "severe character disorders in poor personalities," "some of the most antisocial elements in society" The task was to absorb these social casualties into the transitional community of the unit, to instil some "communal responsibility" into people who had no real place in society before, and to prepare them for their outside rôle after discharge This obviously demands more than average enthusiasm, optimism, energy, and devotion to the idea from all who collaborate in the work, and especially from the nursing staff Probably the most instructive and revolutionary parts of the book are those explaining the nurse's position, the difficulties arising out of the unconventional part she is asked to play in the community of the unit, and the solutions attempted and achieved

Dr Maxwell Jones's colleagues—Dr A A Baker, Dr Thomas Freeman, Dr Julius Merry, Dr B A Pomryn, Mr Joseph Sandler, PH D , and Miss Joy Tuxford—report in separate chapters on their special problems psychotherapy of neurotic inpatients is criticised and justified, techniques of group formations are disentangled, and the special hazards of vocational guidance are described Follow-up study of these patients seems impossible , nevertheless it was tried, and we even find the team in search of a control group of untreated cases They were not able to collect them, but the search disclosed a still more solitary and demoralised layer of unemployable psychiatric patients who refused treatment even in a unit like that at Belmont

Six months after discharge about 100 patients were visited, of whom almost half were working, some of them under sheltered conditions This seems a satisfactory practical result, justifying Dr Maxwell Jones's work It is encouraging to see from his report how his idealism and pioneer spirit have won the support not only of able colleagues, but also of Ministries and other official bodies inside and outside the National Health Service

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[1] Social Psychiatry [illegible] London Tavistock [illegible] & Kegan Paul 1952 Pp [illegible]

KERNICTERUS

KERNICTERUS, a peculiar yellow staining of the nuclear masses of the brain in neonates, has long interested clinicians, pathologists, and hæmatologists Originally this condition, which gives rise to a varied clinical picture,[1 2] was believed to be toxic, possibly hepatogenous , later the cause was thought to be sepsis,[3] but this came to be regarded as only a contributory factor[4] When blood-group incompatibility was correlated with icterus gravis, many thought that the problem of kernicterus was solved , indeed, Claireaux[5] suggested that kernicterus was always due to jaundice resulting from hæmolytic disease of the newborn Aidin et al[6], however, described 25 cases of kernicterus in premature infants without any evidence of hæmolytic disease , and their findings have been confirmed in a further 10 cases by Dr Govan and Dr Scott[7] These workers also examined the brains of 3 premature infants who had lived only 48–72 hours and where there ha been a difficult birth , and in these they found histological evidence of brain damage indistinguishable fro that in kernicterus due to hæmolytic disease of th newborn They concluded that anoxia was the primar cause, and deposition of pigment a secondary factor

This explanation, however, does not accord with a the facts Anoxia does not necessarily accompan the birth of a full term erythroblastotic infant , usuall the infant seems perfectly healthy until it become jaundiced Furthermore, the serum-bilirubin of th neonate destined to have kernicterus is usually, thoug not always, much raised Signs of kernicterus com on pari passu with the jaundice, but the disorde does not seem yet to have been diagnosed at the tim of birth It is doubtful if the theory of antigen antibody reaction in the brain as a cause of kernicterus is any longer tenable , in the worst form of hæmolytic disease of the newborn—namely, hydrops fœtalis—histological evidence of brain damage has not hitherto been described

Experimentally bilirubin can cause a brain lesion similar to that of kernicterus,[8] but only if its level is very much higher than that found in erythroblastosis A familial non-hæmolytic jaundice apparently accounted for kernicterus in five members of a family described by Crigler and Najjar[9], and in a letter that appear on a later page of this issue Dr Forrester and Mr Bev suggest that the cause may be pigment derived from abnormal hæmoglobin metabolism Gerrard[2] concluded that hypoglycæmia was not the cause, and he suggested that neither anoxia nor liver damage, but some primary biochemical dysfunction, such as hexokinase inhibition, might prove the underlying factor Dr Saunders[10] has suggested that the cause may be the withdrawal of an inhibiting substance derived from the placenta

Clearly our knowledge of kernicterus is very far from complete It seems, however, that the kernicterus in erythroblastosis and in jaundiced—and non jaundiced—premature infants should be considered together although the manifestations differ somewhat[11] It seems, too, that replacement transfusion will reduce the risk of kernicterus in infants with hæmolytic disease of the newborn , and early induction of labour where there is any likelihood of hæmolytic disease in the infant should be avoided

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1 Evans, P R , Polani P E Quart J med 1950 19, 129
2 Gerrard J Brain 1952, 75 526
3 Biemond, A van Creveld S Arch Dis Childh 1937 12 173
4 de Bruyne J I van Creveld S Ibid 1948 23 84
5 Claireaux A Ibid 1950, 25 61
6 Aidin R Corner B , Tovey G Lancet 1950 i 1153
7 Govan, A D T Scott J M Ibid March 28 1953 p 611
8 Köster F Krings H Ibid 1950 i 971
9 Crigler J F Najjar J A Pediatrics, 1952 10 169
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11 Aidin R , Tovey G H J clin Path 1950 3 376

THE LANCET

LONDON: SATURDAY, APRIL 25, 1953

Bacteriophage

In July, 1952, the first international congress to be devoted entirely to bacteriophages was held at Royaumont; and the proceedings have been published in the *Annales de l'Institut Pasteur*.[1] At this meeting American workers dealt particularly with methods of phage reproduction, while French workers were concerned more with lysogenicity.

Phage multiplication has been intensively studied with the coliphage T_2; and this work has been aided by the development of electro-microscopic techniques,[2] which have revealed that the head of T_2 phage is hexagonal in shape and is composed of a protein shell filled with desoxyribonucleic acid (D.N.A.). Anderson et al.[2] suggest that the tail seen in these phages is hollow and attaches the head of the phage to the host-cell. By osmotic shock the D.N.A. has been removed from the head, leaving the protein skeleton behind. Primary attachment of the tailed phages seems to be by means of the tail, probably by electrostatic attraction[3]; this primary attachment, which is reversible, appears to be the step inhibited by antisera. Hershey and Chase[4] have shown that the subsequent irreversible change leading to infection is due to the passage of D.N.A. into the host. Most of the phage protein remains outside the cell and appears in a form similar to the skeletons seen by Anderson and his colleagues.[2] Thus the protein fraction appears to act as a syringe which injects the phage D.N.A. into the host-cell. Possibly there is a similar type of union between human viruses and their host-cells; but it would be unwise to suggest close analogies between phage and human viruses.

Once inside the cell the reproduction and the genetic pattern of the phage are apparently controlled by the D.N.A. By means of radioactive isotopes several investigators have found that, while up to 30% of the infecting particle's nucleic acid is transferred to its progeny, little or no protein is similarly transferred.[5] [6] It is noteworthy that Wyatt and Cohen[7] have shown that the phage D.N.A. is chemically distinct from that of its host, while the work of Knight[8] suggests that, in animal viruses at least, the protein pattern is in part a reflection of the host species. This might be expected, since it appears that phage protein is synthesised partly from the metabolic pool in the bacterial cell.

Levinthal and Fisher[9] have observed what they believe to be incomplete virus particles in cells that were prematurely lysed; and De Mars et al.,[10] making use of the observation by Foster[11] that proflavine prevented the production of complete phage but did not prevent cellular lysis, produced large numbers of these incomplete particles and subjected them to electron-microscopic study. The morphological similarity between these incomplete phage particles and the empty heads of the phage particles produced by Anderson[2] by means of osmotic shock is remarkable. These observations suggest that there must be two processes of intracellular multiplication of phage—one leading to the production of the protein shell, and the other to the replication of phage D.N.A. Dounce[12] has lately suggested that D.N.A. may not only be responsible for self-replication but may also form a template for protein synthesis.

The increasing use of phage for the study of genetic problems is reflected by the number of papers on phage in the recent Cold Spring Harbor symposium[13]; and it seems that, because of the ease with which it is manipulated and the rapidity of its multiplication, it may become as important a tool as drosophila in the study of genetic problems. Since the initial observation on phage mating by Delbruck and Bailey[14] a mass of data has been accumulated. To this Adams[15] has added information on heat-resistant phage mutants, and Luria and Human[16] on host-induced mutants. On the technical side the observations of Bresch[17] on the use of dyes to differentiate plaque-type mutants may prove very useful. Unfortunately all these observations are unlikely to be fully explained until the exact mechanism of phage multiplication is fully elucidated. Meanwhile, however, Visconti[18] has put forward a new theory of phage genetics that covers most of the observed facts.

As regards lysogenicity Bertani[19] has observed that mutual exclusion, which is a feature of lytic phages, also occurs with the prophage forms; and he believes that his results can be most readily explained by assuming that prophages form an integral part of the genetic structure of the host-cell and are transmitted at each cell division. Wollman[20] also believes that the prophages are genetically linked; but he suggests that prophage may be a form of cytoplasmic inheritance. In this connection it should be borne in mind that Zinder and Lederberg[21] have transmitted genetic characters from one cell to another by means of bacteriophages.

In considering work on phages it is well to remember that these organisms are probably of much greater value for the study of individual problems of virus multiplication and genetics than as models on which to base generalisations about the behaviour of viruses as a class.

"Natural Childbirth"

There are two ways of investigating attitudes—by tabulating the answers of thousands of people to a few questions, or by making detailed inquiries into the views of a few. By this second method Freedman et al.[22] at Yale, have found that the recent memory of twenty mothers for the events of labour was much the same as that of their attendants;

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1. *Ann. Inst. Pasteur*, 1953, 84, 1.
2. Anderson, T. F., Rappaport, C., Muscatine, N. A. *Ibid*, p. 5.
3. Puck, T. T., Garen, A., Cline, J. *J. exp. Med.* 1951, 94, 177.
4. Hershey, A. D., Chase, M. *J. gen. Physiol.* 1952, 36, 39.
5. Graham, A. F. *Ann. Inst. Pasteur.* 1953, 84, 90.
6. Hershey, A. D. *Ibid*, p. 99.
7. Wyatt, G. R., Cohen, S. S. *Ibid*, p. 143.
8. Knight, C. A. *J. exp. Med.* 1946, 83, 281.
9. Levinthal, C., Fisher, H. *Biochim. biophys. Acta*, 1952, 9, 597.
10. De Mars, R. I., Luria, S. E., Fisher, H., Levinthal, C. *Ann. Inst. Pasteur*, 1953, 84, 113.
11. Foster, R. A. C. *J. Bact.* 1948, 56, 795.
12. Dounce, A. L. *Enzymologia*, 1952, 15, 251.
13. *Cold Spr. Harb. Symp. quant. Biol.* 1951, 16.
14. Delbruck, M., Bailey, W. T. *Ibid*, 1946, 11, 67.
15. Adams, M. H. *Ann. Inst. Pasteur*, 1953, 84, 164.
16. Luria, S. E., Human, M. L. *J. Bact.* 1952, 64, 557.
17. Bresch, C. *Ann. Inst. Pasteur*, 1953, 84, 157.
18. Visconti, N. *Ibid*, p. 180.
19. Bertani, G. *Ibid*, p. 273.
20. Wollman, E. *Ibid*, p. 281.
21. Zinder, N. D., Lederberg, J. *J. Bact.* 1952, 64, 679.
22. Freedman, L. Z., Redlich, F. C., Eron L. D., Jackson, E. B. *Psychosom Med.* 1952, 14, 431.

capacities In the absence of a spirometer a useful indication was the amount the patient could count in one breath

When the patient was in the respirator the aim was to give as normal a respiration as possible, and useful figures to remember were a negative pressure of 15 mm H_2O and a rate of 15 per minute The rate must, however, be modified according to the age of the patient and the degree of pyrexia

Necropsy in these cases nearly always showed a collapse of the lowermost parts, and emphysema or frothy œdema of the uppermost parts, of the lung Changes of posture were therefore very desirable If atelectasis occurred the patient should be put in the prone head-down position and positive pressure used Positive pressure was not uncomfortable provided that the negative pressure was correspondingly reduced to give the same total difference, it was useful in promoting cough, in helping to expel secretion, and in aiding venous return to the heart During the acute phase it was frequently necessary to use a resuscitator while the cabinet was open for nursing

Recording Muscle-power

Mr Donal Brooks said that by 1917 *Lovett*, at Harvard, had devised a system of grading muscle-power which differed only in detail from that proposed by the Medical Research Council in 1943 The M R C grading had many advantages it was simple, it required no apparatus or assistance and it had criteria that were reasonably clear cut, it was surprisingly accurate He thought that its widespread adoption by all concerned with poliomyelitis would prove most valuable Mechanical methods of testing, such as the spring-balance and the strain gauge dynamometer, had little advantage, since the high degree of accuracy required made them exacting to use, and only revealed the "scatter" of variation *normally absorbed* by the "elasticity" of the M R C grading They might perhaps be used for comparing the results of different treatments, but any significant recovery of voluntary power should be readily discernible by the simpler methods

Mr Brooks showed a muscle chart devised for use in poliomyelitis, the muscles were grouped according to their function and not according to their nerve-supply, and in addition there was space for recording the power of a particular movement—e g, flexion of the elbow—so that useful trick movement could receive the recognition it deserved

Resistance to Stretch

Mr George Mitchell showed a film on muscle spasm in support of his contention that painful resistance to stretch of the muscles in poliomyelitis is mainly due to root traction

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SYMPOSIUM ON HUMAN PERFORMANCE

Human performance—one's own or somebody else's—is of interest to practically everyone In one respect, therefore, those who have something to say about it are batting on a safe wicket On the other hand, in so vast a field one must either say little about much or much about little On the whole, the Ergonomics Research Society's symposium at Oxford on April 13-16 tended to deal with particular findings techniques and apparatus, fundamental scientific questions would have been out of place in a gathering of physiologists psychologists, work study engineers, and industrial consultants

The proper function of meetings is catalytic and facilitatory rather than informative, and this "convention" undoubtedly fulfilled its purpose In this connection Prof W E Le Gros Clark F R S, spoke of the valuable stimulus to a university department from contact with applied work, and also the need for the "applied worker" (in this term usage prevails over grammar) to be allowed to give perhaps half his time to fundamental questions

POSTURE

Sir Charles Lovatt Evans, F R S, *in the opening* session, expressed a similar viewpoint in reminding the audience that all science is one He went on to give a brief conspectus of the history of muscle physiology His comment on "so called neuritis" as being probably due to incorrect posture may be associated with the observations, later in the meeting, by Miss Gerda Seiderlin (Copenhagen) on the treatment of aches and pains by muscular re education She insisted that one must go and watch the patient at work (or sometimes at play) Only thus can one detect the habit of posture or movement that is responsible and perceive how to alter it Treatment by rest and by training other muscles does not prevent the patient relapsing into his old habit at work—because, of course, he knows no other He must, in Miss Seiderlin's view, be trained in a better manner of working The principle is not new, and is often impracticable, like so much of common sense, but it deserves to be stated again and again for, like our patients, we are creatures of habit

ENERGETICS

M J Karvonen (Helsinki) recounted some observations on competitors in Finnish lumberjacks' competitions, the finalists are the élite of some 200,000 worker Those who do best are long-bodied and short legged, and—to avoid the jargon-word "correlation"—the bigger they are the better Apparently they do not have to perform those feats of agility that we associate with the Canadian lumberjack "clearing the log jam" Over a third of both the high calorie intake (5460) and the water (4200 g) was consumed at the main meal after work (Metric-Imperial disputants may note the use of grammes as fluid measure)

E H Christensen (Stockholm) argued that the pulse rate is a valuable indication of the physiological load in as much as it signals the stress due, for example, to a hot environment such as a steelworks J G Durnin and his co-workers concluded from their observations on miners in Scotland that this work was, on the whole only "moderately heavy" (i e, 1–1 5 litres of oxygen consumed per minute)

INFORMATION THEORY

W D Garvey (Washington) deduced, from experiments on the coding of stimuli and responses in certain tasks, that it was preferable to arrange that the stimulus response relations could be grasped in terms of spatial rather than verbal dimensions Qualitatively, it is obvious that having to perform some verbal operation such as counting in order to decide on the correct response is a slow business, the importance of the result lies rather in their quantitative aspects E R Crossman presented evidence supporting and extending the now fairly well established law of proportionality between time and reduction of entropy in tasks involving choice (Entropy is a mathematical measure of uncertainty about or disorder in, the material, formally similar to the entropy of physics) The essential feature of the approach is the measurement of "selective power"—i e rate of doing selective work—which is a general criterion of psychological performance, just as horse power (rate of doing physical work) is a general criterion of prime movers However as W E Hick emphasised each can act only as an aid to thought and an indication of fundamental limits Specific supplementary criteria will always be needed for particular cases thrombin; and (3) formation of fibrin. Recent research has tried to analyse these fundamental reactions, especially the first one; and a series of papers from Macfarlane and Biggs and their colleagues at Oxford shows how this can be done, and how ideas on the function of the various factors have been reorientated.

In these experiments the clotting-time of a fibrinogen solution was used as a means of testing the various reactions; and Macfarlane and Biggs[35] used it first to study thrombin generation. A standard commercial preparation of thrombin was diluted and added to the fibrinogen solution, and the clotting-times were recorded: the clotting-time was inversely proportional to the thrombin present. Some fresh venous blood was then put into a glass tube, and small samples were withdrawn at regular intervals until after the blood had clotted. The samples were added to a fibrinogen test solution, and from the clotting-times of the test solution the rate of thrombin generation could be studied. There was a latent period of 2–4 minutes before any thrombin appeared; thrombin generation then reached a peak about 7 minutes after the blood had been drawn, and ceased completely after about 14 minutes. This pattern suggests that an intrinsic thromboplastin is generated suddenly as a result of a slow reaction initiated by surface contact. When thromboplastin—in the form of dried brain—was added to the blood, the latent period was abolished, but the rate of thrombin generation was unchanged. The amount of thrombin formed was proportional to the number of platelets; when these were few—below 20,000 per c.mm.—thrombin formation was much diminished, but the latent period was the same. The latent period was found to depend on the presence of antihæmophilic globulin—the congenital absence of which produces clinical hæmophilia. This finding was put to practical use by Pitney and Dacie,[36] who used citrated plasma, which was recalcified and then used as a means of following thrombin generation in the fibrinogen test solution. They obtained similar thrombin-generation curves, except that with normal plasma the latent period before thrombin appeared lasted for from a few seconds up to 90 seconds. With hæmophilic plasma the latent period in 8 cases was from $2\frac{1}{2}$ to $5\frac{1}{2}$ minutes, and the whole pattern of thrombin generation was grossly distorted. By studying the changes that treatment produced in the latent period and in the thrombin generation curves, they were able to assess the effectiveness of treatment. They found that a transfusion of 600 ml. of 4-hour-old plasma failed to correct the abnormalities completely, even though the whole-blood clotting-time was restored to normal. Similarly, it was difficult to correct the defects with fibrinogen fraction containing antihæmophilic globulin. Using this technique, Pitney and Dacey found that antihæmophilic globulin did not deteriorate significantly in blood stored at 4°C for 1 day, but in 10 days the activity was reduced to 50%.

Biggs and Douglas[37] have used a similar technique in an attempt to make accurate estimates of the prothrombin content of blood. It is now agreed that Quick's one-stage "prothrombin-time" does not measure prothrombin alone; the results are influenced by "accelerator factors," known as factor v and factor vii. Factor v (labile factor, plasma accelerator globulin) is a protein found in the globulin fraction of *plasma*; and it is not adsorbed by inorganic precipitates such as aluminium hydroxide. Congenital deficiency of factor v is known, and deficiency can develop in liver disease or in infection. Factor vii[38] is a protein in the globulin fraction of *serum*; and it is adsorbed by alumina. Its importance lies in the fact that anticoagulants such as dicoumarol and 'Tromexan' (ethyl biscoumacetate) are now believed to act, not by depressing prothrombin, but by depressing factor vii; and further evidence supporting this view is given by Professor Hunter and Dr. Tudhope on an earlier page of this issue. Plasma adsorbed with alumina contains factor v, but not prothrombin or factor vii; on the other hand, normal serum after complete clotting contains little factor v or prothrombin, but does contain factor vii. Consequently the one-stage clotting-time of a plasma deficient in factor v will be shortened by the addition of alumina-adsorbed plasma. If it is deficient in factor vii, the addition of normal serum will have this effect but alumina-adsorbed plasma will not; and plasma deficient in prothrombin will still have a prolonged clotting-time with both reagents. There is no doubt that in many of the cases reported as idiopathic or congenital hypoprothrombinæmia the accelerator factors were also involved. Biggs and Douglas were fortunate in being able to study a case of pure prothrombin deficiency in a man of 26 who had had hæmorrhagic symptoms for 15 months. They adapted the thrombin-generation test to the estimation of prothrombin by carrying out the usual Quick one-stage plasma clotting-time and then following the generation of thrombin in the clotting mixture up to and after the time when the clot formed. They plotted the results as a graph of thrombin units against time, and showed that the prothrombin content of the blood could be estimated by determining the area enclosed by this graph. Their patient proved to have only 11% of normal prothrombin activity, but factors v and vii were not deficient. By this technique, a patient under effective anticoagulant control with tromexan—as judged by the Quick "prothrombin time"—was found to have 68% of normal prothrombin activity. This emphasises the fact that, as Biggs and Douglas point out, this method of prothrombin estimation is no use in the control of anticoagulants. The usual one-stage clotting test, which measures factor-vii deficiency, is still the correct one to use, and Hunter and Tudhope's results confirm that it is suitable for routine use.

The next step was taken in an effort to find out more about the defect in hæmophilia. It is now known that in hæmophilia a factor essential for the development of thromboplastin is absent. Quick called this factor "thromboplastinogen," and it is also known as antihæmophilic globulin. Biggs and Douglas[39] therefore set out to reinvestigate the formation of thromboplastin. While doing so they and their colleagues[40] investigated a disease to which Poole[41]

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35. Macfarlane, R. G., Biggs, R. *J. clin. Path.* 1953, 6, 3.
36. Pitney, W. R., Dacie, J. V. *Ibid*, p. 9.
37. Biggs, R., Douglas, A. S. *Ibid*, p. 15.
38. Koller, F., Loeliger, A., Duckert, F. *Acta haemat.* 1951, 6, 1
39. Biggs, R., Douglas, A. S. *J. clin. Path.* 1953, 6, 23.
40. Biggs, R., Douglas, A. S., Macfarlane, R. G., Dacie, J. V., Pitney, W. R., Merskey, C., O'Brien, J. R. *Brit. med. J.* 1952, ii, 1378.
41. Poole, J. C. F. *Lancet*, Jan. 17, 1953, p. 122.

East and Central Africa the fever is commonly carried by the tick, *Ornithodorous moubata,* but on this occasion in the Gold Coast it was conclusively proved to be transmitted by the body-louse The acting director of medical research, Alexander Ingram, kept three or four lice, which I gave him from one of my many relapsing-fever patients, in a watch-glass fixed on to his wrist by adhesive plaster In his sleep the irritation must have been so intense that he scratched a louse, or its infected excreta, into his skin He went down with an alarming attack of fever, and his blood smears swarmed with *Spirochæta recurrentis* Fortunately, as is usual with this disease, he reacted rapidly to intravenous injections of neoarsphenamine In my experience (limited, it is true, to treating a large number of Zaberrima tribesmen) relapses were unusual after doses of 0 3, 0 45, and 0 6 g on the first, fourth, and seventh day of treatment, provided one was careful to counteract the collapse which often accompanied the startling fall in temperature from, say, 105° to 96°F within twenty-four hours

In 1924 bubonic plague broke out in West Africa Many cases had been reported earlier from the French Senegal, where Dakar is one of the chief ports for the export of ground-nuts—and nuts attract rats It was never definitely established how the infection came to the Gold Coast, but it may have come by car A car belonging to the newly appointed town engineer of Kumasi, the capital of Ashanti, had been mistakenly carried on (like the lady bound for Birmingham) to Lagos in Nigeria Here, the ship had been berthed alongside the wharf. Rat guards on mooring-ropes are notoriously inefficient, and a plague infected rat or two may have got aboard On the return journey the car was disembarked in the Gold Coast and sent up by rail to Kumasi Its performance was not all that had been expected, and on investigation a rat's nest was found under the bonnet Some of the material from which it had been made obviously came from a ship The first people to go down with plague in Kumasi were labourers employed in unloading goods trains at the siding where the car had arrived

Most patients had the bubonic type of plague which itself carried a high enough mortality, but there were also a number with the pneumonic type, which was almost always fatal within forty eight hours of onset I had only one patient who recovered from a plague pneumonia He had large axillary and inguinal buboes, and a typical pneumonia with *Pasteurella pestis* in his bright bloodstained sputum By all accounts, he should have died Instead, I lost my senior male nurse, who was usually very careful with his mask, gum boots, and so on

As in many other plague areas, the black rat (*Rattus rattus*) was the main carrier, although the brown rat (*Rattus norvegicus*) and the pouched rat (*Cricetomys gambianus*) were minor carriers *Xenopsylla cheopis* and *X astia* were the fleas usually found on these rats but, curiously enough, the human plague victims were usually lousy and not flea infested

Malaya

In 1930, I left West Africa and spent the next year or so as chief health officer in the Federated Malay States Here malaria was one of the main causes of ill health On the coast the malarial parasite was carried by *A sundaicus* or *A ludlowi* which can breed in brackish water Further inland, *A umbrosus,* which prefers the shaded water of the plains, was the vector *A maculatus* was the chief enemy in the foothills and along the mountain range, where it bred in fresh clear streams, or in drains or seepages of clean water, exposed to sunlight Recalling the ubiquitous breeding of *A gambiæ* and *A funestus* in West Africa, I should say that these mosquitoes were a slightly greater menace in Africa than, say, *A maculatus* was in Malaya in those days

I came across two types of typhus in the early '30s —the louse borne variety, often in Bengali cowmen, and the scrub variety, carried by the Kedani mite (*Trombicula akamushi*), affecting especially labourers working on red-palm nut estates where rats abound The mite is carried by the rat and gets on the legs of those walking through grass

Two interesting conditions seen in Malaya are probably forms of psychomotor hysteria In latah, the sufferer feels obliged to copy any and every action of his companions For example, a boat is being poled up a river and it is clear that one of the crew is going to have an attack An unkind companion attracts his attention, and pretends to dive in The victim promptly plunges into the water—a cruel trick, for the rivers are usually very shallow and muddy

The second form has been made familiar by the expression "running amok"

One sultry evening several years ago, a Straits steamship, the S S *Klang,* was about to leave Singapore on what was to be the last trip of its master before he retired after many years of honourable service A Malay passenger, who before coming aboard had met with a series of annoyances (pigs had got into his garden, his wife had "made eyes" at his neighbour, and so on), had made a bargain with one of the crew earlier in the day to hire the man's bunk for the voyage When he went below to take possession of it, he found already occupied by another passenger who had given a bigger bribe and who refused to be dislodged The worried and disappointed Malay whipped out his parang and slashed his unfortunate fellow passenger He then went in search of the deck hand who had tricked him In a moment there was an uproar, and crew and passengers flew in all directions, down companion ways and up the rigging, but twelve were not quick enough and were cut down

Hearing the noise, the captain and chief officer went below to investigate As the captain went towards the Malay to persuade him to give up his weapon, he was slashed in the stomach The chief officer then threw a marline spike at the Malay, knocking him into the scuppers When the police came aboard the captain lay dying, the chief engineer and eleven others were dead, and the Malay lay wounded in the head

Hong-Kong

In the early spring of 1938 I landed in Hong Kong The Japanese had attacked China in 1931 and had seized the five Northern Provinces in July, 1937 Refugees were seeking sanctuary in Hong Kong in considerable numbers I had been asked to go there as director of medical services by the then Governor, under whom I had served in West Africa

Within seven months of my arrival in Hong Kong the Japanese had ranged south, landed in Bias Bay, and captured Canton Their flags were soon flying on the hills bordering the Colony's Leased Territories, and they remained there until the morning of Dec 8, 1941, when they attacked us After eighteen days' bombing and shelling they captured Hong Kong

The three years before the attack were spent in organising civil medical defence and in dealing with the difficulties caused by the influx of refugees from China In 1937, the population of the Colony was rather over 800,000, by 1940 it had risen to about 1,750,000 By the time the Japanese attacked, the population had been reduced by repatriations to just over 1,600,000 During the occupation it fell by forcible repatriation, executions, and deaths from starvation to less than 600,000 at the time of the liberation on Aug 31, 1945

When I arrived in 1938 the wards of the Chinese hospitals were full of sick and injured two or more to a bed, many more were on the floor between beds and even under beds, and verandahs and corridors were crowded It took some time to bring order and cleanliness out of this chaos Step by step, the Chinese director view. It is now very clear that the autonomic nervous system, as we understand it, has a very minor rôle in the maintenance of resting blood-pressure, and that this system is not disordered in essential hypertension. Furthermore any benefit from sympathectomy is not closely related to the extent of the sympathetic-nerve section. Although sympathectomy in a rather capricious way sometimes benefits hypertension, there is no agreed explanation of the mechanism.

Blood-pressure in hypertension can be consistently and substantially reduced by a diet low in calories and with an extremely small sodium content (less than 100 m.eq. per day)—for example, the Kempner rice/fruit diet. Unfortunately, indefinite adherence to such a diet is only possible for obsessional patients with a substantial masochistic trait. The prevention of sodium absorption from the alimentary tract by ion-exchange resins, though practicable in the metabolic ward with extensive and skilled biochemical control, is very difficult—indeed dangerous—in routine practice. Many drugs will lower blood-pressure in hypertension. Prominent among these are the polymethylene bis-trimethyl-ammonium compounds, discovered by Paton and Zaimis,[49] which block autonomic ganglia. Hexamethonium bromide is the most popular of this group, and a great deal is now known of its potentialities. Administration by mouth is of little value, since absorption varies and tolerance is rapidly acquired. Injection treatment, however, reduces blood-pressure satisfactorily in a large proportion of hypertensive patients. Unfortunately, they may have very uncomfortable toxic side-effects, such as postural hypotension and gastro-intestinal disturbances. Thus, the use of this drug calls for attentive medical care and intelligent coöperation by the patient, and its use is advisable in only a small proportion of patients; its principal place is in the treatment of the malignant phase. 'Apresoline' (1-hydrazinophthalazine), a comparative newcomer to this field,[50 51] is believed to act by opposing humoral pressor substances such as hypertensin. Riven et al.[50] report results of treatment in 65 hypertensive patients. In the majority the pressure was substantially lowered. They conclude that apresoline is effective in the short-term control of blood-pressure in certain cases of essential hypertension and malignant hypertension, but is useless in renal hypertension. Fully half the patients had unpleasant side-effects, and 10 of the 65 had to discontinue taking the substance. As regards the drug control of hypertension, there is still no agent substantially superior to hexamethonium, with all its limitations.

The latest therapeutic essay consists in subtotal adrenalectomy.[52] From the purely theoretical aspect this has much to commend it; for a large body of physiological data points to the homeostatic rôle of the adrenal cortex in maintaining blood-pressure. Indeed, as physiological knowledge stands at present, adrenalectomy has a far more solid rationale than sympathectomy. Nevertheless, while bilateral adrenalectomy may lead to a better understanding of the origin of hypertension, it is only practicable when cortisone is available to tide the patient over any crisis of hypoadrenalism. Perhaps the hazards of thyroidectomy seemed no less formidable to the clinicians of a previous generation.

Although the immediate prospects of helping the hypertensive patient are poor, the future is full of promise. Meanwhile, the kindest thing to do when one discovers a patient with hypertension but no symptoms is to keep the information to oneself.

GOOD SENSE ABOUT ANTIBIOTICS

THE United Bristol Hospitals have recently produced an excellent booklet of fourteen pages[1] which offers a practical guide to the use of sulphonamides and antibiotics. Members of the teaching staff of the University of Bristol contributed the information, which was arranged to meet the needs of housemen; but the publication contains much of value to a wider audience. Its declared object is to explain the general principles and give enough detailed information to enable a rational plan of treatment to be formulated for individual patients, and to prevent the disappointments and even dangers of starting a line of treatment which has little prospect of success and may interfere with correct treatment later on.

If harm will not result from delay, chemotherapy should await identification of the causal organism and determination of its sensitivity; if necessary the bacteriologist should be brought into consultation. If the patient's condition is so serious that instant treatment is essential, specimens should be taken for laboratory examination before any drug is given, and the essentials of the case should be reported to the person who will examine the specimens. Adequate laboratory examination is a necessary part of properly planned treatment, and clinicians who keep up a close personal relation with the bacteriologist know how much he can contribute if he is given enough information to direct his work to the situation in each case. Conversely, those who treat the laboratory as an automatic machine are likely to find that its response is seriously impaired by their own defective understanding of its methods and functions.

The causal organism and its sensitivity do not alone determine which antibiotic should be used; for there are also questions of toxicity, development of resistance, ease of administration, and cost. Streptomycin, the most toxic of the antibiotics in common use, may cause deafness and vestibular disturbance. For this reason, and because it quickly induces resistance among organisms, it should not be chosen casually if a less toxic drug will serve. In tuberculosis, of course, streptomycin has a special place. Sulphonamides should not be forgotten. Against many infections they are extremely effective, and the newer preparations show very little toxicity if administered with enough fluid to prevent crystalluria. We have still relatively little experience of chloramphenicol, aureomycin, and terramycin, and for that reason have not reached stable perspectives about these drugs. Clearly chloramphenicol has a special place in the treatment of typhoid and rickettsial infections; but it is too early to evaluate fully the risk of aplastic anæmia which is associated with chloramphenicol,[2] and of moniliasis,[3] intestinal dysfunction,[4] and untoward effects on the liver which have all been reported as complications during treatment with the newer antibiotics. Despite occasional reports of sensitivity to penicillin this drug remains the safest of all.

Organisms originally sensitive to a drug may quickly become resistant during treatment; but group-A hæmolytic streptococci and pneumococci do not become resistant to penicillin, whereas staphylococci, especially those found in hospitals, may be resistant to penicillin even before treatment is begun. Gram-negative bacilli are generally insensitive to penicillin. Penicillin and streptomycin must be injected, whereas the other substances are normally given by mouth; chloramphenicol is not suitable for intravenous, intramuscular, or intrathecal injection. Penicillin and the sulphonamides are substantially cheaper than the other antibiotics, and this should be remembered in view of the high cost of private enterprise must play a progressively bigger part and proportionately relieve the Exchequer

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[49] Paton, W. D. M., Zaimis, E. J. *Nature, Lond.* 1948, 162, 810.
[50] Riven, S. S., Pocock, D. G., Kory, R. C., Roehm, D. C., Anderson, R. S., Meneely, G. R. *Amer. J. Med.* 1953, 14, 160.
[51] Hafkenschiel, J. H., Lindauer, M. A. *Circulation*, 1953, 7, 52.
[52] Zimtel, H. A., Wolferch, C. C., Jessers, W. A., Hafkenschiel, J. H., Lukens, S. W. D. *Ann. Surg.* 1951, 134, 351.

[1] A Practical Guide to the Use of Sulphonamides and Antibiotics.
[2] See *Lancet*, 1952, ii, 122, 377.
[3] Taylor, H., Rundle, J. A. *Ibid*, i, 1236. Wolff, F. W. *Ibid*. Annotation. *Ibid*, p. 1247.
[4] See *Ibid*, p. 352.

Turning to the N H S , he said that here the problems were so complex that the Government had sought the assistance of a committee He failed to see why it should be called political cowardice for those who intended to maintain the health service to have it impartially examined, so that those who paid for it, whether political or non-political persons, should get value for money spent

In the course of the debate Mr **Ralph Assheton** declared that in two budgets the Chancellor had proved that the Tories were not out to destroy the Welfare State What they wanted was to make it solvent, and to earn enough money to pay for it and continue the policy of letting the strong help the weak He submitted that we must find ways of doing that, so that the more capable citizens were not crippled in order to benefit those who were less worthy or less industrious

The review of the health service was timely He felt that more financial responsibility might be placed on the hospital boards and that there should be less effort spent in the minute control of expenditure from Whitehall

LESS ON LESS

Mr **Arthur Blenkinsop** pointed out that there was a slight reduction of £20 million in the health service estimates compared with last year, but he agreed that this was largely accounted for by the exceptional expenditure last year on back payments under the Danckwerts award In practice that meant that about the same amount of money was available for the health service as last year It was, however, misleading for the Chancellor to suggest as he did that further increased expenditure was to be made possible The increase of £18 million was only an increase over the estimates of last year and not over the actual expenditure In fact the amount of money available would be about the same

This meant, Mr Blenkinsop declared, that in terms of service much less would be provided for the same money, because £6½–7 million extra would be needed to cover wage and salary advances to hospital staff which had been negotiated during the last twelve months That sum would have to be taken from the money available to the hospital part of the service There would also be a considerable increase in hospital food bills All these increases, he affirmed, could only result in reduced quality of service, unless we had an increase in the now quite artificial ceiling which had been maintained in the N H S for the past four years

In examining the estimates of the health service he found astonishing facts about the reductions secured over last year There was, for instance, a considerable drop in the medical staff, particularly in teaching hospitals This might be partly due to some of the senior registrars going out of the service Despite what had been said about the need for reduction of administrative costs, the estimates showed considerable extra provision for the administrative staff of the N H S Mr **Roland Jennings** interjected that Mr Blenkinsop seemed to be making out a good case for the proposed inquiry into the service But with this Mr **Blenkinsop** did not agree The facts were well known, and no further inquiry was needed It was for the House of Commons to tackle the matter

Continuing his analysis of the estimates he pointed out that for the maintenance of buildings and plant only £8½ million were provided compared with the wholly inadequate £9½ million provided last year All over the country people responsible for the maintenance of hospital buildings were seriously perturbed If we did not carry out maintenance work—such as painting, repairs of plant, heating appliances, and boilers—we should be faced with heavier bills in the future unless we were prepared to close whole sections of our hospitals

Mr **Aneurin Bevan** said that he would support an investigation into the structure of the N H S but asked why the Minister of Health had not been doing it He had plenty of machinery why had he not used it? Mr Bevan alleged that the Conservatives were seeking to undermine the structure of the service, by creating the impression that its finances were extravagant and out of hand, and that some means must be found to bring them under control But in fact, he asserted, if all the charges on the N H S were abolished, and if the whole of the Danckwerts award was set against the expenditure made on the service, the expenditure in 1952–53 would still be a smaller proportion of the national income than it was in 1950 If the Chancellor had any reliefs to offer, had not the aged and sick first claim ?

VALUE FOR MONEY

Mr **Butler**, in his reply to the debate, quoted President Eisenhower's words "The monuments to this new kind of war should be roads and schools hospitals and homes, food and health" That this was precisely the aim also of our Government was, he suggested, borne out by the estimates for education (up by £26 8 million), homes (up by £8 9 million), assistance (up by £24 4 million) He reminded his listeners that the old age pensions had been raised by this Government, and that since October, 1951, assistance scales had been increased by 16 % for a single person and 18 % for a married couple, while the index of retail prices had risen only by 7½ % He admitted that the cost of food in the same period had risen by 15 %, but that was still not as great as the rise in the assistance scales

Turning to the health service he recalled Mr Bevan's comparison, in his resignation speech, of the fate of the health service under the Tories to that of Lavinia, the heroine of *Titus Andronicus* "The Health Service will be like Lavinia—all the limbs cut off and eventually her tongue cut out, too" Mr **Bevan** interposed that taking discussion of the N H S out of the House of Commons and handing it over to a committee was the modern form of taking out the tongue But Mr **Butler** asserted that the committee was appointed to get value for money The committee had been given no total of expenditure to which they had to work but an open remit to report on the health service Mr **Marquand** asked why, then, the terms of reference said they must avoid a rising charge Mr **Butler** went on to say that members of the committee had been chosen with a particular regard to avoid politics If this could be called removing a child which Mr Bevan regarded as his own from his care, Mr Butler believed that the public in general would be delighted to see this particular child boarded out with a respectable committee

Compensation for Partially Disabled Workers

In the House of Commons on April 17, Mr T W **Jones** drew attention to the inadequate rates of compensation payable to the partially disabled under the Workmen's Compensation Acts In his reply, Mr R H **Turton**, parliamentary secretary to the Ministry of National Insurance, announced that the Minister had proposed a scheme to the National Insurance Advisory Committee to remove existing restrictions which prevented a married man on workmen's compensation from drawing his full sickness benefit In what the Ministry regarded as the hardest cases the new proposals would mean a supplementation of 10s a week in some cases and 15s in others for the totally disabled The committee had approved the suggestion, and draft regulations would be introduced

QUESTION TIME

Nursing Services

Replying in the House of Lords on April 16 to Lord Crook, Lord **Woolton**, Chancellor of the Duchy of Lancaster, said that on Dec 31, 1952 there were 47,673 full time nurses and 8381 part time nurses employed in hospitals in England and Wales (including Ministry of Pensions hospitals and those outside the N H S) There were 30 475 student nurses in training Local health authorities employed 6736 full time trained nurses 11 468 part time trained nurses 7723 full time other nurses (including nursery nurses) and [illegible] part-time other nurses Approximately 1700 nurses were findings reported by the different surgeons ranged from 18 to 85%. Minor abnormalities were recorded in from 3 to 45%, and major changes, such as œdema, granulation, or ulceration, in from 0 to 50%. The surgeon who reported the least abnormals (17 out of 91) found no gross changes in any patient; the one reporting the most abnormals (29 out of 34) found major changes in 50%. The prevalence of clinical and radiographic appearances believed to suggest bronchial lesions varied from 7 to 40% at the different hospitals. There were, therefore, wide differences in both clinical and bronchoscopic diagnoses; but there was no clear relationship between the two. Thus, at one hospital 7% were judged to have clinical evidence of bronchial disease and 50% bronchoscopic evidence, compared with 40% and 33% at another hospital. The groups may not have been comparable—it is impossible to judge from the data in the report—but it seems unlikely that the wide differences in bronchoscopic reports were entirely due to differences in the types of patients examined.

Some time ago we suggested that an apparently normal mucosa at bronchoscopy may not exclude gross bronchial disease.[2] In the British Tuberculosis Association investigation 95 patients had a pneumonectomy or lobectomy, and the bronchus at the point of section was examined microscopically. Of the 95, 56 had been reported to have no bronchoscopic abnormality; in only 2 of these 56 was there no microscopic evidence of tuberculosis, while in 32 (57%) there were epithelioid tubercles or a severe inflammatory reaction with tuberculous granulation tissue, ulceration of the mucosa, and fibrosis. Abnormal bronchoscopic appearances had been reported in 39; no microscopic evidence of bronchial tuberculosis was found in 2 and only minor changes in 10 (25%).

It seems that the bronchoscopic report can sometimes give the physician a very inaccurate indication of the state of the bronchi; for there may be great differences not only between the interpretation by different observers of what they see, but also between their reports and the microscopic appearances.

POSTOPERATIVE METABOLIC CHANGES

An operation, like any other injury, produces a characteristic metabolic disturbance. Twenty years ago Cuthbertson[3] described the brisk katabolic phase which after a few days changes rather abruptly to a less intense but longer period of anabolism. Moore,[4] who has studied the matter intensively, has summarised present knowledge. He believes the early katabolism to be due to adrenal hormones and points out that its cessation is marked by features (diuresis and transient eosinophilia) that are also observed on withdrawal of administered cortisone. It is at this stage, too, that wound healing begins in earnest. Moore finds that it takes about a month to rebuild the protein squandered in the katabolic spree, and another month to restore lost fat. This pattern is of course often disturbed by specific effects of particular diseases or operations.

Is all this metabolic to-do necessary? Apparently not, for if a second operation has to be performed within a few days of the first, the katabolic response is absent and yet recovery may be unimpaired. Moore believes that this response is homœostatic, and that the protein breakdown mobilises amino-acids for wound repair. This seems odd, if repair does not get under way until the katabolic phase is over. A clean operation under anæsthesia is such an artificial circumstance that the body's response may not be optimal. The same response, or something very like it, occurs as part of the general illness of inflammation, and its teleological significance should perhaps be sought there.

CATCHING UP WITH THE CLOCK

There are many physiological diurnal variations; the most familiar is the cycle of sleep and wakefulness, and associated with it are the rhythms of body-temperature, metabolic rate, and heart-rate, the fluctuations in the composition of the blood and in renal function, and many other changes.[1–3] Kleitman, who has been one of the most prominent investigators of these changes, has proposed that diurnal rhythms should be distinguished from periodicity by their persistence when, for example, the cycle of sleep and wakefulness is changed. A worker who is transferred from a day to a night shift has to face not only alterations in the social pattern of his life but physiological stresses caused by the persistence of the diurnal rhythms. The daily variation in body-temperature is the simplest of these rhythms to study, and there are many data[2] which show that the commonest pattern consists in a gradual rise of temperature during the day, reaching a peak about 6 P.M., followed by a fall, which may be more abrupt, the lowest level usually being reached between 2 A.M. and 4 A.M. The difference between the highest and lowest body-temperature is usually 1·5°–2·0°F, but there is considerable individual variation from day to day in the same person, and from subject to subject, as well as in the pattern of the fluctuation. When work is changed from day to night, the usual diurnal rhythm changes only gradually, so at first the night worker will have a peak of body-temperature during sleep and a low temperature during work. A new rhythm is eventually established so that body-temperature rises during the night and falls in the day, but this change may occupy a week or more. Once again there is considerable individual variation in the time taken; some people have rhythms which adapt rapidly and others slowly. This individual variation may partly account for the ease or difficulty with which different people can change their hours of work.

Strughold[4] has lately examined another situation in which the day-night cycle is altered. In long-distance flights the aircraft's passengers must change their watches with bewildering frequency; and the "physiological cycle," adjusted to day and night in, say, London, may be very much out of step when the journey ends in Tokyo thirty-six hours later. Strughold has followed (though not in great detail) the diurnal temperature rhythm before, during, and after flights between London and New York, when there is a time shift of five hours. The body-temperature rhythm is out of phase at first, but within a few days the peak is once more reached in the afternoon, with the lowest readings at night. The time taken for this physiological adjustment is probably very variable, but more observations are needed on this point.

Has the fact that the diurnal rhythms are out of step with the day-night cycles any important effect, or is it only of academic interest? The pattern of sleep is disturbed; and the many other rhythms, which have not yet been fully investigated, are also upset. Kleitman has shown, too, that the curve of efficiency in a number of different tasks follows the body-temperature curve. Accuracy and speed of performance increased as the body-temperature rose, and declined when body-temperature fell. There seems, then, to be a good explanation for the traveller's common complaint of fatigue and lack of efficiency in the days following a long-distance flight. Strughold points out that this is certainly not a serious medical problem, but it has its important aspects. Diplomats who fly long distances to attend international conferences may not be as capable as they would normally be, or they may reach their peak of efficiency at the

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[2] *Lancet*, 1951, i, 250.
[3] Cuthbertson, D. P. *Quart. J. Med.* 1932, 1, 233.
[4] Moore, F. D. *Ann. Surg.* 1953, 137, 289.

[1] Kleitman, N. *Physiol. Rev.* 1949, 29, 1.
[2] Kleitman, N. Sleep and Wakefulness. Chicago, 1939.
[3] Mills, J. N. *J. Physiol.* 1951, 113, 528.
[4] Strughold, H. *J. aviat. Med.* 1952, 23, 464.

Care Organisers at their meeting on March 28, when they discussed housing problems of the tuberculous in London

In an opening paper, Dr KENNETH MARSH observed that most of the child contacts of new cases coming to his clinic were already Mantoux positive, and most adolescent contacts showed evidence of healed primary infection He was concerned about the urgent need to teach patients and their families how to live sensibly to minimise the risk of infecting young contacts He emphasised, too, the danger of perpetuating in the new house the unhygienic habits and circumstances of the rehoused family The need to separate careless elderly infective patients from rehoused young and healthy families raised the problem of how to deal with the tuberculous bachelor or widower who could be such a danger lodging in a home where there were young children Dr Marsh said that it was important to avoid rehousing tuberculous workers too far from their workplaces and to discourage rehoused tuberculous families from the temptation to get into debt in refurnishing their new houses

Dr H D CHALKE, an L C C divisional medical officer, described his "points" system used in awarding selective priority to tuberculous rehousing applicants This was based on standardised criteria, which were, in order of "merit," large families, adolescent contacts, infectious cases, shared bedroom, likelihood of prolonged illness, and a real prospect of benefit by rehousing But, he said, a diagnosis of tuberculosis did not, of itself, give automatic advantage in the competition for new houses

Dr VICTOR FREEMAN, medical officer of health for Islington, pointed out that many other sick and disabled persons, apart from the tuberculous, sought and merited priority in rehousing Of the 750 families rehoused by his borough council last year, 6% had been given priority because of tuberculosis 10% of all Islington's accepted family applicants for rehousing were tuberculous, and these 150 applicants were likely to have to wait a considerable time yet before their turn came

Mr J W R PORTER, of the L C C housing department, said that in the past 63 years the L C C had built some 150,000 dwellings housing 500,000 people At present 180,000 families wanted new houses The council regarded 70,000 of these as "most urgent" all sputum-positive tuberculous applicants were in this category Last year the L C C completed 9000 new houses and 700 of these went to tuberculous families It was clear that some time must elapse before even the "most urgent" could be rehoused 5% of newly built accommodation consisted of one-roomed dwellings intended primarily for elderly persons, 15% were two-roomed (i e, 1 bedroom and 1 living room), 40% three roomed, 30% four-roomed, and 10% five roomed It was proposed in future to reduce the proportion of two roomed and of five roomed dwellings The existence of five varieties of house in effect divided the waiting list into five "queues" and explained occasional apparent anomalies in the rehousing of an elderly or young childless couple, needing only two rooms, before a large family, who might have to wait longer for the completion of a four-bedroomed house Tuberculosis commanded more priority points than any other single factor The tuberculous applicant also got special consideration in the allocation of a house which was near to his work, and not too high up in a block of flats The council's system of priorities resulted in 8% of newly allotted houses in any year going to families in which there was active tuberculosis

In discussion, it was said that the L C C has two hostels for ambulant and homeless men with infectious tuberculosis where full board and lodging was provided at charges assessed on each resident's means Some L C C estates outside London now have a prevalence of up to 35 tuberculous persons per 1000 inhabitants—more than three times London's present prevalence Nevertheless it had been established, that the incidence of new cases of tuberculosis on new estates, both inside and outside London, was only one-third or less of what might have been expected from the high comparative prevalence New cases of tuberculosis were rare in rehoused tuberculous families But we cannot yet say whether this is a result of their brighter homes and their new way of life, or the outcome of the heavy attacks already made upon them by the tubercle bacillus

Smallpox

The total of confirmed cases of smallpox in the outbreak in Lancashire and the West Riding had risen to 25 by noon on April 21 There were 2 new cases in the week beginning April 14, and 1 of them, a man aged 61 in Morley, near Leeds, has died, bringing the total of deaths to 6 This man, a claypit worker fell ill on April 13 A rash appeared three days later, and he was admitted to hospital on April 17 He died the same day of hæmorrhagic smallpox An unvaccinated boy of 16, living in Colne Valley, was admitted to hospital on April 15 after six days' illness, now confirmed as semiconfluent smallpox The total does not include a woman in Bury who was admitted to hospital on April 20 with what is in all probability smallpox There is at present no news of the source of infection in the new cases The illness of the Leeds boy, whose death on April 14 we reported last week, has now been confirmed as smallpox

Outbreaks of Communicable Disease in Hospital

In a circular[1] to hospital authorities the Minister of Health reminds hospitals that it is essential to send prompt information to the local medical officer of health on the occurrence not only of a notifiable disease but also of any unusual outbreak of communicable disease, and to give the M O H every opportunity and help in investigating such outbreaks when he considers this to be necessary The circular mentions instances in which outbreaks of, for example, salmonella food poisoning, encephalomyelitis, diphtheria and infantile gastro enteritis came to the notice of the M O H only after considerable delay and by indirect and fortuitous means Quite apart from the question of actual outbreaks, the Minister recommends hospitals to avail themselves of the help the M O H and his staff can give in maintaining the highest standard of hygiene The Minister also urges all hospitals which have not already done so to consider appointing a committee to deal with the control of infection, as recommended in a memorandum prepared by the Standing Nursing Advisory Committee and issued in 1951 The memorandum suggested that a medical officer should be designated by the hospital authority to exercise executive responsibility for the control of infection in hospital and that the M O H of the district should be a member of the committee

Northern Ireland in 1952

The Registrar-General for Northern Ireland reports that the general death rate, the infant-mortality rate and the death-rate from tuberculosis for 1952 were the lowest ever recorded For the first time since records have been kept no deaths were reported from diphtheria The death rate was 10 8 per 1000 population—a decrease of 2 0 compared with 1951 when the death-rate was exceptionally high owing to the severe epidemic of influenza early in the year The death-rate from tuberculosis continued to fall and now stands at 30 per 100,000 population This rate is approximately one third of that of twenty years ago During the same period the infant-mortality rate fell from 83 per 1000 live births to 39 For the past three years the maternal mortality rate has remained unchanged at 1 1 per 1000 live births (which is the lowest rate ever recorded for Northern Ireland), compared with 5 3 per 1000 births in 1932 The elimination of diphtheria seems to be within sight, for only 4 cases were notified during 1952 In 1942 there were 91 deaths and 1100 cases recorded

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[1] R H B (53)40 H M C (53)36 B G (53)39

Special Articles

SYMPOSIUM ON POLIOMYELITIS

A WELL attended symposium on poliomyelitis was held at the Nuffield Orthopædic Centre, Oxford, on March 12.

Prof. J. TRUETA recalled how poliomyelitis first developed severe epidemic proportions at the end of the last century, starting in Scandinavia and then reaching North America whither it was thought by some to have been carried by immigrants. Before that time only small groups of cases had been reported both in Europe and in North America. The first major North American epidemic was in 1907—two years after Sweden had 1200 cases of poliomyelitis with 145 deaths. By 1912 notification of the disease had been made compulsory in 20 of the United States. In 1916 New York State alone had 13,000 cases with a mortality of 27·2% in New York City. Nothing comparable had yet occurred in this country, which did not have its first epidemics until 1947 and 1950; in each of these years 8000 cases occurred in England and Wales. These two recent epidemics, and the severe epidemic last year in Copenhagen with its high proportion of respiratory and bulbar cases, had made it necessary for those responsible for dealing with the disease to plan now for similar large-scale epidemics before they actually occurred.

Professor Trueta recalled that his predecessor in the Oxford chair of orthopædics—the late G. R. Girdlestone—had been one of the first to plan for the severely paralysed victims of the disease. He hoped that Oxford would continue to be a centre of initiative in the fight against poliomyelitis, and that the Oxford region might perhaps take the lead in planning the establishment of quarantine in poliomyelitis.

Poliomyelitis and the Infectious-disease Hospital

Dr. J. B. M. DAVIES, deputy medical officer of health for Oxford, said that poliomyelitis, particularly in the early stages, was extremely infectious; isolation was therefore essential, and this was most easily carried out in infectious-disease hospitals. The present policy of limiting isolation to three weeks was only a "half-loaf" policy, since the excretion of virus in the stools might continue for up to ten weeks; but it more than covered the most dangerous period of a week to ten days when the virus was present in the nasopharynx. Not all infectious-disease hospitals, however, were suitable for the admission of poliomyelitis patients; and certain suitable hospitals should be selected for the admission of these patients. The main objection to this was the distance that patients might have to travel. How far the patient travelled was, however, less important than when he travelled; every effort should be made to obtain admission of these patients when the diagnosis was presumptive rather than in the late stage of spreading paralysis. No practitioner should feel that he ought to await confirmation of the diagnosis before admitting his patient.

Selection of an isolation hospital as a poliomyelitis hospital should be based on "the essential triad" of experienced medical personnel (particularly a resident medical officer and a consultant), experienced nursing personnel based on the ward-sister and the staff nurse, and effective liaison with the orthopædic hospital which would be caring for the patients after the acute stage. In epidemics it would be better to extend the facilities within these selected infectious-disease hospitals, if necessary drafting the staff to work under the experienced staff, rather than to send out trained teams; for these would not only encounter new difficulties but would also be a serious loss to the parent hospital, which was particularly undesirable during an epidemic. Dr. Davies regarded as impracticable the suggestion that special poliomyelitis hospitals should be established since, because of the seasonable incidence of the disease, such hospitals would probably be out of work for two-thirds of the year. The peak poliomyelitis period coincided with the most quiet time for other fevers, and was in fact the most convenient for treating poliomyelitis in the infectious-disease hospital.

Diagnosis and Management

Dr. W. RITCHIE RUSSELL discussed early diagnosis and management. He emphasised the importance of early differentiation between poliomyelitis and the various forms of meningitis, including tuberculous, since these now responded well to chemotherapy. Highly characteristic of poliomyelitis was the association of meningitic symptoms with full consciousness; other suggestive factors were complaints of curious pains and paræsthesiæ in chest, thighs, neck, shoulders, and sacrum, and also fasciculation and retention of urine. Diagnosis could never be certain until lower-motor-neurone paralysis developed; but since physical activity increased paralysis, examination of muscle-power should be limited to 2–3 minutes not more than 2–3 times in the twenty-four hours.

Respiratory impairment or difficulty in swallowing necessitated immediate special care. The mortality-rate from poliomyelitis was nearly 10%; the mortality could probably be reduced by a third or half if there was a proper understanding of the modern principles of keeping the air-passages clear. It was particularly important to distinguish the case with respiratory embarrassment due to mucus in the throat or atelectasis, from one with respiratory paralysis. In the former the use of a respirator often led to disaster; all that was needed was to turn the patient prone without a pillow and elevate the foot of the bed 12–18 *inches*. With *skilled nursing*, tracheotomy was rarely necessary. Dr. Russell thought that the most urgent need was for the training of a pool of trained nurses as specialists in the care of the respiratory tract in these cases, who could be called up to help in poliomyelitis outbreaks. Finally, he criticised the present system by which patients were transferred to orthopædic centres after three weeks; he thought that this caused additional psychological trauma to the child, interrupted treatment at the stage when there was a change from inactivity to supervised activity, and had a bad effect on the staff of both hospitals. He would prefer to see the first three months of the illness handled by the same staff, even though this might mean establishing convalescent sections in the infectious-disease hospitals.

Use of Respirator

Dr. A. B. KINNIER WILSON said that there were three main causes of respiratory difficulty in poliomyelitis:

1. *Failure to swallow and to keep the vocal cords apart (pure bulbar poliomyelitis).*—In twenty-four hours these patients secreted 1·5 litres of saliva and all of it must be emptied by the mouth; they should be placed prone and head downwards on a steeply tilted bed, and fed either intravenously or by an indwelling stomach tube. If they were placed in a respirator they died from forced inhalation of the secretion.

2. *Failure of respiratory rhythm from involvement of the respiratory centres.*—Fortunately this was more rare; it was sometimes difficult to distinguish from (3) and sometimes complicated by (1).

3. *Failure of the prime movers of the thorax—the intercostal muscles, the diaphragm, and the abdominal muscles.*—Here there was a loss of vital capacity, and these were the cases which required a respirator—nearly always a cabin respirator—in the acute stage.

A spirometer was valuable for indicating the need for a respirator; in the acute stage a vital capacity of 2 litres or less was an indication, but in the chronic stage patients could often manage unaided on considerably smaller

Letters to the Editor

HAZARDS OF LUMBAR PUNCTURE

SIR,—Your admirable leading article of April 11 suggests that the risks of lumbar puncture are perhaps greater than they should be.

When lumbar puncture is performed for diagnostic reasons, only two simple rules need be observed in addition to those of asepsis. First, a thin-calibre needle should be inserted with the bevel facing laterally and without the preliminary palaver of a local anæsthetic. The fibres of the dura mater run longitudinally, and so, if split and not cut, they will rapidly close on the withdrawal of the needle. Secondly, for the usual biochemical investigation it should not be necessary to withdraw more than 10 ml. of fluid.

In my experience two types of patient are most likely to suffer post puncture headache: (1) those who have lumbar puncture done for a second or third time, and (2) those with disseminated sclerosis—I regard this feature as an additional point in the diagnosis in an uncertain case. These two types of people have this in common, that they are both upset in an emotional sense. Treatment of tuberculous meningitis necessitates daily punctures, and, in those patients I have seen, some of whom had upwards of 400 lumbar punctures, there has been no incident of headache after the first few occasions, when headache is normally a symptom. In my view, therefore, a post-lumbar-puncture headache can be prevented or, when present, can be simply explained.

Edinburgh. JAMES K. SLATER.

SIR,—In your excellent leading article you emphasise that the use of a fine calibre spinal-puncture needle prevents subsequent leakage and makes post-puncture headache rare. You might have added that such a needle will soon become blunted, twisted, and inefficient unless the skin is previously perforated—for example, with a large bore needle of about 5 cm. length, which may also be used, if desired, to anæsthetise down to the dura. I can bear out Hillman's[1] claim that, if the technique be precisely followed, sepsis and trauma can be eliminated and headache almost completely averted. Though this minor procedure is often easy, there are not a few patients in whom it may be difficult, including the elderly with bony changes and those with rigid or twisted spines. The attainment of uniform success in lumbar puncture calls for experience and a careful and exact technique.

Bradford. PETER MCEWAN.

SIR,—Your leader gives a timely exposition of the discomfort of pneumo encephalography, but an "immediate crashing headache, which builds up," is by no means a constant feature. Much depends on the skill of the operator, and I, for one, would seriously question whether a severe and immediate headache is an invariable consequence of the first few cubic centimetres of air reaching the brain.

Nevertheless, the dismay with which a patient faces a second investigation of this kind is often clear and unmistakable. Therefore, it was with some surprise that I found no reference to the essentially humane method of air encephalography under general anæsthesia. This is regarded as a usual matter with small or even adolescent children.

With regard to the headache following replacement with air, which was described as lasting for several days, this definitely follows air encephalography very commonly. Follow-up of anæsthetic cases prompts me to suggest that the long lasting headache is functional, as it does not occur after the same investigation under general anæsthesia.

It is interesting to note that vomiting frequently occurs as air is introduced when the patient is fully conscious but never (in my own series) when the patient is even lightly anæsthetised.

It seems to me that whatever drawbacks may be implicit in complete replacement in order to obtain complete ventricular visualisation, this investigation is likely to become more, not less, widely used. You rightly stress the importance of a small bore needle in the correct space, especially as the technique is so much more likely to be used as operators are encouraged by the aid of an anæsthetic.

The future drawback to air encephalography would appear to be excessive zeal in manipulation in order to conduct the air from one space to another. There is often an interval between "takes," and an anæsthetist may then usefully inspect the films, not only to assure himself that the bevel of his endotracheal tube is not too firmly impinged against the trachea, but also to look for skeletal deformities or other lesions, particularly in the parts involved in manipulation. When the radiologist's attention is keenly focused on an intracranial lesion, he may not always spare thought for routine technique. In any case, the radiologist may have no means of assessing the effect of relaxants given by the anæsthetist.

National Hospital, Queen Square,
London, W.C.1. J. NOEL JACKSON.

SIR,—Your leading article describes fairly and very fully the hazards of lumbar puncture. There are now a large number of anæsthetists who will follow you in your agreement with Kennedy's[1] plea that spinal anæsthesia should be used only when general anæsthesia is absolutely contra indicated, and many will avoid that method in these cases too.

One reason for this, as you point out, is that grave and permanent neurological sequelæ may follow; but in addition—this point was omitted from your article—there is the almost certain knowledge that if permanent paralysis results a claim for negligence will shortly be laid by the patient against the operator, and probably against the hospital as well. The doctrine of *res ipsa loquitur* will be pleaded and the onus of rebutting negligence therefore becomes the duty of the defendants. It is most noticeable that in actions of this nature and other negligence claims a contest between the several defendants exists. The Ministry of Health has directed that hospitals which have to pay damages to patients for negligence must try to obtain a contribution from the doctors concerned.

I will agree that examination of reported cases of permanent palsy following spinal anæsthesia sometimes shows clear evidence of careless work, or errors in technique which should not have been made by that particular operator. On the other hand, there still remains a small hard core of cases gravely injured after spinal anæsthesia, in which the most exhaustive examination fails to reveal any evidence of negligence. Gunnar Thorsen[2] analysed 2493 cases which had undergone spinal anæsthesia. He found that the frequency of permanent neurological symptoms of one kind or another was at the rate of 1 in 200 cases. Allowing that this complication-rate may be very high, Thorsen was unable to find a cause for the resultant paralysis in 25–30 of these cases.

These were accidents in the true sense of the word and such cases may have been in your own mind when you wrote: "it may sometimes be difficult to decide whether symptoms following spinal anæsthesia are due to the lumbar puncture or to an unusual reaction to the anæsthetic."

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[1] Hillman, O. S. *Lancet*, 1938, ii, 722.

[1] Kennedy, F., Effron, A. S., Perry, G. *Surg. Gynec. Obstet.* 1950, 91, 385.

[2] Thorsen, G. *Acta chir. scand.* 1948, 95, suppl. 121.

WORK STUDY

W. D. SEYMOUR mentioned some effects of varying the speed at which a simple repetitive industrial task is carried out. The durations affected were those of the "grasp" and "position" phases—not, as one might have thought, the movement phases. From this he developed his view of the pre-eminent importance of the perceptual factor in manual operations.

W. E. H.

The Wider World

THE BIGHT OF BENIN AND BEYOND

SOME EXPERIENCES IN THE COLONIAL MEDICAL SERVICE*

Sir SELWYN SELWYN-CLARKE
K.B.E., C.M.G., M.C., M.D. Lond., F.R.C.P.
A PRINCIPAL MEDICAL OFFICER, MINISTRY OF HEALTH

WHY do people choose to leave this excellent country of ours and wander abroad? Is it a form of masochism to want to go to a part of the world, for example, which in my early days overseas was called "the white man's grave"? In the hot and steamy country bordering the Bight of Benin, you live in a bath of perspiration for several months of the year and you are wet with sweat almost as soon as you have dried yourself after a tepid shower. Further inland, when the *harmattan* blows from the Sahara and your furniture, floors, and doors go off like pistol shots as they dry and contract, your nose and lips often crack and bleed. Mosquitoes, carriers perhaps of the plasmodium of malaria or the virus of yellow fever, bite you from dusk to dawn and sometimes during the daytime too. The tsetse fly, with its sleeping-sickness trypanosome, or the smoky-winged chrysops, with its filaria blood-worm causing Calabar swelling, or the vicious midge, *Simulium damnosum*, with its filaria of onchocerciasis, bringing joint swellings or even blindness, may all dog your footsteps. "What a gloomy prospect," you say.

If you were to ask me why I chose a career that took me to such places I think that I should reply that it was partly the result of a dislike for general practice, which seemed to be the only alternative in those days. Why didn't I like being a general practitioner? Chiefly because I disliked asking patients for a fee for a consultation or a visit when I realised that some of them, at any rate, could have the treatment I advised or pay my fee, but not both. And I don't think that I really enjoyed delivering a gipsy woman in a caravan (the old-fashioned horse-drawn kind), with no hot water and with many flies and other insects to cope with. So I joined the Colonial Medical Service and left Liverpool for the Gold Coast in October, 1919.

The Gold Coast

I disembarked at the administrative capital of the Gold Coast, Accra. In 1920, there was an outbreak of smallpox in the Gold Coast, and I had to enlarge the infectious-diseases hospital near Accra by building a large number of huts. The mortality was rather more than 1 in 4—27·8%. To lessen the risk of carrying infection into the densely populated town, I established a cemetery fairly close to the hospital, for the main cemetery was on the far side of the town. But the African superintendent of this hospital used to complain to me that he was "humbugged" and kept awake at night by the ghosts of those buried in this cemetery. One morning, however, I found him in a more cheerful mood. He told me that he had had the graves sprayed with 2% 'Izal' and that this had driven the ghosts away so that he could now sleep in peace.

In those days death certificates from one of the very old African registered medical practitioners sometimes needed rather careful scrutiny. One I received said that a labourer from the Northern Territories had died from "exhaustion due to overwork." This seemed a little unusual in a West African, so I went to inspect the body of the deceased. I found that he had been sharing a room about 12 ft. by 10 ft. with seven or eight other labourers. He was lying on a sleeping-mat and there was "coffee-grounds" vomit over his face, singlet, and blanket. His conjunctivæ were deeply jaundiced. At a post-mortem examination we found that the tissues were heavily bile-stained and there were typical petechial hæmorrhages in the gastric mucosa, with altered blood in the stomach. The liver was fatty, and there was an acute nephritis, with a very small quantity of highly albuminous urine in the bladder. On section, the liver showed the typical degenerative changes produced by yellow fever, from which he had, of course, died.

When I first went to West Africa, thirty-three years ago, it was thought that yellow fever in Africa was confined to a comparatively narrow strip along the coast 200 to 250 miles in depth, stretching from St. Louis (above Dakar in French Senegal) in the north to Northern Angola in the south. It was thought that the disease had existed so long in this region that the Africans had developed some racial immunity and only suffered from the disease in a mild form. Several research-workers felt that yellow fever resembled malaria in this respect. It was a matter of common knowledge that, although malaria killed a great number of infants, those who survived and staggered around as pot-bellied youngsters with huge malarial spleens, grew up with spleens that gradually receded under their ribs until they were only a little larger than normal and might even be impalpable.

The brilliant work of members of the Rockefeller Foundation and of the colonial medical services of the United Kingdom, France, and other countries has now established that yellow fever extends across Africa to the Rhodesias, Uganda, Somaliland, Eritrea, Kenya, and the Sudan, and that it can be carried by many different species of mosquito besides the tiger mosquito (*Aëdes argenteus*) or *A. aegypti* or *Stegomyia fasciata* as it used to be called. In those days, therefore, it was thought that one of the best ways of avoiding yellow fever was for Europeans (the so-called non-immunes) to live in segregation areas separated from African dwellings by a building-free zone of a quarter of a mile in depth. No properly brought up yellow-fever mosquito could, it was thought, fly more than a quarter of a mile. Curiously enough, this was not so ridiculous as it sounds, always providing that intensive anti-mosquito measures were taken within the area itself: for the commoner carrier of yellow fever does show some preference for breeding in and near dwellings. Nowadays, with inoculation and with residual spraying with D.D.T. and gammexane there may be less justification for racial segregation on health grounds alone. Time after time, there were epidemics of yellow fever among white people in areas where both the so-called immunes and the non-immunes (local Africans on the one hand, and immigrants, whites, and Syrians on the other) lived close together. It was not uncommon for yellow fever to kill in five to six days: and although the famous Japanese research-worker, Hidego Noguchi, survived for a fortnight, the next victim, W. A. Young, our director of medical research, who had been helping me to investigate how Noguchi became infected, died within six days.

Another disease, in which fever and jaundice are almost invariable signs, is relapsing fever, and I met with it in West Africa for the first time in 1923. In tion in a large catering department) cites a field in which ordinary indices, such as cost per meal per patient, undoubtedly apply We had in mind the situation in regard to medical and nursing staff—where the cost of a doctor in charge of a department may vary from the minimum for the grade up to the maximum plus distinction award In such cases the financial cost figures may be relatively uninformative compared with figures based upon numbers of individuals or sessions Our main point was that the hospital service is a field in which it is essential to work out a battery of indices giving maximum information We had no wish to suggest that " because hospitals treat patients, business methods are not applicable " What we ask is that the methods should be common-sense adaptations to the special problems, not merely conventional systems applied wholesale —Ed L

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* Based on a talk given to the Whipps Cross Hospital Medical Society on Oct. 3, 1952.

POLIOMYELITIS

Sir,—In your leading article of Jan 10 you advise physiotherapists to introduce without delay active vigorous exercises to the point of fatigue in the treatment *of poliomyelitis This belief is in accord with that of* Ritchie Russell, who has failed to confirm that deliberately induced fatigue harms paretic muscles in the recovery stage

The *following case appears to* disprove this dictum

An intelligent girl of 10 was admitted to Pinderfields Hospital, Wakefield, on Sept 6, 1949 She was taken ill on Aug 18, and on admission she was found to have extensive paralysis of the right leg and partial paralysis of the left leg She stated that she had recovered the use of the right leg slightly prior to admission

During her stay at the isolation hospital she was given daily passive joint movements After admission to Pinder fields there was no pain or muscle tenderness She was started on sling and spring exercises, and treatment in the water tank She was allowed to sit up in bed On Oct 10 —i e, after about five weeks' treatment—there was a surprising relapse in the condition of the right leg The relapse involved the whole limb, and the greatest muscle changes were

	Sept 10	*Oct 10*
Calf	3	0
Tibialis anterior	3	0
Tibialis posterior	3 +	0
Extensor hallucis longus	3 +	0
Extensor digitorum longus	3	0
Peronei	3	0

The results were checked by two experienced orthopædic surgeons and the senior remedial gymnast

Further inquiry revealed that the girl had been advised by her parents to try to get better as quickly as possible The patient told us that she had been getting out of bed daily and trying to stand, and she had also been exercising her legs as much as she possibly could while in bed She herself had noticed that the right leg was rapidly becoming weaker

All treatment was stopped and she was kept at rest in bed The extensors of the big toe and other toes began to recover slowly, and were showing flickers of contraction by Oct 31 On Dec 20 she started walking with a calliper, but it was not until Jan 1 that there was any appreciable recovery in the muscles On that date tibialis posterior was 3, but the calf remained completely paralysed Tibialis anterior peronei, and extensor hallucis longus recovered to 3 but extensor digitorum longus remained at 2 On Jan 27 she went home and had outpatient treatment at her local hospital

At a review on May 3, 1950, there had been further slight recovery, extensor digitorum longus was now 3, but the calf muscles were still completely paralysed No further recovery was noted during the subsequent follow up

This patient had passed the acute stage of the disease and exercises were given, probably to the point of fatigue There was a definite relapse and, in spite of subsequent complete rest the condition on discharge was worse than when she was first admitted to hospital

I should like to see much more definite proof that active vigorous exercises to the point of fatigue are beneficial, rather than harmful, before advising such a technique If the ultimate muscle recovery is going to be jeopardised, even in occasional cases, by the adoption of this method, then its use must be questionable The saving of a few weeks', or even months', treatment in hospital should never be allowed to prejudice the end-result in poliomyelitis

Leeds GEOFFREY HYMAN.

TOO MANY DOCTORS?

Sir,—In your leading article last week you say

> " Oddly enough there are still too few applicants for junior posts as house officers, senior house officers, and registrars in the peripheral hospitals This is partly due to an absolute shortage, but it also to some extent reflects unequal distribution "

As a student about to enter my final year of study, I would point out that a compulsory preregistration year in hospital may appear satisfactory to the authorities, but with the individuals concerned it is not altogether popular Is it not possible that one reason for a shortage of house officers is the pay that they receive ? £350 minus £100 for board and lodging is not much on which to keep a wife and home After six years' work at a university ex-Servicemen who have a wife to support are not going to rush to jobs that hardly keep the wolf from the door In years past between graduating and starting a house job, a newly qualified doctor could earn some money as a locum tenens in general practice and so augment the pay he was to get from his hospital posts This is not possible now, and the financial problem becomes even more acute

This compulsory year in hospital may fill the posts that cannot be filled voluntarily, but is it of benefit to the young doctor who is going into general practice ? Hospital practice is hardly the same as general practice Instead of two six month periods in two departments of a hospital, rotating internships in large hospitals, so that young doctors did three months in the main departments, would be far better

To fill the posts just senior to that of house officer will require one of two moves either better prospects in the hospital service, or compulsory service

Edinburgh G I SLATER

PHARMACEUTICAL ADVERTISEMENTS

Sir,—If Sir Reginald Watson Jones will look again at my letter of March 28 he will see that I applied the word " pernicious " only to the way in which commercial leaflets tend to replace the more orthodox forms of teaching Perhaps if manufacturers of splints enclosed detailed instructions on how to treat fractures he, too, would object He says (April 11) that I complain that " British pharmaceutical firms are not fair or just " The words are his, not mine Everyone knows of the foundations, endowed chairs, and other forms of financial support by means of which the great commercial firms in this country have enriched science Not the slightest criticism was levelled against such ethical firms My letter was referring to some of the manufacturers of antibiotics It is well known that streptomycin, neomycin, aureomycin, and chloramphenicol were all discovered in America, and all the vigour of his language will not alter this simple fact If the facilities offered here are as good, or even better, as he seems to suggest, then the explanation would be that our young research workers are inferior Surely this cannot be his belief

I feel that makers of antibiotics would be well advised if a greater part of their financial reward was spent on medical research and less on circulars In the U S A vast numbers of publications carry the words " supported by a grant from " followed by the name of a commercial firm This is legitimate advertising which benefits of the hospitals were persuaded to discard Eastern herbal treatment, except for a few paying patients. They agreed to treat all cases of cholera, smallpox, typhus, cerebrospinal meningitis, leprosy, and so on, in isolation hospitals and leper settlements, and to segregate patients with pulmonary tuberculosis in special wards.

At the same time, the status and training of nurses were improved beyond all knowledge. The old custom was for nurses to pay 6 dollars a month for their food and to receive no pay for the first two years of their service. Many of them came from families by no means well off, and they lived by accepting money from patients. For example, a patient paid 5 cents for a glass of water and 5 or 10 cents for a bedpan. I was able to persuade the directors to forgo the monthly payment from nurses; and then I gradually got them to agree to pay the nurses an allowance, followed later by a small salary and eventually by the same scale of salaries as in Government hospitals in Hong-Kong. Sister-tutors were introduced and the standard of training was raised until Hong-Kong could claim recognition by the General Nursing Council and the Central Midwives Board for its nursing and midwifery certificates. To fulfil the midwifery regulations, a short course in the United Kingdom was also required.

After the surrender, life became very hard for those who survived the dreadful days of actual fighting. Such civil hospitals as the Japanese allowed to function were manned entirely by Chinese, Eurasian, or neutral nurses and doctors. All the English matrons, sisters, and doctors were interned in a concentration camp. Many of the British and others who were interned took with them only what they could carry. They lived on meagre rations for forty-four months under extremely congested conditions, with no privacy of any kind.

The Chinese and Eurasian staff who—instead of escaping into free China—remained on duty at my request in order to maintain at least a skeleton of the medical and health services, carried their lives in their hands. They were humiliated, insulted, and maltreated, and in several instances "investigated"—with all that that means—and imprisoned for their loyalty to the British cause.

Before the war spread to the Pacific, many Chinese died of beriberi, many wards of the Chinese hospitals were full of patients with beriberi and pellagra, and thousands died of tuberculosis. Despite all this, when peace returned the death-rate and infant-mortality rate fell to a third, and there were few cases of frank deficiency disease—an unlooked for result of nearly four years of semi-starvation under Japanese occupation.

The Seychelles

I left Hong-Kong for the Seychelles in 1947. These islands are spread over thousands of square miles of the Indian Ocean: one-third are of granite and two-thirds of coral. About a third are inhabited by descendants of 18th-century French colonists and their African slaves, and by descendants of slaves freed from Arab dhows by our naval frigates in the middle of last century. There are also a few British officials, Indian and Chinese merchants and their families, and some retired officers of the Army and Indian Civil Service. The island of Mahé, the seat of government, lies only 4° south of the Equator, but it is free from hurricanes, venomous snakes, and anopheline mosquitoes.

The coconut provides the livelihood of the Seychelles: it is exported in great quantities as copra, the dried flesh of the nut. The coconut tree has several enemies: a small brown beetle attacks the lower part of the trunk: a large rhinocerus beetle shears off the young fronds: a minute yellow or black scale grows on the leaves and stifles the tree; and rats attack the growing nuts. Where plantation owners are careless, rats may spoil as much as a third of the crop. The government offers 5 cents for a rat's tail and distributes rat poison free; and owls have been imported from Kenya to catch the rats. The scale alone would have destroyed all the coconut plantations by now had not a clever entomologist, Vesey Fitzgerald, found a ladybird which attacked the scale and kept it in check.

Intestinal infestation by round, hook, and whip worm is very common and causes much ill health. Disposal of sewage and refuse is still primitive, particularly in the more rural areas. A debilitating type of dysentery is found in the Seychelles, amœbic and lamblial forms being far too frequent, and the amœbic type is associated with an unusually high prevalence of liver abscess. The damp hot climate seems bad for patients with pulmonary tuberculosis, which is a fairly common cause of illness and death. There is leprosy too; but almost all the infectious patients are isolated on Curieuse, one of the many islands.

The suicide-rate is rather high, but serious crime is comparatively rare and usually follows a drinking bout. A peculiarly obnoxious drink called *purée,* made out of fermented bananas, pineapples, cassava, and other ingredients, topped up with illicit rum distilled from sugar-cane, has a deadly effect and is responsible for most of the trouble. The Seychelles government itself brews *bacca,* a beer-like drink made from fermented fresh sugar-cane juice, and encourages the inhabitants to drink this instead of the more potent *purée* or rum.

Although the Seychelles are a bit uncomfortable at times, they are particularly interesting and beautiful islands; and there are many friendly and kindly people of all colours, races, and creeds. I shall never regret having spent there the last few years of my Colonial service.

Envoi

To those who are smitten with wanderlust, or who are imbued with a spirit of adventure, or who are interested in trying to help the less developed members of the British Commonwealth to attain a higher standard of living and health, I commend the Colonial Service. The work is often in virgin soil, which is so rich that it produces an unusually good crop, altogether incommensurate with one's efforts.

Parliament

The Social Services and the Budget

SEVERAL references to the social services, including the National Health Service, were made in the budget debate. Mr. R. A. BUTLER, in introducing his budget, pointed out that the social services took 60% of civil supply expenditure—£1264 million. This was an increase of £80 million on last year. Of this increase £24 million was due to there being a full year's cost of the increases in social benefits made in the last budget. The National Health Service, excluding Civil Defence, would cost £411 million, an increase of £18 million, due mainly to rising costs, of which the outstanding example was the Danckwerts award. Education, including the universities, would also cost £27 million more than last year—£286 million.

Of the remaining £567 million, Mr. Butler said that £128 million would go to National Assistance; £183 million to National Insurance and family allowances; £89 million to war pensions; £70 million to housing grants; and £68 million for Exchequer contributions to local revenues. For food subsidies in 1953–54 he had provided £220 million, which compared with the rate of £250 million which he had set in last year's budget.

SOME PRIVATE ENTERPRISE

Wherever appropriate, he believed that the Government should do less and the private citizen more. During the past year by following this line he had introduced some flexibility and more economy. Thus we were entering into a new phase in our housing policy, in which

Although we are unwilling to challenge the histological identity of various types of kernicterus, there must remain considerable doubt about extending this identity The sequelæ in certain children who have survived the neurological damage associated with icterus gravis are well established, these children present definite syndromes most fully and recently described by Gerrard [7] Despite much attention to the development of surviving premature infants there is no evidence which would suggest that their nervous systems have been subjected to any such specific damage Intrinsic pigmentation of the primary dentition is a further feature of icterus gravis which has not so far been described in any other group of children [8]

It appears, therefore, that whatever the measure of identity between the various types of kernicterus some mechanism other than anoxia, anæmia, or blood group incompatibility explains its onset, and this is probably associated in some way with pigment metabolism

Park Hospital
Davyhulme, near Manchester

R M FORRESTER
D C A BEVIS

RARE COMPLICATION OF CHICKENPOX

SIR,—I was interested to see your annotation of April 11 I have just had a case of chickenpox in a married woman of 32, in whom a troublesome cough began the day after the rash first appeared Two days later she sent for me because paroxysms of coughing were making her short of breath She looked very ill, was too weak to sit up, and had bloodstained sputum The only signs I detected in the lungs were rapid respiration and scanty, generalised rhonchi Her condition was unchanged for two days, and thereafter she made a gradual recovery

Winfrith, near Dorchester

P R BOUCHER

PRIMARY REPAIR OF SKIN DEFECTS WITH LOCAL FLAPS

SIR,—It is to be hoped that surgeons will not be carried away by Mr McLaughlin's enthusiastic advocacy of local flaps for the primary repair of skin defects (April 11) Such flaps occasionally necrose, leaving a defect as large as, if not larger than, the original, and the incidence of necrosis varies inversely with the experience of the operator Apart from primary trauma, it must be very unusual for any surgeon to be confronted *unexpectedly* with a large defect in urgent need of immediate repair, since such defects are created by the radical removal of surface lesions, the extent and depth of which can commonly be assessed or at least suspected on clinical examination before operation In other words, the need for a local flap and the design of such a flap can be decided in advance, and it is here that the plastic surgeon with experience of these methods can be of the greatest assistance

In traumatic surgery, and particularly in hand injuries, the need for immediate cover with a vascular skin flap frequently arises, and the technique of such operations is fairly widely known All the illustrations of Mr McLaughlin's paper, however, and most of his remarks, seem to be concerned with defects created by the excision of either malignant or septic lesions and it is very doubtful if primary repair by local flaps of these defects is justifiable apart from two small groups of cases The first group is those defects whose base is unsuitable for free skin grafting because of exposure of extensive areas of denuded bone, tendon, or ligament exposure of the dura or the pleura, or an opening into one of the body cavities The *second group* is those malignant lesions which have recurred after irradiation, and in which it is desired to give further irradiation after excision The use of a local flap of non-irradiated skin will permit this But these instances can almost always be foreseen and planned for in advance, with the aid of a plastic surgeon if necessary, and in most other cases the use of a free skin graft is much more satisfactory, and in malignant cases frequently obligatory Some doubt must always exist as to the completeness of the local excision of a malignant skin lesion no matter how radical the operation, and surely it is wiser to cover such a defect with a thin free graft, and so allow early recognition of any recurrence, than *to mask the area with a thick local flap*, the use of which opens up widely neighbouring tissue planes

We feel that Mr McLaughlin dismisses too lightly the use of free skin grafts They are simple to cut and apply They take readily on freshly cut tissues (with the exceptions mentioned above) Their cosmetic appearance is not always good, but in certain situations they are preferable in this respect to local flaps as a permanent repair The use of free full thickness post auricular skin grafts around the eyelids and nose, or full thickness or thick split grafts for certain defects of hand and fingers, are two examples In other instances they should be regarded as a simple, quick method of achieving immediate temporary cover They then avoid the use of a hastily planned local flap at the end of an extensive operation, they allow a definitive secondary repair to be planned and carried out at leisure and under ideal conditions, they allow skin to be prepared and brought from a *distance when necessary*, *and they allow the delay* of the secondary repair until the risk of local recurrence of malignant disease is minimal

Two of the illustrations invite further comment The repair shown in fig 3, excellent as it is, is only made possible by the lax neck skin of the aged, and might well be disastrous if attempted in a young adult The procedure shown in fig 7 is practically impossible as a *primary* repair, since the inturned flaps must hinge almost on the margin of the excision and would be unlikely to survive Even when carried out as a secondary repair it is frequently better to " delay " such flaps before rotating them into position

Plastic Surgery Unit,
Ballochmyle Hospital,
Mauchline Ayrshire

THOMAS GIBSON
J SCOTT TOUGH

THE PROBLEM OF PEPTIC ULCERATION

SIR,—Sir Heneage Ogilvie (March 21), " at the risk of giving offence," criticised the work of the late Hedley Visick This criticism is obviously sincere, and I hope Sir Heneage will understand if I reply in the same spirit to some of these criticisms and that he will forgive me if I endeavour to correct a misconception

Visick's policy of high gastrectomy was only *undertaken* after much deliberation and discussion, and was more likely the result of undue optimism than a " policy of despair " The primary reason was that early in the series we encountered 5 recurrent ulcers (3 following Polya and 2 following Billroth I resections), these were *submitted* to further and more radical resection, the Billroths *being* converted into Polyas As all 5 patients remained well without further recurrence, it *seemed reasonable gradually* to increase the initial extent of the resection *In my* analysis I tried to indicate this point by classifying 201 patients as " developing measured radical gastrectomy " There is little doubt that a high resection does give a practical, if not an absolute, immunity *from recurrence* but I do agree that the removal of too much stomach is unnecessary and is *one, but only one of the factors* that lead to postprandial symptoms *The difficulty is* to define what is meant by " too much," *for there appears* to be an optimum degree, and it was this *ideal which* Visick was seeking, he hoped that by *measuring the* extent of the stomach remnant, and later *assessing the* results, it would be possible to estimate it It is true that towards the end of the series Visick was abandoning the

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7 Gerrard J *Brain* 1952 75 526
8 Miller J *Brit dent J* 1951 91 121

employed in the nursing services of the Crown; 2650 in school nursing; and 4000 in industrial nursing. In hospitals 11,501 enrolled assistant nurses were employed full-time, and 5300 part-time. The number of beds in these hospitals was 516,114, of which 28,502 were unstaffed.

No information was available as to the number of married women nurses employed. The numbers of male nurses employed in hospitals were 25,178 full-time and 315 part-time; there were no separate figures for male nurses employed by local health authorities, but the number was known to be small. No records were available of the wastage of trained nurses. Hospitals estimated that they required 10,420 additional trained nurses and local authorities 1331.

Hospital Medical Staffs

Mr. A. BLENKINSOP asked the Minister of Health what total reduction in the medical staffs of teaching and non-teaching hospitals he anticipated during the current financial year.—Mr. IAIN MACLEOD replied: I cannot predict the results of the special review of medical staff which I have asked hospital authorities to make. Mr. BLENKINSOP: How many of the registrars are likely to go out of practice during the next 12 months?—Mr. MACLEOD: There is no particular pressure being put on the Ministry of Health in that matter, although it is a difficult one.

Dr. BARNETT STROSS: Is the Minister not aware that many hospitals are finding difficulty in obtaining junior registrars? Has he considered helping them so that they may have the necessary help to carry on their work?—Mr. MACLEOD: The figures for junior registrars have been for some time very closely in accordance with the planned schedule laid down by the Labour Government. There are difficulties there, but the total number of specialist posts becoming available is, unhappily, not as high as was hoped when it was laid down. Mr. BLENKINSOP: How is it, then, that there has been a big drop in the provision made in the estimates for medical staff of the teaching and non-teaching hospitals?—Mr. MACLEOD: The hon. Member is fallaciously comparing this year's estimates with those of last year instead of last year's outlay. There has, in fact, been no change.

Mr. BLENKINSOP asked the Minister if he would give the number of senior registrars whose appointments were being terminated and for whom there were not likely to be vacancies in hospitals; and what action he proposed to take.—Mr. MACLEOD replied: I regret that this information is not available, as the number of hospital vacancies cannot be predicted with any accuracy. I am, however, reviewing the position in consultation with representatives of the profession.

Central Purchasing of Stores

Mr. BLENKINSOP asked the Minister why he proposed to reduce the amount of central purchasing of general medical and surgical stores and appliances, and drugs and vaccines in the current financial year, in view of the economies that had been effected by central purchasing in the past.—Mr. MACLEOD replied: The reduction in estimated expenditure on these supplies in 1953–54 is due mainly to revision of the estimated amount of direct purchases for other Government departments. The amount of central purchasing and contracting for the National Health Service has not been reduced. Mr. BLENKINSOP: Are we to understand that there has been no change of policy to encourage a gradual development in suitable fields of central purchases for the health service?—Mr. MACLEOD: If I can secure economies through this method or any other I will do so.

Dental Treatment and Appliances

In answer to a question, Mr. MACLEOD stated that the numbers of applications made for conservative dental treatment and dental appliances, respectively, in the months of October, November, and December, 1951, and during the corresponding months of 1952 were as follows:

—	1951			1952		
	Oct. (5 wks.)	Nov. (4 wks.)	Dec. (4 wks.)	Oct. (5 wks.)	Nov. (4 wks.)	Dec. (4 wks.)
Conservative dental treatment ..	495,000	363,000	388,000	496,000	414,000	333,000
Dental appliances ..	172,000	124,000	92,000	151,000	121,000	74,000

Public Health

HOUSING LONDON'S TUBERCULOUS

William Farr[1] in 1841 was the first vital statistician to stress the constant relation between the density of a population and its mortality experience. Farr's "law of mortality" postulated that the crude death-rate for districts in England and Wales increased as the sixth root of the population density per acre. In 1922 Brownlee,[2] using standardised mortality-rates, demonstrated that the death-rate for each borough in London was constantly proportional to the tenth root of the density of its population. The more favourable position of the Metropolis in this respect was attributed to the peculiarities in the age-distribution of London's population and in its age-specific mortality-rates. While total mortality may no longer everywhere show this constant parallel between house density and death-rates, there is still a close correlation between tuberculosis morbidity and mortality and crowding of and within houses. Shirley Murphy,[3] London's first county M.O.H., showed how regularly the tuberculosis death-rate in London increased with every rise in the proportion of people living more than two per room; and Robert Koch,[4] discussing "the manner in which tuberculosis takes place," stigmatised this infection as a disease of crowded dwellings.

Improvement in overcrowded-living conditions is not, however, necessarily followed by improved mortality-rates. Newsholme[5] pointed out that, although overcrowding is one of the important consequences of urbanisation that have an adverse effect on tuberculosis rates, beneficial influences such as improved wages and nutrition could nevertheless reduce mortality even in the presence of overcrowding. M'Gonigle[6] clearly demonstrated how the mortality-rate of a rehoused population increased considerably if poor nutrition was allowed to replace overcrowding as an adverse influence. This observation has now been confirmed indirectly by Benjamin[7] in a statistical study of the individual social factors affecting tuberculosis morbidity and mortality in London boroughs. If, then, tuberculosis can and does wane in a district in spite of adverse housing conditions, it might seem questionable, in these days of universal housing shortage, to select the tuberculous for specially generous treatment in the relief of overcrowded living conditions. Moreover, Hartston,[8] in a study of the prevalence of tuberculosis among the contacts of registered London cases, observed that by the time a case is recognised, most of the susceptible contacts have already been infected. By the time the patient has been rehoused all susceptible contacts have been abundantly exposed, and new cases in the household thereafter are uncommon. This may also explain the rarity of new cases of active tuberculosis among the child contacts of colonists at special village settlements.

Does this mean that rehousing of the tuberculous, when it comes, is too late? Should preferential rehousing of overcrowded dwellers be given to those families with young children and adolescents *before* a case of tuberculosis has appeared among them? These questions were considered by the London County Council Chest Clinic

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1. Farr, W. Appendix to Registrar-General's 5th Annual Report, 1841, p. 420.
2. Brownlee, J. The Use of Death Rates as a Measure of Hygienic Conditions. M.R.C. special report no. 60. 1922.
3. Murphy, S. Annual Report of M.O.H. to the London County Council, 1898, p. 46.
4. Koch, R. *Lancet*, 1906, i, 1449.
5. Newsholme, A. The Prevention of Tuberculosis. London, 1908; p. 224.
6. M'Gonigle, G. C. M., Kirby, J. Poverty and Public Health. London, 1936, p. 108.
7. Benjamin, B. *Brit. J. Tuberc.* 1953, 47, 14.
8. Hartston, W. Transactions of 3rd Commonwealth Conference. National Association for Prevention of Tuberculosis. 1952; p. 407.

Friday can have stood outside it—and his parrot might have had words to utter even on this exception

The relationship of trust is manifestly an accident and not the substance of a profession, and this substance has been wisely said to be the fact that the activities of a profession are properly subjected to theoretical analysis and are modified by conclusions drawn from that analysis This process involves the understanding of the natures of the factors involved in these activities Thus, the practice of a profession cannot be disjoined from its theoretical understanding When it is so disjoined it ceases to be a profession and becomes a craft or a technique

This is the criterion by which we may judge the claim to professional status of the ancillary services used by the doctor unless the word "profession" is to be trivialised and to become as meaningless as the word "esquire"

Because everyone in a hospital from matron to ward-maid, from almoner to stenographer, is the doctor's colleague in the sense that each contributes to a common end, it is not rational to assume that each and every one is a member of a profession

Mr Farrer-Brown is kind enough to concede that the doctor must be the leader of the "team," adding that if he is to be a real leader he must have distilled his own and his colleagues' knowledges and experiences This is woolly nonsense, incapable of precise or clear analysis, having only the dubious merit of making his remarks emotionally palatable to a non-medical audience

The doctor's primacy in hospital or at the sick bed rests upon no sentimentalities or snobberies, but upon the scope and quality of his experience, upon his being something more than a craftsman, and, finally, upon the fact that on his shoulders rests the ultimate responsibility in a measure that his subordinates could not bear and would not accept No playing with words that weakens the hierarchy upon which the rational and humane practice of medicine rests should be allowed, and, while Mr Farrer-Brown may not wish to upset it, his tendentious alternative "medical leadership or medical domination" reveals his dangerous failure to understand the complex problem upon which he pontificates so glibly

It is a symptom of this disorderly age that we should find the newest occupation publicly lecturing the oldest profession Long since, when I was young, this activity was known as teaching your grandmother to suck eggs It has never been a highly regarded occupation, or should I say profession ?

London W 1 F M R WALSHE

SIR,—Many of us will have read Mr Farrer Brown's address, with great interest but much searching of the soul But we must surely repudiate his attempt to apply the word "industry to the National Health Service, not at all from pride, but merely out of respect for the Queen's English The relevant definition in the *Concise Oxford Dictionary* is "branch of trade or manufacture," which the National Health Service is not—or certainly ought not to be

Nevertheless it is true that a drastic change in the crazy patchwork of its organisation is bound to come Whatever their faults the medical services of the Forces during the war represented the most highly integrated health services in the history of the world A professional hierarchy from the director general down carried out its duties free from the stultifying control of lay committees Grievances could be raised in Parliament and effectively redressed Perhaps it would be desirable for a similar hierarchy to be established in the National Health Service Before this could be achieved a very thorough rationalisation of local government would be essential

London W [illegible] GEOFFREY G SHEPHERD

SIR,—Mr Farrer-Brown asks for better protection of the public against the incompetent doctor Surely some protection is already provided by the right of every patient to choose his general practitioner and to change, if he so desires I believe that it is as important for the general public to want a good health service as it is for the medical profession to try to make one

Harrow L PICTON DAVIES

Obituary

JOHN GUY

M D Glasg , F R F P S , F R C P E , D P H

Dr John Guy, formerly medical officer of health for the city of Edinburgh, died at his home at Aberlady, East Lothian, on April 11, at the age of 79

He qualified in Glasgow in 1894 and took the D P H at Cambridge in 1899, and the following year proceeded to the degree of M D Before going to Edinburgh he had held posts as assistant police surgeon at Bradford, resident medical officer in poor-law hospitals there and at Leeds, and superintendent of the sanatorium at Bridge of Weir, and for a short time he was tuberculosis officer for Gloucestershire He was elected a fellow of the Royal Faculty of Physicians and Surgeons in 1911 He first joined the staff of the Edinburgh public health department as tuberculosis officer in 1913, and in 1913 he became a fellow of the Royal College of Physicians of Edinburgh Later he was appointed assistant M O H , and deputy M O H , and in 1930 he became M O H for the city He was given this appointment at the time when, under the Local Government Act of 1929, the city took over the former poor-law institutions and hospitals and reorganised its curative medical services He was therefore responsible, in cooperation with the University of Edinburgh, for the conversion of the former poor-law hospitals into general teaching hospitals Thus, the Western General Hospital, formerly Craigleith Hospital, was gradually transformed into an effective general hospital staffed largely by members of the university teaching staff The process was slow, but internal renovation and some new building was undertaken Dr Guy acted, in effect, as administrative superintendent of this and the related hospitals

[Scott & Pictorial Press

Dr Guy was also a lecturer on public health in the university, on tuberculosis at the school of medicine of the Royal Colleges, and on hygiene at the School of Social Study in Edinburgh He collaborated with the late Dr Linklater in a textbook on *Hygiene for Nurses*, and he also wrote a monograph on pulmonary tuberculosis

When he retired in 1938 he went to live on the Island of Coll one of the Inner Hebrides, where he spent the years of the war Afterwards he returned to East Lothian living first at North Berwick and for the last four years at Aberlady

Dr Guy is survived by his wife, three sons, and one daughter

FREDERICK WILLIAM EDRIDGE-GREEN

C B E M D Durh , F R C S

Dr Edridge-Green, who died on April 17 at the age of 89, was the inventor of the first efficient test for colour-blindness His colour-perception lantern is used by the Royal Navy and the railways, and his bead test is used by the National Service boards In 1920 a medical director-general of the Navy wrote "Dr Edridge-Green has deserved well of his country He has given us the means of averting appalling disasters by eliminating the colour-blind from control of vessels and fleets at sea"

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN I am reading a book or a paper in a dream the content seems very clear, and I have a feeling that it is of supreme importance to the human race. But when I wake I cannot remember a word of it. One night last week, however, I was reading obituary notices in *The Lancet* sometime in A.D. 2053. I managed to make some notes as soon as I woke.

The first was of Sir Passit Wellup, O.C.C., chief consultant in cardiac catheterisation (left-sided) to the Ministry. He started to specialise while still at his preparatory school, and studied cardiology for his General Certificate of Education. He took his M.B. in catheterisation, and inclined towards the left immediately after he qualified. He figured in a famous lawsuit in the early years of the century when he was prosecuted for trespass by the Association of Consultant Catheterisers (Right-sided). They alleged that his catheter once passed through a septal defect, natural or (they underlined the "or") maliciously manufactured, and investigated the right ventricle. He was lucky to get off. He sat back with enhanced reputation to invent an anti-dextro-loculus radar catheter tip which prevented repetitions of this painful contretemps. He was one of the first to benefit by the Celibacy of Consultants Act, passed in 1990, owing to the repeated moans from registrars that they could not afford to keep their families on £1500 a year. Being celibate and childless, Wellup could take his statutory five months' holiday per year at all the best seasons, and Madeira, Switzerland, the Riviera, Mars, Blackpool, all the favourite haunts of the consultant, were known to him. He lived to the age of 95, passing catheters to the last. He once did three days' locum in general practice, and though he had to conceal this fact from selection committees he admitted it to his closest friends, and even went so far as to say "It wasn't as bad as all that."

Next there was Dr. Rubber Stamp, a well-known general practitioner, who died at the advanced age of 45, from coronary thrombosis. High-lights in his career were the Compulsory Marriage of General Practitioners Act (2031), which increased the number of unpaid overworked Civil Servants considerably, and the fact that he once achieved the impossible by calling out ten consultants in one Sunday afternoon.

Perhaps I dreamt this wrong. I like to think so. Perhaps this is what I read:

Dr. Good Type, who died at the age of 90, was one of the few doctors who could remember the days when there were such things as consultants and M.O.H.s, and even a College of General Practitioners. He was a pioneer in the legislation which made it compulsory for general practitioners to have been registrars, and for consultants to have been general practitioners. He also supported the movement to abolish the medical schools and institute the apprentice system. At a time when the artificial divisions of consultant, registrar, houseman, and M.O.H. still existed, Type already held his own infant-welfare clinics, gave prophylaxis to his own patients, inspected their own drains, and wrote letters to consultants which gave them a magnificent picture of the background of the patient as well as a very sound clinical diagnosis.

Did I wake up then, or was I just quoting from memory from the obituary of my own great-grandfather, who was a J.P., a respected surgeon, a G.P., M.O.H. for the county borough, and a fellow of the Royal Photographic Society to boot?

* * *

For those who have never run aground in a small cabin cruiser I can recommend it as an interesting experience. As the boat heels over gradually to one side, though never to the point of actually submerging the gunwale, one has time to adjust oneself to the idea of living at an angle of forty-five degrees. During this process of heeling things slide—ballast, oars on deck, or anything unsecured. The contents of open cupboards are vomited across the cabin or galley in a highly projectile manner reminiscent of pyloric stenosis. Crockery and cutlery on the cabin table slide gracefully to the floor. The same applies to anyone who sits on the higher side of the boat, whereas those on the lower side find themselves pressed all too firmly into their seats. To stand upright or to walk about is a considerable muscular effort, and one stands erect at an apparently impossible angle which is very funny to watch. A ball thrown in the air describes a boomerang course. Meals are difficult to prepare and to consume: it is one thing to *feel* inclined to eat; to *be* inclined to eat is quite another matter. On the other hand, one can safely lay a table which looks like the side of a gable roof provided that it is cleared before the boat resumes its normal position as the tide rises.

* * *

It must be seven years since I made Lockyer's acquaintance at a performance of Handel's *Messiah* given in Southwark Cathedral. It was a dull afternoon without much promise; but a remarkable number of people assembled, and when the performance began every available square foot of floor-space appeared to be filled. Three girls had distributed themselves at various altitudes on the pulpit steps, while a few of the audience were sitting beneath the grand piano of the orchestra. I found myself occupying a flagstone in the North Transept, along with Lockyer and his Pills.

I wonder idly what colour they were, what (no doubt multifarious) ills of the flesh they were alleged to cure, and what great figures of the period swallowed them with scepticism or hope. It was, no doubt, a slip of the pen which led my fellow peripatetic to prune a word from the final couplet which should, I think, read:

> "This verse is lost; his PILL Embalmes him *safe*
> To future times without an Epitaph."

* * *

One of the gadgets with which our new operating-theatre was equipped came somewhere between a headphone and a loudspeaker. We did a lot of thoracoplasties under local anæsthetic, and it was felt that distraction might prove the better part of valour. The instrument was accordingly installed in the pillow of the operating-table and the patient offered the choice of Home Service or Light Programme—with a ban on items comical enough to affect the respiratory excursion.

The success of the experiment seemed assured when one patient announced that as the classical music came on he went to sleep "the same as at a concert." But a week later one of the patients undergoing thoracoplasty, who had been very still and quiet, suddenly started to groan pitifully; his pulse-rate and blood-pressure rose sharply. The explanation came later: he had dozed off, and the next thing that he knew was a choir of heavenly voices in the distance singing hymns, followed by a solemn voice referring to the Kingdom of Heaven. An aching body and the smell of the diathermy convinced him that he had gained admission to another world. It was some time before his premedicated mind realised that he was listening to a church service.

Shortly afterwards the headphone was sterilised by boiling by an enthusiastic junior member of the theatre staff. This seemed to upset it, and it was sent to the engineer with a label "Please Repair." That was ten months ago, and we haven't seen it since. We have not pursued the matter.

* * *

Last week, in search of toothpaste, I entered a large multiple store whose wares are conveniently displayed for all to see. Spring was evidently here, for the usual rainbow appearance of the toilet counter was transformed by an all-pervading green. The leading makers were offering their products combined with chlorophyll. Had their research laboratories proved that Nature's pigment was necessary for efficient oral hygiene? Was it in response to public demand? Had an enterprising representative of the Cabbage Growers' Association sold them the idea? As far as I was concerned the answer was simple. In a large family it is convenient for each member to use a tin or tube of differing appearance. There is now a fourth colour in the range of our favourite dentifrice, but I can still taste the peppermint.

* * *

News from the Ministry.—"But the Board would not have to apply for our approval before making . . . an upward adjustment in the half-days of an individual consultant or the appointment of an additional part-time cleaner." [B.G. 24/71/201.]

Notes and News

FACTORIES AND FOGS

AT the beginning of his visit to this country as a senior Fulbright fellow, Prof PHILIP DRINKER, of Harvard, gave a talk last Monday at the London School of Hygiene and Tropical Medicine

Though medical inspection of factories and mines began a century later in the United States than in Britain, "industrial hygiene as we know it" was, he said, an American product Usually the public health engineer was called in not by a doctor but by a management anxious to reduce its production costs, for in the U S A industries mostly ran at a profit or closed down Sometimes health risks were not considered at first, and litigation was the spur, but once managements were convinced that something must be done there was little difficulty in getting their coöperation The rôle of the physician in the appraisal of industrial disease could hardly be overemphasised, but Professor Drinker thought that prevention was the task of the public health engineer Statistics were not the exclusive property of the medical profession

Industrial hygienists in the U S A had been criticised, he continued for preparing official lists of the permissible concentrations of toxic substances It was said that knowledge was insufficient for the fixing of these figures But the first thing the public health engineer was asked was "how clean does this air have to be?" Where the contaminant was carbon tetrachloride or beryllium, for example it was no good answering "we'll follow the records and let you know in three years' time (or may be in fifteen years)" The engineer was used to working to a specification and must give a figure, even if it had to be revised later It was very rare in industry to abolish a poison completely after all, people put up with a certain amount of carbon monoxide from their cooking stoves and their cars But if it could not be reduced to a harmless concentration, or "dosage," at a cost the industry could pay, the process had to be given up

In conclusion Professor Drinker turned to the problem of contamination of the air not of factories but of whole cities In the U S A he said, they had fogs "just as thick and juicy as yours,' though these were quite different in Los Angeles, for example, from what they were in Pittsburgh But fog by itself was not a serious matter what made it dangerous was poisonous pollution The Meuse Valley fog had lasted four days, and had killed 64 persons, as well as many cattle In the Donora disaster there were 20 deaths with none in cattle The London fog last December, with its thousands of deaths, was a vastly different affair Moreover London had provided, for the first time, analyses of samples of air taken at the height of the fog It seemed surprising that the concentration of sulphur dioxide in the London fog reached only 1 3 parts per million, for in the U S.A 10 p p m was regarded as a permissible concentration for workers exposed for eight hours The deaths in London, however were mostly among invalids, infants, and "old people" (over 45!) In experiments in Professor Drinker's laboratory, respiratory reactions had been consistently evident in people breathing a mist containing very low concentrations of sulphuric acid which they could not detect Acetic acid was tolerated at high levels, but the effect of hydrochloric acid was somewhat similar to that of sulphuric acid Recently the experiments had been repeated with sulphur dioxide, and the investigators had been surprised to get a respiratory response in normal people at the very low level of 1 0 or 1 5 p p m The test had then been performed on furnacemen who were habituated to SO_2 concentrations as high as 20-25 p p m or even 30 p p m On exposure to concentrations of 5 p p m and 8 p p m these men showed no reactions whatever to them the mixture was apparently just the same as normal air

At the end of the lecture Dr ANDREW TOPPING, the dean, announced that Professor Drinker had been made an honorary member of the London School of Hygiene Association in token whereof he was presented with the club tie

SURGERY OF VARICOSE VEINS

A 16 mm silent film, dealing with this subject has been prepared under the medical direction of Mr R Rowden Foote Part I which runs for 18 minutes describes the stripping operation The Kodachrome colour is excellent and the film gives a clear exposition of the subject At the beginning there are rather a lot of subtitles, but the sequences of the actual operation are vivid and will convey to the student and general practitioner exactly what the operation involves Surgeons who are going to perform this operation will also find the demonstration helpful, although the introductory explanation, largely by subtitles, will be for them unnecessarily long The film is available on loan from Mr Rowden Foote, 137, Harley Street, London, W 1, who will give an introductory talk at medical society meetings to which the film may be shown

PROBLEMS OF CERTIFICATION

PAID sick leave undoubtedly encourages people to remain at home and nurse their ailments when otherwise they would struggle to work Often their temporary absence from work is, in the long run, a good thing[1], but the tendency to exploit indisposition can also be a bad one for all concerned The doctor is properly careful of the welfare of his patients, but overleniency will not necessarily serve them best, and the doctor who retains the confidence of the administrator is often the patient's best friend

In introducing the estimates of the ministry of labour and national insurance in the parliament of Northern Ireland on April 9, Major Ivan Neill said that the administrator sometimes feels that he does not always receive from the doctor the support he might reasonably expect Last year, he said, his ministry had to ask the ministry of health and local government for a second medical opinion on over 50,000 persons who were claiming sickness benefit Over 7000 of those called for examination did not attend and abandoned their claims, over 10,000 got a final certificate from their doctor, almost 12,000 of those who attended were considered fit for work by the medical referee The impression given by these figures was, he agreed, unduly gloomy, for some of those called for examination would of course have recovered before the examination

But Major Neill was disquieted by the records of some of the doctors "There are," he said, "very wide departures from the general average There are doctors who signed off more than 40% of those of their patients who were summoned for examination In other cases only 20% of the persons called for examination were considered by the referees to be incapable of work at the date of examination I am in consultation with my colleague, the minister of health and local government, about the action which should be taken to secure the necessary improvement in the standard of certification I have no doubt that only a small minority of doctors are at fault, but the fault is serious The acceptance of these certificates at their face value has led to payment of sickness benefit to persons who are not entitled to it, and we must get back to the position where full reliance can be placed on the doctor's certificate in every case I have no doubt that we shall have the support of the medical profession in any steps that may have to be taken "[2]

University of Oxford

The George Herbert Hunt travelling fellowship for 1953 has been awarded to Dr A C Allison, fellow of Exeter College

University of Cambridge

Dr F W Campbell has been appointed lecturer in physiology Dr C W McE Pratt and Dr J D Lever have been appointed demonstrators in anatomy, and Dr H B Barlow and Dr R H Winfield demonstrators in physiology

University of Glasgow

Prof E J Wayne has been appointed to the regius chair of practice of medicine in succession to Sir John McNee, who is retiring

Professor Wayne who is 50 years of age has been professor of pharmacology at Sheffield University since 1934 and professor of pharmacology and therapeutics there since 1942 He graduated B Sc in chemistry in 1921 at Leeds and was elected Sir Swire Smith fellow From 1924 to 1926 he undertook research in biochemistry in the University of Manchester and in 1925 he was awarded the degree of PH D Leeds in that subject In 1929 he graduated in medicine at the University of Leeds and served as demonstrator in physiology there before he was appointed assistant in the department of clinical research at University College Hospital London in 1931 He held this post till he moved to Sheffield in 1934 He was elected F R C P in 1937, and took his M D the following year His papers to medical and scientific journals have mainly dealt with [illegible] endocrinology and drug therapy

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[1] See *Lancet*, Feb 28, 1953 p 428
[2] *Northern Ireland Parliamentary Debates* April 9, 19[illegible] [illegible]

The present legal procedure only allows a public trial for negligence by which an injured patient may try to recover financial compensation for his injury. Humanity dictates that such an injured patient deserves compensation, but I suggest that it is now time for a re-examination of the machinery for assessing claims for negligence in this matter. There are other injuries too, such as brachial-plexus palsy after long surgical operations, in which the possibility of accident may be present.

University College Hospital,
London, W.C.1.
R. W. COPE.

HOSPITAL COSTING

SIR,—It would be interesting to know upon what ground you state (March 28, p. 635) that "it is generally agreed . . . that there is no large-scale extravagance to be exposed, but only different degrees of housekeeping efficiency." So far as I am aware, no authoritative pronouncement has been made to this effect, and I doubt very much whether the Ministry of Health would accept it, since, apart from the decision to set up a committee of inquiry into the cost of the service, the latest memoranda on the control of hospital expenditure and manpower seem to imply—indeed more than imply—that considerable savings are possible.

Again, what is meant by "large-scale extravagance," and does the statement refer to individual hospitals or to hospitals as a whole? What figure have you in mind—£10,000, £20,000, or £30,000, or are you thinking of something in the region of £100,000? The spending of any sum of money by a hospital, no matter how small the amount, is extravagance if a commensurate return in service or goods is not received. It may well reach "large-scale extravagance" if it is repeated in thousands of hospitals all over the country. The estimated expenditure on the hospital service for 1953–54 is £269 million; so if only 5% of this amount were saved by improved methods of organisation and more efficient management, including cost accounting, the demand on public funds would be reduced by £13½ million. Hospital authorities have too readily accepted the "ceiling" laid down by successive Chancellors of the Exchequer as being the amount they should spend, and estimates are made accordingly.

You say that "because salaries are determined on a national basis, there is no point in elaborating the data. The most useful index to the adequacy of staff in any department is not financial: it is a statement of the number of people of different grades who are employed, related to equally simple numbers of patients, or tests, or examinations, or items of service." It may be agreed that this relationship is interesting, but it is certainly not the *most useful* if, indeed, it is useful at all. It relies upon the assumption that the adequacy of staff in any department can be tested by relating numbers of staff to the number of units of work. This plausible suggestion, which seems to offer a short cut to comparisons, fails in practice to detect anything but the grossest disparities in staffing; and if, as you begin by stating, these do not exist, then the method has nothing to commend it in any search for economy.

The most superficial examination of the suggestion shows that, far from being simple, it would soon lead to complications of the utmost intricacy. First, over what period is the number of staff to be calculated, and how is allowance to be made for comings and goings? What is the basis for part-time staff, necessarily ignoring that the cost thereof is proportionately greater? What are the "different grades" referred to, and how far should the differentiation be carried? For example: if one kitchen preparing (say) 1000 midday meals employs a catering officer, a head chef, a pastrycook, two assistant cooks, four kitchen assistants, two porters, and a part-time cleaner, under what system of barter is this to be compared with a kitchen preparing 800 midday meals, employing a head cook, two assistant cooks, five kitchenmaids, and two student nurses for special diets? Are differences in age, experience, and sex, each of which may affect cost, also to be ignored? In practical administration not only are all these factors influenced numerically, and in cost, by considerations of overtime, split duty, and shift-duty payments, but also any crude comparison of the sort suggested would be vitiated by differences in function carried out by "departments" of the same general purpose, one hospital with another. A common factor, understood by all, is required; and the obvious and relatively simple one of cost in terms of money has to be accounted for in any circumstances.

A third statement on which I should like to comment is: "There is a danger that the elaborate methods of costing that have served industry well will be too readily retained in the wholly different context of the hospital service." One may query the introduction of the word "elaborate." There are no doubt some industrial systems which may be considered elaborate, although they may not be so for the particular concerns, but most of them are reasonably simple. The fact to remember is that it is all too easy to instal a supposedly simple system only to find in practice that the simplicity is a myth and in any case is more than counterbalanced by incompleteness. One might argue that the present hospital costing system is simple; but it is extremely costly because it does not provide results which may be put to any useful purpose. An adequate costing system provides results which can be used.

Finally, what is meant by "different context of the hospital service"? In what material way is it different? It is true that hospitals treat patients and industry deals with inanimate "products," and to this extent there is a difference. But does this in itself dictate in any way the type of costing system to be introduced? I would say that it does not. Practically, both have to provide and maintain buildings; instal and maintain equipment, electrical, plumbing, and other services; employ and control staff; make purchases, store and issue supplies, and so on. There appears to be a mistaken idea that because hospitals treat patients business methods are not applicable; that they should be run on easy-going lines and only by those who have direct contact with the patients. If this reasoning is sound why bother about costing or even accounting at all; why bother about the number of staff, their grading, and the amount of work they perform? Why employ qualified administrators; why have committees and meetings? These and many other essentials come under the heading of "business methods." Such methods, which include adequate accounting on the lines proved effective in industry, are applicable in every way to the activities of hospitals—even more so as the cost is met from public funds.

No finance officer wishes to instal a costing system merely for the sake of doing so, but he does want to instal a system which will produce results which can be used by management.

ADMINISTRATOR.

*** On the question of large-scale extravagance we may quote the report of the Nuffield Provincial Hospitals Trust:

> "Dramatic economy will never be possible: there is no dramatic waste to be cured; it is only by eliminating every source of wastage and inefficiency and by making all within the service conscious of cost that the limited funds available for the hospitals will be spent in the best way."[1]

We did not mean to imply that there is no room for ordinary costing analysis in the hospital service; obviously there is, and our correspondent (quoting the situa-

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[1] Report of an Experiment in Hospital Costing. Nuffield Provincial Hospitals Trust. London, 1952; p. 48.

Food-supplies, Population, and War

A conference on this subject will be held by the Medical Association for the Prevention of War at 2 P M on Saturday, May 2 at Church House, Westminster London, S W 1 The discussion will be opened by Dr Duncan Leys and Prof J B S Haldane, F R S The assistant secretary of the association is Dr Richard Doll, 24 Lansdowne Road, W 11

International Medical Congress

The third International Congress of Internal Medicine will be held in Stockholm from Sept 15 to 18, 1954, under the presidency of Prof Nanna Svartz The main subjects chosen for discussion are The Pathogenesis and Treatment of Hypertension and Mesenchymal Diseases (Collagenous Diseases)—their common characteristics and their nature The secretary general, Prof Anders Kristenson may be addressed at Karolinska Sjukhuset, Stockholm 60, Sweden

Child Health in the Tropics

A symposium on this subject is to be held in Jamaica from Oct 20 to 27, immediately after the International Pædiatric Congress (which takes place in Havana from Oct 12 to 17) The provisional agenda for the symposium includes the following sections nutrition, liver disease food poisoning in the tropics, infectious and parasitic diseases, prenatal and neonatal pediatrics, and organisation of child health work in underdeveloped areas Further information may be had from the secretaries of the symposium, Division of Medicine, University College of the West Indies, Jamaica, B W I

Industrial Diseases Committee

The Minister of National Insurance has set up a committee to review the present provisions of the Industrial Injuries Act under which benefit is paid for diseases and for personal injuries not caused by accident and to make recommendations Mr F W Beney, Q C, is to be the chairman, and the 11 members include Sir Ernest Rock Carling, Dr L G Norman, and Dr Alice Stewart

Centenary at Southampton

The Southampton Medical Society, under the presidency of Dr R S Swindell celebrated its centenary on April 18 Two hundred members and their guests were welcomed at the university by the vice chancellor Sir Russell Brain P R C P delivered an oration on Evolution in Medicine A dinner in the evening was attended by a hundred and forty members

The telephone number of Addenbrooke's Hospital Cambridge including the administrative offices of the board of governors of the United Cambridge Hospitals has been changed to Cambridge 5[illegible]71

A *Press guide to British Chemicals and their Manufacturers* has been published by the Association of British Chemical Manufacturers 166, Piccadilly London W 1

Nine consultants in tuberculosis from six overseas countries are taking part in a course arranged by the British Council in Birmingham and London from April 13 to 2[illegible] The course, which has been planned by Prof W H Wynn and Dr C H C Toussaint deals with British practice in the prevention and treatment of tuberculosis and with aftercare

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Diary of the Week

APRIL 26 TO MAY 2

Monday, 27th

University College Gower Street W C 1
4 15 P M Sir Rudolph Peters, F R S Inhibitors and Intracellular Chemical Dissection (First of four lectures)

Postgraduate Medical School of London, Ducane Road, W 12
4 P M Dr Sheila Sherlock Portal Hypertension

Royal Society of Medicine, 1 Wimpole Street W 1
5 30 P M *Section of Odontology* Prof John Boyes Affections of Tongue Mr R Sprinz F D S Sarcoma of Jaw in Black Leopard

Institute of Ophthalmology Judd Street W C 1
5 30 P M Dr Alan Woods (Baltimore) American Approach to Cataract Operation

Institute of Psychiatry Maudsley Hospital Denmark Hill S E 5
5 30 P M Dr E Stengel Lecture demonstration

Manchester Medical Society
9 P M (University of Manchester) *Section of General Practice* Prof W I C Morris The Dramatic in Obstetrics

University of Cambridge
2 45 P M (Department of Biochemistry Tennis Court Road) Prof R Nicolaysen (Oslo) Dynamic and Quantitative Aspects of Calcium Metabolism

Tuesday, 28th

Royal Society of Medicine
8 P M *Section of Medicine* Dr Philip Ellman Dr R A Henson Mr T Holmes Sellors Unusual Manifestations of Bronchial Carcinoma

Institute of Ophthalmology
5 30 P M Dr Woods Pathogenesis of Diabetic Retinopathy

South West London Medical Society
8 30 P M (Bolingbroke Hospital Wandsworth Common S W 11) Mr W A Hervey Recent Advances in Ear Nose and Throat Therapy

University of Dublin
4 30 P M (School of Physic Trinity College) Prof Alf Brodal (Oslo) Pyramidal Tract in Light of Recent Anatomical Research

Wednesday, 29th

Postgraduate Medical School of London
4 P M Dr H A Sissons Growth and Repair in Pathology of Bone and Muscle

University College
5 15 P M Prof George Wald (Harvard) Molecular Basis of Vision

Royal Ear Hospital, St George's Circus Southwark S E 1
5 30 P M Dr A A Guild Symptomatology and Treatment of Cerebellopontine Angle Tumours

Birmingham Medical Institute
8 P M (Medical School Birmingham 15) Prof J Elkes Pharmacological Method in Psychiatric Research

Thursday, 30th

University of London
5 30 P M (University College Hospital Medical School Gower Street W C 1) Professor Nicolaysen Dynamic and Quantitative Aspects of Calcium Metabolism

Royal College of Surgeons Lincoln's Inn Fields, W C 2
5 30 P M Mr Norman Barrett Cardiospasm

Postgraduate Medical School of London
4 P M Dr Ian McMillan Movements of Normal and Pathological Aortic and Mitral Valves, and High Speed Cinematography of Dog's Heart with Simultaneous Pressure Recording (Films)

London School of Hygiene and Tropical Medicine Keppel Street, W C 1
5 30 P M Dr G Gustafson (Malmö) Structure of Enamel

Royal Eye Hospital
5 30 P M Miss M Savory Conjunctivitis

St George's Hospital Medical School Hyde Park Corner, S W 1
5 P M Dr Denis Williams Neurological demonstration

Association of Surgeons of Great Britain and Ireland
9 A M (University of London Malet Street W C 1) Opening of three day annual meeting

Renal Association
4 30 P M (41 Portland Place W 1) Dr H Wirz (Basle) Osmotic Work of Mammalian Kidney

West London Medico-Chirurgical Society
7 30 P M (London Airport) Sir Harold Whittingham Medical Problems of Air Transport

Nuffield Orthopædic Centre Wingfield Morris Orthopædic Hospital Oxford
8 30 P M Mr F W Somerville Congenital Dislocation of Hip

University of St Andrews
5 P M (Medical School Small's Wynd, Dundee) Dr G S Dawes Changes in Circulation at Birth

Friday, 1st

University of London
[illegible] P M (University College Hospital Medical School) Prof J Chassar Moir Use of Radiology in Forecasting Course of Labour

Postgraduate Medical School of London
Noon Prof R A McCance F R S Renal Function Before and After Birth
4 P M Dr J F Goodwin Cardiac Arrhythmias

St Mary's Hospital Medical School Paddington W 2
5 P M Dr Raymond Cohen Dr W D W Brooks Tuberculosis in Pregnancy

Royal Society of Medicine
10 30 A M *Section of Otology* Mr Philip Reading Management of Soft Tissues in Mastoidectomy Mr J [illegible] Stewart Perichondritis Mr C A Hutchinson [illegible] superior Approach to Fenestration (film)
2 30 P M *Section of Laryngology* Dr I B Harman Mr Ronald Foley Mr H D Brown Kelly Hiatus Hernia and Œsophagitis
5 30 P M *Section of Anæsthetics* Dr I R Bromage [illegible] Electroencephalographic Changes Associated with Vascular Hypotension Dr P J Bodman Normorphine

Royal Eye Hospital
5 30 P M Mr A J Cameron Virus Diseases of Eye

Institute of Dermatology St John's Hospital Lisle Street W C 2
5 30 P M Dr I M B [illegible] Eczema

both science and commerce. How often is it seen in this country?

If Sir Reginald Watson-Jones, as an orthopædic surgeon, is satisfied that enough is spent in this way on bacteriological research, there may be others who think otherwise; as "the last straw," their freedom of thought must be respected.

Department of Bacteriology,
St. George's Hospital Medical School. S. D. ELEK.

SITTING DOWN TO SURGERY

SIR,—What a ray of sunshine over Easter was Mr. Sacks's advocacy (April 4) of more sedentary surgery—taboo to all but orthopædic surgeons delving deeply in the palm. But let his team share equally in the general quest for peace and longevity.

His standing assistant must be tall and must peer precariously into the wound from the other side of the table. A short man mounted on a stool or platform would only add to the general instability. With deference, too, it would have been nice to have had a picture of Sister, mellifluent to the last, with her poor feet up.

London, S.W.3. C. I. MURPHIE.

TRICHOMONAS VAGINITIS

SIR,—The original article by Dr. Lanceley and Dr. McEntegart, the extremely interesting editorial, and the valuable letter from Mr. McCullagh in your issue of April 4 prompt me to make some comments.

In a series of cases of trichomonas vaginitis it was possible to find the organism in the prostatic smears from approximately one-quarter to one-third of all contacts tested. The method of testing by urethral scrapings has not yet been attempted, but it seems likely that Lanceley and McEntegart have rendered a real service by introducing this new way of finding the trichomonas in the male.

If gonorrhœa is a venereal disease, so is infestation with *Trichomonas vaginalis*. Of more than 500 patients with proved infestation seen by me in the last six years, only 2 were definitely virgins. Gonorrhœa, too, has on occasion been acquired by non-venereal channels. In a series of 1000 cases of vaginal discharge now being prepared for publication there were 103 cases of gonorrhœa, of which 2 were in virgins.

In cases of trichomonas vaginitis, with really efficient treatment of the vaginal discharge, including if necessary the treatment of trichomonas cystitis, the disease will not relapse if intercourse is eschewed. It will often, however, recur if intercourse without a sheath is allowed.

I have seen severe trichomonas vaginitis with remissions and relapses after several months in a patient whose symptoms began shortly after a repair operation. The remissions followed treatment with acetarsol pessaries; the relapses followed intercourse. Similarly another patient dated her vaginitis from a visit to a practitioner who fitted her for a Dutch cap. Gonorrhœa can be transmitted by rubber gloves as can syphilis or trichomonas. Possibly all three can also be transmitted by lavatory seats, and it is surely reasonable that the U-type seats advocated by Mr. McCullagh should be installed at least in the lavatory in every gynæcological ward.

Commonly, doctors in venereal-disease and gynæcological clinics wear the same pair of rubber gloves for the whole session, merely washing the hands with soap and water between cases. Soap and water will kill most organisms, but detergents are extremely effective trichomonicides. I therefore urge that the gloved hands be dipped into a bowl of detergent before being dried after washing. Detergents should, however, be used with the greatest of care in vaginal douches, and never in bladder washouts, for severe reactions may occur.

London, W.1. ELLIOT E. PHILIPP.

EXTRAORDINARY MEETING OF THE B.M.A.

SIR,—I note that, following the requisition for an extraordinary general meeting of the British Medical Association, the Working Party has been called together in order to take effective steps to investigate and relieve any injustice inherent in the distribution plan. This belated action does in fact secure the main purpose of the requisitionists, for it is accompanied by an assurance that any injustices which are found to exist will be made good retrospectively to April 1, 1953. It therefore appears to me that it is no longer necessary to ask that the implementation of the scheme should be postponed pending a proper inquiry, and I have accordingly submitted an amendment as follows: "To delete all the words following the words 'entry into practice.'" I trust this will be acceptable to the requisitionists, the proposed amended resolution being:

> "That the Association being concerned by the modification of the present method of remuneration by capitation fees agreed in the Working Party's Report requires the Council forthwith to approach the Minister of Health with proposals for the better protection (financial and otherwise) of the small-list doctor and of the doctor newly seeking entry into practice."

May I trespass on your space to add a personal reflection? The Working Party should have taken effective action to inform itself of the nature and size of the problem and to devise a suitable solution not later than last October; had it done so, small-list practitioners and others would have been spared much anxiety and distress, and there would not now be this need for the requisitioning of an extraordinary meeting.

London, W.1. HORDER.

KERNICTERUS

SIR,—Although we are not in a position to comment on the histological evidence of identity of the various forms of kernicterus, we would like to make some observations on the conclusions that Dr. Govan and Dr. Scott draw from their observations (March 28).

They state that anoxia of the brain is the primary mechanism and that the pigmentation is secondary. If this anoxia is regarded as occurring at birth it is difficult to explain the lesions produced in young animals by Eyquem.[1] Here the blood incompatibility was induced postnatally. Further, if the anoxia is regarded as secondary to anæmia it is difficult to explain the development of kernicterus in human infants with comparatively slight anæmia but deep jaundice. This phenomenon is well known to clinical observers and is confirmed by Mollison and Cutbush.[2]

Crigler and Najjar[3] reported a familial type of non-hæmolytic jaundice in which kernicterus was a feature in 5 out of 6 infants. It is difficult to attribute this to anything other than an underlying disorder of liver function of which abnormal pigment metabolism was the outward sign, if not the responsible agent. The direct association between abnormal pigment metabolism and kernicterus has been made clear by Mollison and Cutbush[4] and Diamond et al.,[5] high serum-bilirubin concentrations in the neonatal period being associated with the development of kernicterus. One of us has recently made observations on the antenatal prediction of hæmolytic disease of the newborn[6]; these have shown that the development of kernicterus is directly related to the pigmentation of the liquor amnii and that this pigment is possibly derived from abnormal breakdown of hæmoglobin.

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1. Eyquem, A. *Acta neurol. belg.* 1949, 49, 965.
2. Mollison, P. L., Cutbush, M. *Blood*, 1951, 6, 777.
3. Crigler, J. F., Najjar, V. A. *Amer. J. Dis. Child.* 1952, 83, 259.
4. Mollison, P. L., Cutbush, M. *Brit. med. J.* 1949, i, 123.
5. Diamond, L. K., Hsia, D. Y., Allen, F. H., Gellis, S. S. *Amer. J. Dis. Child.* 1952, 84, 640.
6. Bevis, D. C. A. *J. Obstet. Gynæc.* 1952, 59, 857.

muscles (with their nervous connections), and they may appear to be mentally retarded because their disability has deprived them not only of opportunities for gaining experience of their environment, but also of satisfaction of the instinct to explore And so their conduct or behaviour may lag behind their age

Human Contacts

As yet I have referred only to the physical or material things in a child's environment—the lights and coloured toys, the sounds of rattles, the touch of the mother's breast upon the child's lips These contacts give him experience, provided that he is equipped to make use of them, and with this experience his behaviour develops in a normal, though stereotyped, fashion But it is doubtful whether it influences the conduct of a healthy child in later life, except in a very general sense On the other hand, a child's contacts with human beings *as individuals*, each with a different pattern of behaviour, bring into the picture relationships that make a much more significant and complex impact upon his conduct, both in childhood and in later life

When we try to analyse these intimate relationships we find that most children show at least three marked characteristics—namely, their tendency to imitate, their capacity for hero-worship, and their power of imagination The instinct to imitate is fundamentally protective, and we can well imagine that the infantile death-rate in the animal world would be infinitely greater if the young did not follow closely the pattern of life set by their parents In man mimicry has become less obviously protective in function, though still important because the child is likely to imitate the patterns of behaviour presented to him, whether or not they are desirable from social and ethical points of view Certainly the ability of a child to copy a person's conduct, as distinct from separate physical attributes like quality of voice and gestures, depends largely upon his understanding, and thus the gods and goddesses of one's childhood are more likely to be teddy bears, cricketers, footballers, and ballet-dancers than the types of whom Carlyle wrote, such as prophets and poets

Limits of Understanding

I mention this obvious fact to indicate how often the behaviour of children becomes unnatural and sometimes objectionable when the very limited range of their understanding is not appreciated by those about them It is the reason why, in my view, the well meant endeavours of many parents in the first half of the 19th century to foster their children's spiritual development fell so short of their hopes, and not infrequently resulted in bewilderment, priggishness, and sometimes abject terror You have only to dip into Mrs Sherwood's remarkable book *The History of the Fairchild Family* (1818, 1842, and 1847) to get an impression of the very abnormal effects that might be induced in this way

I will quote only one illustration—the incident when Mr Fairchild found his three children squabbling over a doll After dinner he said to his wife 'I will take the children this evening to Blackwood and show them something there which I think they will remember as long as they live, and I hope they will take warning from it and pray more earnestly for new hearts So he took them to Blackwood and there was a gibbet on which the body of a man hung in chains The body had not yet fallen to pieces although it had hung there some years It had on a blue coat a silk handkerchief round the neck with shoes and stockings and every other part of the dress still entire but the face of the corpse was so shocking that the children could not look upon it There Mr Fairchild made the children sit while he told them the tale of the murderer who had first hated and afterwards killed his brother

Or you may turn to a more gentle illustration, to the *Hymns for Infant Minds* (1811) by Jane and Ann Taylor, who also wrote the famous "Twinkle twinkle little star," and hear in imagination the high pitched tremulous voices singing

I thank the goodness and the grace
Which on my birth have smiled,
And made me, in these Christian days
A happy English child

I cannot lay me down to rest
In quiet on my bed
Until with shame I have confessed
The naughty things I said

Yet the authors, in their preface to these Hymns declared that their intention had been to adapt "Evangelical truths to the wants and feelings of childhood, in language that it understands" As we all know, and as Francis Thompson illustrated so beautifully in his essay on Shelley, it is difficult for an adult to go down to the level of a child's intelligence without making a complete fool of himself—"Know you what it is to be a child?" asked Thompson

"It is to be something very different from the man of today it is to be so little that the elves can reach to whisper in your ear it is to turn pumpkins into coaches, and mice into horses, lowness into loftiness and nothing into everything it is to live in a nutshell and count yourself the king of infinite space "

Imagination

These words are a reminder, too, that children often spend a part of their days in a state of imagination or fantasy, an almost limitless world of make believe which brings them great happiness and fosters many attractive qualities as well as the beginnings of a reverence for Nature I knew a little girl, an only child, who had nine imaginary brothers and sisters—her parents confirmed to me with an obvious feeling of relief that they *were* imaginary !—and she knew not only their names and ages, but what they were all doing from hour to hour, the names of their dolls and dogs and cats, and all about them They were, so to speak, in the direct succession to Alice and John, the dream children of Charles Lamb's reverie, and they provided an outlet for her sympathy and affection

Friedrich Froebel (1782–1852), the founder of the kindergarten system of education, was another who in his childhood was deeply moved by fantasy, especially in the world of plants and flowers He had been neglected and misunderstood, and in his autobiography he says, "Early was I plunged into the painful and oppressive struggle of life" Being brought up in a hard school his fear of punishment sometimes caused him to tell untruths, and to be accused of being a wicked little boy, with the result that his sensitive nature, given to introspection and self analysis, suffered cruelly At the age of 15 he was apprenticed to a forester, and as one who, in his own words, "loved mountains, fields and forests" he developed a religious communion with Nature From this there sprang the conviction, basic to his scheme of education, that man is in essential unity with all things especially with Nature, and that the teacher's chief job is to provide a suitable environment in which the child's faculties may unfold To perpetuate this idea he coined the term "kindergarten" for the first of his schools

Froebel was a vigorous thinker whose contribution to education was considerable and he did much to establish the importance in a person's development of the early years of life The history of his own life illustrates how strongly fantasy in childhood may play a part in leading to significant activities in adult life, for children have still another instinct, what George Sampson called the creative instinct and it is closely allied to their power of imagination In amplifying this theory, Sampson wrote of a common mistake that is made in the upbringing and instruction of children—the mistake of believing that a child is a miniature adult and therefore capable of very extensive resection (leaving 1 × 3 in.), but at the time of his death we had not established the optimum. Even though we have now followed up all his patients for at least four years, it is still unwise to endeavour to define this, as the incidence of symptoms is influenced by so many other factors.

It is difficult to translate clinical results into figures, and I must apologise if my very factual report has given the impression that the results were unsatisfactory. A more human and possibly more accurate assessment has been made by these patients, who, on their own initiative, combined to endow two memorial prizes for nurses. As the amount subscribed exceeded requirements, they have obtained the sanction of the Chapter of York Minster—no easy matter—to erect a panel depicting the Art of Healing through the ages, and incorporating the name of Arthur Visick. This, I understand from the Dean of York, will be the first of its type in any cathedral in the country.

York County Hospital. C. N. PULVERTAFT.

WATER DIURESIS TEST

SIR,—Dr. Oleesky (April 18) proposes a "specific" water diuresis test for adrenocortical insufficiency, which should be a useful simplication of the Robinson-Power-Kepler procedure.

Unfortunately, false negatives are not eliminated by this modification. We have recently studied two undoubted cases of Addison's disease, both of which showed no eosinophil or ketosteroid response to 8-hour infusions of 20 mg. of A.C.T.H. in saline, on two successive days. In each case the maximum rate of urine flow after ingestion of a litre of water exceeded 10 ml. per minute without cortisone. The only *specific* test for adrenocortical insufficiency is the 2-day intravenous A.C.T.H. test, described by Renold et al.[1]

Medical Unit,
Royal Infirmary,
Cardiff. T. M. CHALMERS.

ENDEMIC GOITRE

SIR,—It would indeed be unfortunate if, at a time when new techniques of great value are emphasising the importance of the thyroid hormone in human metabolism, readers of your annotation (April 11) were left with the impression that "most goitres are quite harmless"—an observation which Dr. Stanbury himself did not make. Observations in North India and Nigeria as well as in rural Oxfordshire[2] have also shown that gross thyroid enlargement may have serious economic as well as physical consequences.

The recent introduction of a new grade of fine vacuum salt—dendritic salt—which lends itself to iodisation and can be supplied at a lower cost than coarse uniodised salt for districts where the amount of local salt is inadequate, should go a long way to meet your query as to "whether iodine prophylaxis is worth the effort and expense."

Oxford. DAGMAR WILSON.

AUGMENTING KNEE-JERKS

SIR,—Of all the tricks and artifices employed by doctors to elicit physical signs, few appear more ludicrous and more difficult to follow than the means of augmenting sluggish knee-reflexes.

One asks the patients to clasp their hands and pull, to clench the jaw (or gnash the teeth), to close the eyes or to look at the ceiling and pretend that the doctor does not exist; and to ask any patient to "relax" at once becomes the signal for the body to stiffen into a catatonic state with the legs rigidly extended into the air. What with coaching, coaxing, and correcting, the doctor has often forgotten at the end of it just why he wanted to test the reflexes anyway.

I have found that all these devices may be dispensed with and replaced by a simple manœuvre. With the patient recumbent, lift both knees about nine inches and ask the patient to push both heels gently on to the bed. This contracts the antagonists and automatically relaxes the extensors to be tested. In addition it always augments the knee-reflexes and rarely excites ribald laughter or a gnashing of teeth.

Central Middlesex Hospital,
London, N.W.10. B. I. HIRSCHOWITZ.

UTERINE CANCER AND VAGINAL SMEARS

SIR,—With reference to the remarks in your leading article last week, for the past four years I have been examining the breasts of all patients referred to me for a gynæcological opinion. At the same time the possibility of carcinoma of the rectum has always been remembered when carrying out pelvic examinations. I have discovered four carcinomas of the breast and one carcinoma of the rectum.

The patients with carcinoma of the breast were referred because of: (1) a pelvic-floor prolapse, (2) slight intermenstrual bleeding (a small cervical polyp was discovered), (3) an enormous ovarian cyst which filled the abdomen, and (4) irregular vaginal bleeding which was found to be due to carcinoma corpus uteri (this patient had a double primary carcinoma).

NORMAN KIMBELL
Consultant obstetrician and gynæcologist,
Peterborough area.

PROFESSIONALISM IN THE HEALTH SERVICE

SIR,—The certitudes of the maiden aunt as to how her married sisters should—but do not—nourish and rear their children are known to most parents, but much is forgiven to this well-meaning lady because she has her own virtues. Yet even the most patient of harassed mothers will sometimes ask herself whence the source of the superior wisdom so firmly pressed upon her, and by what right it is proffered.

If he will forgive me for saying so, Mr. Farrer-Brown has constituted himself the most censorious of doctors' maiden aunts in his address to the Institute of Almoners, published in your issue of April 11; but unlike his prototype he has not addressed himself to the persons directly concerned, but publicly to another audience; one that is not responsible for the shortcomings he detects in us, nor able to do anything about them.

I do not seek to fathom why he should have approached us on his delicate mission in this very indirect and public fashion—so that we are the last to hear what he has to communicate—nor to deal with his severe strictures upon those of us who (as he believes) show "consistent incompetence and persistent neglect" in our work. We are too used to the curtain lecture to be unduly sensitive to this latest and most drearily humourless of its many versions.

Yet I do feel that his hazy notions as to what constitutes a profession may usefully be considered, for upon this question are based our relations with the diverse ancillary services that we now have at our disposal in the practice of medicine.

He says that "in so many respects there seems no apparent distinction between a vocation which is generally recognised as a profession and one which is not . . . There seems to be one distinctive feature which is at the heart of the question . . . It concerns the nature of the relations between the professional man or woman and the individual he is engaged to serve." This relation, he goes on to say, is that of trust. But is there any avocation that may bring a man into business or contractual relationship with customer, client, employer, or employé where there does not exist this relationship? Only Robinson Crusoe on his island before the advent of man employment under harsh conditions. It seems probable that childhood delinquency, in our sense of the word, was less widespread than it is today, partly because there was little time available to them to get into mischief, and partly because they were habituated to a stern discipline in the home—sometimes, it is true, a crude form of discipline, and perhaps misguided because the level of general education was so low, but none the less effective because it was repressive. And not infrequently parental control was backed up by threats of divine sanctions, for the doctrine of original sin was fairly widely accepted. There is plenty of evidence that many of the survivors of that epoch, covering the first fifty years of the 19th century, looked back upon their childhood with bitterness.

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[1] Renold, A. E., Garcia-Reyes, J., Jenkins, D. *J. clin. Invest.* 1952, 31, 657.
[2] Medical Research Council memorandum, no. 18. H.M. Stationery Office, 1948.

It is not easy to get a clear picture of what is happening in the minds of children living in corresponding circumstances today. Their parents are better educated, but many are still ignorant and feckless, their housing conditions are lamentable, and there is fairly general agreement that moral and ethical standards are low. It would be surprising if many children brought up under these conditions did not show some undesirable effects in their behaviour, yet we must be cautious in coming to conclusions about the incidence of such effects, because our newspapers see to it that we hear all about the delinquents, and little about the others, and similarly it is the children who steal our flowers and fruit, who scratch our cars, and break our street lamps, that give us reason for remembering them. The wartime evacuation of city children to districts less likely to be bombed was, in one sense, a great social experiment that brought to light many personal shortcomings and social evils, and the report entitled *Our Towns: a Close-Up* by the hygiene committee of the Women's Group on Public Welfare horrified the country by its revelations. Above everything else it revealed the terrible effects of the adult "slum mind" upon children—effects due mainly to ignorance of the care and upbringing of children and of general household management, wrong ideas about the best use of money, evasion or negligence of the duty to instil discipline, and often a sad failure by the adults to set an example of decent, honest living. The children are now back in the cities again, and the public conscience has lulled itself once more into a state of apathy.

It is interesting to look again at the conclusions reached by informed opinion at the time that *Our Towns* and other similar reports were published and to note how much faith was then placed in extending the policy of granting more material assistance, drawn from the national Exchequer, to more families. It must, of course, be admitted that such assistance, in one form or another, is essential for a great many families, if we, as a nation, are intent upon maintaining our reputation for taking care of the needy, our chief problem is to ensure that the help given to parents is educational as well as material. This point has not yet received the attention that it deserves. The homes of the people should be places fit for children to live in, and it is an evasion of the issue to argue that, as an alternative, the younger children should attend nursery schools, and similar places, where they will be taught to keep themselves clean and where they will find a satisfactory diet and opportunities for sound sleep beyond the range of the wireless. As a temporary expedient this might be reasonable, though very expensive, but at a time when the god of planning ranks as deity no. 1 let us first be sure that our aims are fundamentally sound. Do we honestly believe that the home, and all that it stands for as the focus of family life, is worth preserving, or do we think that it can be profitably replaced by schools, centralised restaurants, and other institutions, no matter how well these may be planned and administered?

Excessive Solicitude

You will, I think, have sensed one outstanding difference between the two large groups of children I have been considering, our concern for the less fortunate group—the children of the social class that used to be called the poor—is that we should use all practical means at least to raise them from frank inferiority, while for the more fortunate children, relatively safe from the threats of the five giant evils, and already enjoying a good standard of living, we have opportunities for striving more closely to the ideals we hold. Let me revert, therefore, to the children in our own social group and see whether I can summarise the thoughts which are the basis of this address.

The younger they are, the more their conduct is a measure of their physical endowment and growth, and this "bodily" phase, if I may so call it, has a significance and importance beyond all comparison with physical activity in adult life because the child is actively growing and the full evolution of his behaviour is dependent upon a satisfactory start. Then comes the phase in which relationship with other persons dominates the picture. We have seen that, as a background, good hygiene, exemplified by satisfactory housing conditions, suitable diet, opportunities for sleep and recreation, cleanliness, and so forth is of much importance, and that certain intangible requirements, especially security in the home, discipline, and good example, are perhaps even more important if conduct in childhood is to develop later into sound citizenship. But I do not want to end this address on too austere a note. Childhood should be a period of happiness and we adults must be careful not to smother their spark of gaiety under a mound of excessive solicitude and anxiety for perfection. And as an added warning against over-concern for the young, remember that the "heavy" father—or "heavy" mother, for that matter—may sometimes have to suffer the double annoyance of failing to achieve his object and of making himself appear ridiculous.

> "Auntie, did you feel no pain
> Falling from that apple tree?
> Would you do it, please, again
> 'Cos my friend here didn't see."
>
> *Ruthless Rhymes* (CAPTAIN GRAHAM)

Potentialities

Children are all different and no two sets of circumstances are alike, each must be an individual study. Nor do I feel that I should attempt to answer the interesting general questions that I mentioned earlier, because in human affairs rules are usually found to have too many exceptions. In slum districts, for instance, you will find thousands of families leading exemplary lives despite the most forbidding handicaps, and among "educated" people you will find examples of abnormal childhood behaviour because education has been assumed like a veneer, and has not been absorbed into life as a basis of character. Furthermore, some of those people who have later made noteworthy contributions to life whether in literature, science, the arts, or what you will, have been very strange and difficult children. Shelley, shy and meditative, was at heart a rebel and at times of provocation could be dangerously pugnacious, Keats, though superficially carefree was oppressed by a strange sense of melancholy, John Hunter, the famous surgeon, found much difficulty in learning even the rudiments of reading and writing at the age of ten, and Latin had to be abandoned.

If one leaves out of count those children that have followed an entirely unexpected course in their subsequent development and behaviour, there are good grounds for maintaining that the qualities most sought after because, in our phraseology, they are most civilised are established in the years of childhood, an adventurous, courageous, but disciplined spirit, a character

He was born in London and he studied medicine at St. Bartholomew's Hospital and the University of Durham, where he graduated M.B. with first-class honours in 1887. Two years later he was awarded the gold medal for his M.D. thesis on colour-blindness, in which he attacked the Holmgren wool test and first put forward his theories on the function of the retinal rods and of the visual purple.

Soon afterwards his views received wider publicity when Sir Lauder Brunton presented a paper of his to the Royal Society, and he was appointed a member of the International Code of Signals Committee. But his views did not win immediate acceptance: and in 1892 a committee of the Royal Society unanimously recommended the continued use of the Holmgren test to railway companies and shipowners. Though disappointed by this setback Dr. Edridge-Green published a further monograph on his work, and in 1904 a committee of the Ophthalmological Society confirmed his contention that some cases of colour-blindness cannot be detected by the Holmgren test. Fortified by this support he went to Cambridge at his own expense to obtain further evidence. There, however, he was coolly received and his thesis was turned down. But he continued to press his case, and in 1909 he published a monograph on *Colour Blindness and Colour Perception*. Meanwhile at Oxford Doyne and Gotch had confirmed his findings, and gradually informed opinion turned in his favour.

In 1911 he delivered a Hunterian lecture on colour-blindness at the Royal College of Surgeons, and the following year a committee of the British Association reported in his favour. Questions were asked in Parliament, and in 1915 the wool test was abandoned by the Board of Trade and a lantern based on Edridge-Green's principles was adopted. Five years later he was appointed an adviser to the board. In 1920 he was appointed C.B.E., and the same year he gave the Arris and Gale lectures at the Royal College of Surgeons. In 1930 he was president of honour at the annual meeting of the Ophthalmological Society of Paris, and in 1936 he was awarded the Thomas Grey prize.

Dr. Edridge-Green's own account of these far-away battles, which he published in 1933 under the title of *Science and Pseudo Science*, shows him to have been a trenchant and contentious controversialist, and much of his work on the physiology of vision is at variance with present-day thought. But personal difficulties and scientific differences cannot obscure his real contribution to the safety of transport on land and sea.

In 1893 he married Minnie Jane, the daughter of Dr. Henry Hicks, F.R.S. She died in 1901 and there were no children of the marriage.

ALEXANDER MITCHELL

M.A., Ch.M. Aberd.

Mr. Alexander Mitchell, consulting orthopædic surgeon to the Aberdeen Royal Infirmary, died on April 16, at the age of 72. The record of his family's connections with medical practice is impressive. His grandfather and father practised at Old Rayne, Aberdeenshire, his two brothers were doctors, and one of his sons is Major Patrick Mitchell, R.A.M.C. His first wife was a daughter of the late Dr. Greig of Fyvie, and his second wife a daughter of the late Dr. David Rorie, whose poems, including "The Lum Hat Wantin' the Croon," are well known in the North of Scotland and far beyond.

He graduated M.A. at Aberdeen University in 1901, M.B. in 1905, and CH.M. in 1907. He spent several years in general practice with appointments at Fyvie Hospital and Gray's Hospital, Elgin, but his career in surgery began about 1914 when he was appointed to the Royal Hospital for Sick Children and the Royal Infirmary, Aberdeen. Himself crippled, he had a strong bent for orthopædics which was stimulated by his surgical experience at base hospitals in Rouen during the 1914–18 war and later became his main professional interest. Between the wars he developed an orthopædic department at Aberdeen Royal Infirmary and later, with the help of the Cripples' Welfare Association, an orthopædic service for the whole North East of Scotland. During the late war he became orthopædic consultant to the E.M.S. and the Army Medical Services in the North of Scotland. Undeterred by a first attack of coronary thrombosis in 1942 he carried a heavy burden of work during the war years and, even after retirement from his Aberdeen hospital appointments in 1945, he continued as consultant to the Department of Health and to the North-Eastern Regional Hospital Board under the National Health Service. He was also a vice-president of the Orthopædic Association. Recently he became chairman of the management board of the Aberdeen special hospitals group and, in fact, was presiding at a board meeting when the final coronary attack began.

W. C. W. *writes*: "Distinguished as were his services to orthopædics. Sandy (as he was known to all) will best be remembered for his personal qualities and relations with patients. More interested in men than in affairs, he had a fund of reminiscences and stories and a dry, sardonic wit which made him excellent company. His opinions and judgments were forthright and decided, but always fair and often generous. He had a delightful manner with sick children and a real sympathy for the deformed and maimed. His own standard of service to patients was the highest and he demanded the same from his juniors. In this one could see the influence of tradition and upbringing in a medical family and it is a safe assumption that the tradition has been handed on to many former assistants and students. As usually happens, they were quick to see the sterling qualities of the man and with them his popularity was high. His character has been summed up in the words of an old patient: 'He was a grand gentleman, Sandy Mitchell.'"

Mr. Mitchell is survived by two sons and a daughter and by his widow who gave him great help in his last years.

Births, Marriages, and Deaths

BIRTHS

FORBES.—On April 15, to Pamela, wife of John Forbes, M.D., of Pen-y-wern, near Mold, Flintshire—a son.

FOXELL.—On April 13, at Suffolk House Nursing Home, Stanmore, to Maureen, wife of Dr. Alan Foxell—a son.

MARRIAGES

NEWBORNE—SKELTON.—On April 18, at St. Giles Church, Oxford, Laurence Perceval Anthony Newborne, M.D. Lond., to Mary Skelton, M.C.S.P.

Appointments

BICKFORD, J. A. R., M.R.C.S., D.P.M.: consultant psychiatrist, De la Pole Hospital, Willerby, E. Yorks.

DAVIES, E. B., M.B. Manc.: medical registrar, Rookwood Hospital, Cardiff.

HILL, J. N., M.B. Leeds, D.P.H.: medical director (S.H.M.O.), Leeds mass-radiography unit.

MORTON, J. A., M.B. Edin., M.R.C.P.E.: M.O. (part-time), H.M. Prison, Edinburgh.

TODD, ELIZA, M.B. Aberd., D.P.H.: asst. M.O., Heston, Isleworth, Southall, Brentford, and Chiswick area, Middlesex County Council.

VICKERY, K. O. A., M.D. Lond., D.P.H.: M.O.H. and school M.O., Eastbourne.

Colonial Service:

ALLEN, C. P., M.B., CH.M. Glasg., F.R.C.S.E., D.T.M. & H.: specialist officer, grade A, Federation of Malaya.

COCHEMÉ, M. A. X., M.B. Camb., D.T.M. & H., D.P.M.: specialist officer, grade A, Federation of Malaya.

DRURY, GRAHAM, M.R.C.S., D.T.M. & H., D.A.: A.D.M.S., Kenya.

EDDEY, L. G., M.B. Aberd., D.T.M. & H.: D.M.S., Gold Coast.

FRANKLIN, G. C., M.B. Camb.: M.O., Hong-Kong.

GREEN, R. T. B., M.D., D.T.M.: Specialist officer, grade A, Federation of Malaya.

MOLESWORTH, B. D., M.B. Camb.: specialist officer, grade A, Federation of Malaya.

PALLISTER, R. A., O.B.E., M.D. Durh., M.R.C.P., D.T.M. & H.: specialist officer, grade A, Federation of Malaya.

RYAN, J. C., M.B. N.U.I.: M.O., British Guiana.

SHAW, R. E., M.B. Lond., F.R.C.S.: M.O., Kenya.

SINCLAIR, WILLIAM, M.B. Belf.: M.O., Nyasaland.

Western Regional Hospital Board, Scotland:

CUTHBERT, RICHARD, M.B. Glasg., D.M.R.D.: asst. radiologist (S.H.M.O.), Stirling county area.

HARPER, JAMES, M.B.E., M.B. Edin., M.R.C.P.E., D.P.M.: consultant psychiatrist and deputy physician-superintendent, Crichton Royal Mental Hospital, Dumfries.

TAIT, A. C., M.B. Glasg., D.P.H., D.P.M.: consultant psychiatrist, Crichton Royal Mental Hospital, Dumfries.

TABLE II—CHOLINESTERASE

(µl carbon dioxide per g per hr)

Tumour no	Substrate		
	Acetylcholine	Acetyl β methylcholine	Butyrylcholine
1	6380	1265	8100
2	950	221	1170
3	434	133	27
4	630	34	621
5	1015	292	988
6	1130	636	109
7 (a) Pure	—	—	—
(b) Edge	1020	65	712
(c) Centre	2580	1160	1830
8	2010	1130	1740
9	4830	2060	793
10	784	—	—
11	147	41	319
12	0	0	25
Cortex adjacent to abscess	898	470	733

glioma obtained from the child that the content in pressor amines, particularly noradrenaline, far exceeded that in all the other tumours The amine oxidase content was also high, but not outside the range of that in several other tumours Cholinesterase activity, especially the non specific or pseudocholinesterase, as shown when butyrylcholine was used as a substrate, was also very high in tumour no 1 The values for amine oxidase in gliomas varied over a wide range they exceeded the amounts found in the meningiomas and in most cases there was also more cholinesterase How difficult it is however, to obtain a definite correlation between cell type and enzyme activity is shown by tumour no 7, of which three different portions were investigated The sample of the astrocytomatous part of the tumour was too small to permit estimation of more than the amine oxidase The part of the tumour which was infiltrating the brain showed more amine-oxidase activity than did a portion taken from the centre, whereas the cholinesterase activity was higher in the centre of the tumour than in the peripheral portion An ependymoma of the spinal cord (tumour no 8) resembled most of the gliomas in its enzyme content as well as in its content of pressor amines This finding was interesting because the ependymomas are usually classified histologically with gliomas A neurofibroma of the acoustic nerve (tumour no 9) contained very low amine oxidase activity but very high cholinesterase activity, especially the specific or true cholinesterase, as shown when acetyl-β methylcholine was used as a substrate In two meningiomas no amine oxidase activity could be estimated, and in the third it was the lowest value found Similarly, the cholinesterase content was very low in the three meningiomas (tumour nos 10 11 and 12)

The question asked at the outset—whether neuroglia contains enzymes concerned with the metabolism of nervous transmitter substances—has been answered in the affirmative For comparison with the activity found in the brain tumours the values found in one specimen of human cortex from the right temporal region adjacent to an abscess removed at operation are given at the end of tables I and II In addition we are greatly indebted to Prof R H S Thompson and Dr A Tickner for their permission to cite results obtained on areas of the human brain shown in table III These values agree fairly well with those published by Birkhäuser (1940) on human brain cortex, when recalculated and expressed in the same terms, though the activity found by Birkhäuser in the thalamus and caudate nucleus was higher

TABLE III—AMINE OXIDASE ACTIVITY OF HOMOGENATES OF HUMAN BRAIN

(R H S Thompson and A Tickner, unpublished)

Area	µl oxygen per g per hr (in presence of cyanide)
Cerebral cortex grey matter	20[illegible]
Frontal	228
Parietal	170
Temporal	127
Occipital	
Cerebral subcortex white matter	1[illegible]1
Frontal	112
Parietal	27[illegible]
Internal capsule	[illegible]
Red nucleus	1[illegible]4
Corpus callosum	132
Cerebellum (grey)	1[illegible]7
(white)	

The amine oxidase activity which we found in glia tumours (table I, nos 1–8) falls within the range of that in various parts of the brain (table III), but the activity of the meningiomas (table I, nos 10–12) is well below

Perhaps the presence of pressor amines, particularly noradrenaline, in some of the tumours is even more significant than that of amine oxidase, which has a far wider distribution in the body Vogt (1952a and b) found 1–2 µg of noradrenaline per g of fresh tissue in cat's hypothalamus and about 1 µg per g in dog's hypothalamus, parts of the mid brain and medulla containing 25–30% of these figures Adrenaline, when present, was found in quantities of only a tenth of those of noradrenaline Tumour no 1 contained more pressor amines than did any of the areas investigated by Vogt (1952a and b) The amounts found in nos 2 and 3 are close to normal figures in dog's thalamus A sample of human cortex adjacent to an abscess contained none

In eight samples of brain tumours (table II, nos 1, 2, 5, 6, 7b and c, 8, 9) cholinesterase activity was found to be very high and of the order reported by Ord and Thompson (1952) for substantia nigra, cerebellum, thalamus, and red nucleus But, whereas in these areas the activity was mainly due to true cholinesterase, in six tumours histologically classified as gliomas, the pseudocholinesterase activity was very much higher than that of true cholinesterase This is interesting in view of the suggestion of Ord and Thompson that the function of pseudocholinesterase may be connected with processes in neuroglial elements Tumour no 1 contained more pseudocholinesterase than did any normal human brain area investigated by Ord and Thompson On the other hand, tumour no 9 with high total activity (a neuroma arising from the acoustic nerve) contained the greatest amount of true cholinesterase of all

SUMMARY

Glia tumours made up predominantly by glia cells may contain as much enzyme activity as normal brain tissue in which glia constitutes only a fraction of the different cell components Amine oxidase activity was of the same order as that in normal brain areas

Cholinesterase activity in six out of eight gliomas was greater than in normal cerebrum (grey and white) and of the order found in the thalamus, mid-brain, and cerebellum, but, in contrast to these, it was mostly due to pseudocholinesterase

One glioma (in a child) contained a larger amount of noradrenaline than has yet been found in any area of the normal central nervous system

We are greatly indebted to the late Sir Hugh Cairns and to Mr Joe Pennybacker for providing the material obtained at operations

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University of London

Dr. Miles Weatherall, senior lecturer in pharmacology at London Hospital Medical College, has been appointed to the readership in pharmacology at the college. Mr. L. F. Lamerton, PH.D., senior assistant physicist at the Royal Cancer Hospital, has been appointed to the readership in physics applied to medicine at the Institute of Cancer Research at the hospital.

University of Birmingham

Dr. Edwards A. Park, emeritus professor of pædiatrics in Johns Hopkins University, will deliver the Leonard Parsons lectures at the university on Tuesday and Wednesday, May 5 and 6, at 4 P.M. The subject of the first lecture is to be the Effects of Severe Infection and of Malnutrition on Normal Bone Growth and their Influence on Rickets; and of the second, Zones of Increased Density in Growing Bones and Underlying Mechanisms.

University of Dublin

Dr. F. M. R. Walshe, F.R.S., is delivering the Frederick Price lecture on Friday, April 24, at Trinity College. He is speaking on the Interpretation of Clinical and Experimental Observation in Neurology. On Tuesday, April 28, Prof. Alf Brodal, of the University of Oslo, will give the John Mallet Purser, lecture on the Pyramidal Tract in the Light of Recent Anatomical Research. Both lectures are at 4.30 P.M.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on April 13 with Dr. Andrew Allison, the president, in the chair, the following were admitted fellows of faculty:

E. B. Hendry, Sheriar Jamshed Irani, J. H. R. Ramsay, Chellappa Ratnavel, R. S. Walker, qua physician; Muhammad Ismet Anwar, qua surgeon.

Almroth Wright Lectures

Dr. Leonard Colebrook, F.R.S., will give the first of this series of weekly lectures which is to be held at the Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London, W.2, on Tuesdays at 5 P.M. from May 5 to June 16. Dr. Colebrook is to speak on Almroth Wright—Pioneer in Immunology. The other lecturers are: Mr. J. G. Davis, D.SC., Brigadier J. S. K. Boyd, F.R.S., Prof. C. L. Oakley, Prof. J. R. Squire, and Prof. Gerhard Domagk. Further particulars will be found in our advertisement columns.

International Congress of Blood Transfusion

The fifth International Congress of Blood Transfusion will take place in Paris from Sept. 13 to 19, 1954, immediately after the International Congress of Hæmatology, which will be held from Sept. 6 to 12. Further information can be had from Colonel (méd.) Julliard, 57, Boulevard d'Auteil. Boulogne sur Seine, France.

Irish Medical Schools and Graduates Association

At the annual dinner of this association at the Rembrandt Hotel, London, S.W.7, on May 7, Dr. W. R. F. Collis, the president, will present the Arnott medal to Mr. Terence Millin, and will invest Mr. Ian Fraser with the badge of presidency for the coming year. The hon. secretaries of the association may be addressed at 149, Harley Street, W.1.

Kingston and Malden Victoria Medical Foundation

The first report of this foundation, established in 1951 with the aim of setting up a new voluntary hospital, shows that in the *nineteen* months up to Dec. 31, 1952, receipts totalled £9747. Expenditure amounted to £2918, leaving a balance of £6828.

Stock-taking Time for Nursing

Opening the new preliminary nurse training-school at Orpington Hospital on April 16, Miss Patricia Hornsby-Smith, parliamentary secretary to the Ministry of Health, said that although the total nursing force had reached a record level of over 167,000, there were increasing claims on the country's woman-power. "It is, therefore, essential," she said, "that the time and skill of every nurse should be properly and efficiently used, and at this moment there is, as it were, a stock-taking in the nursing profession. "To make the best use of available nurses we must decide what were the proper tasks of the nurse, and the Minister had invited his Standing Nursing Advisory Committee to set up a small study group to report on the practical implications of this problem.

Areas in Scotland Needing More Doctors

A revised list of areas needing more family doctors has been prepared by the Scottish Medical Practices Committee, and is being issued to executive councils throughout Scotland. The Department of Health state that an initial practice allowance will be payable to a doctor setting up in single-handed practice in these areas.

Association of Occupational Therapists

This association is holding a conference at Church House, Westminster, London, S.W.1, from April 30 to May 2. Lord Webb-Johnson will open the conference, and other medical speakers will include Sir Russell Brain, P.R.C.P., Dr. Morris Markowe, Dr. J. G. Howells, Prof. J. Whillis, Mr. John Barron, Mr. J. P. Heron, and Prof. R. E. Tunbridge. Further particulars may be had from the secretary of the association, 251, Brompton Road, London, S.W.3.

Blood Donors

In 1952 gifts of blood to hospitals in England and Wales through the National Blood Transfusion Service totalled 647,009—over 50,000 more than in the previous year. It was the highest total since the record of 669,000 in 1944. 107,881 new donors were enrolled, and the donors' panel at the end of the year numbered 487,660; but the service still needs over 135,000 more donors, to do away with the need to call on anyone more than twice annually, to make good the loss of those reaching the retiring age of 65, and to provide a reasonable reserve of blood-plasma.

Association of British Pharmaceutical Industry

Speaking at the annual dinner held in London on April 15, Mr. Iain Macleod, the Minister of Health, said that the total bill for pharmaceutical services in the National Health Service was about £60 million a year, of which about £7 million was paid by patients. He was not much comforted when told that, looking at the cost of the service as a whole, this represented only about a penny in the shilling: by any reckoning £60 million was a vast sum—only a million or two less than what was needed to take 6*d.* off the income-tax. He well knew that the pharmaceutical industry made a very important contribution to exports and also that it was very important to continue the research that had brought such benefits. But he thought it fair to tell the industry that this Government, like the previous Government, was deeply concerned over the size of the drug bill—a subject that was (to use an official bromide) under earnest and constant and continuous review. He was, he added, deeply conscious of the industry's assistance to the Ministry, which had always had its willing and public-spirited coöperation.

Mr. Charles Saul, president of the association, said that the industry was more than anxious to help in effecting economies in the N.H.S. The cost of certain drugs was high, but so was the cost of research and of production; and the use of expensive drugs could be an economy if they shortened illness. The money value of the industry's exports had risen from £3·28 million before the war to £31·65 million last year, and every effort would be made to improve on that figure. But at no time had the industry been faced with greater difficulties than those of today—currency and quota difficulties, import restriction difficulties, and registration difficulties, to say nothing of increasingly severe competition from the U.S.A., Germany, the Continent, and even Japan and certain countries which benefited from incentives on exported goods. A new difficulty was the attempt in certain Continental countries to link the selling price in those countries *to the retail selling price in the country of origin*—a policy that would defeat its own object because the low-priced preparations would be driven off the market. While the Ministry of Health naturally pressed for the lowest possible price for all medicaments, the Board of Trade, wanting the greatest possible volume of exports, was not unwilling to see the manufacturer get a high price for his product. It was just not practicable, however, to charge a low price in this country and a much higher price abroad—one reason being that foreign importers could buy the product here through their agents. Exhorted to reconcile two irreconciliable policies—one to keep down prices in the home market, the other to increase export revenue or die—most manufacturers would undoubtedly prefer to export. If there were a single central body which at the highest level could look at any problem from the domestic and export standpoints simultaneously, the industry would give it full coöperation.

Mr. Richard Law, M.P., replied to the toast of The Guests.

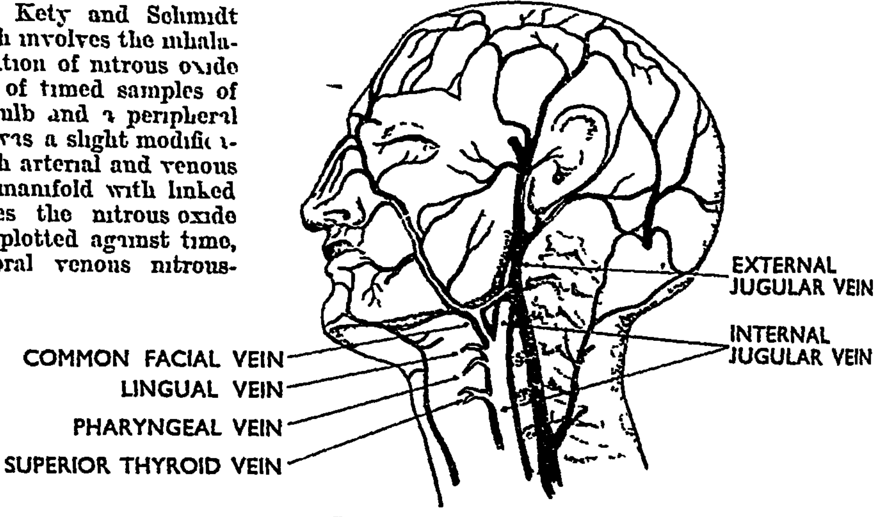

Fig 3—Venous anatomy

In the first 2 cases the estimations were made according to the original technique of Kety and Schmidt (1945, 1948) and Kety (1948), which involves the inhalation of a non-anæsthetic concentration of nitrous oxide for ten minutes and the removal of timed samples of blood from the superior jugular bulb and a peripheral artery during this period There was a slight modification in that one operator drew both arterial and venous specimens by means of a double manifold with linked pairs of syringes In these cases the nitrous oxide concentration in the samples was plotted against time, and the integrated arterial-cerebral venous nitrous-oxide difference $(\int_0^{10}(A-V)dt)$ was calculated from the curves by the trapezoid rule, relevant corrections having been made in the timing and for the dilution due to the dead-space volume of the catheter and tubing Otherwise the calculation was as described below

In the subsequent 4 cases the modification due to Scheinberg and Stead (1949) was adopted and continuous constant-rate withdrawal from artery and jugular bulb was maintained during the ten-minute period, the nitrous oxide content of each sample then represented the integral value for the whole period

It seemed to us that manual withdrawal at a constant rate was subject to an undesirable degree of human error and an electrical device was therefore constructed for the purpose Timing was by stopwatch and allowed for the evacuation of the dead-space volume, which was filled with heparinised saline solution, subsequent corrections were made for the corresponding dilution of the samples In other respects the technique resembled that of Scheinberg and Stead, a cerebral venous blank being taken immediately before each estimation, and final arterial and cerebral venous specimens at the end of the ten-minute period, nitrous oxide inhalation was continued until the latter were collected Arterial sampling was through an indwelling needle placed in either the left brachial or the left femoral artery The nitrous oxide mixture, which was supplied commercially (N_2O 15%, O_2 21%, N_2 64%), was conducted to either a face mask or a mouthpiece by way of a system incorporating an anæsthetic bag and inspiratory and expiratory valves Steps were taken to guard against possible leakages in this system

The blood samples were analysed for nitrous-oxide content in a Van Slyke Neill manometric apparatus according to the technique of Orcutt and Waters (1937), modified by Kety and Schmidt (1948) The analyses were all done by one of us (A R J), and eight pairs of duplicates submitted for statistical analysis showed a standard error of ±0 1 mm The mean cerebral blood-flow (C B F) was calculated from the formula

Mean C B F (ml of blood per 100 g of brain per minute)

$$= \frac{CV_{10} \times S \times 10}{\int_0^{10}(A-V)\,dt}$$

where CV_{10} is the nitrous oxide content in volumes % of the cerebral venous specimen taken at the end of the tenth minute S is the partition coefficient of nitrous oxide between brain and blood

$$\frac{\text{Solubility of N}_2\text{O per g of brain}}{\text{Solubility of N}_2\text{O per ml of blood}}$$

which has previously been found to approximate to unity (Kety et al 1948) and $\int_0^{10}(A-V)\,dt$ is the integral of the arterial cerebral venous nitrous oxide difference over the ten-minute period determined from the difference between the nitrous oxide contents of the two integrated specimens The theory and validity of the procedure have been extensively discussed elsewhere (Kety and Schmidt 1945 1948, Scheinberg and Stead 1949)

Arterial blood-pressure was measured by the auscultatory method in the right arm before, during, and after each estimation of blood-flow, and the mean arterial pressure for the period was calculated by adding a third of the average pulse pressure to the average diastolic pressure

The cerebral vascular resistance (C V R in C V R units) was taken as the quotient

$$\frac{\text{Mean arterial blood pressure in mm Hg}}{\text{Mean C B F in ml blood per 100 g brain per minute}}$$

A C V R unit may be considered as the mean pressure in mm Hg required to drive 1 ml of blood through 100 g of brain in one minute The theoretical standard error of the estimation of C B F in this way depends on the standard error (S E) of the manometric readings and on the magnitude of the difference in nitrous oxide saturation between the continuous samples of arterial and cerebral venous blood

Where the S E on the manometric apparatus is ± 0 1 mm the S E of the C B F method expressed as percentage of C B F is ± 3 5% for a difference of 4 mm in the manometric readings of samples $\int_0^{10} A\,dt$ and $\int_0^{10} V\,dt$ and decrease to a value of ± 2 3% for a difference of 6 mm Where the S E of manometric analysis is ± 0 2 mm these are correspondingly doubled The S E of C V R estimation is about ± 5%.

It was not considered justifiable to submit patients to successive C B F estimations to see how far observed differences confirmed these estimates, but duplicate estimations done in one patient were well within the predicted range Further, four other pairs of successive estimations performed under conditions which would not have been expected on a priori grounds to alter the C B F significantly all showed agreement within the range of the theoretical standard error It was thus thought unlikely that any other [illegible] variables were operating in the method as performed by us

With a single exception, no sedatives were given, and cardiac premedication was limited to quinidine gr 3 by mouth, which was administered at least two and a half hours before the first estimation of blood flow The exception was patient no 2, who received quinidine gr 6 and 'Sodium amytal' gr 3 by mouth three hours beforehand

The catheter was kept clear by a slow drip of heparinised physiological saline solution during catheterisation of the heart and between the first and second estimations of C B F Procaine was not used except for the intravenous injection of not more than 1 ml of [illegible] solution of the hydrochloride when the catheter was first introduced into the left antecubital vein Th

BEHAVIOUR IN CHILDHOOD*

NORMAN B. CAPON
M.D. Lpool, F.R.C.P.
PROFESSOR OF CHILD HEALTH IN THE UNIVERSITY OF LIVERPOOL

"... 'Tis Nature's plan
The child should grow into the man."—LONGFELLOW.

WE use the word "behaviour" in many different senses, and sometimes apply it even to inanimate objects. I should explain therefore that what I have in mind here is much more than the display of any single characteristic, such as deportment, sociability, or even personality; I am thinking of the sum total of an individual's activities, whether they spring from deliberate taking of thought, or whether they are due to habit or to subconscious reflexes.

Naturally the components of human behaviour are extremely complex; and the pattern is constantly changing. Just as a flower bears little resemblance to the seed from which it has grown, so in the transformation of behaviour from childhood to adult life the picture is likely to alter out of all recognition; or, to vary the metaphor, the central core of behaviour displayed during early life is sure to be concealed under the new accumulations of experience added year by year. Nevertheless the process is one of evolution, each successive phase bearing some sort of relation to what has gone before. Behaviour during childhood is in some measure the mould which gives shape and form to subsequent development.

Individuals and Groups

There are at least three ways of considering behaviour in childhood. The first is to take individual children and to observe their actions and how they conduct themselves in various circumstances. This is the way that interests most parents; it is personal, intimate, and factual. A second way is to select certain groups of children, and note whether the behaviour of the individuals composing each group has features that are common to all, or perhaps to a majority. Examples of such groups might be "only" children; or children born into the so-called problem families; or the children of artistic parents, like musicians or poets; and I might also add other groups—if it were not to tread on dangerous ground—such as the children of pædiatricians or of psychologists.

The third way is to consider the behaviour of much larger groups of children, and to face up to questions that have to be answered on the basis of general impressions rather than detailed observations. Can we, for instance, claim that the children of today have better manners than those of a hundred years ago? Is childhood delinquency on the increase or not? Does the use of political propaganda in schools in certain countries affect the character and conduct of the pupils when they become men and women? These are problems that greatly concern statesmen, politicians, sociologists, the members of debating societies, and indeed each one of us; but I need not remind you that generalisations are easily made but seldom convincing, and one must always be cautious both in making and accepting them. And whether or not we decide to tackle such interesting but elusive problems, we must first give some thought to the "individual" mode of approach, and ask ourselves about the factors that probably play a part in determining the behaviour of children.

Tendencies

Undoubtedly there are inherited tendencies, but these are curiously bizarre in their transmission; and when a child displays a parent's characteristics there is always the possibility that mimicry rather than heredity has been responsible. (One fact stands out in my experience—that any unfavourable trait shown by a child is commonly ascribed by the mother to direct transmission from the father's side of the family.) Then there are those strange and amazingly vigorous urges that we call instincts: these play a big part, especially in regard to feeding and to self-preservation, and though they become modified by experience and memory they are potent directives of behaviour during the whole of childhood. And there are many other instincts, less fundamental though still noteworthy: of these I will mention only the urge to dominate others and to have possessions: the herd instinct, linked with social customs and with local loyalties, whether to school or to crime-gang: and the instinct to explore and gain experience, which later may become the most significant weapon used by the scientist, the theologian, or the expert burglar. And behind all these instincts there works the inexhaustible energy of childhood, giving momentum and, as we adults often think, inexplicable direction to their activity simply because the child's reasoning capacity is underdeveloped. As one little boy said to me when I mildly rebuked him for his restless and rather foolish behaviour, "But I never know what I'm going to do until I've done it."

Sensations

The power of discrimination is also immature in childhood, but it may be seen even in the instinctive behaviour of animals still in their infancy; and a human baby will not suck and swallow more than a mouthful or two of a bitter solution offered instead of milk. It would be idle to pretend that this choice in respect of diet in infancy possesses the full conscious significance of an adult's preference for, say, a dry sherry, but it is certainly a more elaborate and selective response than the contraction of a muscle in a nerve-muscle preparation. And at an early age—certainly by the third month—a baby indicates, by smiling or grimacing, that his actions bring him contentment or vexation, that is to say a range of feelings less sharp-edged than vivid pleasure or pain. These sensations, which later become increasingly complex, like a spectrum of colours derived from a single beam of white light, eventually play a part in fostering those conscious choices which the adult describes as preferences, tendencies, leanings, and so forth, and undoubtedly constitute an important factor in determining behaviour. And even in early life, their expression by facial and bodily movements is a channel by which the child makes his contribution to the to-and-fro tossing of messages between himself and the people that surround him.

The younger the baby, the smaller is his space-world—that is, the surrounding area available to him for gaining experience. Things must touch his skin, and objects must be placed immediately in front of his eyes, before he becomes aware of their presence; and as yet his brain can make only a crude interpretation of the impressions received by his sense-organs. But soon, with the gradual opening up of nervous pathways between his eyes, ears, and brain, he learns to follow the movement of a bright object or attractive sound, and then he puts out his hand to grasp it. But he shows little diagnostic acumen—for instance, he would try to take hold of a red-hot poker. Nevertheless, these active responses of the young baby to things happening within his very circumscribed world are the beginnings of his adventure out into the larger world—a development that will proceed much more quickly when he learns to move about the room, at first crawling and later walking. When children are slower than normal in their development the fault may lie in their sight, hearing, brain, or

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[*] From the presidential address given at the Liverpool Medical Institution on Oct. 9, 1952.

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engineering, King's College Newcastle upon Tyne, for constructing the syringe withdrawal device, to Mr H Campbell for his invaluable aid with the statistical analysis, to Dr Whately Davison and Dr C K Warrick for radiological facilities, to Mr C J Duncan and his staff of the department of photography, King's College, Newcastle upon Tyne, for the reproduction of the radiographs and for the diagram of the venous drainage of the head, to Dr N A Wynne for help and criticism, to Mr L P Lassman, of the department of neurosurgery, Newcastle General Hospital, for the observation referred to in the text, and to Mr T Copeland for his willing help at all stages of the investigation

Addendum

Since this paper was written, a group of workers in the United States have reported on the effects of intravenous tolazoline on the cerebral circulation (Scheinberg et al 1953) They did not observe any significant change in cerebral vascular resistance in the patients studied, most of whom belonged to the age-group when cerebral vascular disease is usually present though not clinically evident It seems likely that tolazoline is not effective in such patients

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PROGNOSIS AND TREATMENT IN ACUTE PERFORATED PEPTIC ULCER

A REVIEW OF 206 CASES

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THE annual number of admissions for peptic ulceration and its complications at the Royal Victoria Infirmary, Newcastle, averages about 1400 Of this total acute perforations account for about 15% I review here the 206 cases of acute perforation in peptic ulcers admitted under my care in 1946–50 and examine the possibility of making a prognosis which would be a guide in their treatment Although we know that some patients appear to be "cured" of their ulcers for long periods after surgical suture of their perforations we do not yet know how to distinguish these at operation from those who suffer recurrent ulceration

The 206 patients were operated on by different members of my clinic They were all treated by laparotomy simple suture of the perforation and toilet of the peritoneum combined with the use of sulphonamides or other antibiotics when necessary and postoperative gastric suction *Modern methods of anæsthesia* facilitated operation and diminished chest complications Several points of general interest call for brief comment

ULCER SITES AND DISTRIBUTION BY SEX

TABLE I—AGE DISTRIBUTION IN 206 CASES OF PERFORATED PEPTIC ULCER

Age (yr)	Males	Females	Total
10–19	1	—	1
20–29	43	1	44
30–39	43	1	44
40–49	44	4	48
50–59	35	—	35
60–69	26	1	27
70–79	4	—	4
80 or more	3	—	3
Total	199	7	206

This series of perforations comprised 160 duodenal ulcers (77 7%), 43 gastric ulcers (20 8%), and 3 stomal ulcers (1 5%) 199 (96 6%) were in males and 7 (3 4%) in females, 4 being duodenal and 3 gastric Of the 43 gastric perforations 24 were on the lesser curve, 11 on the pyloric canal and 8 on the body of the stomach The high percentage of duodenal cases accords with general experience, and the preponderance of males over females is striking

Though men suffer more than women from peptic ulceration, acute perforations seem to occur much more often in men In 1950 if perforations are excluded, 1210 patients with peptic ulcer were admitted to the R V I Of these, 1030 were males and 180 were females—a ratio of 5 7 males to 1 female The same year there were 187 acute perforations, 179 being in males and 8 in females—a ratio of about 22 males to 1 female In the present series the ratio is 28 males to 1 female Men with peptic ulcer thus appear to be between four and five times as liable to perforation as are women with ulcers

No adequate explanation has yet been given of the relative immunity of the female sex to peptic ulceration DeBakey (1940) recalls the suggestion that it may be due to a protective mechanism which is *hormonal* and operates during the years of sexual maturity, particularly during pregnancy In the search for the cause of peptic ulceration or its prevention this aspect of the problem should not be overlooked

AGE-DISTRIBUTION

Table I shows the age distribution in the present series. A prominent feature of this table is the relatively even distribution of the cases between the ages of 20 and 59 The oldest male was 85, and the oldest female 67 The youngest male was 10, and the youngest female 21 The average age of the males was 44, and of the females 42, 43% of the ulcers perforated before the age of 40, and 57% after that age The statistician who has reviewed these figures states that an interesting comparison can be made between the age distribution of males with perforations and the age distribution of all males in the Northern Region at the 1951 census (table II)

Although it is difficult to argue from hospital admissions to the incidence in the whole population, the R V I has always received most of the surgical emergencies from Newcastle and the county of Northumberland, and acute perforations have consistently totalled about 200 annually for many years The figures do not suggest that there is any particular period of adult life when males are more susceptible to perforation The fall in the incidence of perforation in later years corresponds to the smaller adult male population in those years It thus appears true that peptic ulceration occurs throughout the years

TABLE II—COMPARISON OF AGE DISTRIBUTION OF PERFORATIONS IN MALES WITH AGE DISTRIBUTION OF ADULT MALES IN NORTHERN REGION AT 1951 CENSUS

Age (yr)	Males in Northern Region 1951	Percentage of adult males	Number of perforations in males	Percentage of perf in males
20–39	451 000	43	86	43
40–59	390 000	38	79	40
60 or more	200 000	19	33	17

conviction by intellectual means; while in defiance of such reasoning, as he wrote, the small girl turns with indifference from the expensive doll, to cherish her beloved golliwog which lives and moves and has its being at her word, which comforts her in sorrow and soothes her at last to sleep.

Home

In speaking of the relationship of children with adults, I have so far limited myself to some observations upon the characteristics of the child. What can be said of the adults and their contribution? This is where a knowledge of abnormal tendencies in childhood behaviour comes in to support the view—now widely held in this country, but not always put into practice—that the stability of home life, and the exercise of reasonable, fair, and consistent discipline provide what most children need for the full development and maturation of their potentialities.

To speak of home life is to run the risk of giving way to sentiment, and after two world wars our mood is to take a tight grip of ourselves and to do what we can to keep our emotions in check; so please bear with me if I quote Ruskin's words "This is the true nature of home—it is the place of peace; the shelter not only from all injury but from all terror, doubt and division." This is a sensible statement, and the general idea it contains may be backed up, in lighter vein, by reminding you of Winston Churchill's shaft of ridicule when the Government of the day was toying with the idea of substituting the words "accommodation unit" for the older term "house" or "home." He pointed out that the modern version of "Home, sweet home," would now be "Accommodation Unit, sweet Accommodation Unit, There's no place like my Accommodation Unit"; and by this sally of humour he made a telling point.

When a child's home circumstances are satisfactory he enjoys the care and affection of his parents, the friendship of brothers and sisters, decent living conditions, and many other blessings that are perhaps too obvious to mention. But I doubt if we fully appreciate their influence upon his behaviour unless we make a contrast and review the lives of children living under less satisfactory conditions—not only the so-called problem children and the delinquents, but also those relatively less distressing cases that some of us meet daily in professional practice.

Two years ago I analysed, for another purpose, a series of 450 children referred to me with complaints which seemed to me to be due to their upbringing rather than to any physical disease or to subnormal intelligence. In such a series the complaints are found to be varied, and therefore difficult to classify satisfactorily. I divided the children tentatively into four groups, the first including habit spasms, some speech disorders, and breath-holding attacks; the second, abnormal forgetfulness and incapacity for mental concentration; the third, cases characterised by anxiety neuroses, phobias, including night-terrors, refusal to eat, sleep, and play, abnormal outbursts of temper, and so forth; and the fourth group, children with antisocial behaviour, such as pilfering, truancy, and cruelty to other children and animals.

By studying the histories of these children I was able to form an impression of the home conditions under which they had been living. One could not expect, of course, to find any common pattern—human life is far too varied for that; but I was convinced that the lives of most of them had lacked one or both of those two cardinal advantages which I have previously mentioned—namely, security at home, and reasonable discipline. As examples of insecurity at home I would instance death of one or both parents; divorce; discord or loss of agreement and mutual respect between parents; and the unwanted child. Such children are liable to become the victims of what I can only call emotional ill health; and the efforts made by other relatives, such as grandparents, to give the affection that has been denied to them, are not always successful, chiefly because they are likely to be tinged with "over-protection," or excessive care to guard the child from further accident or distress. Under these circumstances the spirit of adventure is opposed, the healthy urges of childhood are too much restricted, and the child's reaction may be a disorder of behaviour. Similarly, when there is a lack of discipline the child is liable to become unattractive, wilful, or perhaps highly nervous, strained, and fretful. For the essential basis of discipline is that adults should make decisions for the child in respect of those matters which his understanding cannot fully comprehend, and should require compliance with their orders. And the most successful parents teach by their personal example even more than by their commands; they make the most of those childhood characteristics of mimicry and hero-worship to which I have already referred. Furthermore, they do what they can to allow the child some latitude for trial and error in order that imposed discipline may become the ground plan upon which the highest form of discipline—namely, self-discipline or self-control—is built up.

The Less Fortunate

These thoughts based upon experience with children at our own social level lead naturally to the question of behaviour as shown by the children of the masses, especially in large industrial areas. If you turn your minds for a moment to the early years of the industrial age when such men as the seventh Earl of Shaftesbury, William Farr, Sir John Simon, Sir Edwin Chadwick, and Charles Dickens were among the pioneers of reform, you will be shocked to find that the public conscience was so deaf and blind to the disreputable conditions under which many children lived, and all too frequently died. As Simon wrote in one of his masterly reports (1857):

> "Those places where infants are most apt to die are necessarily the places where survivors are most apt to be sickly; and where, if they struggle through a scrofulous childhood to realise an abortive puberty, they beget a still sicklier brood than themselves, even less capable of labour and even less susceptible of education. It cannot be too distinctly recognised that a high local mortality of children must almost necessarily denote a high local prevalence of those causes which determine a degeneration of race."

The five giant evils that in more recent years formed the main topic of the Beveridge report—namely, want, Disease, Ignorance, Squalor, and Idleness (or as we should today say, Unemployment) were rampant on all sides. Children of tender years were putting in long hours of work in mills, factories, and other places of employment, and even in 1869 the Registrar-General's report recorded the deaths of 145 children under the age of fifteen who were killed in coalmines, and 2 of these victims were under the age of ten years. Samuel Hutton has recorded that at seven years of age he was set to work in a silk mill, where he toiled each day from 5 A.M. until 7 P.M. for the weekly sum of one shilling. "This," he wrote, "paid for my board and lodging, and rendered me independent of my father, except for the clothes I wore."

In those times families were large, and the parents in the social group under consideration were uneducated and expected nothing better than a life of toil and drudgery, and a never-ending struggle against penury. Naturally it was upon the children that these dreadful conditions operated most harmfully; yet it can be said that in these families, hedged in by so many threatening forces, the bonds of affection were fostered and it would be wrong to conclude that the children lived stunted lives emotionally, no matter how much they suffered physically and through the frightening ordeal of their episodes of medical or surgical treatment in hospital for pain, for bleeding, or for previous perforation

Modes of Perforation

The records show that the perforation occurs in one of two ways

(1) As the culminating crisis in an attack of peptic ulceration, or

(2) As a sudden event with no preliminary symptoms of dyspepsia

In the first instance a painful dyspepsia leads up to the moment of perforation, whereas in the second case this feature is absent In the former the perforation may be visualised as the result of active ulceration In the latter the catastrophe strikes the patient when he is apparently in normal health, and the underlying pathological process is painless Whatever the true explanation of these two modes of perforation, they occurred in cases of both acute and chronic ulceration and in considerable numbers

Pathological Appearances of Perforation

There is usually no difficulty in recognising the type of perforation present at operation

In *acute ulcer perforations* the stomach or duodenal wall is pink or red and mobile, and the perforation is small After preliminary symptoms the wall surrounding the perforation has become œdematous and soft, making sutures tend to cut out, the colour is whitish-pink, the perforation is small, and the bowel is still mobile After a longer period of ulceration before perforation there is more induration of the wall, the peritoneal coat is thicker and whiter, the perforation is less easy to infold with sutures, and the parts remain mobile

In *chronic ulcer perforation* the hole may still be small but it tends to be larger than in the acute ulcer The condition of the wall reflects previous pathological changes It is usually more fibrotic and stiff and may show some scarring, mottling, and deformity There may be thickening of the peritoneal folds, particularly of the lesser omentum, leading to deep fixation which interferes with mobility There may be adhesions between the ulcer area and neighbouring viscera, or penetration into the liver or pancreas Sometimes stenosis complicates the picture, or a posterior ulcer increases the deep fixation

Thus, by correlating the preoperative clinical history with the pathological changes found at operation, the type of ulcer associated with each perforation was diagnosed, and the results are set out in table IV The most noteworthy feature which emerges from this study is the relatively high proportion of acute ulcer perforations (64%) to chronic-ulcer perforations (36%) in this series This conflicts with the commonly accepted view that most perforations occur in chronic ulcers, but it is confirmed by the investigation of the late results, which, though very uniform in each type of ulcer, are different in character

Table IV also shows the distribution of the two modes of perforation Symptomatic ulceration ending in perforation occurred in 103 cases (57%) and sudden acute perforation in 78 cases (43%) Acute perforation was the first and only symptom in 16 cases (9%)

TABLE IV—CLINICAL TYPES OF PERFORATING PEPTIC ULCERS

Type of ulcer	Previous history	Mode of perforation		Total	
		During attack of dyspepsia	With no symptoms of dyspepsia		
Acute	None	35	16	51 (28%)	116 (64%)
	Vague	31	34	65 (36%)	
Chronic	Recurrent	37	28	65 (36%)	
Total		103 (57%)	78 (43%)	181	

TABLE V—RELATION OF CLINICAL TYPES TO LATE RESULTS

Type of ulcer	Late result		Relapses		Total
	Satisfactory	Moderate	Medical	Surgical	
Acute	62	28	15	11	116
Chronic	—	—	24	41	65
Total	62	28	39	52	181

Prognosis in Perforations of Acute and Chronic Ulcers

In seeking to establish the prognosis the after history of each case was assessed, and table V gives the results This shows the clear contrast between the after histories of acute and chronic ulcers

Of the 116 acute ulcer cases 62 (54%) were satisfactory, 28 (24%) were moderately good, and 26 (22%) were poor results Thus, the ultimate prognosis of perforating acute ulcer is good in more than 75% of these cases, less than 25% tend to relapse, and less than 10% required further surgery It should also be remembered that there were no deaths in this group

In contrast with this the ultimate prognosis of perforating chronic ulcers is poor in all cases Of the 65 chronic-ulcer cases all relapsed, 24 required further medical treatment, and 41 had already undergone further operation for perforation, for hæmorrhage, for stenosis, or for painful crises causing loss of work As a group they account for 70% of all the relapses in the series Further, it should be recalled that the immediate mortality rate of this group was 15%

Such differences in the immediate and ultimate prognosis of perforations in acute and in chronic peptic ulcers clearly indicate the need for individual consideration

METHODS OF TREATMENT

Laparotomy and simple suture are a life saving procedure, safe and adequate for the acute ulcer which perforates, but less so for the chronic ulcer The results of published series of perforations have shown a considerable drop in the mortality-rate comparable with that of the present series, but this mortality is almost wholly due to perforations in chronic ulcers, which form the kernel of our problem and are responsible for more than 70% of all relapses What alternative method is there which will yield better results in perforated chronic ulcers ?

The ideal treatment for perforations would, of course, be preventive in known cases of chronic ulcer Medical treatment, however, is powerless to prevent it, as witness those ulcers which perforate while undergoing medical treatment even in hospital Surgical intervention before the age at which the mortality from perforation begins to mount—i e, 40–45—therefore seems to offer the best hope Failing this prophylactic attack, acute perforations will continue and alternative methods of treatment require to be considered

The conservative method of treatment was first advocated in this country by Hermon Taylor (1946) who used continuous gastric aspiration, intravenous fluid replacement therapy, and antibiotics to tide the patient over the crisis of acute perforation Surgical measures are held in reserve to deal with the residual collections of fluid in the abdomen, with cases in which escaped air accumulates in the peritoneal cavity, and with cases which do not respond to aspiration and which show signs of peritoneal infection This method requires constant vigilance from a team of trained and enthusiastic surgeons and nurses, along with routine radiography It depends on the natural defensive reactions of the peritoneum to close the perforation Various reports indicate that this method yields a mortality rate of 8–10% More important is the observation that it that shuns meanness and is unselfish, gay, and reverent; a nature that is sociable and attractive. It is usual to find that these qualities evolve gradually; like good wine, they take years to mature. But—and this is my final note—the more closely human life is viewed, the more unexpected seem its twists and turns.

I cannot claim to have done more than bring to your notice some of the factors affecting children's behaviour, which in turn bears a relation to the behaviour and character of adults. The Welfare State, with all its advantages, has still not found the key that will unlock the hearts of the people, wherein are stored fine qualities that need an airing. Let me quote to you a sentence from Lord Radcliffe's Reith lectures, 1951.

> "The British have formed the habit of praising their institutions, which are sometimes inept, and of ignoring the character of their race, which is often superb. In the end they will be in danger of losing their character and being left with their institutions; a result disastrous indeed."

Is there not a good case for believing that of all the resources given to men to guide their future none offers better promise than the upbringing they give to their children? For in it lies one of those potentialities that "makes mighty things from small beginnings grow."

AMINE OXIDASE, PRESSOR AMINES, AND CHOLINESTERASE IN BRAIN TUMOURS

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This investigation was undertaken to ascertain whether, besides serving as a supporting and nutritional tissue, neuroglia participates in the formation and breakdown of substances such as acetylcholine, adrenaline, and noradrenaline which play a part in the transmission of nervous impulses. All samples of the central nervous system are necessarily a mixture of nervous tissue and neuroglia; but by examining samples of brain tumours, particularly glioma tissue, we hoped to obtain some correlation between enzyme activity and the histological classification of the tumours—i.e., the preponderance of certain cell types. Some of the results have already been briefly reported (Bülbring 1953).

The presence of amine oxidase in the central nervous system was first shown by Pugh and Quastel in 1937, and Nachmansohn (1939) first studied in detail the distribution of cholinesterase in the brain. Birkhäuser (1940) published quantitative data on the contents of both enzymes in certain areas of the human brain. The findings of Ord and Thompson (1952) on cholinesterases and of Thompson and Tickner (1952) on amine oxidase in human brain were obtained by the same technique as we have used and are therefore more suitable for comparison with our results obtained in brain tumours. Noradrenaline and adrenaline have been found by Vogt (1952a and b) in certain parts of cats' and dogs' brains.

MATERIAL AND METHODS

Samples from twelve intracranial tumours removed at operation were studied, adjacent portions being used for histological, biochemical, and pharmacological investigation. Seven gliomas of the astrocyte series (one in a child), one ependymoma, one acoustic-nerve tumour, and three meningiomas were studied. The meningiomas, which do not originate from brain tissue, and the acoustic-nerve tumour served to some degree as controls. The gliomas showed a mixture of cell types and varied in the amount of anaplasia from tumour to tumour and from part to part of the same tumour. In table I the less anaplastic ones are designated astrocytomas and the more anaplastic ones glioblastomas. The presence or absence of mitoses is also indicated to give some guide to the degree of variation from normal adult tissue and the rapidity of growth. The histological sections of the meningiomas and the acoustic-nerve tumour showed no nerve-cells. Although in gliomas most of the cells are of glial origin, they are usually diffusely infiltrating tumours, and it is common to find nerve-cells even quite deep inside the tumour. In most of our cases there were at least some nerve-cells visible and in some cases fairly well preserved nervous tissue. Furthermore, in the centre of the tumour there was often much necrosis.

Enzyme activity was estimated manometrically by Warburg's technique. Adrenaline and noradrenaline were estimated by biological assay.

RESULTS

The amine-oxidase activity and content of pressor amines in the twelve tumours are shown in table I. Cholinesterase activity, using various substrates, is shown in table II.

With the exception of tumour no. 1, from a child aged 3 years, all the tumours were from adults. It was in the

TABLE I—ANALYSIS OF TUMOURS

Tumour no.	Age of patient (yr.)	Diagnosis	Mitoses	Presence of nervous tissue	Amine oxidase (µl. oxygen per g. per hr.)	Noradrenaline (µg. per g.)	Adrenaline (µg. per g.)
1	3	Astrocytoma	−	+	241	7·5	0·75
2	53	Glioblastoma	+++	+	206	0·63	0·024
3	43	Glioblastoma	−	(−)	151	0·58	0
4	38	Glioblastoma	−	+	224	0·15	0·002
5	32	Astrocytoma	−	+	97·4	0	0
6	60	Multiforme	+	−	86·3	0	0
7	32	(a) Astrocytoma (pure tumour)	−	(−)	202	..	..
		(b) Astrocytoma (infiltrating edge) ..	−	+	323	0·02	0
		(c) Glioblastoma (centre of tumour) ..	++	−	69	..	0
8	19	Ependymoma of cord	−	−	213	0·2	0·02
9	42	Acoustic-nerve tumour	−	−	69	0	0
10	55	Meningioma	−	−	49·2	0·2	0·0125
11	37	Meningioma	−	−	0	0	0
12	30	Meningioma	−	−	0	0	0
Cortex adjacent to abscess	52	..	−	−	482	0	0

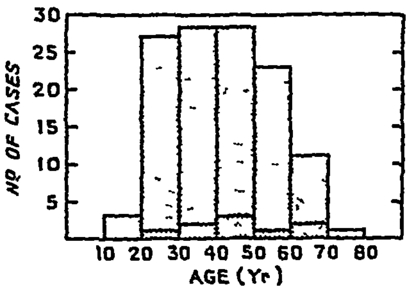
to control thyroid overactivity, and any toxic effect on bone-marrow and other extrathyroid tissues may be correspondingly reduced

Material and Methods

The 120 patients, of ages ranging from 16 to 72, comprised 92 with primary thyrotoxicosis (9 of them post operative recurrences) and 28 with toxic nodular goitre, the ratio of females to males being 12 5 1 (see figure).

DIAGNOSIS

In all the cases the diagnosis was established on the basis of clinical judgment, basal metabolic rate (B.M.R.), and radioactive iodine tracer studies uptake curve, thyroid plasma clearance-rate (Pochin 1950), urine excretion, and additional topographical survey in nodular glands Electrocardiograms were made in all the cases Serum-cholesterol and serum-creatine levels were also determined



Age and sex distribution in 120 cases of thyrotoxicosis stippled, female hatched, male

The size of the goitre was estimated clinically by palpation and the maximum neck circumference measured at intervals during treatment All glands removed at operation were weighed, thus providing a guide for subsequent clinical estimations The size of diffuse enlargements could be gauged fairly accurately, but nodular goitres were often underestimated owing to retrotracheal or subclavicular extensions inaccessible to palpation

Table I shows the distribution of different forms of thyrotoxicosis in relation to goitre size Goitres were classed as small when the estimated weight, or the weight of the gland removed, was up to 40 g Medium sized goitres had estimated or actual weights of 40–60 g Large goitres all weighed more than 70 g The cases were tabulated in this way, throughout the present study, to see whether a correlation could be found between the size and variety of goitre, the amount of drug required, and the rapidity of response to anti thyroid medication

TABLE I—TYPES OF THYROTOXICOSIS IN 120 PATIENTS

Size of goitre	Treatment		Primary thyrotoxicosis		Post-operative recurrent thyrotoxicosis		Toxic nodular goitre		Average initial dosage of neomercazole (mg daily)
	Curative	Preoperative	Curative	Preoperative	Curative	Preoperative	Curative	Preoperative	
Small	41	9	28	6	5	1	8	2	22 7
Medium	38	12	31	5	2	1	5	6	25 6
Large	11	9	10	3			1	6	29 5
Total	90	30	69	14	7	2	14	14	

NEOMERCAZOLE

At the beginning of this clinical trial neomercazole was given in small doses of 10–20 mg daily in accordance with the first published reports on the dosage of methimazole (Reveno and Rosenbaum 1950) Some of the slow responses to neomercazole in the patients treated early in this series are undoubtedly due to insufficient medication It is now considered that 15–20 mg daily is an adequate initial dose for mild cases with small goitres, 30 mg for cases of average severity, and 40–45 mg for severe cases with large goitres, or in patients with small goitres who respond slowly to 30 mg

Neomercazole is tasteless (mercazole is bitter) and is administered in tablets of 5 mg or 2 mg thrice daily

Clinical response was gauged by return of B.M.R. to normal, increase in body-weight, return of pulse rate to normal, loss of restlessness and tremor, and gain in general well-being of the patient The serum cholesterol level proved useful in assessing response a rise of 40% over the initial level confirmed other signs of over-treatment and occasionally helped to give warning of hypothyroidism before symptoms appeared A white cell count was always made before giving neomercazole Initial pretreatment counts below 4000 per c mm were sometimes found but were not a contra indication since they remained at the same level during prolonged administration of neomercazole White cell counts were not repeated as routine, since they provide no safeguard against agranulocytosis (Young 1949)

The B.M.R.† was estimated weekly in the preoperative group and in patients admitted to hospital for the initial period of medical treatment Most of the patients on curative treatment with neomercazole were treated entirely as outpatients and only spent one or two nights in hospital to undergo B.M.R. and I^{131} tests Most of them continued their usual occupations throughout the treatment Patients were seen fortnightly until their B.M.R. returned to normal, and subsequently every four weeks, with a B.M.R. test at each visit After six months the test was only done every two or three months

The preoperative group were given neomercazole for three or four weeks, with added Lugol's solution of iodine for five days before operation This group comprised patients with toxic nodular goitres, patients sent from distant towns where follow-up was impossible, and patients who did not respond rapidly enough and wanted an operation

As soon as the clinical condition and B.M.R. returned to normal, the dose of neomercazole was cut down gradually The rate of decrease of B.M.R. and the general improvement indicated how rapidly and to what maintenance level neomercazole could be reduced It was aimed to keep the B.M.R. between 0 and −5%, a few goitrogenic reactions occurred when it was allowed to drop below −10% After four to twelve weeks of the initial dosage neomercazole could be cut down in early remission to two-thirds or a half of the initial dosage, and after six months' treatment 5–10 mg a day sufficed for maintenance in average cases Mild thyrotoxics were maintained on 2 mg a day within three months Patients who responded slowly to neomercazole usually required higher maintenance doses, even after nine months' treatment Treatment was stopped when the patient was able to remain euthyroid on 2–5 mg of neomercazole daily for about six months To date, about twelve months' treatment has been found necessary Decrease in the size of the gland was also a good prognostic sign

Thyroid was administered together with neomercazole in 5 cases showing goitrogenic reactions due to over-treatment and in 2 patients with malignant exophthalmos

3 patients became pregnant while under treatment with neomercazole It is hoped to continue their treatment to term with the least amount of neomercazole necessary to keep the B.M.R. on the high side of normal (Astwood 1951)

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† Aub and Du Bois standards were used (normal range − 10 to
Two ten minute tracings were obtained at each test

INFLUENCE OF TOLAZOLINE HYDROCHLORIDE (PRISCOL) ON CEREBRAL BLOOD-FLOW

IN PATIENTS WITH MITRAL STENOSIS

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WE present here the results of estimations of cerebral blood-flow by the nitrous-oxide method in 6 patients with mitral stenosis before and after intravenous injections of the vasodilator tolazoline hydrochloride ('Priscol'; 2-benzyl-4 : 5-imidazoline hydrochloride). This study arose from the desire to ascertain if there were a rational basis for the use of tolazoline in the emergency treatment of cerebral embolism.

So far as we are aware, no reports have been published on the effect of this drug on the cerebral blood-flow and vascular resistance in man.* Certain facts, however, suggest that it may influence cerebral hæmodynamics:

(1) Besides the cutaneous warmth in the extremities and face and the consciousness of increased cardiac action which follow intravenous injection of tolazoline, there develops also a sensation of fullness in the head which may become very intense at the height of the subjective effects (Ahlquist et al. 1947).

(2) Measurements of the retinal vessels have shown increase in calibre of the arterioles after the administration of tolazoline (Cholst et al. 1952). Engel (1952), using the skull-window technique, has demonstrated prompt dilatation of pial arteries and arterioles in the cat after an intravenous injection of tolazoline, an effect which he also observed in the presence of postconcussional vasospasm. A similar response of the pial vessels of man was recently observed during an intracranial operation (Lassman 1952).

(3) In patients with cerebral ischæmia improvement has been reported after treatment with tolazoline by mouth (Roch and Roch-Besser 1947).

(4) Smith and Turton (1951) have described the case of a patient with peripheral arteriopathy who was admitted to hospital suffering from depression and mental disturbance together with motor aphasia; his disability underwent a temporary but remarkable improvement in response to intravenous tolazoline, which was repeated on several occasions, control substances (physiological saline solution, vitamin B_1, and nicotinic acid) proving completely ineffective. More gradual improvement was later produced by oral administration, although ultimately tolerance to tolazoline developed. On the basis of this report and of the experimental work of Engel, the *British Medical Journal* (1952) has suggested that it might be worth while to make an extended trial of tolazoline in suitable patients with cerebral arteriosclerosis.

In view of these facts it seemed important to determine whether the brain participates in the increase in the total peripheral blood-flow produced by tolazoline.

Methods

Six patients, with mitral stenosis, undergoing routine cardiac catheterisation before valvotomy, were studied. The cerebral blood-flow was estimated in the supine position after measurement of the right-heart pressures in all the patients except case 3, in whom it was estimated immediately before.

The cerebral venous blood was sampled through a cardiac catheter, the tip of which had been placed in the left superior jugular bulb under fluoroscopic control.

The internal jugular vein joins the subclavian behind the inner end of the clavicle, and the catheter, which in each instance had been passed up the left arm, was rotated in the subclavian vein until its curved end pointed upwards, and there was usually not much difficulty in securing its entry into the left inferior jugular bulb. Rotating the patient's head to the right, depression of the patient's left shoulder, and deep expiration by the patient assisted this entry.

At the upper end of the inferior jugular bulb, about 1 in. above its junction with the subclavian vein, lie two valves. Sometimes the catheter passed through them swiftly and without any difficulty, but in other instances sharp obstruction was met, and then deep inspiration, compression of the opposite internal jugular vein, hyperextension of the head, and, on one occasion at least, rotation of the patient's head to the left, combined with withdrawal and readvancement of the catheter, usually overcame it.

The catheter was then advanced upwards to the base of the skull and, when its position there had been confirmed by fluoroscopy and radiographed, it was kept steady by tying it in the antecubital vein. Fig. 1 shows a catheter in position.

Rarely a catheter would stick short of the base of the skull, usually because its tip had caught in the junction of a tributary vein, but in most instances rotation enabled it to advance to the full distance. The cerebral blood-flow was not estimated unless this full advancement had been attained. The highest tributary bringing extracranial blood to the internal jugular vein is the common facial vein. Fig. 2 shows the catheter in this vein. Fig. 3 shows the venous anatomy of the region.

Catheters U.S. nos. 6, 7, and 8 were used at different times, and occasionally one size would pass where another would not.

Attempts to catheterise the left internal jugular vein succeeded in 15 of 22 patients (68%). Of the 7 failures, in 5 the catheter was held up at the valves, and in the 2 others it was arrested much higher; in 1 of these cases "stickiness" of the catheter in the veins was responsible, probably because of the time spent previously in catheterising the heart. Of the last 6 cases attempted, success was attained in 5. No complications were met with; 1 patient experienced pain in the ophthalmic division of the left trigeminal nerve; but this was promptly relieved by withdrawing the catheter a centimetre or so.

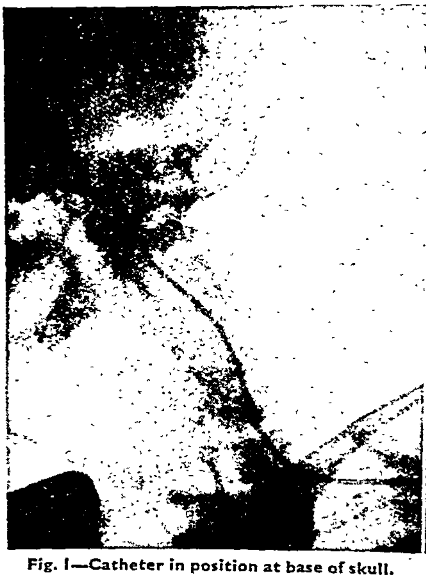
Fig. 1—Catheter in position at base of skull.

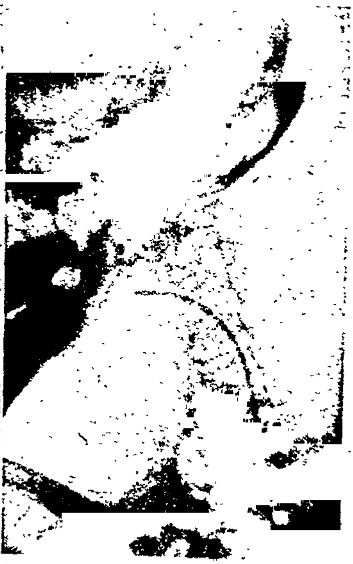
Fig. 2—Catheter in common facial vein.

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* Such a report has appeared since this paper was written (see Addendum).

TABLE III—ANALYSIS OF 90 CASES TREATED CURATIVELY

Response to neomercazole	Size of goitre	No of patients	Average age and age range (yr)	Average initial B.M R	No of patients with primary thyrotoxicosis	No of patients with toxic nodular goitre	Mean initial dosage of neomercazole (mg daily)	Average maintenance dose in patients treated 5 mos or more (mg daily)	No of patients who discontinued treatment
Rapid (B M R to 0 in 2–8 weeks)	Small (est wt 25–40 g)	30	43 4 (*22–62*)	+29	29 (3 post operative recurrences)	1	22 6	4 (range *2–10*)	5 all in remission 2–7 mos
	Medium (est wt 40–60 g)	33	32 5 (*16–50*)	+32	29 (2 post operative recurrences)	4	27 0	7 (*[illegible]–20*)	3 (1 relapsed after 6 weeks 2 with toxic nodular goitre had operation)
	Large (est wt more than 70 g)	9	32 (*19–50*)	+54	9		32 5	14 (*10–15*)	
Slow (controlled after 3–6 mos	Small	11	61 5 (*35–72*)	+35	4 (2 post-operative recurrences)	7	30 0	18 (*6–30*)	1 defaulted
	Medium	5	35 (*28–47*)	+38	4	1	23 0	11 (*5–20*)	2 (1 defaulted 1 remission 4 mos)
	Large	2	56 and 23	+32 +2[illegible]	1	1	30	20	
Total		90			76	11			

ment The B M R was down to −11% in 1 patient and −14% in the 2 other patients, and the neck circumference increased by $^3/_4$ in in 2 of the patients The goitres became larger and firmer This goitrogenic reaction subsided rapidly when the dosage of neomercazole was reduced to 5 mg daily The 4th patient showed the most dramatic response of the whole series (see case 2 below) She received 40 mg of neomercazole daily Her B M R fell from +63% to +7% in twenty one days, during which her pulse rate dropped from 132 to 68 a minute This shows the importance of regular attendance during therapy

It appears from table III that the size of a goitre does not influence rapidity of response to neomercazole An equal percentage of large goitres is found in the two groups, and more medium sized goitres responded rapidly The type of goitre appears more significant Toxic nodular goitres account for half the slow responses and only for 7% of the group responding rapidly Elderly patients with small long-standing nodular goitres responded slowly on the whole It is also seen from this table that a higher maintenance dosage is required for large goitres and for all goitres showing slow response

Goitrogenic Reactions

Goitrogenic reactions were seen in 7 of the 120 patients 2 patients responded excessively quickly (see above) 1 patient showed an increase of her goitre after ten weeks' treatment with neomercazole 20 mg daily with a B M R of 0 her neck circumference increased by $^1/_2$ in Goitrogenic reactions developed after several months in 4 patients who were over-treated their B M R s at the time were −17% −11%, −11% and −13% and they were receiving 15 mg, 10 mg, 10 mg, and 25 mg, of neomercazole per day, respectively

1 patient had a very large goitre with primary thyrotoxicosis of three years' standing, and was ultimately operated on owing to pressure symptoms In each of the remaining 6 patients the thyroid returned to its previous size or less when the dose of neomercazole was reduced Over-treatment can take place without an increase in the size of the goitre 2 patients became almost myxœdematous with B M R.s of −30% and −18%, while taking neomercazole 15 mg daily, without any change in the size of their goitres

Most undue goitrogenic reactions can be avoided with neomercazole if the size of the goitre is watched carefully and the B M R kept between 0 and −10%

Decrease in Size of Goitre During Long continued Treatment

The thrill felt over superior or inferior thyroid arteries was the first sign to disappear—usually within one or two months, or even less At the same time pulsation diminished, the bruit became less loud, and then less blowing, until it finally disappeared In well controlled patients the gland became substantially smaller and softer

It is desirable to reduce the dose of neomercazole to the minimum compatible with adequate control throughout the period of treatment and to adjust the dose if an exacerbation of thyrotoxicosis develops 6 patients had a temporary exacerbation of toxicity after being controlled from six to nine months on a small dose of neomercazole After taking an increased amount of neomercazole for a few more months they were again controlled with the smaller dose

Of 90 patients 16 gave a history of increased psychological stress at the time they became thyrotoxic, and attributed the onset of their symptoms to their mental trauma 13 of these patients responded normally and became euthyroid in two to eight weeks, but 2 showed exacerbations with each emotional crisis and required larger dosage Both went into complete remission when their problems were solved, and discontinued treatment with neomercazole without recurrence The remaining 3 responded slowly

Auricular fibrillation was present in 6 patients treated without operation 2 of them had recurrent post-operative thyrotoxicosis, 1 having had two previous thyroidectomies The 4 other patients had old standing nodular goitre, and their average age was 64 The cardiac rhythm returned to normal in only 2 of these patients after long treatment

EYE SIGNS

Of the 90 patients followed up 37 had no eye signs 11 had only lid lag and 7 had malignant exophthalmos The rest all had some exophthalmos but no œdema, chemosis, or ocular muscle palsies Of the cases of malignant exophthalmos 2 were severe and progressive 2 were of long standing and 3 were mild 4 occurred was at least an hour before the cerebral studies were begun. At least twenty-five minutes between the first and second estimations was allowed for nitrous-oxide desaturation: two to three minutes before the second flow was begun 20–30 mg. of tolazoline in 0·8–1·2 ml. was injected intravenously, the exact amount being determined by the subjective and objective effects of a test dose administered the previous day. These included a feeling of fullness in the head, facial flushing, conjunctival injection, and lacrimation. In all other respects the conditions of the second estimation were identical with those of the first.

Results

The results of the studies are shown in the accompanying table.

Discussion

The results showed a striking and significant decrease in the cerebral vascular resistance (C.V.R.) after tolazoline, from a mean value of 2·0 to one of 1·5 ($t = 5·6$, $p < 0·01$); this was accompanied by increases in the mean cerebral blood-flow (C.B.F.) averaging 25%, which are also statistically significant (mean increase 11·7 ml. per 100 g. per minute, $t = 2·9$, $p < 0·05$). In 5 of the 6 patients the mean arterial blood-pressure (M.A.B.P.) fell slightly, the average decrease being 6%. The data are therefore sufficient to demonstrate that in this age-group with this order of dosage, and where no abnormal cerebral condition is present, appreciable and significant changes in the cerebral hæmodynamics follow the intravenous administration of tolazoline. These changes represent dilatation of the cerebral vessels (assuming the blood viscosity and the intracranial pressure to remain constant) and increase in mean cerebral blood-flow per unit weight of brain tissue.

RESULTS OF ESTIMATIONS OF CEREBRAL BLOOD-FLOW

Case no.	Sex	Age (yr.)	C.B.F.		M.A.B.P.		C.V.R.	
			C	E	C	E	C	E
1	F	29	38	47	75	70	2·0	1·5
2	F	38	42	73	77	77	1·8	1·1
3	F	22	58	62	81	73	1·4	1·2
4	F	32	48	59	91	85	1·9	1·5
5	F	38	28	37	78	74	2·8	2·0
6	M	39	47	53	93	86	2·0	1·6
Mean values		33	45	55	83	78	2·0	1·5

C.B.F., mean cerebral blood-flow in ml. of blood per 100 g. of brain per minute over ten-minute period of estimation.

M.A.B.P., mean arterial blood-pressure in mm. Hg over ten-minute period of estimation.

C.V.R., mean cerebral vascular resistance in mm. Hg per ml. of blood per 100 g. of brain per minute over ten-minute period of estimation.

C, control period.

E, period following intravenous injection of 20–30 mg. of tolazoline in 0·8–1·2 ml.

Hendrix et al. (1947) found that the skin-temperature of normal people and in vasospastic states rose with doses of tolazoline (0·5–1·0 mg. per kg. body-weight) considerably less than those required for sympatholysis or for adrenolysis, judged by diminution, loss, or reversal of the normal reflex and adrenaline pressor responses (2·0–3·5 mg. per kg. body-weight), and they suggested that this effect might be due to a histamine-like action on the vessels. The dosage in the present studies did not exceed 0·6 mg. per kg. body-weight, and a similar mechanism seems possible. The fact that sympathetic block has a negligible effect on the cerebral circulation (Harmel et al. 1949, Scheinberg 1950, Naffziger and Adams 1950) is compatible with this hypothesis. Further, histamine has been shown to be an effective cerebral vasodilator although it produces no concomitant increase in the mean cerebral blood-flow (Shenkin 1951, Alman et al. 1952). Both Alman et al. and Kety (1950) considered that the failure of histamine to increase the C.B.F. was most probably the result of the fall in arterial pressure produced by it. Shenkin (1951) analysed his figures regarding this point and found that the response of the C.B.F. varied with the degree of alteration in the head of pressure: where the fall in M.A.B.P. averaged 23%, the flow was not materially affected, whereas increases and decreases respectively occurred with falls in M.A.B.P. averaging 12% and 50%. Inspection of the present results shows a strikingly similar trend, and there proves to be a high degree of correlation between the changes in C.B.F. and those in M.A.B.P. ($r = 0·94$, $p < 0·01$).

Although there is no independent observation of C.V.R. measured as the ratio of M.A.B.P. to C.B.F., the changes in this value are more stable than those in the other two. This is in accord with the fact that the decreases in C.V.R. show the highest level of significance of the changes occurring after tolazoline, and suggests that the primary action of tolazoline is vasodilator, its effect on the C.B.F. being a function of its effect on the mean arterial pressure. It therefore seems reasonable, especially in view of the chemical and pharmacological resemblances between the substances, to regard the action of tolazoline on the cerebral circulation as essentially histamine-like but differing from that of histamine in that effective cerebral arterial pressure is *maintained with consequent increase in mean flow-rates.*

Further work is clearly needed to confirm and to extend these findings, especially as regards the effect of higher doses of tolazoline and to find whether a similar response takes place in acute and chronic cerebral ischæmia and where the blood-vessels are diseased. The experiments of Engel and the clinical reports referred to above suggest that, so far as acute ischæmia is concerned at least, tolazoline is likely to be effective. Such a result would be consistent with its frequently demonstrated efficacy in ischæmia and vasospasm elsewhere in the body. It may be noted, however, that Cholst et al. (1952) found by angioscotometry that the increase in calibre of the retinal arterioles which they consistently observed after intravenous tolazoline in normal people was much diminished in the presence of more than a moderate degree of retinal arteriosclerosis.

Pending both the results of further investigations along these lines and controlled clinical assessment of the practical value of tolazoline, we suggest that the use of tolazoline in the emergency treatment of cerebral embolism in young patients with rheumatic heart-disease is justified on theoretical grounds, since augmentation of the cerebral circulation by dilating the vessels and increasing the blood-flow through them is clearly the aim of such therapy.

Summary

The effect of tolazoline hydrochloride ('Priscol'; 2-benzyl-4 : 5-imidazoline hydrochloride) on the cerebral circulation has been determined by the nitrous-oxide method in 6 patients with mitral stenosis.

The results demonstrate significant changes in the cerebral hæmodynamic values after intravenous administration of tolazoline in doses of 20–30 mg.: a fall in the mean cerebral vascular resistance averaging about 25%; and an increase in the mean cerebral blood-flow per unit weight of brain tissue of a similar order.

The possible mode of action of tolazoline in this respect is discussed.

Modifications in the nitrous-oxide technique for estimating the cerebral blood-flow are described, including the sampling of cerebral venous blood through a cardiac catheter placed in the superior jugular bulb and the withdrawal of constant-rate blood samples by means of an electrically operated syringe device.

We wish to thank all those who have kindly assisted us in this study. We are especially indebted to Prof. A. F. Burstall and his staff, of the department of mechanical

This case shows that neomercazole is a potent anti-thyroid drug, since 15 mg daily produced almost complete myxœdema in four months It also illustrates the fact that *it is safer to reinforce clinical judgment* with B M R estimations In this case the serum cholesterol level did not rise above normal limits with over-treatment

Discussion

Neomercazole is probably hydrolysed to methimazole before it exerts its anti-thyroid action Its increased efficiency must be due to the maintenance of a steadier blood level produced by the slow release of methimazole

In assessing the activity of a new anti thyroid drug it often proves misleading to apply the results of experiments in rats, because of variations in response due to species differences For example, propylthiouracil is ten times more active and methylthiouracil *only half as* active in the rat as in man In the rat neomercazole did not prove superior to methimazole, it was slightly less goitrogenic weight for weight and was proportionally less effective in decreasing the consumption of oxygen by the rat

Stanley and Astwood (1947) advocate the testing of new anti thyroid drugs by their ability to inhibit the uptake of I^{131} by the normal human thyroid gland This method also proved misleading since it showed methimazole to have a potency a hundred times as great as that of thiouracil, which was not borne out in practice Neomercazole tested by this method inhibited the uptake of I^{131} more than methimazole did The blocked iodide uptake (Stanley and Astwood 1948) in thyrotoxic patients showed that 30 mg of neomercazole inhibited the synthesis of thyroxine completely in two thirds of the cases tested, whereas 50 mg was fully effective in all the tests made so far I^{131} tests do not take into account the cumulative properties of drugs and are therefore not a true measure of their clinical effectiveness

The objections to testing new anti thyroid drugs by treating thyrotoxic patients are the length of time required for clinical trials, *the great variation in the rate* of response to a full dose of anti thyroid drug, and the individual differences in the *minimal effective dose* The rate of clinical response is also affected by the amount of hormone stored in the *thyroid gland*, especially when iodine has been previously administered

These objections can be overcome if the final assessment of the anti thyroid drug is based on a large number of observations continued for a sufficiently *long time* Toxicity-rates can only be assessed after treating a large number of patients

A summary of the published reports on the use of methimazole is given below for comparison with results obtained with neomercazole

Stanley and Astwood (1949) who first tested methimazole, tried it on 30 patients but did not publish their results in detail, they gave 15 mg daily (personal communication to McGavack) Reveno and Rosenbaum (1950) gave as little as 6–15 mg daily but only 6 of their 18 patients seem not to have had previous treatment The rest were more or less already controlled with propylthiouracil when *methimazole* therapy was started, hence a maintenance dose could have been sufficient Their new *patients* improved on this dosage but were not completely euthyroid after three months

Beierwaltes (1950) tried methimazole in 9 patients and found the optimum initial dose to be 40 mg daily His average period of observation was two months, ranging from two weeks to six months, but his results are comparable with ours, where only 30 mg of neomercazole was given daily Taylor et al (1951) gave 30 mg or more to 23 *patients* Hallman and Bondy (1951) treated 35 patients and gave 20–60 mg, but most of their cases were *preoperative* and were treated for short periods None of these workers reported any toxic reactions—probably because of the smallness of dosage or the brevity of the trials

Bartels and Sjogren (1951) presented the first large series 100 patients given 30–50 mg daily Their maintenance dose of 2 5–5 0 mg daily is similar to ours They reported 6% of toxic reactions, mostly skin rashes, but 1 case of granulopenia was later seen by them With additional experience their toxicity rate was revised to 7 5% (Bartels 1952) Kendrick et al (1952) treated 32 patients with 30–45 mg daily and had 3 rashes Irwin et al (1952) treated 45 patients and decided on a dosage of 15 mg for small goitres, 30–45 mg for moderate goitres, and 60 mg for large goitres with severe toxicity The average dose administered was 38 8 mg Their incidence of toxic reactions was 6 6% For 1100 patients treated all over the U S A up to 1951 a toxicity-rate of 4 8% was cited (Hines 1951)

It seems that most of the larger series of patients treated with methimazole received a rather higher dosage than we find necessary with neomercazole The rate of response appears comparable to ours only in the series in which the larger dosage was used

The toxicity-rate of *methimazole seems definitely* related to the dosage (the most serious toxic reactions developed *in patients taking more than 40 mg daily*) and to the length of observation Where upwards of *30 mg daily* was *used*, all the workers reported toxic reactions except Hallman and Bondy (1951), most of whose patients had only 20 mg daily and short preoperative courses

For more than a year we have given 30 mg of neomercazole a day as an initial dosage without seeing any toxic reaction The reason for this becomes clear when one considers the molecular weights of the two drugs that of methimazole is 114, and that of neomercazole 186 The difference between these molecular weights is accounted for by the completely harmless and non toxic carbethoxy group Thus 30 mg of neomercazole contains only 18 5 mg of methimazole but is clinically as effective as 30–40 mg of methimazole The highest dosage of neomercazole found necessary in our series, 45 mg *contains 27 4 mg of methimazole*—barely the average dose of methimazole administered by other workers

4 cases of agranulocytosis have followed the use of methimazole (Croke and Berry 1952, Bartels 1952), and theoretically the possibility of this complication exists with neomercazole, but it is extremely unlikely in view of the small amount of the potentially toxic methimazole used when neomercazole is administered Probably neomercazole will have a toxicity rate only a fraction of that of methimazole, with a weight for weight efficiency which promises to be somewhat higher

The final remission-rate and total duration of treatment with neomercazole will have to be assessed when more patients have finished their course The correlation between intensity of treatment and permanent cure is not yet established

Astwood (1949) thinks that a higher proportion of permanent remissions is obtained when the initial dose is continued until the signs of early myxœdema appear and a maintenance dose given which will keep the patient in a state of normal or slightly subnormal thyroid function McGavack (1951), on the other hand, advocates *keeping the* B M R *between* +5% and +15% and avoiding the risk of goitrogenic reactions One of the objections *to definitive* anti thyroid therapy is the possible development of adenomas in the treated gland, and the remote possibility *of future malignant* changes Both these dangers are greatly enhanced in the over-treated thyroid, when the thyrotrophic hormone of the pituitary gland exerts its unopposed influence *In our* treatment with neomercazole we have therefore preferred to reduce the dosage as soon as the patient became euthyroid We have tried to avoid over treatment by checking the required dosage by regular B M R estimations The usual objections to the B M R test *do not* apply to patients who follow a prolonged course of medical treatment and *thus become* accustomed to the performance of the test, especially if the tests and the entire management of the case are personally supervised by the same physician of man's greatest activity, that once established it tends to persist, and that the risk of perforation remains even in old age.

MORTALITY-RATE

The mortality-rate of an operation is the yardstick by which its immediate success or failure is measured. In this series of 206 perforations there were 13 deaths—a mortality-rate of 6·3%. This accords with that of other series recently published (Chamberlain 1951, Heslop 1951, Beattie 1951), which show a mortality-rate of about 8% and mark an important improvement that is agreed all over the country. The recent study of this subject by Avery Jones et al. (1950) attributes this lessened mortality to the use of antibiotics and to better techniques in anæsthesia. In the present series none of the 7 women died, and in 55 consecutive cases all the patients recovered, including 4 who had suffered perforation for more than twelve hours, and 3 for more than twenty-four hours. Several factors appear to influence the immediate mortality-rate.

Time factor.—It is generally agreed that delay in operating on perforations tends to increase the mortality-rate. It is satisfactory to report that 164 patients (80%) were operated on within twelve hours of perforation, with 5 deaths—a mortality-rate of 3%. With a delay of twelve to twenty-four hours 3 of 17 patients (18%) died. With delay of over twenty-four hours 4 of 10 patients died—a mortality-rate of 40%. In 15 cases the exact times are not recorded, and 1 of the patients died. These figures show the importance of early operation.

Age factor.—As might be expected, a significant rise in the mortality-rate accompanies age, particularly after 60:

Under the age of 40, 1 of 89 patients died (mortality-rate 1%).

Between the ages of 40 and 59, 6 of 84 patients died (mortality-rate 7%).

Of those aged 60 or more, 6 of 33 patients died (mortality-rate 18%).

These figures illustrate the increasing risk which advancing years add to perforations.

Site of ulcer.—There were 160 duodenal perforations with 7 deaths (mortality-rate 4·4%). Of 43 patients with gastric perforation 5 died, and of 3 with stomal perforation 1 died. The figures of gastric and stomal ulcers are too few to be statistically significant, but they suggest that there is a greater risk with gastric and stomal perforations. This is perhaps due to the fact that such patients are often ill-nourished and debilitated; their perforations are sometimes difficult to suture, particularly when the ulcer is chronic; they are usually more shocked than patients with duodenal perforation; and there is usually a greater degree of peritoneal soiling because of the wider spread of acid gastric contents.

Type of ulcer.—Perhaps the most important factor affecting the immediate mortality-rate is the proportion of chronic ulcers in any series of perforations. In this series there were 119 patients with perforated acute ulcer, and none of these died. In contrast there were 87 patients with perforated chronic ulcer, and 13 of these died. This reveals the important fact that the total mortality-rate of 6% was wholly attributable to the chronic ulcers, and that as a group their mortality-rate was about 15%.

REMOTE RESULTS

In assessing the remote results of our 206 cases we have to exclude the 13 patients who died while in hospital and 4 others whom we failed to trace. This leaves 189. Of this number 8 have since died: 5 from intercurrent disease; and 3 from conditions directly associated with the original peptic ulcer—namely, abscess of the lung following subphrenic abscess, reperforation of a mid-gastric ulcer in an old man, and an acute duodenal-ulcer hæmorrhage during an attack of infective hepatitis. These 3 patients all died at home from three to five months after leaving hospital, and should properly be regarded as an increment to the mortality of perforated ulcer. We have therefore 181 survivors for the completion of this review. The remote results have been classified on a clinical or symptomatic basis into three main groups:

(1) *Satisfactory cases.*—This includes all who express themselves as "perfectly well." They are symptom-free and working regularly.

(2) *Moderately well.*—This group comprises all those who, though admitting to a mild degree of dyspepsia at times, have not required medical care and have not lost work.

(3) *Poor results.*—This covers all who have had recurrent ulcer symptoms, who have had further medical or surgical treatment, and who have lost a considerable amount of work.

Table III shows the remote results in 181 survivors after perforated peptic ulcer. These results differ a little from a former series (Gilmour and Saint 1932), in which the satisfactory cases were 38·6%, fair results 25%, and poor results 36·4% after five years. Grey Turner (1931) found that 50% of his patients with sutured perforations had further symptoms; and Illingworth et al. (1946) reported 40% relapse in a year, rising to 70% at the end of five years. The present analysis reveals again the striking tendency towards further relapse, which 50% of all the patients undergo, and calls for further consideration.

TABLE III—THE REMOTE RESULTS IN 181 SURVIVORS AFTER PERFORATED PEPTIC ULCER

Results	Duodenal cases	Gastric cases	Total
Satisfactory ..	52 (*36%*)	10 (*29%*)	62 (*35%*)
Moderate ..	25 (*17%*)	3 (*9%*)	28 (*16%*)
Poor	68 (*47%*)	21 (*62%*)	89 (*50%*)
Total	145	34	179

There were also two stomal ulcers which as such were poor results.

PROGNOSIS

Method of Assessment

In a study of this kind it is not enough to recognise that late results may be good, moderately good, or poor, or even to know the percentage of such results. We desire to know, if possible, which ulcer patient will probably remain well after recovering from his perforation, and which will probably relapse. The problem is therefore to establish a rational basis for such prognosis, so that the patient may be given the best advice and treatment as early as possible. To do this we have to rely on ascertainable facts, such as the preoperative history and the type of ulcer. If it can be shown that such are in any respect constant in each of our three groups of late results, and that there is a relationship between the clinical type and the grade of late result, something tangible will have emerged to aid us in making such a prognosis.

Clinical Types of Perforations

The preoperative clinical histories show that perforations may be classified into two main groups:

(1) Those which occur in a first acute attack of peptic ulceration, acute ulcers.

(2) Those which complicate an acute exacerbation of a known chronic peptic ulcer.

In group 1 there is either no previous history of dyspepsia whatever, or the history of indigestion is so vague that *peptic ulceration* is neither suspected nor diagnosed. Pain is not a feature in the history of these mild gastric disorders.

In group 2 there is always a record of recurrent bouts of painful dyspepsia, marked in many instances by which it was reduced to 10 mg twice daily, or even 5 mg twice daily

Case 1 —A woman aged 29, with a three months' history, had a large hyperplastic gland B M R +55% Receiving 30 mg neomercazole daily for 9 weeks, she became symptom free and gained 9 lb The dosage was then reduced to 20 mg daily, given with thyroid sicc As she was two months pregnant and the thyroid was still enlarged subtotal thyroidectomy was advised and was performed a month later The gland (82 g) showed typical diffuse hyperplasia but some colloid formation At operation the gland was firm with no undue vascularity and stripped readily from its fascial capsule There was no postoperative reaction

Case 2 —A woman of 58 had for 3 months had asthenia, anorexia, and palpitation Her thyroid was not visible or palpable but her B M R was +35%, her pulse rate was 160, and she had lost 46 lb She was given neomercazole 30 mg daily A fortnight later her husband had a fatal coronary occlusion, but after another 2 weeks her B M R was +19%, her pulse rate was 96 and she felt well At the end of 6 weeks, dosage was reduced to 20 mg daily At the end of 3 months, with B M R −13%, she had put on 11 lb weight and felt well After another month, the supply of neomercazole ran out, but she has kept well on mild sedation

Case 3 —A woman of 46 had developed her symptoms some 6 months after a hysterectomy In the next 6 months she had been given iodine and sedation but she had lost 21 lb and her thyroid had enlarged She had then received methyl thiouracil and 4 weeks later developed agranulocytosis with a temperature of 105°F and ulcerated throat This was quickly controlled but her B M R was +30% I gave her neomercazole 20 mg daily for 10 days and then 30 mg daily After 4 weeks her weight had increased by 8 lb and her B M R was −3% Dosage was then reduced to 10 mg daily, and 6 weeks later her B M R was +10%, but as she was symptom free the same dosage was maintained After another 6 weeks her B M.R was −17%, her thyroid was apparently normal, she had put on 7 lb weight, and she was symptom free After 2 further months on mild sedation she was still well During treatment with neomercazole her leucocyte count rose from 7400 (neutrophils 62%) to 13,000 (neutrophils 67%)

Case 4 —A man, aged 32, had become ill 5 years previously when his B M R was +65% After 3 months his condition had improved but in view of the large, very vascular thyroid and his poor physical state, the surgeon refused to operate After a further 9 months the surgeon again refused For another 2–3 years he was in poor health and 6 months before I saw him his B M R was +41% When given methyl thiouracil in large doses he developed a reaction with fever, vomiting, and increased asthenia As the thyroid had enlarged very much, operation was again refused, and he was given large doses of iodine When I first saw him his condition was parlous he had a very large hard vascular thyroid his pulse rate was 140, and he could not walk Treatment with propyl thiouracil reduced the leucocytes to 4900 with 58% neutrophils He was then given neomercazole 30 mg daily, and in 4 weeks felt a new man and had gained 5 lb leucocytes 6350 but neutrophils only 48% The dosage of neomercazole was increased to 45 mg daily, and in 4 weeks he gained 4 lb pulse rate 100, leucocytes 5350 (neutrophils 85%), B M R +21% The thyroid was still very large but its vascularity seemed less After a further month (15 mg daily for 2 weeks and then 30 mg for 2 weeks) he entered hospital and was given iodine for 5 days prior to operation This was carried out without any difficulty and very little blood loss The gland was large but moderately firm, it was easily handled, and the tissue planes stripped readily The whole right lobe, the isthmus, and the greater part of the left lobe was removed the tissue removed weighed 210 g and its microscopical appearance was that of a colloid goitre with small areas of hyperplasia There was no postoperative reaction and in 3 months he had put on a further 7 lb and had resumed work after 5 years invalidism

Case 5 —A woman of 36 Her illness had an acute onset in October 1951 when her B M R was +96% She received large doses of methyl thiouracil for 2 months and after 3 months showed hypothyroidism and a greatly enlarged thyroid At this time a bout of alcoholism necessitated 4 weeks institutional treatment at the end of which her B.M R was +26% and her pulse rate 108 She was then given methyl thiouracil 0 3 g daily with thyroid sicc gr ½ daily but after 3 months she had not settled, B M R +27% After 4 weeks' treatment with neomercazole 30 mg daily her B M R was +5% and her pulse rate 70 She had gained 6 lb, had lost the puffiness of her face, and felt like her old self After another 4 weeks she was symptom free and the thyroid had receded to almost normal proportions As the supply of neomercazole was now exhausted she was given methyl thiouracil 0 2 g with thyroid sicc gr. ½ daily, and has maintained her good condition for a further 3 months

Case 6 —A woman of 47 with symptoms for 12 months Methyl thiouracil, tried on four occasions, had always caused a toxic reaction with swelling of face and hands Her blood pressure was 220/90 and she was showing signs of congestive cardiac failure B M R +20% Neomercazole, 30 mg daily, was commenced, and in two weeks her B M R had fallen to −12%, her weight had risen by 9 lb, and she was symptom free As her thyroid had been enlarged for some years, operation was advised and performed some 2 weeks later by a colleague, who commented on the ease of operation and the slight blood-loss The tissue removed showed many vesicles containing colloid with considerable hyperplasia She made a rapid recovery

Case 7 —A man of 31 with symptoms since October, 1951 He had been given methyl thiouracil and iodine for 7 months with marked improvement but had relapsed within 8 weeks of ceasing treatment, when his B M R was +28% and his pulse rate 140 He had a large adenomatous thyroid After 8 weeks on neomercazole 30 mg daily, his B M R was +10%, and his pulse rate 80 Total thyroidectomy was then performed without difficulty or blood loss The gland weighed 175 g and showed colloid adenomata with hyperplasia in the surrounding gland tissue There was no postoperative reaction

Case 8 —A woman of 47 had noticed her thyroid enlarging for 2 years, and in the last 6 months had lost 12 lb B M R +47% Toxic symptoms were alleviated by methyl thiouracil but the thyroid grew rapidly and seemed very vascular Although the dose of methyl thiouracil was reduced and she was given thyroid sicc the gland enlarged still further and her pulse rate was 108 B M R −1% She was then given neomercazole 15 mg daily, and after 8 weeks was so much improved that operation was undertaken Total thyroidectomy was performed with removal of a very large gland which was firm and easily handled without any undue bleeding and fascial planes were clear

Case 9 —A woman of 65 gave a 4 years' history of weight loss with increasing asthenia For the last 3 months she had been in hospital with fibrillation For many years she had had a small adenoma in the left lobe of the thyroid B M R +15% Despite a leucocyte count of 3400 (neutrophils 34%) she was given methyl thiouracil and within a week had agranulocytosis though without febrile reaction With treatment, the leucocytes rose in 2 weeks to 6400 (neutrophils 68%) She was then referred for operation, but because of a low hippuric acid excretion (63% of normal), her poor physical condition which suggested adrenal deficiency, and the recent agranulocytosis neomercazole was advised, 30 mg daily For 3 weeks she seemed to be much the same but in the next 3 weeks she improved rapidly and though she still had a slow fibrillation total thyroidectomy was performed without any trouble There was a degenerating cysto adenoma in the left lobe of the thyroid with diffuse generalised hyperplasia in the rest of the gland tissue There was postoperative aggravation of the fibrillation which was not controlled for some 3–4 weeks She has put on weight and has resumed her ordinary activities

I should mention that ancillary treatment was given in all my cases for example, phenobarbitone was prescribed as a sedative, and iron where there was anæmia The patients received vitamin B, or, in cases with much weight-loss, mixed vitamin compounds

CONCLUSION

Experience in this small number of cases suggests that 'Neo Mercazole' is superior to any of the thiouracil compounds, not only for control of thyrotoxicosis but also for reducing the vascularity of the gland before operation In the dosages employed it reduces the basal metabolic rate more slowly than the thiouracils but it does not induce or increase thyroid hyperplasia and it does not interfere with the leucocytes It therefore appears to be a safer remedy and there is reason to treatment commonly fails with cases of chronic ulcer. The larger perforation and the rigid margin of the ulcer make closure by adhesions more difficult to achieve, and delay *in operating in these cases can only increase* the hazard. Further, when adhesion does occur between the base of a chronic ulcer and the liver, there may be a risk of converting a perforating into a penetrating ulcer. *On theoretical grounds the method seems to be more* suitable for the small acute-ulcer-perforation, where the peritoneal reaction sometimes leads to sealing off, which is facilitated by the flexibility and mobility of the viscera. *Indeed these cases are probably responsible for the* measure of success which has attended this mode of therapy. Its value in the presence of associated conditions, such as coronary and pulmonary disease, and in neglected cases, *for which it was first proposed by* Wangensteen (1935), is freely acknowledged. It might also be suitable for patients with a perforation that have to travel many miles to hospital, who might first have the stomach contents aspirated.

Primary partial gastrectomy for perforation has been practised in Continental clinics for fully thirty years and Nuboer (1951) draws attention to the great possibilities of this operation in the hands of the skilled surgeon. A mortality-rate of 3·8% in 131 cases is eminently satisfactory, especially when it is remembered that this procedure deals not only with the perforation but also with the ulcer and its possible sequelæ. It is pertinent to point out, however, that in using this operation as the standard treatment for all perforations Nuboer includes the relatively acute-ulcer cases with the chronic ulcers. The present investigation has shown that the acute-ulcer cases number 64% of the total, and that less than 10% of them have required further surgery within the five years; they also include the youngest patients. For these reasons such a drastic operation in an acute-ulcer case seems unnecessary, particularly when these cases can be dealt with safely by simple suture, and any evidence of recurrence can be treated by a planned operation. It is in the treatment of perforated chronic ulcer that primary partial gastrectomy may have its proper place, if it can be proved to be associated with a lower mortality-rate and morbidity-rate than simple suture. This experiment seems well worthy of trial; and if, as Nuboer says, the cases are easier to do in the presence of œdematous tissue planes than some planned operations for chronic ulcer, the patient should benefit from such timely intervention.

When any doubt exists about the practicability of the operation, the surgeon can revert to simple suture and leave his resection to a later date. Conversely, when he finds a large chronic ulcer whose rigid walls will not approximate, when there is reason to believe the ulcer is carcinomatous, or when there is an associated hæmorrhage, the surgeon may profitably proceed with the partial gastrectomy. Success will depend on the wise selection of patients, and *gastrectomy should be considered only* in those patients who are deemed fit enough to withstand the operation and exhibit no signs of peritonitis. A more serious attempt is needed to reach an accurate preoperative diagnosis of the type of ulcer involved in the perforation, so that adequate measures may be invoked to deal with it.

SUMMARY

Of 206 acute perforated *peptic ulcers 119 (58%)* were found to be acute ulcers and 87 (42%) chronic ulcers.

Treatment consisted in laparotomy and simple suture of the perforation.

The over-all mortality-rate was 6·3%. All 13 deaths were in the group of 87 cases of perforated chronic ulcer; in this group the mortality-rate was 15%, compared with nil in the 119 cases of perforated acute ulcer.

My thanks are due to Mr. J. D. Rose and to Mr. J. D. T. Jones, successively my assistant surgeons, and to Mr. C. J. Evans, Mr. K. Turnbull, Mr. F. I. Herbert, Mr. I. Marks, and Mr. W. G. Ferguson, who have been my surgical registrars during the period covered by this paper. The successful treatment of these emergency cases is largely due to their efforts, and to the nursing skill of Sisters Mackie, Atkinson, and Burke and their nurses. I must also acknowledge the assistance of Mr. W. G. Ferguson in the conduct of the "follow-up," and of Mr. H. Campbell, statistician in the department of *industrial health in the medical school, who reviewed the* tables and the conclusions based upon them. Finally, I am greatly indebted to Mr. J. D. T. Jones and to Mr. H. J. B. Atkins for much helpful advice and criticism in the preparation of this paper.

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TREATMENT OF THYROTOXICOSIS WITH 'NEO MERCAZOLE' (2-CARBETHOXYTHIO-1-METHYLGLYOXALINE) *

REPORT OF 120 CASES

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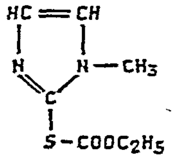
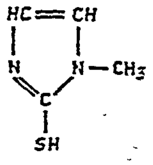
This paper presents the results of a clinical evaluation of the anti-thyroid compound 2-carbethoxythio-1-methylglyoxaline ('Neo Mercazole') in the treatment of thyrotoxicosis. In 30 cases it was used to prepare patients for operation, and in 90 cases it was used as a definitive form of treatment. In these observations, made between April, 1951, and February, 1953, no toxic reactions were seen.

The preliminary experiments on animals were reported by Lawson et al. (1951), and the first few cases by Lawson and Barry (1951).

Neomercazole, formerly called C.G.1, is a modification of 1-methyl-2-mercaptoimidazole (methimazole; 'Mercazole' in Great Britain, 'Tapazole' in the United States) (Stanley and Astwood 1949), which has been increasingly used in the U.S.A. since 1948 as an alternative to thiouracil derivatives. Methimazole has a tenfold anti-thyroid potency and a toxicity-rate of about half that of the older drugs. Neomercazole was synthesised by Lawson et al. (1951) in the hope of further reducing the toxicity-rate, which for methimazole is still considered by most workers to be 3–6%.



Neomercazole



Methimazole

The theoretical advantage of neomercazole over methimazole is that in neomercazole the active part of the molecule is blocked by a carbethoxy group: methimazole is probably released gradually by hydrolysis and the thyroid receives a more constant supply of the active thiol group. Thus a smaller quantity of the active drug may suffice.

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* This investigation was supported by a grant from the endowment funds of the Royal Free Hospital. The author's thanks are also due to the research grants committee of the Middlesex Hospital, London, W.1.

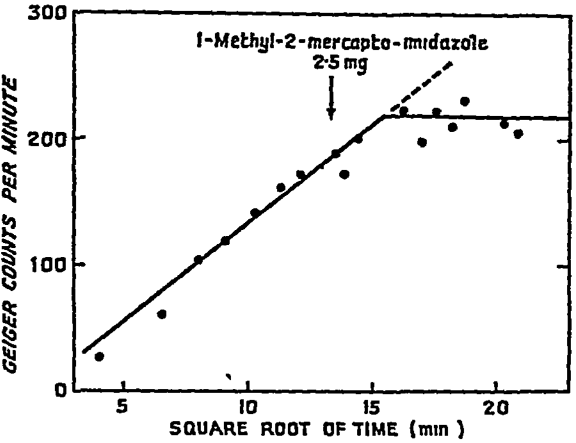

Fig 3—Effect of 2 5 mg of 1-methyl 2-mercapto-imidazole on accumulation gradient in thyroid gland

below 2 5 mg was very transient, whereas fig 2 shows a fairly prolonged effect due to 0 5 mg of C G 1 It has always been suggested that the former drug be taken in frequent divided doses because of the transient nature of the inhibition produced

Our own limited experience of the clinical use of these drugs suggests that they are both effective anti thyroid agents, but considerable caution should be exercised in the transfer of the results of potency trials of this type to the clinical field of therapy These radioactive-iodine tests suggest a potency possibly fifty times greater than that of methyl thiouracil This does not imply, however, that the therapeutic dose is correspondingly low Most observers now agree that 1 methyl-2-mercapto-imidazole has to be administered in very much higher dosage than was originally assumed to be necessary, and weight for weight, it is probably about ten times as active clinically as methyl thiouracil In the same way, where C G 1 is being used extensively, the dose necessary to achieve adequate control is higher than that first recommended (Lawson and Barry 1951)

The role of anti-thyroid drugs in the management of hyperthyroidism is now clearly defined, and, with the increasing availability of radioactive iodine for the therapy of thyrotoxicosis, their use is predominantly in the treatment of young patients and in the preliminary preparation of the patient for operation Both methyl thiouracil and propyl thiouracil are satisfactory members of the group, and to compete with them a new drug must have definite advantages A lower absolute dose is of little value in itself unless it can be shown to be accompanied by fewer undesirable side effects Dunlop and Rolland (1950) found that undesirable reactions to methyl thiouracil, sufficient to necessitate the abandonment of treatment, occurred in 7% of cases, and Iversen (1951), using the same drug, had to discontinue treatment in over 10% of his patients In contrast, most workers with 1-methyl-2 mercapto-imidazole have reported a low incidence of toxic reactions, but Stone Petit, and Starr (1952) have found that, when it is used in effective clinical dosage, its toxicity is somewhat higher than that of propyl thiouracil, and they had toxic reactions in 8 out of 29 patients (27%), two of the reactions being serious

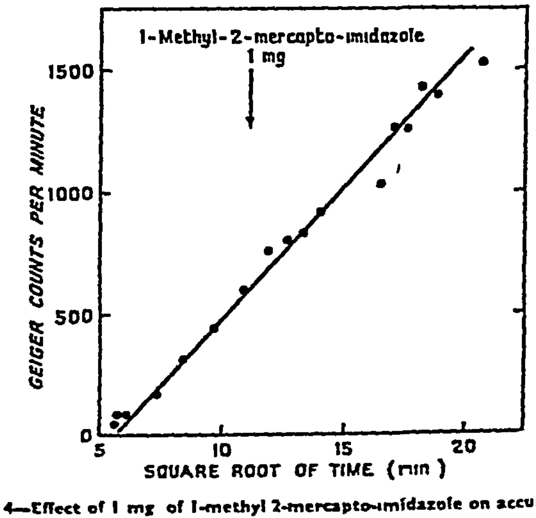

Fig 4—Effect of 1 mg of 1-methyl 2-mercapto-imidazole on accumulation gradient in thyroid gland

Very large numbers of patients will have to be treated with the new drugs before statistically valid comparisons can be made

SUMMARY

The anti-thyroid activity of 2 carbethoxythio 1 methylglyoxaline (C G 1) and that of 1-methyl 2 mercapto imidazole have been compared by the technique of Stanley and Astwood (1947)

Both drugs are fully effective in a single dose of 2 5 mg, but 2 carbethoxythio 1 methylglyoxaline appears to be consistently slightly more potent than 1-methyl 2 mercapto-imidazole in doses below this level

The present rôle of the anti thyroid drugs in therapy is briefly discussed Considerably higher doses of the new compounds are required in clinical practice than was originally recommended

We are grateful to Prof C Rimington for the supply of C G 1, and to Prof E J Wayne for his interest in these observations We should like to thank Miss Lorna Mann for her technical assistance

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CRYOGLOBULINÆMIA IN ALCOHOLIC CIRRHOSIS

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THE term "cryoglobulin" (Lerner and Watson 1947) describes a protein which is precipitated from serum or plasma on cooling and redissolves on warming Cases have been described by Shapiro and Wertheimer (1946), Hill et al (1949), Rorvic (1950), Blades (1951), Luckey et al (1951), and McFarlane and Dovey (1952) Most of these were cases of multiple myelomata, but the anomalous protein has occasionally been found in nephrosis (Wertheimer and Stein 1944), endocarditis (Lerner and Watson 1947), polyarteritis nodosa (Lepow et al 1949), and infective arthritis (Rorvic 1950)

In the case to be described here cryoglobulinæmia developed while the patient was under treatment

Two tests, which are commonly used in the United States but not in this country, have been used in this laboratory for some time In both of these the globulins are precipitated and estimated turbidimetrically de la Huerga and Popper (1950) use as reagent a saline ammonium sulphate solution, and Kunkel (1947) a barbitone and zinc sulphate solution Both are specific precipitants for γ globulins, but the Popper reagent also precipitates fibrinogen and consequently should be used only on serum The normal values are Popper 0-6 units and Kunkel 2-12 units

TABLE II—ANALYSIS OF 30 CASES TREATED PREOPERATIVELY

Mode of response to neomercazole	Size of goitre	No. of patients	Average age and age range (yr.)	Average initial B.M.R.	No. of patients with primary thyrotoxicosis	No. of patients with toxic nodular goitre	Mean dosage of neomercazole (mg. daily)
Good clinical response (mean B.M.R. fall = 1·5% per day)	Small (mean wt. 30·3 g.)	3	37 *(32–44)*	+30%	3	..	25
	Medium (mean wt. 48 g.)	10	40·7 *(22–51)*	+47%	5 (1 postoperative recurrence)	5	23
	Large (av. wt. 109 g.)	8	48 *(25–64)*	+37%	3	5	26
Slow response (mean B.M.R. fall = 0·3% per day)	Small (av. wt. 26 g.)	6	49 *(40–65)*	+33%	4 (1 postoperative recurrence)	2	23·3
	Medium (wt. not recorded)	2	49 *(32 and 66)*	+46%	1	1	40 and 20
	Large (wt. 102 g.)	1	43	+21%	..	1	20
Total	..	30	..	..	16	14	

Results

PREOPERATIVE MEDICATION

The preoperative group included 14 patients with toxic nodular goitre and 16 with primary thyrotoxicosis (2 having had previous thyroidectomies). Table II shows their response. The mean percentage in B.M.R. fall was calculated by taking the difference between initial B.M.R. and last preoperative B.M.R. and dividing by the number of days' treatment. For the 21 patients who responded well clinically the mean fall in B.M.R. was 1·5% per day. The 9 remaining patients showed a slow clinical response, and their B.M.R. fell by 0·3% a day. The two groups contained the same proportion of toxic nodular goitres, and there was no significant difference in the amount of neomercazole administered or in the initial B.M.R. However, there were more small goitres and the patients were older in the group showing slow response. Dosage was low in the first cases treated, and some patients were operated on while their B.M.R. was still between +10% and +25%.

Four of the patients with toxic nodular goitre were referred from the cardiac department—2 with auricular fibrillation and early cardiac failure, and 2 with hypertension. All were successfully prepared for operation, but 2 of them responded slowly and required both neomercazole and supportive treatment for three months.

None of the goitres enlarged during the short course of treatment. At operation the goitres were not particularly friable or more difficult to remove than in patients prepared with iodine only. Histologically the glands showed great variations and on the whole looked active.

DEFINITIVE TREATMENT

90 patients were treated medically with neomercazole for periods varying from a few weeks to twenty-one months. 76 patients had Graves's disease, including 7 postoperative recurrences; 14 patients with toxic nodular goitre received curative treatment for various reasons; 6 refused operation; 2 had ocular muscle palsies; 4 were old and hypertensive, with a small goitre; and 2 were well controlled with neomercazole but were ultimately operated on because of deviation of the trachea at the thoracic inlet, present before operation.

So far 6 patients have terminated their course of treatment and have remained well from two to seven months. In 2 other cases treatment was stopped, but symptoms recurred and neomercazole therapy had to be resumed:

The first patient was a postoperative recurrent thyrotoxic who had been well controlled for twelve months and had a maintenance dose of 6 mg. daily and a B.M.R. of −18%. Symptoms recurred within six weeks, with a rise of B.M.R. to +14%.

The other was a patient who had had a large nodular goitre for forty years with signs of toxicity for two years and auricular fibrillation when first seen. She refused operation and was treated with neomercazole for eighteen months, being well controlled on 10 mg. daily. Symptoms and signs returned within two months of ceasing treatment.

Table III shows the responses in these 90 patients: 72 showed a rapid clinical response and became euthyroid in two to eight weeks. Included are the results in 8 patients previously treated with methythiouracil, who all remained well when neomercazole 2·5 mg. was substituted for every 25 mg. of methylthiouracil. In mild cases with small goitres the B.M.R. usually returned to normal in two to four weeks; more severe cases took four to eight weeks to become euthyroid. 2 mild cases gave a delayed response due to previous saturation with Lugol's iodine.

Slow Response

18 cases responded slowly and were finally controlled after three to six months except for the 2 patients who defaulted. Here again, of the small goitres a large proportion were in elderly patients, of whom 7 had long-standing nodular goitres.

In 3 patients insufficient dosage was probably responsible for the delay in response. One of these, a postoperative recurrent thyrotoxic, was ordered 30 mg. a day but took the neomercazole irregularly to an estimated average of 10–12 mg. daily. She was controlled as soon as she was persuaded to take the full dose. 2 other patients were given 16 mg. and 20 mg. daily, a dose believed to be adequate early in the trial but now proved to be insufficient as an initial dose in severe cases. In 3 patients excessive psychological stress may have retarded the response to neomercazole, but 1 of these had only 20 mg. daily.

4 patients responded slowly to 30 mg. daily though they were straightforward primary thyrotoxics of average severity. An iodide trap test (Stanley and Astwood 1948) done on 1 of these showed that neomercazole 50 mg. blocked the synthesis of thyroxine completely, suggesting normal uptake of neomercazole by the thyroid. This patient responded rapidly when the dose was increased to 45 mg. daily. Possibly the patients who respond slowly to an average dose of neomercazole detoxicate or excrete it more rapidly and therefore need a larger amount to maintain a sufficient blood level.

Rapid Response

In contrast to these slow responses 4 of our patients reacted to neomercazole with unexpected rapidity. The B.M.R. (initially +49%, +34%, and +42%) returned to normal in two weeks on 30 mg. daily in 3 cases. After four weeks on this dose they showed signs of over-treat-

New Inventions

DOUBLE SUTURE-PASSER

SURGEONS brought up in the tradition of Ernest Miles, who use thread ligatures passed with his suture-passer, will appreciate the advantage of being able to pass a pair of parallel sutures with a single manipulation

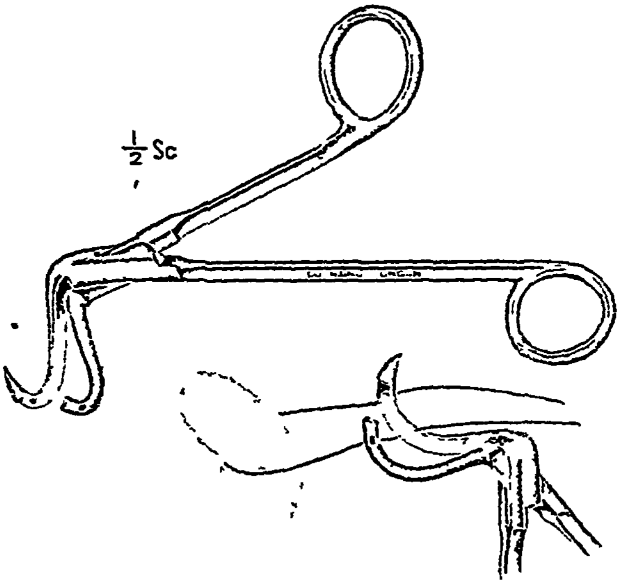

Fig 1—The double suture-passer After the instrument has been passed, the blades are opened to enable the thread to be hooked out by the finger

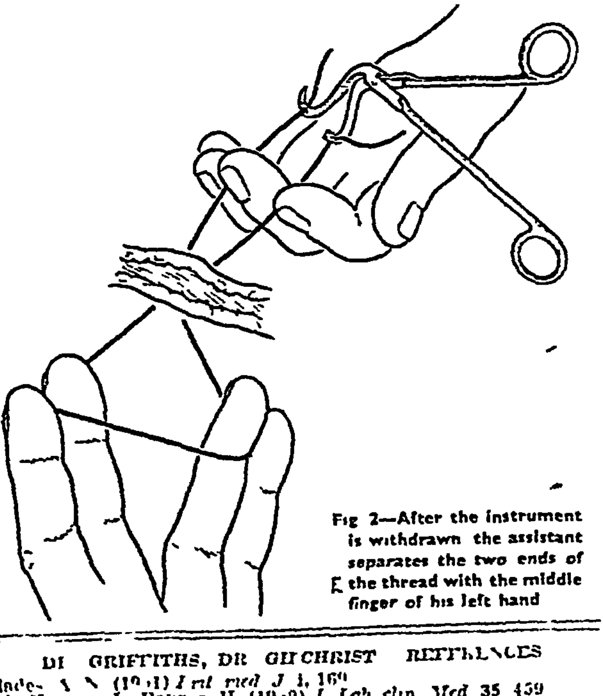

Fig 2—After the instrument is withdrawn the assistant separates the two ends of the thread with the middle finger of his left hand

The instrument here illustrated (fig 1) is a combination of aneurysm needle and Miles suture-passer, set on the handles of a Gillies needle-holder It is threaded with the blades closed, so that the double eye lies at the middle of the thread which trails to the right over the handle After it has been passed through the tissue (mesentery omentum or blood-vessel) which is to be doubly ligated the jaws are opened thus stretching the centre of the thread so that it can be hooked out by the operator's left middle finger Then the instrument is withdrawn the blades being *almost closed as they pass through the* hole in the tissue and opened again so that the assistant may separate the two threads with the middle finger of his left hand (fig 2) Finally the operator then cuts the centre of the thread, leaving two parallel ligatures

In major gastric and intestinal resections this instrument reduces the number of manipulations with the suture-passer, and by ensuring that both sutures pass through the same hole it lessens the risk of bleeding Also it saves much time

It is made by Down Brothers and Mayer & Phelps

St Bartholomew's Hospital,
London

A H HUNT, F R C S

Medical Societies

MANCHESTER MEDICAL SOCIETY

Mitral Valvotomy

ON March 19 Dr MAURICE CAMPBELL, discussing the Selection of Patients for Mitral Valvotomy and the Results, said that fifty years ago Lauder Brunton had suggested the surgical relief of mitral stenosis and had carried out some experiments on animals and in the necropsy room, but he could not find a surgeon who was interested More than twenty five years ago the first unsuccessful attempts were made, though the approach through the left auricle by Allan and the use of the finger for splitting the valve introduced by Souttar were valuable steps

Dr Campbell's figures were based on the first 100 patients operated on by Mr R C Brock and seen by Dr C G Baker, Dr Paul Wood and himself, with 50 others operated on since then Nearly all these patients were seriously disabled before operation After operation two thirds of them had returned to work and were often able to walk two miles or more, in many cases the improvement was dramatic Nearly all the patients had been followed for more than a year, and the first 50 for two to four years Mitral regurgitation did not follow a successful operation, but the murmurs generally remained, although they might disappear completely, as might the murmur of pulmonary regurgitation

There were 13 deaths in the first 100, but since the first 20 the mortality has fallen to 8% It was twice as high in those with auricular fibrillation as in those with normal rhythm Of the survivors 1 in about 5 could not be helped or was only moderately improved, but the two thirds obtained great help and could lead reasonably full lives It was soon realised that the young patients with signs and symptoms of pulmonary congestion, and often without much enlargement of the heart, were greatly improved Further experience showed that success could also be gained in older patients with larger hearts and in a wider variety of cases including patients who had had emboli or congestive right sided heart failure

The greatest disappointment of the operation was the frequency with which auricular fibrillation followed it Often this was paroxysmal and stopped spontaneously or could be stopped with quinidine, but in too many it remained established In the only 2 deaths that Dr Campbell himself knew of it was a factor the 1st patient died suddenly and unexpectedly a few hours after normal rhythm had been restored with quinidine nineteen months after a successful operation, the 2nd died from a large pulmonary embolus due to venous thrombosis in

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patients who had undergone excessive psychological stress. 2 cases were severe enough to require lateral tarsorraphy. 3 of the patients became worse while taking neomercazole. In benign cases the eye signs subsided with toxicity or did not progress appreciably.

TOXIC REACTIONS

No rashes, drug fevers, arthralgias, sore throats, or leucopenia occurred in any of the patients, and no other toxic manifestations have been seen to date. 3 of our patients had previously shown toxic reactions with methylthiouracil and 1 with 'Itrumil,' but had no ill effects from neomercazole.[‡]

Illustrative Case-records

TYPICAL RESPONSE IN AVERAGE CASE

Case 1.—A housewife, aged 32, was seen at the Royal Free Hospital in August, 1952, with five months' history of nervousness and irritability, insomnia, palpitations, and breathlessness on exertion. Loss of weight 11 lb. in five months.

On examination the thyroid showed firm generalised enlargement, estimated weight 40 g., with palpable thrill over both superior poles and intense systolic bruit over entire gland. Marked tremor. No eye signs. B.M.R. +34%. Pulse-rate 96, regular. Weight 115 lb. Serum-cholesterol 187 mg. per 100 ml. Maximum uptake of I^{131} 82% (normal 20–50%) at five hour (half-maximum in thirty minutes), declined to 78% at twenty-four hours. Thyroid/plasma clearance-rate 330 ml. (normal 10–42 ml.). Urine excretion 7% in twenty-four hours (normal 30–60%).

Aug. 26: treatment with neomercazole, 20 mg. daily, started.

Sept. 18: B.M.R. +10%; pulse-rate 80; weight 118 lb.; no thrill, bruit less loud.

Oct. 17: B.M.R. −10%; pulse-rate 78; weight 126 lb.; thyroid softer, bruit practically gone. Neomercazole reduced to 5 mg. a day.

Nov. 20: B.M.R.=0; pulse-rate 82; weight 128 lb.: thyroid now quite soft, no bruit. Neomercazole reduced to 4 mg. a day.

Dec. 30: B.M.R. not estimated; pulse-rate 76; weight 133 lb.; goitre soft, about 35–40 g., no bruit. Feels perfectly well on neomercazole 4 mg. daily.

RAPID RESPONSE

Case 2.—A housewife, aged 30, was first seen at the Royal Free Hospital in January, 1953, with four months' history of ravenous appetite, intolerance of heat, and severe nervousness, two months' history of swelling of neck, and five weeks' history of prominent eyes. No family goitre and no precipitating causes.

On examination she was severely toxic, thin, shaky, and breathless, with staring and restlessness. The thyroid showed firm generalised enlargement, estimated weight 70–80 g.; neck circumference $14^1/_2$ in.; palpable thrill over right upper pole; loud systolic bruit over entire gland but loudest on the right. Exophthalmometer readings R 16, L 15. Slight supraorbital swelling; moderate lid retraction and lid lag; no ophthalmoplegia or chemosis. Warm moist skin; fine and coarse tremor of hands. Initial B.M.R. +66% and repeat B.M.R. +63%, pulse-rate 130, regular; weight $119^1/_2$ lb.; height $67^1/_4$ in.; blood-pressure 185/55 mm. Hg; serum-cholesterol 104 mg. per 100 ml., thymol turbidity 5 units, flocculation positive. I^{131} iodide trap test uptake blocked with neomercazole 30 mg.= 34% of the dose taken up at $1^1/_4$ hours, decline to 30% at $2^1/_2$ hours. Administration of 1 g. of potassium thiocyanate was followed by rapid loss of iodide to 12% of the administered dose.

Jan. 9: treatment with neomercazole 40 mg. a day started.

Jan. 30: patient said she felt a different woman. Had gained $4^1/_2$ lb.; B.M.R. +7%; pulse-rate 68; blood-pressure 130/80 mm. Hg. Neomercazole reduced to 25 mg. daily.

Feb. 20: B.M.R.=0; pulse-rate 72; weight $127^1/_2$ lb.; exophthalmometer readings R 17, L 16; neck circumference $14^1/_2$ in., goitre size unchanged, thrill still present with loud bruit; no tremor. Neomercazole reduced to 20 mg. daily.

SLOW RESPONSE

Case 3.—A married clerk, aged 38, was first seen at the Middlesex Hospital on Feb. 19, 1952. In October, 1951, there had been a rapid onset of intolerance to heat, with excessive sweating, severe breathlessness on exertion, and palpitations at night. *In December, 1951, swelling of neck first appeared.* Weight had been lost from 10 st. 7 lb. to 8 st. $5^1/_2$ lb. in the last five months in spite of good appetite. Generalised pruritus.

On examination the patient was restless and looked worried, with a slight stare. The thyroid showed considerable, uniform, and moderately firm enlargement; estimated weight 60 g. Neck circumference 14 in. Much pulsation of goitre, with thrill over both superior poles. Intense systolic bruit over entire gland. Skin moist and warm; fine tremor of hands. B.M.R.=+45%; pulse-rate 106; weight 117 lb.

Feb. 22, 1952: treatment with neomercazole 30 mg. daily, started.

After four weeks' treatment pruritus had disappeared, and all other symptoms improved. B.M.R.=+29%; pulse-rate 92; weight 123 lb.

After eight weeks' treatment B.M.R.=+20%; pulse-rate 88; weight 126 lb.; goitre smaller and softer, estimated weight 50 g., no thrill, soft bruit only.

After sixteen weeks' treatment B.M.R.=−3%; pulse-rate 76; weight 137 lb.

After twenty-four weeks' treatment neomercazole was reduced to 15 mg. daily.

September, 1952: B.M.R.=+18%, pulse-rate 80. Dosage not changed, because patient still felt well.

November, 1952: recurrence of symptoms. B.M.R.=+14%; pulse-rate 100; weight 132 lb.; skin moist; slight tremor; goitre size unchanged, but bruit loud again. The dosage of neomercazole was increased to 30 mg. again.

Three weeks later all the symptoms had been controlled.

Follow-up.—Patient now on neomercazole 20 mg. a day; neck circumference is $13^1/_2$ in., and bruit is still present. Feels well and works full time besides running own home.

This patient may well come to operation, for after a year's treatment it has been impossible to reduce the dosage of neomercazole to a small maintenance dose.

OVER-TREATMENT

Case 4.—An engineer, aged 40, was admitted to the Royal Free Hospital on Aug. 30, 1952, with three months' history of lack of energy, nervousness, and shakiness, increased sweating, and intolerance of heat. He had lost 1 st. weight in a year, and for the last month had had palpitations on exertion.

On examination he weighed 9 st. $10^1/_2$ lb. Sweating was profuse. The thyroid was easily palpable; estimated weight 30 g.; soft bruit over both lobes. Fine tremor. No eye signs. Pulse-rate 100. Blood-pressure 180/90 mm. Hg. B.M.R. +38%.

After ten days' rest and 'Sodium amytal,' B.M.R. +27%, I^{131} maximum uptake 76%, half-maximum reached at fifty minutes, thyroid/plasma clearance 280 ml. per minute, urine excretion 6% in twenty-four hours. Serum-cholesterol 166 mg. per 100 ml.

Treatment and progress.—After ten days' treatment with neomercazole 30 mg. daily the B.M.R. was +3% and pulse-rate 90, and the patient had gained $6^1/_2$ lb. The dosage of neomercazole was reduced to 15 mg. a day, on which dosage the patient was discharged.

From October, 1952, to January, 1953, the patient attended another clinic, continued to take neomercazole 15 mg. daily, but did not have his B.M.R. estimated. From November, 1952, onwards, he had pain in his shoulders and back, slowing down and excessive sleepiness, and increasing sensitivity to cold. His skin became dry. No constipation.

On Jan. 12, 1953, he was seen again at the Royal Free Hospital, when his B.M.R. was −30%, pulse-rate 80, weight 11 st. 4 lb., eyes puffy, and speech slow and slurred. Neomercazole therapy was stopped. A week later his B.M.R. was −23%, serum-cholesterol 184 mg. per 100 ml.; thyroid still small and soft (estimated weight 30 g.), and no bruit was heard.

[‡] The number of patients treated with neomercazole has since increased to 150, and still no toxic reactions have been seen.

Recent Advances in Pathology

6th ed. Editor: GEOFFREY HADFIELD, M.D., F.R.C.P., Sir William Collins professor of pathology, Royal College of Surgeons of England. London: J. & A. Churchill. 1953. Pp. 367. 30s.

THIS well-known work can no longer be called Hadfield and Garrod, because it is now written by nine contributors under the general editorship of Professor Hadfield, while Professor Garrod, owing to increasing commitments has retired after sixteen years of collaboration. The large body of new knowledge which has accumulated since the last edition appeared six years ago is set out, mostly in clear and readable reviews.

In some chapters, notably those on liver diseases and pneumoconiosis, a little judicious cutting of older work, which tends to conflict with modern knowledge, would have given greater clarity; but on the whole this book presents clearly and concisely most of the advances of recent years. It is unfortunately inevitable that a survey of this kind is partially out of date before it appears, and we can only regret that it is not produced more often and the time taken in publication reduced; but the postgraduate student preparing for higher examinations and the busy practising consultant who wishes to get abreast of modern advances in specialties other than his own will find that it adequately fills the gaps in their reading.

Advances in Carbohydrate Chemistry

Vol. 7. Editors: CLAUDE S. HUDSON, National Institute of Health, Bethesda, Maryland; MELVILLE L. WOLFROM, department of chemistry, Ohio State University, Columbus; SIDNEY M. CANTOR, American Sugar Refining Co., Philadelphia. New York: Academic Press. London: Academic Books. 1952. Pp. 370. 60s.

THIS is a book for the research-worker specialising in the chemistry of carbohydrates and will probably be of little value to the general reader or even to many biochemists. For those actively engaged in this field however, it provides critical reviews on the chemistry of various carbohydrates and their derivatives written by experts. The high standard of the reviews published in earlier annual volumes of the series has been fully maintained in this. Of the eight reviews those dealing with derivatives of fucose, with fructose and its derivatives with 2-amino sugars, and with the size and shape of polysaccharide molecules have the most interest in medicine, but all are essentially chemical in viewpoint. Information about the molecular weights of various polysaccharides, including glycogen, bacterial dextrans, inulin, bacterial polysaccharides, chondroitin sulphate, blood-group polysaccharides, heparin, and hyaluronic acid, is summarised. The book is illustrated with numerous structural formulæ, and contains tables of chemical properties of carbohydrates and their derivatives.

The Stranger's Son

JOHN J. KEEVIL. London: Bles. 1953. Pp. 230. 21s.

THIS biography of Baldwin Hamey the younger, a leading physician of seventeenth-century London and the most liberal of all the benefactors of the Royal College of Physicians, is a sequel to the same author's *Hamey the Stranger*,[1] but is complete in itself. It is based on unusually intimate and previously unexamined manuscripts, mostly written in Latin, which give a detailed account of his youth and medical education at Leiden, Oxford, and London.

Through them can be seen his rise to eminence as a physician and his great influence over the college though he refused an invitation to be its president. Hamey successfully steered his way through the divided loyalties of Cromwellian England while secretly forming a collection of Stuart relics now at Windsor Castle. He lived to experience the plague in London and to witness the great fire from his new home in the country at Chelsea. A classical scholar he could read and write Latin prose and verse with fluent ease and when occasion demanded with wit. When the college building at Amen Corner near St. Paul's was subject to confiscation in 1651 Hamey redeemed the property out of his own private purse and preserved it for the college. He contributed liberally to the rebuilding fund after the fire. In addition he presented the wainscoting of fine Spanish oak which now adorns the censors' room, and made over to the college an estate in Essex to double the premium of the Harveian orator. He had no children, a good inheritance, and a lucrative practice. He was always well off and used his wealth with generosity all his life. He made gifts to London's churches, to Charles II and on several occasions he paid for the education of boys whose scholarship seemed deserving of help.

Dr. Keevil has assembled his facts into a readable and entertaining story and he gives a vivid picture of life in London at the time and of the administration of the college. The translation of medieval Latin must have been a big labour and is a work of scholarship and distinction.

Die Sprache des Menschlichen Antlitzes

4th ed. FRITZ LANGE. Munich: J. F. Lehmann. 1952. Pp. 237. D.M. 20.50.

WE all have to work out for ourselves a rough and ready gallery of correspondence between face and character, and we all suffer from the lack of an assured system. There have been many failures to reinstate Lavater or improve on him, but efforts to find a sound basis for this necessary art continue. Professor Lange, an orthopædic surgeon, has pursued the study of faces throughout his long life, in the belief that only anatomical analysis of expression and structure can provide the essential data for reading character. Consequently his book is rich in descriptions, which are precise about muscles and movements but woefully loose about traits of personality. Many of Dr. Lange's illustrations are of historical personages about whose character we know little, so he has had to rely on anecdotes and scanty or biased accounts. Some of his notions are very old fashioned: thus he suggests that much intellectual activity may make the brain grow more, thus bringing about in a young man the broad and high forehead of the thinker. The book contains much information much uncritical guesswork, and a pleasant seasoning of prejudices.

Traitement de la tuberculose par l'acide para-amino salicylique P.A.S.

Editors: JEAN PARAF, médecin de l'Hôpital Bichat, JEAN FOUQUET, Médecin de la Salpêtrière (Service des enfants). Paris: Masson. 1952. Pp. 404. Fr. 3200.

para-Aminosalicylic acid is considerably less effective than streptomycin and, though it is a valuable adjunct through its partial inhibition of resistance to streptomycin when the two are given together, its use alone has not been very popular in this country; indeed many consider that it should not be used by itself at all. But numerous patients have undoubtedly been treated with P.A.S., and the paucity of reports in the English journals suggests that the results have not been satisfactory. Much more attention has been given to it in France, and this book assembles the experience gained there. The section dealing with chemistry, pharmacology, and laboratory studies is useful and adequately documented, but the clinical section is too uncritical in the presentation both of reports from published work and of the authors' own observations. It is unlikely that the results described with oral or intravenous P.A.S. will change the present judgment in this country of the rôle of the drug in tuberculosis.

Polyglot Medical Questionnaire (London: H. K. Lewis. 1953. Pp. 62. 12s. 6d.)—Ten years ago[1] Dr. Chalmers Parry drew our attention to his polyglot medical questionnaire in 27 languages, then awaiting publication. Now, at long last, 12 of his 27 languages have been published and it is a pity that all 27 are not here. To communicate with a patient the questioner finds the required phrase numerically keyed in his own tongue, and points out to the patient the same number in the foreign tongue concerned. This method of communication does away with difficulties of pronunciation and phonetic spelling and unintelligibility of the patient's reply which is nearly always "yes" or "no". This questionnaire is limited to English, German, Dutch, Norwegian, Swedish, Danish, French, Spanish, Italian, Portuguese, Russian, and Polish.

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[1] See *Lancet*, 1952, ii, 1209.

[1] *Lancet*, 1943, ii, 750.

Summary

A report is presented on the use of 2-carbethoxy-1-methylglyoxaline ('Neo Mercazole') a new anti-thyroid drug related to methimazole.

120 thyrotoxic patients treated with neomercazole were followed for periods up to twenty-one months. Of these, 30 patients received neomercazole preoperatively and 90 as curative treatment.

The optimum initial dosages were 15, 30, and 45 mg. a day for mild, average, and severe cases respectively.

Of the 120 patients, 93 became euthyroid within two to eight weeks, and 27 responded more slowly. Of the latter, 9 were operated on and the rest were controlled in three to six months.

Goitrogenic reactions were avoided, in all except 7 patients, by careful control of the maintenance dose.

No toxic reactions were seen.

The results are compared with those obtained with methimazole by other workers. Weight for weight, neomercazole seems to be at least as effective as, and very much less toxic than, methimazole.

I am grateful for constant encouragement and guidance to Miss G. Barry, senior surgeon at the Royal Free Hospital, under whose direction this work was done and who initiated the clinical trial in April, 1951, and operated on 30 patients. I am indebted to Sir Daniel Davies, Dr. P. E. Thompson Hancock, and Dr. Frances Gardner, physicians to the Royal Free Hospital, for allowing me to cite 15 cases treated by them. Dr. Gardner also supervised the cardiac aspect in our patients. Mr. R. Vaughan Hudson, senior surgeon at the Middlesex Hospital, gave me facilities to treat and to follow up 34 cases in his clinic: I wish to thank him for his keen interest and valuable help in this study. I also want to thank Mr. A. Lawson, PH.D., university reader in chemistry at the Royal Free Hospital, for his advice and help; and the physicists and the staff of the pathology departments in both hospitals for investigating our patients.

The drug used in this investigation was supplied by Glaxo Laboratories and by the British Schering Company.

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"The closing sessions of the annual meeting of the American College of Physicians offered today a striking example of what a medical leader described as indifference by doctors to economic and social aspects of practicing medicine. Only fifty-three physicians among the 4,700 attending the week-long session went to hear Dr. Louis H. Bauer, president of the American Medical Association, and a panel of five medical authorities discuss how the public can pay for the excellent medical treatment that science now can provide. At the same moment, well over 1,000 crowded into another room of Convention Hall for an erudite clinical-pathological conference. Strictly scientific, the conference presented in detail two medical cases, at autopsy, which the average practicing physician would infrequently see in normal practice."—ROBERT K. PLUMB, *N.Y. Times*, April 18, 1953, p. 5.

THYROTOXICOSIS TREATED WITH 2-CARBETHOXYTHIO-1-METHYLGLYOXALINE

('NEO MERCAZOLE')

Sir HUGH POATE

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AFTER the first reports on the anti-thyroid activity of 'Neo Mercazole' (Lawson, Rimington, and Searle 1951, Lawson and Barry 1951), a small supply was sent to Sydney in May, 1952, for clinical trial.

PREAMBLE

With the advent of the "thio" compounds, introduced by E. B. Astwood, the treatment of thyrotoxicosis has undergone profound change. Medical treatment will now cure the majority of patients with early acute primary thyrotoxicosis—in my experience nearly 85%—while the remainder can be subjected to an operation of convenience. In the late stage of primary thyrotoxicosis, or in thyrotoxicosis secondary to an old colloid or adenomatous thyroid, the toxicity can be controlled in 2–3 months and the patient then treated by an operation which usually requires only 7–10 days in hospital, followed by rapid convalescence. Though the technical difficulty of operating on large glands is much the same as when iodine is administered to prepare the patient for operation, with adequate preparation there is no postoperative reaction to worry surgeons and nurses.

Of the various "thio" compounds, I finally selected methyl thiouracil as a standard means of treatment, with propyl thiouracil in reserve. However, a number of patients proved intolerant to both these compounds, and agranulocytosis kept occurring as wider use was made of this form of therapy by general practitioners. Hyperplasia of the thyroid has become common, because of overdosage and failure to give thyroideum siccum when control of toxocity has been obtained, while inadequate treatment, on the other hand, has resulted in many recurrences of thyrotoxicosis. What was wanted was a compound which would reduce the vascularity of the gland but would not interfere with the white blood-cells, induce hyperplasia of the thyroid, or cause perithyroiditis or reactions such as fever, rashes, or joint pains. Judging by experience up to date, neomercazole comes closer to meeting these requirements than any other compound yet introduced.

Compared with methyl thiouracil, neomercazole seems to have a more persistent effect on the thyroid and to cause greater regression of the hyperplasia with restoration of colloid storage. The glands of those operated on have shown relatively slight hyperplasia, and the longer the preparatory treatment the less the hyperplasia becomes. If confirmed, this observation will be important for long-term therapy; for in cases treated with methyl thiouracil recurrence takes place only in patients whose glands remain enlarged after adequate therapy: if the gland reverts to a normal size, there is no recurrence. Also it seems that neomercazole induces resolution of hyperplasia much more quickly than does methyl thiouracil.

THE CASES TREATED

Of the nine thyrotoxicosis cases I have treated with neomercazole, the first two were examples of acute primary thyrotoxicosis in which a good response to methyl thiouracil would have been expected. Having obtained good results I then tried the drug in cases where thiouracil had proved unsatisfactory or had produced side-effects. The usual dosage was 10 mg., three times daily until thyrotoxicosis was controlled, after

"I dread the rustling of the grass"

WILLIAM WORDSWORTH

No sooner has the blossom languished
and spring shed her coat of many
colours than the tall grasses ripen The air is
again pollen-laden To those who love the countryside
these richly-clothed meadows are a joy to
sufferers from hay-fever they are
merely the signal for a fresh period of acute discomfort
Yet there is a solution — BENADRYL,
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may be taken just before and during the
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PARKE, DAVIS & Company, Limited [illegible] Hounslow, Middlesex Telephone Hounslow 2361 think that, once control of a primary thyrotoxicosis is obtained, a comparatively short period of maintenance therapy will bring about complete cure.

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ANTI-THYROID ACTIVITY OF 2-CARBETHOXYTHIO-1-METHYLGLYOXALINE

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THE first account of 2-carbethoxythio-1-methyl-lyoxaline (C.G.1) was published by Lawson, Rimington, nd Searle in 1951, and Lawson and Barry (1951) have eported on its clinical use in thyrotoxicosis.

Lawson et al. (1951) included in their report an account f the effect of C.G.1 on the metabolism of iodine as easured with the isotope I^{131}, and they showed that s effect was very similar to that of 1-methyl-2-mercapto-midazole, but the inhibitory effect on the uptake of iodine y the thyroid gland appeared to be more prolonged.

FFECTS OF 1-METHYL-2-MERCAPTO-IMIDAZOLE AND C.G.1 ON THYROID UPTAKE

ase o.	Drug	Dose (mg.)	Effect
1	1-methyl-2-mercapto-imidazole	10·0	Uptake completely inhibited
2	,,	2·5	Uptake completely inhibited (fig. 3)
3	,,	1·0	No effect
4	,,	1·0	No effect (fig. 4)
5	,,	0·5	Very transient partial suppression of uptake
6	2-carbethoxythio-1-methylglyoxaline	10·0	Uptake completely inhibited
7	,,	10·0	Uptake completely inhibited
8	,,	2·5	Uptake completely inhibited (fig. 1)
9	,,	1·0	Partial suppression of uptake
10	,,	1·0	Partial suppression of uptake
11	,,	0·5	Slight partial suppression of uptake
12	,,	0·5	Slight partial suppression of uptake (fig. 2)

We have assayed C.G.1 ('Neo Mercazole,' British chering) by the standard technique of Stanley and stwood (1947), so that its potency might be readily ompared with that of the numerous other compounds imilarly assayed. The technique has previously been pplied by Goodwin, Miller, and Wayne (1949) to other ubstances.

METHOD

After the administration of a tracer dose of radioctive iodine, a dose of an anti-thyroid drug is given to a atient. This changes the normal curve of accumulaion of iodine in the thyroid gland. In a normal person, f the activity of the thyroid is plotted against the quare root of the time, the curve persists as a straight ine for about ten hours, and any deviation from the ine is easily detected. Within limits, the extent of the eflection from the straight line can be related to he potency of the drug and the size of the dose.

The inhibitory effect of 1-methyl-2-mercapto-imidazole ras studied by Stanley and Astwood (1949), and we have ompared the action of this drug with that of C.G.1.

RESULTS

Graded doses of both drugs were administered to patients with normal thyroid function (see table) and typical results are illustrated in figs. 1–4.

In doses of 10 mg. both drugs caused complete inhibition of uptake of radioactive iodine by the thyroid gland during the whole period of observation, and a similar effect was observed with doses of 2·5 mg. of each drug (figs. 1 and 3). The effect is comparable to that of 200–300 mg. of methyl thiouracil.

At the 1 mg. dose level C.G.1 caused a definite but smaller depression of the curve, and even in a dose of 0·5 mg. the shape of the curve was consistently affected (fig. 2). With 1-methyl-2-mercapto-imidazole, however, no effect was noted in either of two patients to whom 1 mg. doses were given (fig. 4); and, except for one patient in whom a very transient inhibition of uptake was observed after a dose of 0·5 mg., we did not notice any effect in any patient with doses of this order.

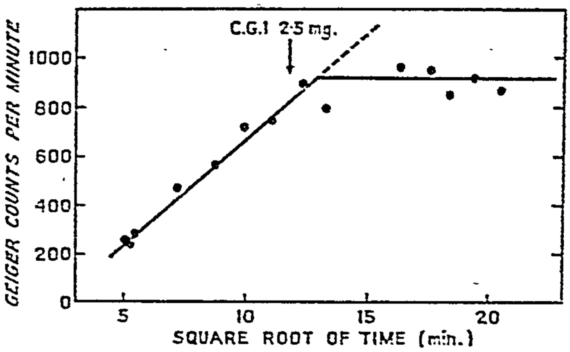

Fig. 1—Effect of 2·5 mg. of C.G.1 on accumulation gradient in thyroid gland.

DISCUSSION

Stanley and Astwood (1949) reported a definitely demonstrable effect with doses as low as 0·5 mg. of 1-methyl-2-mercapto-imidazole, but this was not invariable in our experiments. On the other hand, the anti-thyroid potency of C.G.1 is certainly as great as that of the other compound; and it may well be greater, for more consistent inhibition was obtained with single doses of it at levels of 1 mg. or less.

Further, the possible positive effect obtained in one patient with 1-methyl-2-mercapto-imidazole in dosage

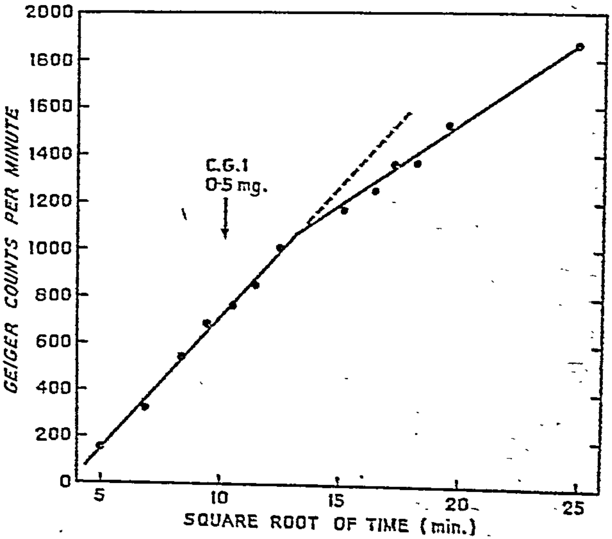

Fig. 2—Effect of 0·5 mg. of C.G.1 on accumulation gradient in thyroid gland.

contamination with carcinogens cannot be entirely excluded in any surroundings where they have been used, so readily do they become dispersed. Mere contamination was, however, an unlikely explanation of the malignant change in untreated cultures, for precautions were taken to avoid it, and FIROR and GEY[3] found, by chance, a similar transformation in the course of experiments requiring continuous culture of rat mesenchyme. This occurred in a laboratory into which no chemical carcinogen had knowingly been introduced. These workers also noticed altered appearances which led them to suspect malignant conversion. On inoculation into rats malignant tumours developed. In this case stray gamma radiation due to storage in the laboratory, at the time of early cultivations, of 50 mg. of well-shielded radium had to be considered as the effective cause of the change. On measuring the radiation in the region of the roller-tube drum about $^1/_{20}$ rontgen per day was detected; this applied to two out of three instances of malignant change but not to the third and possibly more.

Yet another example of malignant change in vitro, associated this time neither with chance nor with known carcinogen but with a deliberate attempt by other means, has now been reported by GOLDBLATT and CAMERON[4] in two cultures derived from 5-day-old rat heart. The means used to effect the change were intermittent deprivation of air and the substitution of nitrogen during prolonged propagation. Work was begun by GOLDBLATT in 1930 on a theoretical basis derived from WARBURG's studies of metabolism of various normal and malignant tissues in vitro. This work was abandoned and could not again be resumed until 1949, when GOLDBLATT and CAMERON started to test the idea that because surviving or temporarily growing tumour cells characteristically use the glycolytic mechanism as a source of energy, the enforcement of this mechanism on growing normal cells might impose the malignant conversion. It now appears that intermittent exposure to anaerobic conditions, with replacement of air by nitrogen in the culture-tubes, has twice, short of killing the cells, brought about, or been attended by, eventual malignant change. Five cultures of myocardium so treated died or were discarded on account of poor growth. A sixth culture was divided, and from it three substrains were grown. One line of cells was propagated in the usual way and never exposed to nitrogen. It eventually developed into a strain of pure fibroblasts which served as controls throughout the experiments. Its progeny underwent no further unusual morphological variation and did not give rise to tumours on inoculation into rats; the other two strains were deprived of air and exposed to nitrogen intermittently, the second being derived from the control subculture one year later than the first. The cells of both developed striking morphological alterations in about a year and after several unsuccessful attempts, gave rise on inoculation, using a special device, to serially transplantable fibrosarcomas. The special device, due to a technique used by H. S. N. GREENE, was the inclusion with the test inoculum of a small fragment of embryo rat lung from the same rat strain. Subcutaneous nodules then became visible and palpable in 3 or 4 days and grew progressively and in serial transplants.

GOLDBLATT and CAMERON suggest, but do not claim to have proved, a causal relationship between intermittent anaerobiosis and malignant conversion. They recognise the difficulty of reconciling their findings after deliberate intervention with the apparently spontaneous transformations of EARLE and of GEY and his associates. They think that in fact GEY's cultures may often have been exposed inadvertently to oxygen lack under the experimental conditions used. Some morphological and biological observations by LUDFORD and BARLOW[5] on cultures of mammary carcinomas of mice under ordinary conditions must also be taken into account. These observations suggested—though they never finally proved—that accompanying connective tissue cells had undergone sarcomatous transformation. Only further work undertaken to test whether results are repeatable sufficiently often to be relied on and duly controlled will settle the relation of anaerobiosis to malignant conversion. As in the natural history of malignant disease, time again appears to play a ruling part. Perhaps epithelium and cells from animals other than rats will now be tested by the same methods. Malignant change is notoriously easily induced in rat connective tissues, but this does not detract from the value of these stimulating experiments.

Puerperal Mastitis

UNTIL recently interest in the painful condition of puerperal mastitis was directed more towards treatment than towards prevention. Typically mastitis and breast abscess develops rather late in the puerperium—most commonly in the third and fourth weeks. Thus obstetricians and midwives, whether they work in or outside hospital, do not see nearly all the instances of this complication; it is the surgeon and the pædiatrician who are continually reminded of it.

Careful observation has shown that mastitis is closely associated with early breast engorgement and feeding difficulties due to abraded or cracked nipples. Where lactation starts by sudden engorgement, the nipples become œdematous and thus especially liable to damage. This liability is further increased because the baby, unable to get the areola in his mouth, munches the nipple; and once damaged the nipple is open to infection. Only about 30% of women are so fortunately fashioned that their nipples protract well and there is no obstruction to the outflow of breast secretion in the later months of pregnancy, or of milk after delivery. In such cases the baby takes the nipple well into his mouth; his gums are applied to the areola, and milk squirts almost effortlessly down his throat; there is little or no engorgement; and there is a minimum of friction of, or of danger of damage to, the delicate epithelium of the nipple since no force is applied to it. The majority of women, however, need help and instruction, not only to remedy nipple defects antenatally, but also so that they may learn in good time how to express secretion in the later months of pregnancy and clear the way for the free flow of milk after delivery. Anatomical

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[3] Firor, W. M., Gey, G. O. Ann. Surg. 1945, 121, 700. Gey, G. O., Gey, M. K., Firor, W. M., Self, W. O. Acta Un. int. Cancr. 1949, 6, 706.

[4] Goldblatt, H., Cameron, G. J. exp. Med. 1953, 97, 525.

[5] Ludford, R. J., Barlow, H. Cancer Res. 1945, 5, 257.

CASE-RECORD

A man, aged 63, was referred to us by Mr. H. S. Gild because of recurrent epistaxis. In 1946, when he had his first attack, he consulted another otolaryngologist, who cauterised his nose without benefit. In 1947 he was admitted to another hospital with severe anæmia. On the basis of a high colour-index, pernicious anæmia was diagnosed and the patient was transfused with a pint of whole blood, after which he had an intermission of five months before his symptoms returned. He had then, on the average, an attack every 7–10 days. He was admitted to Farnborough Hospital on Nov. 10, 1949. His family history contained nothing significant. He admitted taking four or five pints of beer a day since the age of 20.

On admission physical examination showed no abnormality, apart from some dilated venules on the nose. The liver was not enlarged, and the reflexes were normal. Examination of his blood showed red cells 2,900,000 per c.mm., Hb 7·85 g. per 100 ml., white cells 4700 per c.mm., erythrocyte-sedimentation rate (E.S.R.) 148 mm. at 1 hour (Westergren), bleeding-time 2 min. 30 sec. (Dukes), clotting-time 3 min. (Lee and White), prothrombin 100%. Of liver-function tests; the thymol turbidity and thymol flocculation tests were negative, and the Kunkel test showed 1·5 units. A sternal-marrow count showed no evidence of pernicious anæmia.

Treatment and Progress.—The patient was treated with iron, his anæmia improved, and he was discharged.

On readmission on Nov. 22, 1950, with a history of epistaxis during the past year, his liver was not enlarged and his tendon-reflexes were all present. Blood examination showed red cells 2,700,000 per c.mm., Hb 8·39 g. per 100 ml., white cells 5700 per c.mm., E.S.R. 155 mm. at 1 hour (Westergren); bleeding-time 19 min., clotting-time 9 min., prothrombin 100%, calcium 10 mg. per 100 ml., uric acid 0·9 mg. per 100 ml. Liver-function tests: serum colloidal gold nil, thymol turbidity +1, thymol flocculation nil, Kunkel 1 unit, Popper 30 units. Galactose tolerance was normal, and the urea-clearance 125%. The serum gave a very strong formol-gel reaction without turbidity. Radiographs of all the bones were normal.

After discharge the patient attended as an outpatient. His Hb never increased above 9·29 g. per 100 ml., nor his red cells above 2,900,000 per c.mm. The anæmia was normocytic throughout. The E.S.R. was 140–155 mm. at 1 hour (Westergren). Wassermann and Kahn tests were negative.

On readmission on Aug. 6, 1952, he had a sallow complexion, with dilated veins and a nævus on his nose; there were also dilated veins on the face and at the thoraco-abdominal junction. His liver was palpable 4 in. below the costal margin in the right midclavicular line; it was firm, regular, and not tender. There were a few firm enlarged glands in both groins. The pupils reacted normally to light and on accommodation. Reflexes in the upper limbs were normal, and the abdominal reflexes were brisk. The knee-jerks could be obtained with reinforcement, the ankle-jerks were absent, and there was a normal plantar response. Sensation was everywhere normal, and the tendo Achillis on each side was sensitive to pressure.

Blood Examination.—Very great difficulty was met with in making any pathological examination, because his blood set almost immediately into a solid gel. However, by taking blood with a warm syringe and doing all the tests at 37°C it was possible to obtain the following results: red cells 2,000,000 per c.mm., Hb 7·8 g. per 100 ml., bleeding-time 8 min., clotting-time 8 min. 30 sec., prothrombin 100%, calcium 10·8 mg. per 100 ml., blood-urea 25 mg. per 100 ml., uric acid 6·4 mg. per 100 ml. (normal 2–4 mg. per 100 ml.), and cholesterol 65 mg. per 100 ml. (normal 140–310 mg. per 100 ml.). Liver-function tests: serum-colloidal gold nil, thymol turbidity +1, thymol flocculation nil, Kunkel 1 unit, Popper 37 units. Urea-clearance and bromsulphalein tests were normal. Biopsy of sternal marrow showed a normocytic picture.

Diagnosis.—Chronic alcoholism with cirrhosis of the liver was diagnosed, the anæmia being due to a combination of these factors and the frequent epistaxes.

SERUM-PROTEINS

In this patient the serum-proteins were estimated on three occasions, with the following results:

	Nov. 24, 1950	*Jan. 18, 1951*	*Feb. 20, 1951*
Total protein	5·4	7·8	8·45
Albumin	1·4	2·5	2·90
Globulin	4·0	5·3	5·55
A/G ratio	1 : 2·2	1 : 2·1	1 : 1·93

On readmission on Aug. 6, 1952, electrophoresis of the serum-plasma and urine (Griffiths 1952, 1953) showed the presence of an abnormal fraction situated between the β and γ fractions but distinct from fibrinogen, the result being:

Total protein	11·70 g.	Fibrinogen	1·10
Albumin	2·77	Cryoglobulin	6·15
α_1-Globulin ..	0·44	γ-Globulin	0·32
α_2-Globulin ..	0·33		
β-Globulin	0·59		

The addition of 0·1 *N* NaOH to the serum produced an immediate solid gel of the consistence of india rubber; this was slowly reversible on neutralisation. Two-dimensional electrophoresis (Kunkel and Tiselius 1951) showed the homogenicity of the abnormal fraction and suggested that the albumin consisted of two components of slightly different mobilities. The urine contained a trace of protein; 200 ml. of this was dialysed against 50% dextran to dryness and resuspended in 0·5 ml. of saline solution and run electrophoretically. This protein had the same mobility as the abnormal fraction in the blood.

Prolonged centrifuging of serum or of plasma in the cold failed to separate the cryoglobulin. Hill et al. (1949) reported in their case similar negative results after blood-transfusion, and no doubt the blood received prevented the development of this phenomenon.

In one experiment in the present case the proteins were precipitated by the method of Popper and the centrifuged deposit was dialysed against water and resuspended in physiological saline solution. This fraction on electrophoresis consisted entirely of the abnormal protein, but the reconstituted serum did not exhibit the cold precipitation of cryoglobulin. It therefore seems that reversible cold precipitation is not an inherent property of this type of protein but depends on some other factor not yet identified. de la Huerga et al. (1950) showed that the Popper method is almost specific for γ-globulin; this is true for serum, but we have found that fibrinogen is also precipitated by this method, and the results obtained are due to the close relation between the cryoglobulin and true fibrinogen.

Judging by the Popper reaction of 30 units in 1950 the blood in the present case was already beginning to form the abnormal protein, but it was not until a year later that its presence was manifested by the difficulty encountered in performing the usual blood examinations.

McFarlane and Dovey (1952) have described a case very similar to ours. This was in a younger man, aged 42, who also presented with epistaxis. The abnormal protein migrated between the β and γ peaks. In this case abnormal plasma cells appeared in sternal-marrow biopsies in the later stages and were found in the abdominal lymph-glands and liver after death. In view of these findings we have re-examined the marrow smears taken in 1949 and 1952 and can find no evidence of abnormal cells. As the patient has also an enlarged liver and a few enlarged lymph-glands, we cannot say that he will not eventually have multiple myelomata. At the time of writing he is comparatively fit and we have no evidence that our clinical diagnosis is incorrect, but the possibility remains.

SUMMARY

Cryoglobulinæmia developed in a patient with chronic alcoholism.

Experiments are described in which an attempt was made to identify the abnormal protein.

The reasons why this is regarded as an abnormal fibrinogen fraction are given.

Our thanks are due to Miss V. Anne Brews, our senior biochemical technician, for her aid in this investigation.

References overleaf

from infections to cancer[14,15] and might be extended still further Doctors who are interested will find guidance on methods of making and using maps for different purposes in a book[16] by two members of the department of geography in the University of Liverpool Doctors as well as the "historians, economists and ethnologists" for whom the publishers recommend the book will profit from instructions about the technique of drawing maps and from examples of the use of maps to portray an area's physical characters, and its climate, economics, population, and settlement The book will also assist in the choice of suitable diagrams to convey the facts elicited from statistical tables—a choice made expertly by Cohn and Lingg[17] Modern cartography can, like modern meteorology, bring help to medicine, and the results of cross fertilisation between the sciences may be both fascinating and useful

OBSERVATION AND INTERPRETATION

In the radiological assessment of pulmonary tuberculosis it is fairly easy to define the extent of the disease, but its character is much harder to estimate with accuracy The radiologist first describes shadows in the lung that is an observation If he then calls them "primary," "post-primary," "recrudescent," "exudative," or "fibrotic," he makes a deduction from the observation And at present deduction from radiographic to pathological appearances is by no means exact Sometimes it is pure guesswork, and sometimes it is based on reasonable probabilities There are therefore two main sources of error in radiological interpretation errors due to observation and errors due to deduction The latter are the commonest, and, therefore, the extent of the disease is more accurately recorded than its type

Several analyses of observer error in the *interpretation* of chest radiographs have been made in America in the past few years[18-20] And in this country Cochrane and Garland[21] found that among British radiologists the error was much less when the appearances were classified as "inactive" or "clinically significant," including two subgroups, "active" and "inactive, but clinically significant," instead of simply "inactive" or "active" There are those who regret the lack of any generally acceptable and workable classification based on pathological changes, but there are serious difficulties in the way of making and using such a classification The interpretation of a particular shadow or set of shadows in terms of morbid anatomy is often a matter of dispute Moreover, different people use identical terms for different things—"fibrosis" and "infiltration" are examples Last year a committee formed by the Joint Tuberculosis Council, the Faculty of Radiologists, and the Society of Thoracic Surgeons published a valuable report[22] which aimed at overcoming the difficulty of terminology The general adoption of its recommendations would certainly make radiological deductions more precise and helpful

A recent article by Edwards et al[23] illustrates some of these difficulties Over 4000 Americans rejected for military service on the ground of abnormal chest radiographs were re examined after an interval of approximately two years, and the lesions were classified as "stationary," "regressive" or "progressive" The object of the study was "to determine whether it was possible to separate certain types of minimal lesions according to their relative risk of progression on the basis of their roentgenographic appearance" The classification of the American National Tuberculosis Association was used, and the films were read by two observers independently It was originally intended to analyse progression-rates by pooling the two readings, but, because of the difference in interpretation, separate analyses had to be made—which illustrates the importance of the subjective factor in applying the N T A classification There was reasonably close agreement on the extent of the lesion, but "the two interpreters appear to have somewhat different patterns of classification for type of lesion" While Dr A said that 34 9% of the initial films of people under 25 showed "exudative" or "exudative productive" lesions and 46 1% showed "productive" and "fibro-productive" lesions, the corresponding figures for Dr B were 24% and 57 7% Moreover, Dr A found "exudative" and "exudative-productive" lesions to be twice as common among non-whites as whites, while Dr B interpreted both groups of patients as showing the same relative frequency Subjective variations in individual radiological interpretation cannot, of course, be eliminated, but these differences suggest that this particular classification is unsatisfactory It is an attractive step—and a logical one—to classify the radiographic changes of pulmonary tuberculosis pathologically, but it will not really clarify a confused subject until the deductions can be made with more accuracy Meanwhile, the correlation of pathological findings in the many resected specimens now available, with previous radiographic appearances would be helpful

CRYOGLOBULINÆMIA

Serum, as every schoolboy knows, is the fluid expressed from the clot of shed blood Much serology, however, consists in the study of a very *different* fluid, often obtained from blood kept in a refrigerator for hours or days, centrifuged more or less vigorously (perhaps while still cold), and immersed in a hot water bath (hot enough for example, to kill many organisms) Most known antibodies appear to survive this onslaught and remain detectable by established techniques, but in looking for components in serum of possible significance in disease the serologist is handicapped if he confines his attention to such serum Cold precipitating globulin may be an instance This has been described mainly in conditions accompanied by hyperglobulinæmia (e g, multiple myeloma, kala-azar, malaria) and interest has centred chiefly on the associated Raynaud like symptoms which have been attributed to the peculiar physical property of cryoglobulins

These proteins commonly precipitate on standing in the cold (4°–11°C) and redissolve on warming Electrophoretically, they apparently resemble gamma globulin,[1,2] but in this issue Dr Griffiths and Dr Gilchrist report a case where the abnormal protein fraction in the blood seemed to be more closely related electrophoretically to the fibrinogen fraction Concentrations found in the blood vary over a wide range Barr et al[1] describe a case of multiple myeloma where routine laboratory investigation of serum showed a total protein level of 7 7 g per 100 ml, with globulin 2 6 g per 100 ml The grossly abnormal, jelly like nature of the blood on withdrawal led to re estimation of protein on a sample kept at body temperature until clot retraction was complete, total protein was then found to amount to 15 g per 100 ml, with 11 g of globulin, 8 9 g of which was cold precipitable It is clear, then, that cryoglobulinæmia especially when mild is easily missed

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[14] Stocks P Regional and Local Differences in Cancer Death Rates Studies in Medical and Population Subjects no 1 H M Stationery Office 1947

[15] Cruickshank D B *Brit J Cancer* 1947 1 109

[16] Monkhouse F J Wilkinson H R Maps and Diagrams London, 1952 Pp 323 25s

[17] Cohn A E Lingg C The Burden of Diseases New York 1950

[18] Birkelo C C Chamberlain, W E Phelps, P S Schools P E Zacks D Yerushalmy J *J Amer med Ass* 1947 133, 359

[19] Garland L H *Radiology* 1949 52 309

[20] Yerushalmy, J Harkness J T Cope, J H Kennedy B R *Amer Rev Tuberc* 1950 61 443

[21] Cochrane A L Garland L H *Lancet* 1952 ii 505

[22] See *Lancet* 1952 i 1195

[23] Edwards, H R Reisner, D Bellows M *Amer Rev Tuberc* 1952 66 666

[1] Barr D P Reader G G Wheeler C H *Ann intern Med* 1950 32 6

[2] Dreyfuss F Libnach G *J Lab clin Med* 1952 40, 489

the leg that had followed a period of failure in the adequate control of fibrillation four months after operation, although the size of the valve opening had been greatly increased.

No patients were included who were thought to have active rheumatic carditis, aortic valvular disease, or mitral regurgitation as the main lesion. Good results were not prevented by some degree of aortic disease, mitral regurgitation, calcification of the mitral valve, thrombosis in the left auricle, or functional tricuspid regurgitation. The whole valve mechanism might be so fibrosed and deformed that improvement in its function was impossible until the surgeon could be given more time and freedom by some form of artificial heart. The combination of mitral regurgitation, gross calcification, and a large heart made success unlikely, because the valve was almost certainly beyond help. The best indication of free mitral regurgitation was a loud systolic murmur heard at the apex and well conducted. Expansile pulsation of the left atrium seen in the anteroposterior view on radioscopy was confirmatory evidence; but some mistakes were still difficult to avoid, and so far catheterisation had not helped.

Considerable pulmonary hypertension with systolic pressure above 100 mm. Hg did not prevent excellent results, and the pressure in the pulmonary artery might fall to half its previous value or less. Most of the excellent and good results were in patients who had had pressures in the pulmonary artery of 60/35 mm. Hg or more. There had, however, been a few good results where the pressure at rest was hardly raised; probably in these cases the pressure rose unduly on even the slightest exertion, with little or no increase in the cardiac output. Pulmonary hypertension was, therefore, often an indication for operation; but generally the decision could be taken on clinical evidence alone.

Mitral valvotomy should be considered in all patients with mitral stenosis who were progressively disabled. Orthopnœa, cardiac asthma, pulmonary hypertension, and recurrent pulmonary œdema were special indications. Active rheumatic carditis, gross mitral regurgitation, and right-sided congestive heart-failure that could not be relieved were the main contra-indications.

So far there was no evidence that the good results were not lasting, but patients had been observed for only from two to four years.

Reviews of Books

The Neurophysiological Basis of Mind

The Principles of Neurophysiology. JOHN CAREW ECCLES, F.R.S., professor of physiology, Australian National University, Canberra. Oxford: Clarendon Press. 1953. Pp. 314. 25*s.*

LAST year Professor Eccles delivered his eight Waynflete lectures to an audience which seemed to grow larger week by week. The lectures were delivered in the manner of brilliant extemporisations: this book is their closely reasoned and fully documented source. Its publication is an important landmark; for in it one of Sherrington's collaborators surveys the working-out of many conceptions which when first framed were less readily amenable to experimental testing than they are today.

The first two chapters review the Cambridge school's account of ionic relationships in excitable tissues. They might be taken from some future textbook of advanced physiology: they may not be read as substitutes for the original articles and reviews; their purpose is to state at the outset those properties of peripheral plasma membranes in terms of which central processes may be tentatively interpreted. The main interest lies in the middle four chapters, which deal with the themes of Eccles's own experimental work—peripheral and central junctional transmissions and the coördinating function of the spinal cord. Study of the physiological reactions of spinal motoneurones has been revolutionised by the intracellular microelectrode technique. This has furnished proof of the postsynaptic nature of excitatory and inhibitory effects, for it records the lowering and raising of membrane potential when the neurone is bombarded by excitatory and inhibitory synapses, as well as the reversal of membrane potential when an impulse is discharged. These are over-all potential changes across the cell-membrane. The microelectrode presumably penetrates the soma or larger dendrites, and local and propagated activity in the outlying dendritic forest still needs to be elucidated.

The foregoing analysis measures time on a millisecond scale. A specially interesting chapter presents new evidence that even the most elementary spinal reflexes may be more enduringly modified by repetitive stimulation, and suggests that similar long-duration reactions may be the basis of conditioning and learning. A theoretical chapter on the cerebral cortex attempts an interpretation of its known spontaneous and evoked electrical potentials in terms of spinal motoneurone properties and cortical histology. The last chapter, on the mind-brain problem, is frankly disappointing. Different readers will find it so for different reasons, and especially, perhaps, readers who agree that "for the scientist there should be no doubt that the problem of interaction of mind and matter is a real problem and not a pseudo-problem arising from confusions in the usage of words."

One of the most stimulating characteristics of the book is its highly articulated argument. The results of each step in the analysis are used to the full in the interpretation at each succeeding stage. Thus the ionic hypothesis is used in the interpretation of fundamental neurone properties: inhibition of a motoneurone, for example, is supposed to be due to the action of a specific chemical transmitter on the pumping of sodium ions outwards across its membrane. And neurone properties are used in their turn in the explanation of spinal reflex activity and cerebral activity. But the detailed nature of such explanations is not meant to imply that we already know all the neurophysiology we need to know. Professor Eccles has always used detailed and elaborate working hypotheses, and he has never hesitated to discard them—as for example in the cases of the Golgi-cell theory of inhibition and the electrical theory of synaptic and neuromuscular transmission—if later experiment has convinced him that they were wrong.

Textbook of Pædiatrics

Editors: G. FANCONI, M.D., professor of pædiatrics, University of Zürich; A. WALLGREN, M.D., professor of pædiatrics, University of Stockholm. Editor: W. R. F. COLLIS, M.D., F.R.C.P., lecturer in pædiatrics, University of Dublin. Translator and co-editor E. KAWERAU, M.B., M.SC. London: Heinemann Medical Books. 1952. Pp. 124. £7 7*s.*

THIS, the leading Continental textbook of pædiatrics, was conceived by two of the most famous European pædiatricians at the end of the late war. It is based mainly on the pædiatric centres of Switzerland and Sweden, of which Fanconi of Zürich and Wallgren of Stockholm are the respective leaders; but there are are also contributions from eminent pædiatricians in several other European countries. The work, first published in German in 1951, represents the contemporary outlook of pædiatricians on the Continent. For the more recent English edition it has been revised, and a new chapter on megacolon added by Dr. M. Bodian. Among other subjects its 23 chapters cover the sociological aspects of pædiatrics, heredity, the psychology of the normal and the abnormal child, diseases of the skin, diseases of the eyes, surgical conditions in childhood, and diseases of childhood peculiar to hot climates. The views expressed correspond closely, in general, with those in British and American pædiatric works, although in the chapter on disorders of nutrition in infancy, some will regret the tendency to perpetuate the hypothetical classification and outlook of Czerny and Finkelstein. The immense task of translation has been creditably accomplished, though occasional imperfections might have been eliminated by stricter editing.

spread by the biopsy. The full cooperation of the patient is essential, and it says much for the technique developed by Christian that not one of his patients refused a second biopsy when it was necessary.

A report[3] from the hepatitis centre for Japan and Korea illustrates particularly well the importance of liver biopsy in the work of such a unit. During nine months in 1950–51, 2351 patients were seen at the centre, and 84 biopsies were performed on 73 patients without a single untoward incident. In 35 cases the biopsy was required because the diagnosis was still in doubt, despite considerable clinical and laboratory inquiries. It is interesting that in only 13 of these was the diagnosis of infective hepatitis confirmed; in 12 liver disease other than hepatitis was discovered; and in the remaining 10 the liver was excluded as the cause of the patient's symptoms. In another 35 cases the biopsy was performed because the disease was particularly severe or lasted a long time. There was continued activity of the inflammatory process in 21 of these livers, postnecrotic scarring in 8, and fatty metamorphosis in the remaining 6. Despite the claims to the contrary,[4–6] *no correlation could be established in this series between any of the laboratory or clinical findings and the pathological changes in the liver.* In the 3 remaining patients biopsy was performed because the jaundice returned after apparently complete recovery. All 3 showed the histological picture of acute hepatitis, and complete recovery followed a further period of hospital treatment.

Liver biopsy is also a help in evaluating specific methods of treatment. In fatty infiltration, for example, the administration of lipotropic substances produces a progressive diminution of fat, which may readily be assessed by biopsy. With the greatly increased safety of needle biopsy, the value of many other methods of *treatment may be convincingly demonstrated in this way.*

HMCs ON NHS

LIKE the rest of us, the council of the Association of Hospital Management Committees do not believe that all is for the best in the best of all possible hospital services. But they think that much less is wrong than might have been expected considering its size and complexity. Furthermore much of what is wrong is due to national economic difficulties rather than to a change of administrative heart. "The policy of centralisation carried out over the past four years is not necessarily the result of original sin on the part of successive Ministers and their advisers . . . and may even have been opposed *to their desires*." The association deplore the ever stricter financial control which has been imposed, but they recognise that the service has achieved a good deal even in four fairly difficult years, and they feel that it would be *folly to scrap the present system* without giving it a chance to prove itself in easier conditions. In their realistic report[7] on the N.H.S. they have therefore contented *themselves* with suggesting amendments within the present administrative framework.

Most of the criticisms of the health service are directed to the relation of the various statutory bodies to each other and to the Ministry. "Increasing financial control has upset the delicate balance of the different bodies and the H.M.C.s *have* been brought more and *more* into a position of . . . direct administrative responsibility to the Ministry." But the association do not altogether welcome this rapprochement, for they fear that, if the R.H.B.s were not there, "the place would inevitably have to be filled by something else, which would presumably be the regional officers at the Ministry." They reiterate the familiar complaint that greater centralisation has led to delay, inefficiency, and frustration, but they prescribe an injection of independence and responsibility rather than administrative reorganisation.

The system of appointment to R.H.B.s and H.M.C.s is also often criticised. Some would like to claim the right for groups or interests to appoint their own representatives. But the association stoutly oppose *this suggestion* and indeed believe *that* the representation of special interests on hospital authorities has already *gone too far. Instead they ask for more effective* representations of the patient. This can best be achieved, they hold, by confiding to laymen the chief responsibility for administration. They show a praiseworthy detachment in their opposition to the suggestion that every *H.M.C. should* be represented on the appropriate R.H.B., and they declare that it would "be fatal if Regional Boards were to become the battleground for Hospital Management Committees in competition for the Board's limited resources." A person with wide experience of hospital work should be allowed to serve on both bodies, but he must remember that he is a member of the regional board because of his personal qualifications and not as spokesman of his own H.M.C. The association are also against the suggestion that local authorities should have a right to representation on hospital authorities. Not only would they regret the encroachment of party politics on the neutrality of the health service, but they think that many an excellent person would be lost to the hospital service if he had first to pass a local authority sieve. In opposing election from below, the association also support selection from above. They regard it as no more than reasonable that the Minister *who* is responsible for the working of the service should have a say in the choice of people who are helping him in this task, and in particular of the chairmen. They see no *evidence that the present system has produced* "a class of chairmen who are 'Yes Men' or that those who have been appointed have failed to secure the confidence of those over whom they preside."

TRANSILLUMINATION OF THE STOMACH

As a method of clinical examination, transillumination *has limited value, and commonly the information that* it yields is misleading. Celli[1] has applied transillumination to the stomach. First a gastroscope is introduced; then, with the patient in the left lateral position, the illuminating bulb of the gastroscopy is used as the source of light. The bulb is directed towards 11 o'clock from a position in the middle third of the body of the stomach. By premedication Celli aims to decrease stomach tone, make insufflation easier, and thus improve the transillumination. The contra-indications are those of gastroscopy, with the addition of gastric resection and a very thick abdominal wall, which cuts down the amount of light at the skin surface. The whole of the stomach may be outlined except part of the fundus, and even the first part of the duodenum may be seen. Peristaltic waves can be observed, and when there is rigidity of the curvatures the contraction shadows are not present and the rigid area remains illuminated continuously. Celli claims that it is possible to estimate gastric tone by this method, and even to recognise the position of the vascular network running along the curvatures of the stomach.

Celli's article is illustrated by coloured drawings of his observations. These are interesting, but perhaps few at present would care to substitute transillumination for the established *methods of investigation.*

THE next session of the General Medical Council will open on Tuesday, May 19, at 2 P.M., when Prof. DAVID CAMPBELL, the president, will deliver an address. The Medical Disciplinary Committee will meet on Wednesday, May 20, at 2 P.M.

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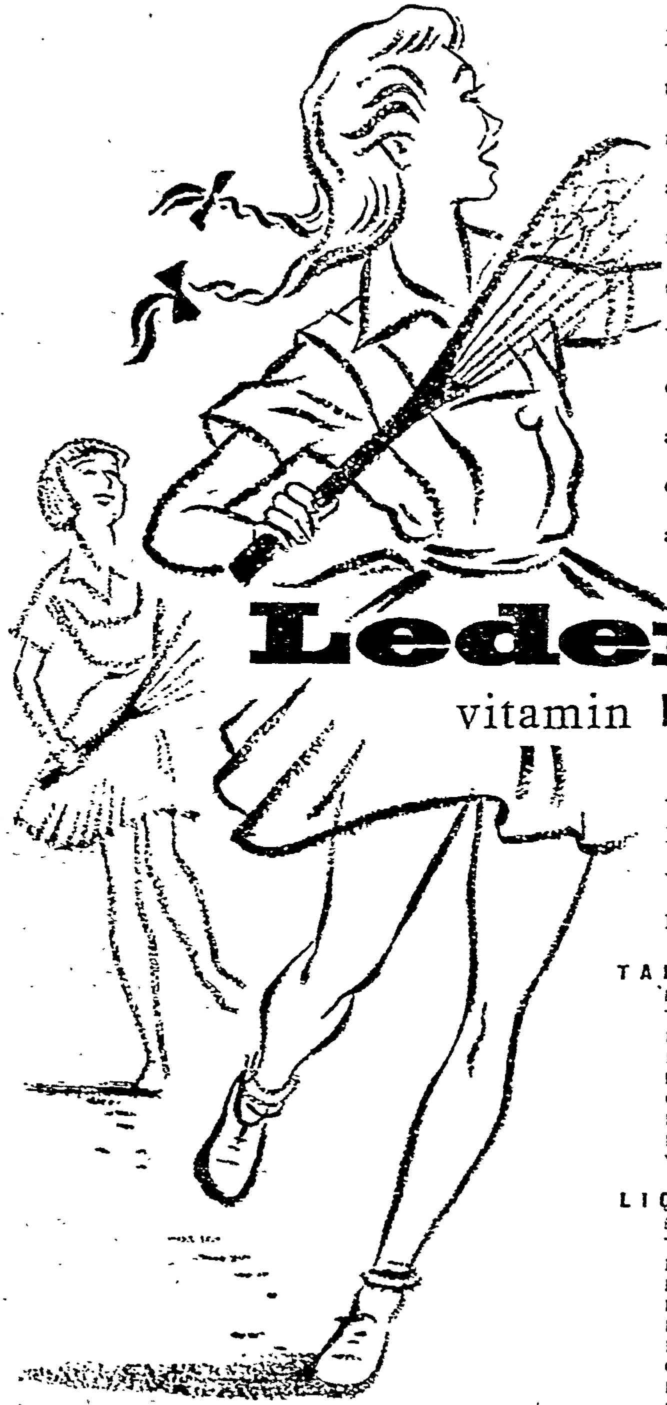
[3] Deschamps, H., Steer, A. *Ibid*, p. 674.
[4] Popper, H., Franklin, M. *J. Amer. med. Ass.* 1948, 137, 230.
[5] Wehn, G. *Acta med. scand.* 1952, suppl. [illegible]
[6] Weinbren, K. *J. Path. Bact.* 1952, 64, 395.
[7] Obtainable from the secretary of the association, Mr. H. B. Shelswell, Salford Royal Hospital, Chapel Street, Salford 3.

[1] Celli, L. *Minerva med.* 1953, i, [illegible]

Good health for all . . .



If every child in the world could have the physical advantages of these children, many of the ills that plague juvenile and adult life would disappear. Good health and nutrition go hand-in-hand; but, unfortunately, *well-fed* does not always mean *well-nourished.* Where there is any deficiency of the factors of the B complex, as the result of malabsorption, deficiency in the diet, or other causes, an ideal supplement and therapeutic aid is . . .

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Pyridoxine HCl (B_6)	0.1 mg.
Calcium Pantothenate	3.0 mg.
FOLVITE Folic Acid	0.2 mg.
Insoluble Liver Fraction	250.0 mg
Vitamin B_{12}	1.0 microgram

LIQUID

Each teaspoonful (4 cc.) contains:

Thiamine HCl (B_1)	2.0 mg.
Riboflavin (B_2)	2.0 mg.
Niacinamide	10.0 mg.
FOLVITE Folic Acid	0.2 mg.
Pyridoxine HCl (B_6)	0.2 mg.
Pantothenic Acid	2.0 mg.
Choline	20.0 mg.
Inositol	10.0 mg.
Soluble Liver Fraction	470.0 mg.
Vitamin B_{12}	5.0 micrograms

Tablets: Bottles of 100 and 1,000
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didactic Generally speaking it was felt that the trained social worker should play a responsible part in administering services that sought to meet the needs of people Certainly he was required for carrying out such services, and where he undertook personal work it was the continuity of his rôle that was important breaks in human contacts impaired the chances of building constructive relationships with clients

There seemed to be unanimous recognition of the need to increase the use of general family case workers in the social services and to reduce the types and uses of specialist workers This recognition had obvious implications for training There should be a common basis of training for all types of social work and strengthening of the case-work training now provided Special attention should be paid to the needs of those already employed by means of in-service training, to refresher courses as a normal accompaniment to professional life, and to special courses for tutors and those with responsibility for supervising staff One group had suggested the need to set up a professional institute to set standards of training and to approve qualifications put forward

There was apparently cordial recognition of the part that can be played by volunteers, who were said to be increasingly ready to accept the idea of some measure of training The extent to which the health visitor with a radically revised training might fulfil a still wider rôle as the general family visitor was frequently referred to So, too, was the possibility of developing a local authority family welfare service, this was sympathetically discussed, particularly as it appeared to present the best hope of a coordinate and preventive service

Coordination of existing services, rather than more workers, was said to be the crying need Workers in the various services were still not sufficiently familiar with one another as individuals or with each other's methods and objectives One department of the local authority might act as a main inquiry centre for individual cases and see that these were appropriately referred The case conference method now used by most local authorities in connection with neglected children brought together administrative officers and field workers from their departments and from voluntary bodies This method came in for commendation and was thought to be applicable to individual cases of other types

Conclusion

This conference made many people think, and it is noteworthy that the thinking was on the whole objective Our social services have now reached a stage when some rationalisation and realignment is again due To the consumer confusion must be obvious, but the solution obscure It is to the credit of these assembled social practitioners that they tried to look afresh at the services in which they are engaged, to point out the problems and some possible solutions They and the community at large appear now to deserve some further help and guidance from those engaged in teaching and research and those who determine policy

COLLEGE OF GENERAL PRACTITIONERS

At the end of March, when the college was three months old, the number of foundation members was 1807 Their geographical distribution throughout the British Isles is shown on the accompanying map

It has been suggested that the regional faculties (whose names are printed in italics) should comprise the following areas.

ENGLAND

London —County of London

Home Counties South —Kent, Surrey, Sussex, Hampshire, and the Isle of Wight

Home Counties North —Middlesex, Essex, Hertfordshire, Bedfordshire

Oxford —Oxfordshire, Berkshire, Buckinghamshire

Cambridge — Norfolk, Suffolk

Bristol —Wil Dorset

Exeter —Dev

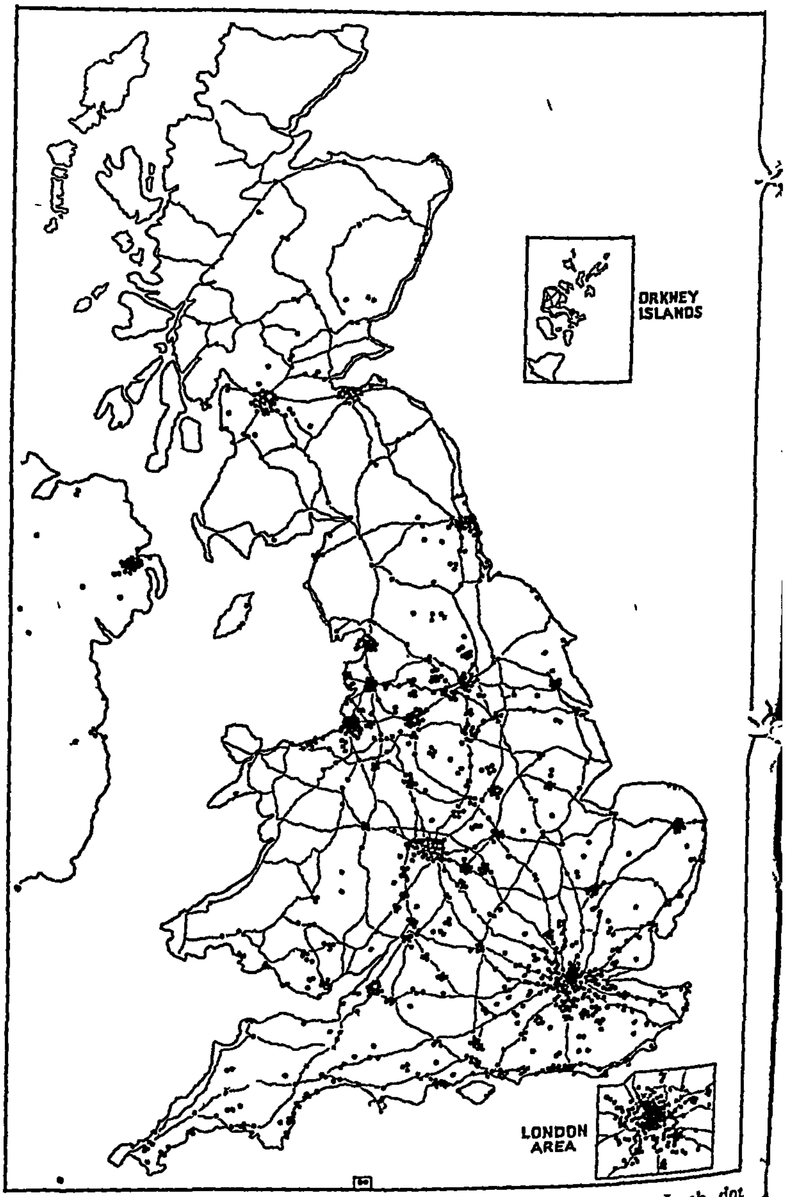
Birmingham —Warwickshire, Shropsh Herefordshire, Worcestershire St and Northamptonshire

Sheffield Lincolnshire

Leeds — Riding)

Manchester —North and East Lancashire (East of the London Glasgow road A 6) East Cheshire Westmorland

Liverpool —South West Lancashire, West Cheshire, North Wales and the Isle of Man



Foundation members of the College of General Practitioners Each dot represents a member The dots in the small square labelled "London" represent members in London additional to those shown on the larger map (Based on an Ordnance Survey map with the sanction of the Controller of H M. Stationery Office, Crown copyright reserved)

THE LANCET

LONDON: SATURDAY, MAY 2, 1953

The Medical Defendant

NEWSPAPER headlines and correspondence columns indicate that medical practitioners are increasingly being made a target for claims based on allegations of negligence. Let it be conceded at once that, if a surgeon or physician injures patients by his carelessness or incompetence, he is not to be shielded from those legal remedies to which his patients are entitled. But, if he honestly does his best, employing at least such reasonable care, skill, and knowledge as the law is content to expect of him, he ought not to be harassed by plaintiffs as if he guaranteed the accuracy of every diagnosis, insured them against every accident or setback, and promised that every operation would result in permanent cure.

How can we explain this undoubted increase in the litigation against the medical profession? Are those observers correct who ascribe it to the coming of the National Health Service? Is it an inevitable feature of the new régime in which everybody has a right to medical care and the members of hospital staffs are known to be paid instead of giving their services for nothing? Are men and women becoming so health-conscious that they demand too much from medical science? Has the replacement of the old system of voluntary hospitals induced an exaggerated estimate of the resources of the State? Are patients encouraged to go to law because they read of the heavy damages already awarded to others? Does the general preoccupation with football pools lead people to try their luck in a different field? Are they backing their fancy that, whatever one doctor has done, another doctor will say it would better have been done differently? It will not be forgotten that there is now another national service besides that of health. Although the Legal Aid and Advice Act is not yet fully operative, the State-aided plaintiff has his free run. An ordinary litigant often takes advantageous advice to settle his case before the parties get into court; but State-aided litigation tends to be fought to a finish without compromise. An ordinary plaintiff is in some measure controlled by certain procedural restraints. The rules allow a defendant, while denying liability, to pay into court a sum which he says is sufficient to satisfy the claim; the plaintiff, if he decides not to take out the money but to continue his action, runs the risk that, should he finally recover a less amount, he must pay the costs incurred by his unjustified persistence. No such check deters the State-aided plaintiff. Why should he break off the fight? Costs mean nothing to him. Apart from all these questions, a defendant who is a medical practitioner nowadays faces another embarrassment. The hospitals, if his work is done there, now find themselves liable in damages as his "employers." The patient who complains of some alleged negligence in the ward or the operating-theatre will sue both the hospital and the practitioner. If so, the hospital may seek to put all the blame on the practitioner, so that he finds himself attacked not only by the plaintiff but also by a fellow defendant. These conditions, of course, mean more anxiety for those responsible for medical defence. They also mean, as commentators have not been slow to point out, that the practitioner, if increasingly menaced by the threat of writs for damages, may incline to play for safety when a bolder course might be to the patient's advantage. Though care and caution are virtues, more harm than good will be done if doctors become obsessed with the need to cover themselves against criticism. For one thing the resources of the service will be wasted by keeping patients in bed unnecessarily long and by subjecting them excessively to radiological and other examinations.

No other profession is comparable with that of medical practice. Solicitors, it is true, have from time to time been attacked in the courts on the ground of their professional misconduct; they contribute to a statutory Compensation Fund from which a client's losses, if due to a solicitor's dishonesty, can be recouped. Solicitors are occasionally sued on the ground of negligence, but fraud has more often been the basis of the proceedings. A doctor has not the same temptation to financial malpraxis. The special element in his daily work is the risk and danger to life and health. "There is always a chance," said the Lord Chief Justice a year or two ago, "that, without negligence on the part of anybody, some unfortunate result will happen, sometimes fatal. Any person who submits himself to any surgical operation is voluntarily submitting himself to a risk. No practitioner is an insurer that no accident will happen. He does no more than profess and undertake to use ordinary skill and care." Lord GODDARD was delivering judgment in a case where the "unfortunate result" had followed an injection. His words would be equally true of any surgical operation and any medical treatment. How is that truth to be taught to the public?

Malignant Change in Vitro

A CHANGE from normal to malignant during the propagation of cells in vitro was first recorded by EARLE.[1] In a culture-medium that included methylcholanthrene (a powerful carcinogen) connective-tissue cells underwent an irreversible morphological variation which had previously been noticed by EARLE and VOEGTLIN.[2] On inoculation of subcultures into living animals the cells continued growing and gave rise to malignant tumours. At the same time a most unexpected result was encountered: fibroblasts derived from the same source but propagated without the carcinogen sometimes underwent the same morphological variation, and on inoculation these also gave rise to malignant tumours. Chance

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experiments lasted only three or four weeks, but they were repeated on several occasions during many months The best opinion at the moment is that there would be a deficiency of calcium in the national diet of 30% if we did not add to the flour

Dr STROSS Is the Minister aware that no one denies the validity of the specific experiment which he mentioned but that recent research has shown that chalk in flour is not needed, for the human body adapts itself to the increased phytic acid which is found in wholemeal flour ?—Major LLOYD GEORGE As the hon gentleman appreciates, this is a technical matter While I should be only too happy to discuss it with him, I think that it would be far better if he discussed it with someone with greater knowledge than I possess

Flour-improvers

Dr BARNETT STROSS asked the Minister of Food whether he now recognised vitamin C as a flour improver, and how far his investigations showed this substance to be harmless for such a purpose —Dr CHARLES HILL replied I share the hon member's desire for a speedy conclusion of the investigations which are in progress, but he will understand the time that such scientific inquiries usually take On the face of it vitamin C seems a reasonable and hopeful proposition but the investigations are not yet complete

Hospital Costs in Scotland

Mr WILLIAM ROSS asked the Secretary of State for Scotland the current average daily cost of maintaining a patient in hospital —Commander T D GALBRAITH replied The returns or 1951–52 show an average cost per patient over all hospitals of *21s 5d* per day

Replying to a further question, Commander GALBRAITH said that in 1952 and 1953 just over £1$^1/_2$ million had been allotted for hospital building work and just over £1 million for essential maintenance

Scottish Tuberculous Patients in Switzerland

In answer to a question, Mr JAMES STUART, Secretary of State for Scotland, said that under the National Health Service 195 tuberculous patients from Scotland were receiving treatment in three sanatoria in Switzerland The average daily cost of treatment was about *30s*, or *34s 4d*, allowing for transport and incidentals such as dental treatment The average daily cost in Scottish sanatoria was about *23s 6d*

B C G Vaccination

Mr JOHN RANKIN asked the Minister if he would extend the use of B C G vaccination to include school leavers —Commander GALBRAITH replied It is proposed in the near future to issue advice to all local health authorities on the extension of B C G vaccination to children about to leave school

Mr ARTHUR WOODBURN Are we to take it from the answer that the Department is now satisfied that B C G is effective and that advisory scientists are satisfied that it is quite safe and reliable as a preventive for tuberculosis ?—Commander GALBRAITH I would not go so far as that, but we believe that trials are far enough advanced to enable a general extension to school leavers 14 out of the 55 local authorities in Scotland have already been specially authorised to provide vaccination for school leavers

Replying to further questions, Commander GALBRAITH said that as there was no difficulty in getting adequate and satisfactory supplies of vaccine from abroad, it had not so far been considered justifiable to incur expenditure on manufacture in Scotland At the moment the vaccine was costing £600 a year One of the biggest manufacturers in this field in this country would undertake production of the vaccine at short notice if necessary

Shortage of Nurses for Mental Deficiency Institutions

Replying to a question, Commander GALBRAITH said that some 30 additional nurses were required to staff the 141 unstaffed beds in Scottish mental deficiency institutions Additional accommodation for mental defective patients was, however, needed and various developments were in view for which considerable numbers of further nurses would in due course be needed

Health Visitors

Replying to a question, Miss HORNSBY SMITH, parliamentary secretary to the Ministry of Health, said that on Dec 31, 1951, the number of health visitors employed by local health authorities (counting two part time as roughly equal to one whole-time) was 0 9 per 10,000 of the population

In England Now

A Running Commentary by Peripatetic Correspondents

COUNSEL for the prosecution in a recent case suggested that a doctor gave "dangerous advice" when he said that he could "find nothing wrong at the moment" If the medical profession takes this to heart we may soon hear conversations on the following lines

Patient Tell me doctor, you don't think it's anything serious do you ? I'd rather know

Doctor (LL B, M.R C P) Hmm, I should rather hesitate to be as dogmatic as that I cannot be absolutely certain, without the performance, in duplicate, of certain test or tests, as to what is or will be the true nature of your alleged illness We shall be safest if we call in two specialists [*Specialists, both* Q C, L M S S.A, *arrive*]

This, gentlemen, is Mrs Litigious She alleges that she experiences er let me quote her signed testimony "headache"

After cautioning the patient that anything she says in her history will be recorded on tape machine for possible medico legal purposes later, the specialists take her history and examine her The doctors then retire to discuss the prognosis.

Well Symes old man, what's going to happen in this case ?

Oh I think we are going to be all right here, it's pretty well wrapped up By the way could you lend me an Investigation Refusal Form ? She's unlikely to want the full Without Negligence drill for headache We always advise burr holes in the skull nowadays, since that case where the ventriculograms were omitted

Ah, sad case that, heavy damages No we can't be too careful You never know what a patient will do As my old teacher used to say "If you know your Law you know your Medicine" Remember his book on *Litogenesis* ? Classic Should be in every doctor's brief case and on every doctor's desk Treatment in this case had best be on expectant lines We mustn't run the risks of supplying her with drugs.

But as a matter of cold fact a patient did say to me yesterday "Tell me doctor what you think I'd rather know I won't hold it against you"

* * *

I have been looking again (as the politicians say) at the Doctrine of Reminiscence in Jowett's admirable translation of Plato All that stuff about education being a drawing out and not a putting in, as quoted by Jeeves and other scholarly types, takes a bit of swallowing We are all tired of hearing that the toddling Mozart was already composing song hits at the age of five, and how that little swot Macaulay could get a *Times* leader by heart by reading it through once In most of us such virtuosity seems to be painfully and curiously lacking To feel, however, that it is all there even if we can't get at it, is immensely comforting and inspiring Whenever I can't remember the dose of the latest wonder drug, I reflect that what I don't know about, let us say, the differential calculus, astrophysics, Syrian dialects, and conversational Chinese is probably not worth knowing

* * *

The only real disadvantage that I can see to living in a cave would be the lack of a front door No doubt the local cave-agents extolled well-situated, sheltered, desirable, well-built caves in rural surroundings, secluded yet not isolated, with beautiful aspect and open views. But for my taste these would have been all too open, and the nightly chore of stoking the home fire burning in the entrance hall would have been irksome, even though it did keep the wolf from the cave No, give me a proper front door like the one behind which I grew up Every night it was shut with solemn ritual Two heavy bolts were shot, a large key turned, the hasp slipped over, and finally a huge iron chain was fastened across as if to make assurance doubly sure This done, everyone could sleep in peace, heedless of whether the back door had been left locked or unlocked according to the caprice of the cook

The heavy, studded oak doors of earlier days were strong, with hinges of wrought-iron a yard long and barred inside by a sapling There is no fairer tribute to the Queen's peace which we all enjoy than the disappearance of these fortifications from new buildings faults, however small, must first be corrected. Much can be achieved even where the nipple is at first so retracted that correction seems well-nigh impossible; the nipple shields designed by WALLER [1] for wearing during the antenatal period are effective even when there is a severe anatomical fault. In the later weeks of pregnancy the daily manual expression of colostrum seems a reasonable practice, to prepare the breasts for lactation and to keep open, and even to open up, the milk ducts. Women taught to do this can help themselves when engorgement threatens; this reduces pressure on the midwifery staff, who then have more time for cases of serious engorgement. Furthermore, lactation will have a better start before the mother leaves hospital; and so she will be very much more likely to continue breast-feeding at home, and to find it satisfactory. Satisfactory lactation cannot be said to be fully established until the nursing or draught reflex is fully conditioned, and in the young primipara this reflex may take a month or so to become established; its inhibition or delay by pain and engorgement needs to be more generally recognised. When engorgement is severe, the breasts should be well supported and feeding temporarily stopped; stilbœstrol in doses of 5–20 mg. helps in the control and probably does not inhibit lactation, though it may delay it temporarily. In less severe cases gentle expression of the breasts relieves the fullness and engorgement, especially around the areola, and so allows the baby to get the nipple well into his mouth and suckle normally. Pain on suckling is a bar to nursing until the nipples are healed.

No less important than antenatal preparation for lactation is a careful aseptic technique in the lying-in period; and infection, where it does set in, should be treated at once with penicillin or aureomycin, before it has passed beyond the stage of cellulitis.[2,3] The organism most often responsible for mastitis is *Staphylococcus aureus*,[4] though others are sometimes found alone or in conjunction with it. Mastitis is favoured by stay in hospital; and when the carrier-rate for staphylococci among the hospital staff or visitors reaches a certain level, epidemic outbreaks of mastitis are likely to ensue unless very strict precautions are taken. Opinion on the mode of infection has varied; sometimes the baby has been regarded as the main agent, and sometimes the environment and hospital personnel. In Germany during the late war it was thought that forcible stripping of the breasts occasionally caused trauma and that infection could take place with organisms circulating in the blood.[5] It seems certain that milk stasis promotes the multiplication of any infecting organism that may be about.[6,7]

A low incidence of mastitis goes hand in hand with successful breast-feeding; and for this reason, if for no other, everything possible should be done to increase the proportion of women who successfully suckle their young. Further progress in the prevention of mastitis calls for close coöperation between the antenatal, lying-in, and postnatal services.

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Annotations

MAPS AND MEDICINE

IT was a map drawn by his young stepson that stimulated Robert Louis Stevenson to write *Treasure Island*. Looking at maps can revive memories of past holidays and work-places and raise hopes of traveller's joys to come. There may therefore be pleasant associations at the back of one's mind when thinking about the use of maps in medicine.

The spot map which John Snow drew of cholera cases in 1854 showed how they were concentrated round the Broad Street pump in Soho. His investigation is recounted, and his map reproduced in the new edition of *Rosenau's Preventive Medicine and Hygiene*.[1] By using Snow's work on cholera as a model for teaching students the Baltimore School of Epidemiology has honoured his achievement, as did Underwood [2] in this country. Spot maps are used routinely in the investigation of epidemics. Recent examples of their use in poliomyelitis,[3–5] infective hepatitis,[6] and influenza [7] show how they can reveal a geographical spread and draw attention to the "odd cases out" which often repay close investigation by providing clues about the mode of spread of infection. Moving, to borrow a phrase from Prof. John Gordon, from "parish pump epidemics" to the study of pandemics over "several centuries and across the seven seas," there are maps of the distribution of poliomyelitis [8] which show that these can summarise the enormous number of data in the records of national and international health organisations.

A further stimulus to the use of maps in medicine is provided by the *Climatological Atlas of the British Isles*.[9] The maps in it are models of clarity and set out vividly the information collected over many years by many observers, a large proportion of whom are amateurs. The amount of detail will surprise those who do not know much meteorology. Thirty-year averages of daily means, maxima, and minima for the year and for each month are mapped for barometric pressure, temperature, rainfall, humidity, and sunshine. There are also data about daily variations of temperature, about wind and snow and frost, and about record rainfalls and droughts. Materials are here for testing any hunches doctors may have about the effects of the weather on their patients and also for studies of the sort proposed by Dr. Jacques M. May under the title of Medical Geography.[10] The necessary medical data are in the reports of the Registrar-General and of medical officers of health and in recent studies by the Social Survey, by regional hospital boards, and by general practitioners. There is here a vast field for studies which would be in the lineage of *Airs, Waters and Places* and *Historical and Geographical Pathology*. Recent papers on the influence of absolute humidity on respiratory infections [11] and on the relation of variations in temperature and humidity to epidemics of poliomyelitis [12,13] encourage the belief that valuable results would accrue.

The study of interregional and international variations in the incidence of disease and death has been extended

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predictions based on these For example, we might assume that general practice is to continue in its present form, or alternatively that group practice (specifically defined) is to be promoted over a period of x years Acting on these or other assumptions, reasonable predictions are possible There is an advantage to making more than one prediction based on more than one premise

Our American cousins are the world's best collectors of data, calculators of national requirements, and "projectors" into the future In most detailed and elaborate fashion they have "worked out" the need for doctors in the U S for the year 1963, and have correlated this to the needs of medical education They have even gone so far as to attempt to budget on this basis In so far as they have had to deal with the amorphous mass of totally unplanned medical service and "free trade" medical economics, their task is much harder than that confronting us in Great Britain If we wish, we can learn a great deal from them as to what to do, and what not to do, in this regard That the American medical profession has recognised this need for assessment of "doctor requirements," without the stimulus of a planned medical service, is itself significant They have shown us that it is possible and practical to establish certain premises and then to make reasonably accurate predictions of need They have even been kind enough to show us some of the premises from which we should *not try to work for example, straight doctor/population* ratios without consideration being given to important modifying factors The big U S cities are a working demonstration of the bad effect of over doctoring and over competition on medical morale, ethics, and performance But that is another story

The N H S is itself our guarantee that we will never reach the high point of over doctoring that characterises some areas of American medicine, but we cannot afford even a degree of this The cost in both professional and financial terms is enormous What we must grasp, and act on, is that in a planned medical service serious over-doctoring (or under doctoring) can be prevented, or if *present and detected* early can be cured If not detected, either of these can be as disastrous as any other form of malignant growth The key to this problem is a careful assessment of needs

The newly formed College of General Practitioners, as well as the Medical Practices Committee, could interest themselves *in this problem* with great benefit to everyone

Lerici La Spezia,
Italy

JOSEPH S COLLINGS

UTERINE CANCER AND VAGINAL SMEARS

SIR,—It is surprising to read a leading article in your journal (April 18) which seems to favour the partial conversion of gynæcological outpatient departments to "cancer prevention clinics" The accurate diagnosis of lesions of the breast and rectum is one of the most difficult problems facing the general surgeon Gynæcologists are not competent to undertake this work, even if they were they could only do so by neglecting their gynæcology

Because the misapprehensions in this article are widespread, it may be desirable to comment on a number of the interesting points raised

The correct diagnosis and treatment of cancer requires considerable experience and knowledge Doctors with this training are in very short supply all over the world, and their services must be used to the best advantage

"Cancer prevention clinics" have developed in parts of the U S A in connection with the cancer education campaign Their object is to detect "symptomless cancer"—i e, to bring the cases to suitable treatment at a stage when good results are probable Observation satisfied me that "the mental and physical trauma in borderline cases, eventually found to be free of cancer" is greatly exaggerated I did see a few very unfortunate examples of this, but I was satisfied they should be attributed to lack of training in the doctors, not to the "cancer prevention clinics" as such The steps to be taken by a gynæcologist to diagnose or exclude carcinoma of the uterus are definite, precise, and reliable A good gynæcologist will not create neuroses, even if he is much afflicted by neurotics

Early cancer is *difficult to diagnose* American experience shows clearly that an education campaign will bring the patients to the doctors earlier, often much earlier Unfortunately the medical profession as a whole is not able to diagnose these early cases as well as it should, and the proportion of doctors' errors has therefore risen considerably This is very serious because the delay due to the patient alone is of the order of 12 weeks, but after reassurance by the doctor it is 56 weeks Most patients think we know more than we do, and they do not return until the error is painfully obvious

A good cancer campaign would not begin with the general public, as in the U S A, but would proceed in three definite stages (1) establishment of competent tumour clinics in all our major centres (the various types of consultant required to staff these clinics, and the necessary diagnostic departments, cannot go to cottage hospitals, &c), (2) education of general practitioners in the correct use of tumour clinics, and (3) education of *the general public to make use of their suitably trained* family doctor—he should be our "cancer prevention clinic"

About half the cancer patients are far from hopeless if well managed when first seen There is no such thing as the "cancer specialist," coming along and working wonders after early bad management

The figures you quote of deaths from malignant disease do not represent the true incidence of the different forms of cancer Figures from my disease index of pathologically proved cases (surgical plus necropsy material) are open to the same objections but they are similar 2222 cases of six forms of cancer of current interest are composed of tumours of the breast (807), uterus (369), *colon* (319), rectum (300) (1 7 males to 1 female), stomach (220), and lung (207)

Because good results may be obtained in the treatment of carcinoma of the colon and rectum the gynæcologist would have to diagnose the former as well as the *latter* If he has to spend "some 500 hours of work necessary to reveal one carcinoma" of the uterus (a statement far from true in the gynæcological outpatient department as distinct from the "cancer prevention clinic"), he would have to spend at least 1500 hours to diagnose one carcinoma of the rectum Lack of training and boredom would almost certainly make him miss that one, hence he would probably do far more than 3000 hours for each "positive"

For routine hospital investigations we now consider the cytology section just as *essential as the* hæmatology, bacteriology, and biochemistry departments It is foolish to say biochemistry is more important than hæmatology, and equally foolish to say cytology is more or less important than the other divisions

The steady growth in demand for vaginal *cytology* was really all we needed to prove its value When we passed our 5000th smear some months ago I nevertheless asked the gynæcologists to assist me in determining the value of the method

The gynæcologist does far more than *diagnose* and treat cancer, likewise the merits of vaginal *cytology* are not confined to cancer work With *minor* variations we agreed that its value was, in order of importance (1) diagnosis of cancer, (2) diagnosis of trichomonas infection, for which it has proved the *method of* choice, (3) rough estimation of the œstrone *level*, (4) bacterio

The case described by Griffiths and Gilchrist, and other reported cases where abnormal blood-protein was excessive, have been associated with liver disease. Cryoglobulinæmia has also been reported occasionally in disseminated lupus,[1] in rheumatoid arthritis,[2] and in polyarteritis nodosa.[3] Several workers have found a high proportion of sera positive for cryoglobulins in subacute bacterial endocarditis [1 4 5]; and now Dreyfuss and Librach [2] have found small but definite amounts in 42 out of 50 cases at some time during the course of this disease. Hyperglobulinæmia was present in most sera throughout the disease; but cryoglobulinæmia was independent of this, and appeared to be related more closely to increased euglobulin content. Positive findings were also independent of the species of the infecting organisms, which included staphylococci, non-hæmolytic streptococci, and hæmophilus strains, as well as *Streptococcus viridans*.

The production of cryoglobulins, therefore, seems to be a special type of reaction in a predisposed host, rather than a response conditioned by a specific bacterial stimulus. If this is so, it would be of interest to know whether cold-precipitating globulins are formed in endocarditis lenta where the primary heart lesions are congenital and not rheumatic. A distinction emerging here might throw light on more than the academic significance of cryoglobulins.

MEN AND MANNERS

> "In dealing with human beings, science is not enough; you must also have good manners."

Lord Percy of Newcastle, in his presidential address last Tuesday to the Royal Sanitary Institute's congress at Hastings, thus neatly stated a perennial truth, and added that it is good *public* manners that are the hardest to learn. Dr. Richard Scott developed this thought further in his paper on the training of medical students in the practical aspects of preventive medicine. Coördination in the three great arms of the health service—the hospital and specialist service, the local-authority service, and the general-practitioner service—depends among other things on human relationships, and more especially on "that surprisingly complex form of human relationship" operating between professional people. In medicine it should not be as difficult as it sometimes seems to foster sympathy between colleagues in different branches; for the consultant, the medical officer of health, and the general practitioner trained in the same medical schools, and were for six years nourished in the same traditions and curriculum. Edinburgh University has always tried to give its medical students a sense of the indivisibility of medicine, by sending them out in their final year to see patients as the general practitioner sees them. At one time students used to attend the public dispensaries; but of late years one of these dispensaries has been developed into a general practice under the National Health Service, staffed by two doctors, a public-health nurse, an almoner, and a secretary, all of whom are employed by the university; and the students learn about general practice from this team. Dr. Scott described the original unit some years ago in our columns,[6] but since that time a second unit has been added, largely thanks to the help of the Rockefeller Foundation.

At the congress he was able to report some of the effects on students of attending these units. They graduate from listening-in during the doctor's surgery to the responsible care of patients, and more particularly to care of a family (using the clinic doctor as consultant); and they join in the daily case-conferences where the medical and social treatment of the patient are discussed and agreed on by the team. Dr. Scott noted that the student, when he first comes, is often disappointed that "major, dramatic and urgent pathology is so relatively uncommon"; and moreover he is disturbed to find how often it is impossible to reach a final satisfactory diagnosis. His disapproval, however, gives way to a second phase in which he becomes increasingly impressed with the psychosomatic aspects of disease, and sometimes declares that general practice "is really psychiatry." He begins to talk more freely to patients, and then to make his first home visits, where a new lesson comes home to him. Most of the patients are poor, and he becomes obsessed with the economic and social components in ætiology: his doubt of the powers of medicine to help much plunges him into therapeutic nihilism. Return to the wards is some corrective for this, but he is now able to receive his clinical teaching with a broader, more balanced mind. One message passed on to him during his last weeks at the unit is that as a practitioner he will have a duty to keep his colleague, the medical officer of health, informed of the medicosocial problems presenting themselves in general practice, and to work alongside him as a field intelligence officer. But his chief gain is in the insight he acquires into patients as people, and his sudden grasp of the fact that this girl in her 'teens, brought by her mother, is not someone who will pass in and out of his ken by way of a hospital bed, but the same girl who will be coming to him for antenatal care in ten years' time, and who in twenty years' time will be bringing her own daughter to him for advice. He is, in fact, not just "seeing a case," but making a lifelong acquaintance with whom he must collaborate.

As Lord Percy reminded the congress at the outset, the true base of operations for good family doctoring is not in any system of model health centres, but in the homes of the people.

NEEDLE BIOPSY OF THE LIVER

SINCE the introduction by Roholm and Iversen, of needle biopsy of the liver[1] its value in the study of hepatic disease has been repeatedly demonstrated. At first it was justifiably regarded as carrying considerable risk, but common-sense precautions have rendered it "a most useful procedure with a gratifying degree of simplicity, efficiency and safety."[2] It is, in fact, indispensable for accurate diagnosis in many cases in which disease of the liver is suspected. Its value is clearly shown in Christian's report[2] from New Orleans. In as short a period as eighteen months, needle biopsy was found necessary in 91 patients; and of the 73 in which it was performed purely for diagnostic purposes, the prebiopsy diagnosis was shown to be wrong in 35 cases. In other words clinical and laboratory methods combined gave a correct diagnosis in only half the cases investigated. Apart from its value in the diagnosis of diseases of the liver itself, needle biopsy has often provided definite evidence of conditions difficult to diagnose, such as the chronic granulomata, including brucellosis, sarcoidosis, and histoplasmosis, as well as miliary tuberculosis and non-specific granulomata in patients with pyrexia of unknown origin.

The chief contra-indication to aspiration biopsy is any condition in which there is a tendency to bleed. Fortunately this can often be overcome by preliminary treatment with vitamin K or by a blood-transfusion. In severe or prolonged jaundice from biliary obstruction, there is also some risk of bile peritonitis from perforation of one of the greatly dilated intrahepatic ducts. It is also wise to exclude patients who may have a subphrenic or hepatic abscess or other local infection that might be the proportion of registrars to consultants which will provide for replacement and "healthy" competition is not even remotely related to the present staffing of hospitals, particularly in departments of general medicine and surgery

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[3] Lepow, H., Rubinstein, L., Woll, F., Greisman, H. *Amer. J. Med.* 1949, 7, 316.

[4] Wertheimer, E., Stein, L. *J. Lab. clin. Med.* 1944, 29, 1082.

[5] Lerner, A. B., Barnum, C. P., Watson, C. J. *Amer. J. med. Sci.* 1947, 214, 416.

[6] *Lancet*, 1950, ii, 695.

[1] Roholm, K., Iversen, P. *Acta path. microbiol. scand.* 1939, 16, 427.

[2] Christian, E. R. *Amer. J. Med.* 1952, 13, 689.

In the bad old days hospitals were staffed by housemen and by "consultants," of whom many were also in general practice Chief assistants were found mainly in teaching hospitals, and smaller hospitals would have a R S O and perhaps a R M O Yet there was still competition for specialist appointments Now every hospital is littered with registrars, and the consultant unblessed with at least one is small beer indeed

Dr Forrester and Dr Walton suggest that displaced senior registrars be encouraged to pursue their dwindling hopes from post to post Rather than prolong this dismal muddle, would it not be kinder to give their ambitions the *coup de grâce* forthwith, by Purge or Inquisition ? Or, alternatively, to eliminate all new registrar appointments except for those men genuinely in training for prospective vacancies, and spend the salary of £890 on paying a new consultant for the appropriate number of sessions ? There are many who would *rather* be indigent surgeons than poor G P S But perhaps the present part-time consultants would not approve

London S W 10 **AUBREY LEACOCK**

RENAL DUCTS OF BELLINI

SIR,—In reply to Mr Ross (April 18), I cannot see how the use of 'Neoprene,' post mortem kidneys, and an unnatural physiological way of approach can give the conclusion of irrefutability to his experiments If this were so it would be logical to expect that before obtaining a back-flow retrograde pyelogram it should in every case be possible to inject the Bellini ducts, but, as is obvious from radiological evidence, this is not so

I would add two observations firstly, the finding of uric acid precipitate in the kidneys of an eleven-month old girl who died from a non-kidney disease, showing that its elimination is not as easy as has been accepted, and, secondly, if comparative anatomy is of some value to the study of human functions, it may be of interest that the kidney of the cat, which has only one pyramid, has no Bellini ducts at all, and the larger tubules are orientated parallel to the renal pelvis, and not perpendicular to it

Department of Pathology,
Booth Hall Hospital
Manchester

F DURAN-JORDA

DISORDERS OF MOTILITY OF THE SMALL BOWEL

SIR,—The cases described by Mr. MacPhee (April 4) and by Dr Frankel and Dr Moore (April 18) both illustrate the development of ileojejunal insufficiency following Polya type gastrectomy These cases are occurring with increasing frequency Having recently studied several such patients in some detail, we are inclined to attribute this disorder of small-intestinal function to the presence of a cul-de sac In one of our cases the operative restitution of the normal duodenal pathway led to complete cure of the steatorrhœa and wasting Megaloblastic anæmia, as found in Frankel and Moore's case, is due to a vitamin-B_{12} deficiency and occurs only rarely Possibly it is due to the same mechanism that causes megaloblastic anæmia in man and other animals after the formation of intestinal cul-de sacs

On searching through the literature we have found a large number of cases of steatorrhœa, creatorrhœa, and wasting which have developed after the formation of intestinal cul de-sacs After a Polya-type gastrectomy this may occur, especially if the afferent loop is long and antecolic In all cases in which it has been tried, restitution of the normal continuity of the gut has cured the condition

It is possible, as Mr MacPhee suggests, that th ileojejunal insufficiency is associated with a refle disorder of intestinal motility, but there must also b a considerable disturbance in the chemical, physical and microbiological environment within the intestine

Reporting our own observations and experiments i a paper shortly to appear, we have used the comprehensive term "intestinal cul de sac phenomena" t describe the syndrome

J NAISH
Bristol W M CAPPER

CONTRACEPTIVE TECHNIQUE

SIR,—We have noted with some misgivings the appearance for some months past in your journal of commercial advertisements concerning a certain contraceptive jell which is recommended to be used "without a diaphragm" or the simultaneous employment of that or other barrie pessary the implication being, of course, that this jelly method alone is a safe one

Experience at the clinic of the Society for Constructive Birth Control over the past thirty years has convinced us that for effective contraception in all cases the use of a mechanical barrier to the entry of spermatozoa into the cervical canal, as well as a chemical substance (preferably a suppository with a greasy base) to inactivate the spermatozoa, is essential to reliable contraception Evidence of the repeated failure when one method alone has been used to prevent fertilisation is continually accumulating from the case histories of patients who attend this clinic after other methods have failed them

We believe that this opinion is shared by most of the clinics concerned with birth-control in this country, and we are therefore dismayed to find that a purely commercial institution is able through your advertisement pages to promulgate claims which are entirely at variance with the majority views of scientists in this country who have special knowledge of this aspect of preventive medicine

MARIE C STOPES
President
M BEDDOW BAYLY
Chief Medical Officer,
C B C Clinics

Society for
Constructive Birth Control
106, Whitfield Street,
London, W 1

BACT COLI IN THE CAUSATION OF INFANTILE DIARRHŒA

SIR,—The isolation in Japan by Prof Tohru Ogawa and Prof Jiro Ogawa (March 21) of *Bacterium coli* of the serological types 0 111 B4 and 0 55 B5 from infants suffering from diarrhœa and vomiting provides a further instance of the association of these organisms with this disease

That one of these two serological types may predominate over the other at different periods in the same area has already been demonstrated,[1] and is again illustrated by the results of bacteriological examination of rectal swabs taken from infants on admission to the gastro-enteritis unit of this hospital Thus, during the past four months, December, 1952, to March, 1953, *Bact coli* 0 55 B5 was isolated from 24 out of 90 children admitted, and *Bact coli* 0 111 B4 from only 4 These results contrast with those of *1949* when *Bact coli* 0 111 B4 was isolated from 38 of 153 admissions and *Bact coli* 0 55 B5 from 12 It was found [2] that 9 of the 12 *Bact coli* 0 55 B5 strains isolated in 1949 possessed H6 antigens (thus conforming in flagellar type to the strains originally isolated in Aberdeen [3 4]), 2 possessed H2 antigens, and 1 had H7 In the current series, all of the 24 *Bact coli* 0 55 B5 strains possessed H2 antigens The infants from whom they were isolated came from various places in North and East London,

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1 Smith, J Galloway, W H, Speirs A L *J Hyg, Camb* 1950 48 472
2 Wright J, Villanueva R *Ibid*, 1953, 51 39
3 Giles C Sangster G Smith, J *Arch Dis Childh* 1949 24 45
4 Kauffmann, F, Dupont, A *Acta path scand* 1950, 27, 552

Special Articles

THE FAMILY

CONFERENCE IN LONDON

OVER 500 people assembled for the British National Conference on Social Work, held in London on April 16–18 under the chairmanship of Sir WILSON JAMESON, with The Family as its comprehensive theme.

The Family as a Social Institution

Prof. RICHARD TITMUSS remarked that the family, which used to be a private affair, had now become a public institution; and since the health and stability of the community were recognised as depending on the health and stability of the family, even the quality of its internal life had become a matter of public concern. As society made the business of being a parent more a matter for expert advice, parents became more self-conscious and more anxious. Professor Titmuss suggested that there was a risk in seeking to impose general standards of child care and health education throughout a community when these might only be assimilable within certain strata of society, with the result that the self-confidence of parents might be seriously disturbed and they might fade into a state of inert irresponsibility. He pleaded for re-examination of the training of all professional persons directly concerned with the health and welfare of the family.

In drawing attention to the implications for the family, and in particular for the mother, of the decline in the birth-rate and the emergence of the small family as the typical modern family unit, Professor Titmuss referred to "problem families" as apparently less numerous than before the war and recruited from the rapidly dwindling group of large families. "They are reproductive deviants;" as such they might soon become anthropological curiosities.

The revolutionary reduction in the time devoted by women to bearing and nursing children compared with the last years of the 19th century, estimated at $3^{1}/_{2}$ as against 12–15 years, and the 35-year expectation of life after 40 years of age, by which time the business of child care was largely over, led Professor Titmuss to urge the need for re-examining woman's rôle in society. Figures for married women in employment, now apparently at a peak, also suggested a shift in social practice to which social policies should bear some intelligible relation. Of all mothers with children 10% worked outside the home during the first 5 years of marriage, and the figure increased to 24% when the marriage had lasted 15 years. We ought to know why this was so.

Professor Titmuss disposed of the popular belief that most divorces occur in the first few years of married life: he declared that the rate of divorce in the early years of marriage was comparatively insignificant (less than 30 in every 100,000 couples), and that the rate became much higher after the marriages had lasted 10–20 years.

Throughout his address Professor Titmuss effectively illustrated his main thesis that the family has never been a static institution, but has continually evolved in response to internal and external forces of change.

Statutory and Voluntary Effort

In the absence of the Minister of Health, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry, testified to the importance of the subject-matter of the conference. She spoke of the vital importance in our social services of a wise combination of statutory and voluntary effort; and, in emphasising the importance of dealing with the family as a whole, she reminded the conference that the three-tier family was still an important unit of social responsibility.

Special Problems

Dr. JOHN BOWLBY made a plea for more biology teaching in the training of social workers; he suggested that this would bring new strength to the study of personal relationships. Like Professor Titmuss he feared that many mothers were disturbed by misleading standardised teaching, and he lamented that our services were not built round the idea that a child's relation to his mother was of first importance. If this fact were recognised we should be less prone to break up the problem family or to spend large sums on caring for sick children away from home. He regarded additional psychological study as essential in the training for social work.

Reports on Discussion Groups

At the final session three rapporteurs reproduced the findings of the twenty-nine groups which during the conference had been engaged in more or less detailed discussion of the main themes. It was clearly impossible for them to reproduce precisely the findings of these groups, or indeed to convey the extent to which the findings were unanimous. Nevertheless it seemed that a large measure of agreement lay behind the reports, which included the following conclusions.

IMPACT OF SOCIAL SERVICES

The family was accepted as a social institution vital to the healthy life of the community, and this healthy life depended largely on the quality of individual relationships. There was a growing feeling against removal of children from their families, including the children of problem families. As to the employment of mothers there were differences of views, and judgment might depend on the reasons for which they went out to work.

Anxiety was expressed that the social standards set by present-day services might require from the ordinary family a response which involved strain. The parent who felt that he or she fell short in a visitor's eyes in matters of budgeting, cleanliness, or child care was the more liable to try to cast responsibility on to the State which seemed to have so much to offer.

There was disquiet, too, at the services that had been enumerated that might lead to disruption of the family group in endeavouring to provide for the homeless, the handicapped, the aged, or children; at the current emphasis and expenditure on curative services; and at the lack of a social policy directly designed to strengthen and support the family.

As a subject for discussion the problem family appeared to have exercised a fascination out of all proportion to its numerical importance. Whatever was done should be done for the family as a unit, always remembering that material standards were here of secondary importance to considerations of emotional and mental stability. The need for intensive personal work over a long period was recognised: such work should be with the family in its own setting, aimed at a standard within its reach and at fostering a relationship of friendliness and trust as an essential preliminary to building up other social relationships.

Discussion of evicted families had given rise to some criticism of housing policies which led to homeless families becoming a heavy financial burden on public funds. There were often alternatives to eviction which should be fully explored. Where evicted families came into the care of a local authority, case-workers might be appointed to undertake individual work and bring in voluntary effort.

SOCIAL WORKERS

It appeared that in discussing the rôle and training of social workers the groups had not been disposed to be

It may be thought impertinent for someone from the South of England to make comments on this situation, but the problem of tuberculosis in the British Isles is surely indivisible

The pathetic housing programme must receive the most urgent attention in Government circles, and, at the same time, the medical and nursing profession in Glasgow should rise to meet the demands of their local population It is essential that the facts should receive the widest publicity in the national press and on the air, in order that there may be quickening of response to this tremendous human need

Central Middlesex Hospital,
London N W 10 **Horace Joules**

EPIDEMIOLOGY OF STREPTOCOCCAL INFECTIONS

SIR,—In their very interesting review of the epidemiology of streptococcal infections in your issue of April 11, Professor Dingle, Professor Rammelkamp, and Dr Wannamaker refer to their finding that, in a number of instances, infections due to hæmolytic streptococci of type 12 have been particularly commonly followed by acute glomerulonephritis It is clearly of considerable interest to see whether a similar association can be shown in Britain The Streptococcal Reference Laboratory at Colindale and the regional laboratories of the Public Health Laboratory Service at Cambridge, Cardiff, and Oxford would be very glad to collaborate with pædiatricians or others who may have an opportunity of making such an investigation and to undertake the type identification of group A streptococci that have been isolated in circumstances suggesting that they may have initiated an attack of nephritis

Streptococcal Reference Laboratory
Public Health Laboratory Service
Colindale, London, N W 9 **R E O Williams**

TRAINING OF PHYSIOTHERAPISTS

SIR,—Prominence has been given lately in medical journals to the training of physiotherapists, and we feel that certain points ought to be clarified

Physiotherapists in this country belong to three groups (1) the Physiotherapists Association, (2) the Faculty of Physiotherapists, and (3) the Chartered Society of Physiotherapy The Cope report, drawn up by a committee of nine members, six of whom were in active association with the Chartered Society, whereas the other two bodies were not represented, recommended hospital authorities to employ exclusively members of the Chartered Society, and the first circulars of the Ministry of Health were drawn up in this spirit The injustice of this report, however, has been rapidly realised, and the Minister of Health stated in Parliament on March 19 that the Cope report would not be implemented, and that he would further withdraw the temporary instructions in the Ministry circular referring to the employment of chartered physiotherapists, and make new regulations fair to all associations

We are at a loss to understand this tendency of the Chartered Society to monopolise physical treatment in this country Apart from the fact that it goes against the liberal principles that dominate medical work, nothing has demonstrated the superiority of the members of the Chartered Society over those of other associations of physical-treatment practitioners We must emphasise that hospitals employing members of the Physiotherapists Association and the Faculty of Physiotherapists are perfectly satisfied that the training of members of the association and the faculty is not inferior to that of the Chartered Society

The education plan formulated by the Physiotherapists Association, and supported by education authorities, experienced teachers, and the medical profession, provides for the cooperation of technical colleges and teaching hospitals Physiotherapy training schools should be part of a university, and the physiotherapist's qualification should be a recognised university diploma The real aim is to enable the physiotherapist to take his place as an accepted member of a medical team, receiving alike the support of the medical profession and the confidence of the public

A P Cawadias
President

Physiotherapists Association,
31 Dover Street London, W 1

S S Knight
General Secretary

PHARMACEUTICAL ADVERTISEMENTS

SIR,—Could not the British pharmaceutical firms serve the community even further by including in all their copious advertising matter the price of the preparation advocated ? Of course, the resulting reduction in profits would mean less funds for research, but I venture to suggest that, on balance the community would benefit more

Rickmansworth Herts **A W Anderson**

ENLARGED HILAR GLANDS

SIR,—It is to be hoped that your annotation on this subject (April 18) may act as a catalyst, and promote some useful reaction amongst those of your contributors who are interested in a problem which is still very much in the melting-pot

It would be of great interest to know how frequent these cases of asymptomatic hilar-gland enlargement really are in this country, and how they fit in to the broader general picture of hilar adenopathies in young adults It is well known that bilateral hilar gland enlargement at this age is much more common in Scandinavian countries than in the British Isles In recent years large series of such cases have been reported, from Sweden in particular

Lofgren, for example, has made a special study of the question, and he has recently published[1] two papers in collaboration with Lundback, in which 212 cases of "the bilateral hilar lymphoma syndrome" are studied in relation to (1) age and sex incidence, and (2) tuberculosis and sarcoidosis Of these patients, 161 were women and 51 men, and in 113 cases the syndrome was associated with erythema nodosum (107 females, 6 males) The maximum incidence was found in the age group 25–29 In the female group, a *relation to pregnancy and lactation* was observed in some cases

In 100 cases tuberculin sensitivity was absent, even to 1 mg of tuberculin Complications, tuberculous in type, developed in only 1 case A diagnosis of sarcoidosis could be established by histopathological examination on an average in 26 4% of cases, but during the later stages of the investigation, 23 out of 49 cases (47%) were proved to be sarcoidosis

The conclusion drawn is that this syndrome is independent of tuberculosis from the point of view of ætiology The authors interpret it as being a manifestation of sarcoidosis, and more exactly, as the primary stage of pulmonary sarcoidosis

Our own short paper[2] reported 6 cases of bilateral hilar-gland enlargement, all in relatively young women with erythema nodosum In 5 cases the Mantoux reaction was positive, and in the 6th it was negative at 1 in 10,000 There was a history of recent pregnancy in 2 cases No clinical manifestations of sarcoidosis were found, though, if it had been possible to make the intensive search for biopsy material mentioned by Lofgren and Lundback, the result might have been different in some cases

Chaves and Aboles[3] whose paper, entitled Transient Undiagnosed Intrathoracic Lymphadenopathy in Apparently Healthy Persons, you mention, lay down as criteria for their cases the spontaneous regression of enlarged glands and the absence of evidence of pulmonary or other visceral involvement throughout the period of observation From the large volume of material available for screening, coming from

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[1] Lofgren, S, Lundback, L *Acta med scand* 1952 142, 259
[2] Dunner, L Hermon R *Brit med J* 1952 ii 1076
[3] Chaves A D Aboles H *Amer Rev Tuberc* 1953 67, 46

Newcastle.—Durham, North Riding of Yorkshire, Northumberland, Cumberland.

WALES

Cardiff.—South Wales, Monmouth.

SCOTLAND

Edinburgh (South East Scotland). *Glasgow* (South West). *Dundee* (East). *Aberdeen* (North East). *Inverness* (North).

NORTHERN IRELAND

Belfast.

SOUTHERN IRELAND

Dublin. Cork. Galway.

Members or associates will be free to choose the faculty to which it is convenient (for transport or other reasons) for them to belong.

Members or associates who care to make further suggestions or comments upon the areas covered by these regional faculties should write to the Secretary, the College of General Practitioners, 14, Black Friars Lane, Queen Victoria Street, London, E.C.4.

Parliament

British Hospital in Paris

IN the House of Lords on April 22, replying to a question by Lord AMULREE, the MARQUESS of READING, parliamentary under-secretary for Foreign Affairs, said the Hertford Hospital in Paris was closed to patients last year. At that time the difference between regular income and expenditure which had to be met by donations or out of capital had risen from £15,000 in 1948 to £26,000 in 1951, and out of a normal complement of 50 to 60 beds an average of only between 21 and 25 were occupied. Last autumn the Charity Commissioners prepared a scheme whereby £30,000 was to be raised from endowments for the modernisation of the hospital, which was founded in 1871. At the same time Sir Bernard and Lady Docker offered a sum of £30,000, not towards the support of the existing hospital but for the construction of a new Docker Wing of 10 beds for fully paying patients.

Lord Reading added that although remittances for the continuance of British charitable works abroad were normally approved without difficulty, remittances for capital expenditure on new developments must obviously be carefully scrutinised; and one of the points on which the Treasury would need to be satisfied was that the new works would constitute a viable proposition. It was upon this aspect of the scheme that the Treasury felt obliged to obtain fuller information than had been received when Sir Bernard and Lady Docker's offer was withdrawn. He understood that at a meeting of the hospital committee on March 31, the chairman was asked to work out a fresh scheme to ensure the continued existence of the hospital. The Chancellor of the Exchequer would be prepared to consider sympathetically the remittance, both of the capital sum needed for the cost of the new wing and of such future sums as would be required for the maintenance of the hospital as a whole, if he could receive satisfactory assurances that the hospital's income from fees and donations would be adequate for its future needs.

Earl JOWITT hoped that Lord Reading would realise that there was an element of prestige involved in this matter. The hospital had a long and honourable tradition, and in his view it would be a grave misfortune if it had to close through lack of funds. The MARQUESS of READING said that he appreciated this point and that the Chancellor was prepared to consider the situation. At the same time, while not prejudging the matter, it was a serious question whether in present conditions, and with the decrease in the British population in Paris, there was a case to be made for a viable hospital on those lines.

Pharmacy Bill

In the House of Commons on April 24, Mr. JOHN HALL moved the third reading of the Pharmacy Bill, which had passed through Standing Committee unamended. Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said she was sure that the whole House would welcome the Bill which, although a domestic measure mainly sponsored by the Pharmaceutical Society, tidied up the matter of the two registers which formerly operated for pharmaceutical chemists and chemists and druggists. The Bill was read the third time and passed.

QUESTION TIME

Food Hygiene and Infectious Disease

Mr. G. H. OLIVER asked the Minister of Health what steps were taken to ascertain whether persons employed in the preparing, cooking, and serving of food in hotels, restaurants, and road-side cafés were free from infectious diseases such as tuberculosis.—Miss M. P. HORNSBY-SMITH replied: There is no general power to require the persons concerned to be medically examined for this purpose, and the Minister is advised that the present state of our knowledge does not suggest that such a power would be justifiable as a means of preventing the spread of infection.

National Health Service Inquiry

Dr. BARNETT STROSS asked the Minister to what extent the terms of reference of the committee which was to investigate the costs of the National Health Service included powers to consider salaries paid to medical and non-medical staff, and the economies that might be effected by employing consultants on a full-time basis only.—Miss HORNSBY-SMITH replied: The Minister would certainly not expect the committee to deal with actual rates of pay. For the rest the Secretary of State for Scotland and the Minister are anxious not to hamper the committee in their work by seeking to restrict their field of inquiry.

Doctors and Litigation

Air Commodore A. V. HARVEY asked the Minister what steps he was taking to safeguard doctors from litigation resulting from their work in the health scheme.—Miss HORNSBY-SMITH replied: Officers of the department are at present discussing with representatives of the profession the relations, financial and other, between hospital authorities and their medical staffs when legal actions are brought against either or both.

Tuberculin-tested Milk

In answer to a question Sir THOMAS DUGDALE, the Minister of Agriculture, stated that under the Milk (Special Designation) (Raw Milk) Regulations, 1949, applications received after Sept. 30, 1954, for the issue and renewal of licences to use the designation "Tuberculin-Tested" would only be approved in respect of attested herds. The success of the attested herds scheme had made it possible to add this more stringent test to the present requirements of animal health and hygiene in the dairy. The scheme was going extremely well and we were getting more and more absolutely clean milk in the country.

Calcium Content of Flour

Dr. BARNETT STROSS asked the Minister of Food the number of days involved in the original experiment in 1942, when, after a diet in which 50% of the calories were supplied from flour of 92% extraction, it was noted that absorption of calcium decreased; his reasons for continuing the fortification of bread with chalk; whether, in view of recent research, he would consider revising his policy; whether he had noted the fact that the human body could and did acclimatise itself to high intakes of phytic acid if ingested over a prolonged period; and whether he would now cease to fortify bread with chalk.—Major GWILYM LLOYD GEORGE replied: In the 1942 experiment the subjects were under observation for 21 to 28 days. Calcium carbonate is now added to flour to ensure that total food-supplies provide sufficient calcium to meet nutritional requirements. Flour provides nearly 30% of the total amount of calcium in the diet; and any adverse effect of phytic acid on its absorption is of small importance in relation to that amount.

Dr. STROSS: Does the Minister think that after all these years we should still be tied to one single experiment which lasted only three or four weeks, as a result of which we have been imbibing or ingesting large quantities of chalk in our bread ever since? Has not he been informed of more recent work which shows that phytic acid is not detrimental to human beings and that we do not need to nibble away the cliffs of Dover entirely against a danger which we feel now does not exist at all? Will not the Government look at the matter again?—Major LLOYD GEORGE: We are prepared to look at anything, because this is a matter of tremendous importance to the nation as a whole. It is true that the week in patients in the isolation hospital here Encouraged by the results, I introduced heat and the muscle relaxant drugs to relieve spasm, and by the end of 1949 I had no hesitation in beginning not only passive movement but active exercise as soon as pyrexia had subsided

Final proof of efficacy could be obtained only by comparing patients so treated with themselves as they would have been if otherwise treated—a manifest impossibility I have certainly had a lower-than-average incidence of contractures, and an impressive proportion of my patients have been discharged to their homes, requiring only outpatient physiotherapy and remedial exercises to complete their treatment I have had no case in any way corresponding to that reported by Mr Hyman

I have, however, tried to follow a policy of asking no muscle or group of muscles to bear disproportionate strain. So long as the patient is in bed this is easy, for no limb can be called on to do more than raise its own intrinsic weight, and if the muscles cannot raise the limb from the bed they do not even have to bear that weight In other words, they are not asked to carry a load until they have shown themselves capable of making a reasonable attempt to do so

When the patient gets out of bed, the case is altered and the legs are at once called upon to support the weight of the whole body, even if they are not ready to do so I cannot help suspecting that this may have been the determining factor in Mr Hyman's patient, and that the golden rule, especially in dealing with enterprising schoolchildren and other impatient people, is to keep them strictly in bed, except for tank exercises, until there is evidence that the muscles of the legs are ready to make at least a fair attempt to carry out their normal duties

Myland Hospital, Colchester JOHN D KERSHAW

AUGMENTING KNEE-JERKS

SIR,—However "ludicrous" the traditional methods of augmenting the knee jerks may appear, they are certainly preferable to the method suggested by Dr Hirschowitz (April 25) If, for example, a patient has a one-sided partial paralysis of his lower-limb flexors, then when he pushes into the bed, the degree of reciprocal inhibition of the extensors so produced may, and probably will, produce a spurious inequality of the knee jerks This is one of the reasons for insisting on complete relaxation where possible, however tedious it may be to obtain

Hoddesdon, Herts BARBARA SIMONDS

TRICHOMONAS VAGINITIS

SIR,—I have been interested in the recent articles and letters on trichomonas vaginitis While supporting Mr McCullagh's laudable plea (April 4) for the "gap" seat in lavatories, I think he is being rather hopeful when he says that we could expect cases to be reduced by 90% if the gap seat were universal

For the last four and a half years I have been in practice in North-east India and East Pakistan, where the Eastern squatting position is universal, and in my experience the prevalence of trichomonas infestation there is almost as great as it is in this country Gonorrhœa, of course, is the main cause of infective vaginal discharges, but trichomonas runs it a close second

I am of the opinion that transmission is mainly venereal, with perhaps a small percentage of cases caused by infective clothing During routine prostatic smears, of which we perform very many in a busy outpatient hospital practice, I have come across two instances of *Trichomonas vaginalis* in the resting phase Is it not possible that in the male the parasite lodges in the seminal vesicles or the prostatic ducts without causing any symptoms, and that it multiplies and causes symptoms only in the favourable medium of the vaginal secretions ?

Perhaps observations on husbands of infected women with a series of non infected couples as controls might give a convincing answer to the vexed question—is this mainly a venereal or a non venereal disease, and, if venereal, can any treatment be directed at the husband as well as the unfortunate wife ?

Glasgow J T PATRICK

THE GAP SEAT

SIR,—The correspondence (April 4 and 18) about the value of the gap seat brings back old memories to me, for it was I who first thought of it in 1905 I was at that time R M O at the Lock Hospital for Women Harrow Road We then had the old type of oval lavatory seat, and though the lavatories themselves were labelled *syphilis* and *gonorrhœa*, I soon found that the patients disregarded the labels and used them indiscriminately, leaving obvious signs of use on the front sections of the seats

Cross infection between gonorrhœa and venereal warts certainly occurred, and probably trichomonas also, and I was so worried by this that in the top ward I had a section of the front of each oval cut out and rounded off, thus making a horseshoe shaped seat It was one of those things that once thought of seemed surprisingly obvious The hospital architect saw it, gave it his approval at once, and had the lavatories in all the wards similarly treated

I thought no more of it after I left Harrow Road until some years later when I began to find it was being supplied to other hospitals, and I have never until now troubled to claim any credit for it—it seemed so simple But undoubtedly it is a definite hygienic improvement and probably should be made compulsory in all public lavatories It also has the advantage that the seat need not be lifted by men

Dr Hudson (April 18) suggests that it would be even better still to use the squatting platform one finds in Turkey and the Near East That certainly is true, but we are so conservative in this country that his advice is extremely unlikely to be followed So may I still recommend my gap seat, at any rate until something better is invented !

London, W 1 J JOHNSTON ABRAHAM

CHLORAMPHENICOL BY INJECTION

SIR,—In your annotation last week entitled "Good Sense about Antibiotics" you say that "chloramphenicol is not suitable for intravenous, intramuscular, or intrathecal injection" May I point out that the antibiotic has been successfully administered by each of these routes ? A solution of chloramphenicol in aqueous dimethylacetamide has been widely employed [1,2] both intravenously and intramuscularly A number of reports [3,4] have appeared on the intramuscular use of an aqueous suspension of microcrystalline chloramphenicol As chloramphenicol readily penetrates the blood brain barrier,[5] intrathecal injection is not usually necessary, but as an adjunct to oral therapy it has been considered desirable, on occasion, to use this means of rapidly raising the cerebrospinal fluid level Intrathecal injections, in the form of sterile aqueous solutions, have been well tolerated [6]

Medical Service Department,
Parke Davis & Co Ltd ,
Hounslow Middlesex C BEAVEN

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[1] Orr, W W , Preisser, W G Ross, S , Burke, F G , Rice, T C *Antibiotics*, 1951, 1 63
[2] Moseley, V , Baroody W G *J S Carolina med Ass* 1951, 47, 157
[3] Harb, F W , Simpson, W G , Wood, C E *J ven Dis Inform* 1951, 32, 177
[4] Ross, S , Rice T C Burke, F G , McGovern J J , Parrott R H McGovern, J P *N Engl J Med* 1952, 247, 541
[5] Kekwick, A *Lancet*, 1952, ii 630
[6] Anderson K F Ellis, F G *Brit med J* 1951, ii 1067

One of the few remaining traces is a grille—but in England a grille makes one think of nuns peeping out, whereas in Spain it makes one think of bandits peering in.

A wide panelled Georgian front door, surmounted by a glass and wrought-iron fanlight, is a thing of beauty, and I know one modern door in London, richly black, with silver-plated accessories, which breathes an atmosphere of dignity and calm. But for sheer enchantment look for those doors painted like jewels in vermilion, turquoise, or palest jade. They replace the glowing colours of my childhood days, brilliant in memory with window-boxes, striped awnings, flower-sellers, and monkeys in red flannel jackets, who, with their Italian organ-grinders, brought a Southern sunshine to our streets.

* * *

He was a man after my own heart; an urbane and cultivated doctor with a taste for the arts, exquisite manners, and a kind of quintessential aristocracy. There are wines by nature of royal vintage.

He was principal in our firm of three, and in ten years of intimate association I never saw him ruffled, nor heard an intemperate remark. He had achieved the greatest gift of a family doctor—the envied quality of every man of civilised habits—the power of living *tempo moderato.* The fever and the fret of life passed him by. He was never involved in it.

He was a great reader and a great talker. I never knew a man who relished words more than he did. He responded to a felicitous phrase as a woman to a compliment. And yet there were gaps in this most integrated personality that might puzzle and intrigue his Boswell. He spoke to me only once of religion and that was to claim, with his own characteristic confection of conceit and simplicity, that he considered himself "deeply religious—though bad at being religious."

On the eve of his retirement we were taking brandy together after a dinner en famille.

"In your long years of medical practice have you any regrets?"

"Yes, that I have so seldom, in the Pauline and proper sense of the phrase, *visited the sick.*"

* * *

In the otolaryngological outpatient department of a Dublin hospital recently the surgeon in charge—and a senior one at that—took a patient into the darkroom for transillumination, accompanied by his house-surgeon and a nurse. The lights were turned out and the test completed, when an eerie purple glow was seen in the darkness. On investigation this funereal light proved to come from the dermatologist's ultraviolet lamp, which had been accidentally turned on.

"I see you have a false tooth, sir!" said the nurse, a pert young blonde.

The surgeon looked at his face in a hand mirror kindly provided for him, and saw that his single false incisor shone a bright buttercup yellow.

"Well, I may look a little peculiar, but have you seen yourself?" said the surgeon, slightly shaken, as he handed the mirror back to nurse.

Nurse looked at her face in the mirror, emitted a scream, and fled. She was soon recaptured, and solaced by cups of tea when the fit of the giggles which succeeded the screech of horror had subsided. And the cause? Her eyebrow pencil, which had caused her brows to phosphoresce like two brilliant bars of Neon light in the midst of a jade-green face.

* * *

Your annotation last week (p. 839) on the physiological difficulties of air travel reminds me of the story of the American explorer who made a forced march through a tropical jungle for a couple of days. On the morning of the third day, he found his native bearers sitting about, chatting and smoking their pipes. When he indignantly asked the head bearer why they were not getting ready for the day's journey he was told that the men felt they had left their souls behind them in their rapid progress and must now wait until these caught up.

* * *

The poetic young man at our sanatorium now calls the lady doctor who refills his A.P. the Lass with the Delicate Air.

Letters to the Editor

TOO MANY DOCTORS?

SIR,—In your leading article of April 18, you raised the serious question of supply, demand, and placement of doctors in the future, and touched briefly on the matter of distribution. In this you stated: "The Medical Practices Committee emphasises the difficulties of attempting to predict future requirements of doctors in the present changing situation. Nevertheless the attempt should be made."

I would like to endorse your plea for such an attempt and stress the urgency of beginning at once in spite of the very obvious difficulties. In professional, and in lesser degree in economic, terms failure to make such calculations with reasonable accuracy is perhaps the greatest hazard facing the N.H.S. in the years ahead.

Too many doctors, or "bottlenecks" which slow down or prevent a steady professional advancement, thus artificially creating a state of over-supply at different levels in a planned medical service, are destructive not only to the morale of the doctors concerned but to the quality of the service as a whole.

An assessment of the supply of doctors needed should be attempted concurrently with the inquiry into the costs of the N.H.S. The two are intimately related (more so in the long run), and the one can lend force and direction to the other.

In approaching this problem of supply of doctors it would be desirable, in the first instance, to try to disregard the limitations and difficulties imposed by the existing administrative and legislative framework of the Act, and to concentrate on *real* needs. If these can be assessed with some accuracy—and I believe they can—it should be possible then to modify them in terms of the present Act, or better still to make intelligent modifications to the legislation and administrative machinery so that the *real* needs can be met. There is always a tendency to accept the existing terms of reference of a service like the N.H.S. as more or less immutable and to gear our thinking and predictions to these. If we concede to this tendency the terms soon do become unchangeable. One way to avoid this danger is to take stock about every five years, in absolute terms as suggested above, and then to review legislation and administration in this light. We have now reached this point and the need is apparent.

How difficult is the problem of predicting "future requirements of doctors in the present changing situation"? At the level of specialist services it should not be too difficult; certainly not so far as the hospital aspect is concerned. A great deal is now known about the incidence of illness requiring hospitalisation, the number of special and general hospital beds necessary per unit of population, and the specialists required to service a good modern hospital properly. This then becomes a big, but not too difficult, problem in statistics.

Predictions relating to general practice are much more difficult; and, before these can be made with any degree of accuracy at all, certain premises need to be established. How much and in what direction is general practice going to change? Are the present trends of more and more specialist services, and a lower and lower level of general-practitioner services, to continue? Will the general practitioner go on working alone or in a form of loose partnership agreement? Is properly planned and organised group practice to replace the inefficient and outmoded form of individual practice? Sound assessments of national requirements for general practitioners depend on answers to these questions. If they cannot be answered in absolute terms, it becomes necessary to establish certain theoretical assumptions and to make profession is not its skilled labour nor the citizen its raw material The medical profession is continuing within the service the work it was already doing before the service existed The citizen can use it or not as he sees fit A bad mistake was made at its christening—at once the consequence and the cause of much confused thinking "N M S," not "N H S," should have been its name, but at least we were spared "National Health Industry", and this is just as well, for if the "industry" conception prevails both doctor and citizen-patient must expect a curtailment of liberty in the interests of industrial efficiency far greater than that which occurs when a free, self-governing profession becomes a profession within a service

London N W 3 **Lindsey W Batten**

ALCOHOL PAIN IN HODGKIN'S DISEASE

Sir,—Not only Danish beer has the effect on Hodgkin's disease described by Professor Bichel and Dr Bastrup-Madsen (April 18)

In July, 1950, a man of 56 was referred to me because of severe hypogastric pain after drinking alcohol I could find no abnormality and advised him to stop drinking For five months he did so and had no pain, then he tried a glass of beer and was as bad as ever Because he had lost weight he came to see me again, and I found rubbery glands above both clavicles Biopsy, response to irradiation, and subsequent death were all typical of Hodgkin's disease

It seems odd that this striking symptom should not have attracted notice before this relatively abstemious age

London, W 1 **C P Petch**

Medicine and the Law

Alleged Negligence in Blood-transfusion

In Crawford *v* Board of Governors of Charing Cross Hospital [1] a practitioner was held to have been negligent in respect of the posture of the arm during a blood-transfusion The patient, a man aged 52, was undergoing a bladder operation, and for this purpose was placed in the Trendelenburg position with his head and shoulders lower than his pelvis His left arm was extended and secured at right angles to his body so that the transfusion could be given during the operation After the operation the extended arm was partially paralysed The right arm was already almost useless as a consequence of infantile paralysis in childhood

The patient sued the hospital governors, their servants or agents, for damages for the injury to his left arm Mr Justice Gerrard held that the operation itself had been completely successful and observed that allegations of negligence against the surgeon had been rightly withdrawn The only charge of negligence which had been proved, he said, was that the anæsthetist who administered the blood-transfusion had been at fault in the particular circumstances of the case in not avoiding the extension of the left arm "at any rate to the degree he permitted" for longer than was necessary The anæsthetist was in this respect negligent and his negligence had contributed to the very severe degree of brachial paralysis suffered by the plaintiff His Lordship assessed the damages at £4000, taking into account the evidence that the patient's state of health was very poor and that his expectation of life was no more than eight years Judgment, therefore, was given for the plaintiff, but a stay of execution was granted, pending appeal It would seem difficult, indeed, to establish the moment at which the extension of the patient's arm, if initially placed in a proper position, became negligent

Public Health

Smallpox

In the outbreak in Lancashire and the West Riding, the illness of a woman in Bury, mentioned in last week's report, has been confirmed as smallpox There have been no more cases and no more patients have died The total of confirmed cases is 26, including 6 deaths

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Statistical Review of 1951

The medical tables included in the Registrar General's statistical review of England and Wales in 1951 were published this week [2] They contain detailed mortality statistics analysed by sex, age, and cause of death Many of the figures are also shown on a geographical basis The recent report of the chief medical officer of the Ministry of Health cited many of these statistics, some of which we mentioned in our summary of the report [3]

1952 in Eire

The birth-rate in Eire increased from 21 2 per 1000 population in 1951 to 21 8 per 1000 in 1952 [4] The infant mortality rate fell to 41 per 1000 registered births—the lowest figure yet recorded The death-rate of 11 9 per 1000 population was 2 4 less than in 1951 The decline in the number of deaths from tuberculosis continues, the death-rate in 1952 was 0 5 per 1000 population, and the figures for 1952 are less than half those for 1947

Pneumoconiosis in Boiler-scalers

Boiler-scaling is added to the occupations which are covered for pneumoconiosis under the National Insurance (Industrial Injuries) Act by regulations [5] made by the Minister of National Insurance Under these regulations, which came into operation on April 22, boiler-scalers who suspect that they have contracted pneumoconiosis may claim benefit under the Act

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At its meeting on April 23 the London County Council health committee expressed its appreciation of the work of the London Ambulance Service personnel who helped to deal with the accident on the London underground railway at Stratford on April 8 The mutual assistance arrangements between the L C C and the ambulance service authorities whose areas border on the County of London worked very effectively The committee was told that as a result of experience gained in the Harrow railway disaster in October, arrangements had been made to keep an ambulance, fully loaded with a comprehensive reserve supply of first-aid equipment, standing

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[1] *Times*, April 23

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[1] Registrar General's return for the week ended April 18, 1953 H M Stationery Office Pp 20 1*s*

[2] The Registrar General's Statistical Review of England and Wales for the Year 1951 Tables Part I Medical H M Stationery Office Pp 474 12*s* 6*d*

[3] See *Lancet* April 18 1953 p 790

[4] Quarterly Return of the marriages births and deaths registered during the December quarter 1952 and yearly summary 1952 Government Publications Sale Office, G P O Arcade Dublin Pp 25 6*d*

[5] The National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment Regulations, 1953 S I 1953 no 609 H M Stationery Office 3*d*

logy (on duplicate smears); and (5) estimation of "radiation response."

Cytology certainly misses a small proportion of the cases of cancer of the uterus, but biopsies are not infallible. The methods are not rivals, and our gynæcologists have shown that they want the additional information and safeguard of the vaginal smear. I have been worried about the danger of occasional potentially misleading cytological reports. It was pleasing to learn that the three gynæcologists discount this entirely. We are agreed, however, that the cytologist must have proved his reliability in other fields of gynæcological pathology, and that the work cannot be left to beginners and technicians.

Vaginal cytology need not be confined to "larger teaching centres where adequate funds and skilled staff are available." The method is less expensive than bacteriology, and we have proved that hospitals can be served by the existing staff. The confusion again comes from cytology done for "cancer prevention clinics": the thought of checking every woman in the Kingdom once or twice a year certainly makes one shudder. That is very different from checking every woman who complains of some symptom that ought to be investigated.

We do not employ Papanicolaou's five classes because they give the impression that a woman may have "a touch of cancer," and that cytology can say how bad the disease is. Actually one of the greatest values of cytology is its inability to distinguish between carcinoma-in-situ and the most advanced invasive squamous-cell carcinoma.

You are also wrong in saying that "the diagnosis can only be provisional." In most, but not all, it is just as certainly a cancer cytologically as histologically. Cytology does not determine the extent of a tumour, its invasiveness, or its method of treatment.

I believe that you are also wrong in stating that there is continuous desquamation from the columnar epithelia of the cervix, endometrium, and fallopian tube; and in suggesting that cyclical changes in desquamated epithelial squames enable us to recognise the different phases of the menstrual cycle in humans.

Cytology comes into disrepute when it is practised by those who are inadequately trained, and when pretentious reports are made. I feel certain that in a few years from now no pathological laboratory will be considered good if it lacks a reliable cytology section.

Derbyshire Royal Infirmary, Derby.

G. R. OSBORN
Pathologist.

SIR,—In spite of the shortcomings of the vaginal smear technique, "its expense and the tremendous time it takes," a considerable literature in many languages has accumulated to testify to its value to the endocrinologist and the gynæcologist. The list of references and the summary account in your leading article might lead the reader to suppose that the method is designed for cancer detection alone.

Even if this one application be considered, the method deserves a wider trial than it has yet been given in this country. Five hundred hours spent "searching for an elusive cancer cell in vaginal smears" is well spent if that particular cancer could not have been detected clinically or by other means. What other diagnostic procedure can detect a cancer which is symptomless, which has not yet given a sign to indicate the site from which a biopsy may with advantage be taken, and which is, moreover, at a stage when it can almost certainly be eradicated? It is the question of alternatives that is of paramount importance when the value of a method is to be assessed, not its hypothetical cost in working hours. Who would care to put a price in working hours upon the life of his daughter or his wife?

Royal Free Hospital,
London, W.C.1.

MARY E. EGERTON.

HAZARDS OF LUMBAR PUNCTURE

SIR,—In your leading article (April 11) you said that "the occurrence of headaches in 40% of ambulant patients in Sciarra's series confirms the idea that twenty-four hours' rest in bed is advisable after lumbar puncture."

Our experience is at variance with this statement and supports the findings of other authorities, especially those of Torbert,[1] who found the incidence of headaches after lumbar puncture to be 22% in inpatients, compared with 20% in outpatients, and Blau[2] who observed headaches in 22% of patients who rested at the clinic and at home, compared with 39% in those rested at home only and 13·6% in those who had no rest at all. Underwood[3] noted 25% headaches with eight to twenty-four hours' rest, 17% headaches with less than eight hours' rest, and 15% headaches with no rest at all; while Emory's statistics[4] showed that 39·5% had headaches with immediate bed rest, 38·8% had headaches with bed rest after four hours, and 35·5% had headaches with no rest at all.

In this department experience based upon control investigation over the past six years, has led us to believe that the majority of patients fare no worse if the twenty-four hours' rest is omitted. After allowing for the greater incidence of headaches in those with normal cerebrospinal fluids, we agree with Dattner,[5] who observed that absolute bed rest following lumbar puncture may result in more headaches than lively activity; and it is apparent that neither is effective in counteracting all the unpleasant sequelæ.

Department of Venereology,
Newcastle General Hospital,
Newcastle upon Tyne.

W. V. MACFARLANE
R. PICK
C. B. S. SCHOFIELD.

THE SENIOR REGISTRAR

SIR,—The letter from Dr. Forrester and Dr. Walton (April 18) draws attention to the senior registrar crisis, but seems to understate the magnitude of the problem. Their investigations have discovered 279 senior registrars in their fourth or subsequent years, with more returns still to come in. But what really matters is the number now in the market for consultant posts; and to estimate this, one must add to the 279 + the number now employed as research assistants or junior lecturers and the number of ex-senior-registrars who are not employed at all, or working from month to month as locums. It seems improbable that these luckless ones could figure in any regional board return; and, indeed, the only way of counting their heads would appear to be to ask them to write to the chairman of the Registrars' Group.

Young men are wise in their reluctance to embark on the long grind of specialist training, for there seems to be little comprehension among their seniors of the gross excess of men in training over prospective consultant vacancies. Consider a hospital where 15 consultants are employed. If appointed at the age of 35, a consultant's professional life is thirty years. The hospital will therefore have 15 consultant vacancies in thirty years, and should train 15 men to be consultants in that time. A senior registrar is appointed for four years; if the hospital employs only two senior registrars it will train 15 consultants in thirty years. Since a registrar is appointed for two years only, the number employed should be half the number of senior registrars if the appointment is to be regarded as the first step on the consultant ladder. No doubt there should be a slightly higher proportion of men in training to allow for early coronary thromboses among consultants and for consultant exports to a diminishing Empire. But

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1. Torbert, H. C. *Arch. Derm. Syph., N.Y.* 1934, 30, 692.
2. Blau, A. *Urol. cutan. Rev.* 1941, 45, 239.
3. Underwood, L. J. *Amer. J. Syph.* 1946, 30, 249.
4. Emory, M. L. *Amer. Practit.* 1948, 2, 451.
5. Dattner, B. The Management of Neurosyphilis. London, 1944 p. 32.

profession is not its skilled labour nor the citizen its raw material The medical profession is continuing within the service the work it was already doing before the service existed The citizen can use it or not as he sees fit A bad mistake was made at its christening—at once the consequence and the cause of much confused thinking "N M S," not "N H S," should have been its name, but at least we were spared "National Health Industry", and this is just as well, for if the "industry" conception prevails both doctor and citizen-patient must expect a curtailment of liberty in the interests of industrial efficiency far greater than that which occurs when a free, self-governing profession becomes a profession within a service

London, N W 3 LINDSEY W BATTEN

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[1] Registrar General's return for the week ended April 18, 1953 H M Stationery Office Pp 20 *1s*

[2] The Registrar General's Statistical Review of England and Wales for the Year 1951 Tables Part I Medical H M Stationery Office Pp 474 *12s 6d*

[3] See *Lancet* April 18 1953 p 790

[4] Quarterly Return of the marriages births, and deaths registered during the December quarter 1952, and yearly summary 1952 Government *Publications* Sale Office, G P O Arcade Dublin Pp 25 *6d*

[5] The National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment Regulations, 1953 S I 1953 no 669 H M Stationery Office *3d*

Flagellar antigen determinations provide a means of undertaking more detailed epidemiological studies of the *Bact. coli* types associated with infantile diarrhœa and vomiting. Inclusion of H-antigen typing is of advantage in cross-infection investigations[5] made in a particular locality, and may also be of value, in view of the occurrence of these *Bact. coli* types in cities as far apart as Nagoya and London, in the study of the possible spread of these strains from one country to another.

St. Ann's General Hospital,
London, N.15.
JOYCE WRIGHT.

CARDIAC ASTHMA

SIR,—Dr. Kynaston's comment (April 4) on his patient who had 67 attacks of cardiac asthma is surprising. That the condition should recur so frequently would appear to refute his conclusion that "morphine is the drug par excellence in cardiac asthma."

It is unusual for a hypertensive patient to survive the first attack of cardiac asthma for more than two years, but during this time attacks may not only be aborted but lessened in frequency by administering aminophylline, which has been shown to alleviate pulmonary congestion—perhaps most strikingly in hypertensive left ventricular failure, but no less effectively in aortic stenosis and mitral stenosis and also to a lesser extent in cor pulmonale.

Aminophylline (theophylline with ethylene diamine) is effective intravenously but of little use by any other route. My own practice in treating cardiac asthma is to combine injectio mersalyl *B.P.* 2 ml. with 18 ml. injectio aminophylline *B.P.* (containing 0·45 g. aminophylline), given during 10 minutes, provided that the patient has shown no intolerance of intramuscular mersalyl.

I should appreciate enlightenment as to whether my impression that slow intravenous injections of mersalyl are safer than quicker injections is well founded.

Guernsey. BRIAN WEBBER.

AN UNUSUAL TYPE OF HERNIA

SIR,—I have just read Mr. Howard's article (Feb. 21). This reminds me of a West African man of about 40 years of age on whom I operated two years ago in Nigeria.

> He had complained of pain in his left groin for 6 months and of swelling in each groin for many years. There were small, rounded lumps in each inguinal region over the site of the external ring; they were soft and partly reducible and had a cough impulse. At operation a mass of fat presented at the external ring. It was about 7 cm. in length and placed above the cord and separate from it. On dissection I found, to my surprise, that there was no hernial sac associated with the cord, but that there was a narrow sac inside the mass of fat; and this sac had its neck directed medially and its fundus laterally. It was in fact lying obliquely in the line of the inguinal canal, but with its neck at the external ring instead of the internal ring. Careful dissection of the neck showed that this passed through a small circular aperture in the conjoined tendon just deep to the place where the upper crus of the external ring meets the reflected inguinal ligament. Muscles and tendons were in good condition and the aperture had every appearance of being congenital in origin.
>
> The sac was too narrow to admit the little finger and was 6 cm. in length. A pair of artery forceps passing down the sac and through the neck entered the abdominal cavity in the direction of the fundus of the bladder, and the forceps could not be turned into any other direction while in this situation. The sac contained a little clear gelatinous fluid only and had evidently never been stretched by the entry of gut into it, at least in adult life. The cord and testis were of normal appearance and size. Operation on the other side revealed an identical type of hernia, and I could find no explanation why only one side had caused him pain. In each case, the sac was tied at the neck and removed, and the small aperture in the conjoined tendon closed by one stitch. This aperture was just medial to the pubic tubercle, and about 3 cm. above it.

This hernia had every appearance of being congenital, but I am quite unable to explain its site. After finding it I had plenty of opportunity to examine other cases of indirect inguinal hernia in Africans of the same tribe, but found nothing about their conjoined tendons to give a clue. It resembles in site a supravesical hernia, but I have so far found nothing in accounts of rare hernias that quite compares with it. The resemblance of this hernia with that described by Mr. Howard lies in the fact that both simulated indirect inguinal herniation and both came through minute openings in the transversalis and internal oblique muscle planes, although these openings were widely divergent.

Methodist Hospital
Segbwema, Sierra Leone.
J. R. ROSE
Superintendent.

TUBERCULOSIS IN GLASGOW

SIR,—There has been much speculation about the high incidence of tuberculosis in Glasgow, but a short visit by one not acquainted with local conditions will soon reveal some of the most important causes.

The housing conditions of many of the people are appalling by Southern standards. They have been described on many occasions. However, a visit with a general practitioner to an unselected patient in Anderson Ward revealed a little of this problem. The patient, a boy of six, the eldest surviving child in the family, was in bed in the "house."

> This was of the usual Glasgow type—one all-purpose room with the parents' bed in an alcove and another very small room just big enough to take the double bed in which all the children slept. The "house" was approached through a dark, damp corridor and then up three flights of the common stairway, ill lit, with a common lavatory on each floor. Off this floor five doors led to five "houses," each of which held a minimum of four people.

The patient, who had a temperature of 102°F, was ill with his sixth episode of bronchopneumonia. The mother was eight months pregnant and the father had just arrived home from Territorial Army training. He told us a little of their housing problem. They had been on the housing list for eight years. Twelve months previously, when the wife was in hospital having their fourth child, the rats were so troublesome that they took possession of the children's room and consequently the family slept in one large bed. Two days after the mother returned from hospital the newly born child was overlain and died. No open inquiry is held in Scotland in such circumstances. The parents assured me that their conditions were better than those of many others. Thousands of families live in such conditions, and it is to circumstances such as these that many patients return when hospital treatment for tuberculosis is finished.

I was amazed to learn that no consultant in tuberculosis had yet been appointed to the whole region of South-west Scotland, of which Glasgow is the centre. I met a doctor who as senior hospital medical officer is in charge of 350 beds and has many clinic responsibilities as well.

There has been little or no secondment of nurses from general hospitals to sanatoria or other hospitals where tuberculosis is treated. I was told that a doctor, prominent on administrative committees, had stated that if secondment from general hospitals was accepted he would withdraw his daughter from nursing. If this is the attitude which obtains in influential quarters there seems little hope of an intelligent approach to the nursing problem of tuberculosis.

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[5] Wright, J. *Mschr. Kinderheilk.* 1953, 101, 108.

profession is not its skilled labour nor the citizen its raw material. The medical profession is continuing within the service the work it was already doing before the service existed The citizen can use it or not as he sees fit A bad mistake was made at its christening—at once the consequence and the cause of much confused thinking "N M S," not "N H S," should have been its name, but at least we were spared "National Health Industry", and this is just as well, for if the "industry" conception prevails both doctor and citizen-patient must expect a curtailment of liberty in the interests of industrial efficiency far greater than that which occurs when a free, self-governing profession becomes a profession within a service

London N W 3 LINDSEY W BATTEN

ALCOHOL PAIN IN HODGKIN'S DISEASE

SIR,—Not only Danish beer has the effect on Hodgkin's disease described by Professor Bichel and Dr Bastrup-Madsen (April 18)

In July 1950, a man of 56 was referred to me because of severe hypogastric pain after drinking alcohol I could find no abnormality and advised him to stop drinking For five months he did so and had no pain, then he tried a glass of beer and was as bad as ever Because he had lost weight he came to see me again, and I found rubbery glands above both clavicles Biopsy, response to irradiation, and subsequent death were all typical of Hodgkin's disease

It seems odd that this striking symptom should not have attracted notice before this relatively abstemious age

London W 1 C P PETCH

Medicine and the Law

Alleged Negligence in Blood-transfusion

IN Crawford *v* Board of Governors of Charing Cross Hospital[1] a practitioner was held to have been negligent in respect of the posture of the arm during a blood-transfusion The patient, a man aged 52, was undergoing a bladder operation, and for this purpose was placed in the Trendelenburg position with his head and shoulders lower than his pelvis His left arm was extended and secured at right angles to his body so that the transfusion could be given during the operation After the operation the extended arm was partially paralysed The right arm was already almost useless as a consequence of infantile paralysis in childhood

The patient sued the hospital governors, their servants or agents, for damages for the injury to his left arm Mr Justice Gerrard held that the operation itself had been completely successful and observed that allegations of negligence against the surgeon had been rightly withdrawn The only charge of negligence which had been proved, he said, was that the anæsthetist who administered the blood-transfusion had been at fault in the particular circumstances of the case in not avoiding the extension of the left arm "at any rate to the degree he permitted" for longer than was necessary The anæsthetist was in this respect negligent and his negligence had contributed to the very severe degree of brachial paralysis suffered by the plaintiff His Lordship assessed the damages at £4000, taking into account the evidence that the patient's state of health was very poor and that his expectation of life was no more than eight years Judgment, therefore, was given for the plaintiff, but a stay of execution was granted, pending appeal It would seem difficult, indeed, to establish the moment at which the extension of the patient's arm, if initially placed in a proper position, became negligent

Public Health

Smallpox

IN the outbreak in Lancashire and the West Riding, th illness of a woman in Bury, mentioned in last week' report, has been confirmed as smallpox There hav been no more cases and no more patients have died Th total of confirmed cases is 26, including 6 deaths

First Quarter in England and Wales

The Registrar-General's provisional figures for Englan and Wales for the first quarter of 1953[1] show that th stillbirth-rate has fallen to a new low level and that th infant-mortality rate was the second lowest recorde for any March quarter There were 3597 stillbirth registered, giving a rate of 22 5 per 1000 total birth compared with 4146 and a rate of 23 3 per 1000 in th first quarter of 1952 (The figures for the first quarter o 1938 were 6185 and 38 3 per 1000) The infant mortalit rate was 33 8 per 1000 live births, compared with 33 4 p 1000 in the corresponding quarter of 1952, which wa the best March quarter on record The birth rat fell slightly to 15 8 per 1000 population, in the firs quarters of 1951 and 1952 the rate was 16 3 and 15 per 1000 population respectively

Statistical Review of 1951

The medical tables included in the Registrar General's statistical review of England and Wales in 1951 wer published this week[2] They contain detailed mortality statistics analysed by sex, age, and cause of death Many of the figures are also shown on a geographical basis The recent report of the chief medical officer of the Ministry of Health cited many of these statistics, some of which we mentioned in our summary of the report[3]

1952 in Eire

The birth-rate in Eire increased from 21 2 per 1000 population in 1951 to 21 8 per 1000 in 1952[4] The infant mortality rate fell to 41 per 1000 registered births—the lowest figure yet recorded The death-rate of 11 per 1000 population was 2 4 less than in 1951 The decline in the number of deaths from tuberculosis continues, the death-rate in 1952 was 0 5 per 1000 population, and the figures for 1952 are less than half those for 1947

Pneumoconiosis in Boiler-scalers

Boiler-scaling is added to the occupations which are covered for pneumoconiosis under the National Insurance (Industrial Injuries) Act by regulations[5] made by the Minister of National Insurance Under these regulations which came into operation on April 22, boiler scalers who suspect that they have contracted pneumoconiosi may claim benefit under the Act

The Stratford Accident

At its meeting on April 23 the London County Council health committee expressed its appreciation of the work of the London Ambulance Service personnel who helped to deal with the accident on the London underground railway at Stratford on April 8 The mutual assistance arrangements between the L C C and the ambulance service authorities whose areas border on the County of London worked very effectively The committee was told that as a result of experience gained in the Harrow railway disaster in October, arrangements had been made to keep an ambulance, fully loaded with a comprehensive reserve supply of first-aid equipment, standing

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[1] *Times*, April 23

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[1] Registrar General's return for the week ended April 18, 1953 H M Stationery Office Pp 20 1s

[2] The Registrar General's Statistical Review of England and Wales for the Year 1951 Tables Part I Medical H M Stationery Office Pp 474 12s 6d

[3] See *Lancet* April 18 1953 p 790

[4] Quarterly Return of the marriages births and deaths registered during the December quarter 1952 and yearly summary 1952 Government Publications Sale Office, G P O Arcade Dublin Pp 25 6d

[5] The National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment Regulations 1953 S I 1953 no 609 H M Stationery Office 3d

23 chest clinics and survey units of the Bureau of Tuberculosis, these criteria were satisfied in 20 cases.

With 1 exception, the patients were between 19 and 31 years of age. 10 patients were negative to 1 mg. of Old Tuberculin, and 1 was negative to 0·01 mg., while 4 were positive to 0·01 mg. and 4 to 1 mg. (in 1 case no test was made). 18 patients had bilateral, and 2 unilateral, involvement. Paratracheal-gland enlargement was seen in 7 patients. In 11 patients who could be reviewed at sufficiently frequent intervals, complete disappearance of glandular enlargement was observed in from ten weeks to nine months. All of the patients studied for a mean period of five years have remained in good health, without evidence of recurrence or other visceral involvement.

During the last few years, only 3 cases of apparently asymptomatic hilar lymphadenopathy have been discovered in the Hull district by means of mass miniature radiography. These cases are being kept under observation, and if the numbers warrant it, they will be reported in more detail later.

Here, then, are some of the questions to be answered:

(1) How many of these cases are there in Great Britain? How many of these have (*a*) no symptoms; (*b*) erythema nodosum (excluding obvious cases of primary tuberculosis); and (*c*) clinical and histopathological evidence of sarcoidosis.?

(2) What is the age and sex incidence, and the reaction to tuberculin?

(3) Is there any seasonal incidence (as in erythema nodosum)?

(4) Why is the condition so much commoner in Scandinavia?

(5) Has this geographical difference any relation to the later age at which primary tuberculous infections tend to occur or to the more general use of B.C.G. in Scandinavia?

(6) Are some of these asymptomatic cases *formes frustes* sarcoidosis?

(7) What virus or bacterial infections can give rise to tuberculin-neutralising effects?

(8) What is the true value of the Kveim test?

Hull.

LASAR DUNNER
R. HERMON.

CIRCUMCISION OF THE NEWBORN

SIR,—Is there not a real danger of serious bleeding from hæmorrhagic disease of the newborn if circumcision is carried out at birth, as reported in your annotation last week? This danger may well have been the reason for ritual circumcision being delayed till the eighth day of life.

London, W.1. DAVID MORRIS.

ACRYLIC PROSTHESES

SIR,—In recent months a number of Judet acrylic prostheses have had to be removed from patients because of mechanical failure. These failures may be due to one or more of the following factors: (1) unsuitability of the materials employed; (2) design; (3) manufacturing methods; (4) sterilisation procedures; (5) position of insertion of the prosthesis and fit of the acrylic head in the acetabulum. In collaboration with Mr. J. M. Zarek, PH.D., of the faculty of engineering, King's College, University of London, experimental work is being carried out, the results of which it is hoped may shed some light on the cause of these failures.

The number of cases to which we have access is naturally limited. It would be of the greatest assistance if surgeons and pathologists who remove from a patient any prosthesis (which may or may not be broken) either at operation or post mortem, would be kind enough to send it to me at the Plastics Research Unit, Institute of Orthopædics (University of London), Royal National Orthopædic Hospital, Brockley Hill, Stanmore, Middlesex. The following information is required:

(*a*) A brief preoperative and postoperative case-history with the actual or estimated weight of the patient. Personal details which might identify the patients are not required.

(*b*) All radiographs in which the prosthesis can be seen. These will be returned.

(*c*) Details of method of sterilisation and, if possible, information on whether the prosthesis has been sterilised on a number of occasions.

(*d*) The prosthesis.

It is hoped that all those interested in this problem will coöperate, as an investigation of this kind can only be of value if as many as possible of the failures are investigated.

JOHN T. SCALES.

POLIOMYELITIS

SIR,—Your leading article of Jan. 10 has provoked several letters from orthopædic surgeons; and this is not surprising, as this leader exaggerated somewhat the recent views on treatment put forward by various people including myself.

I would, however, make a special plea to my orthopædic colleagues to widen their thoughts beyond muscle resting and the avoidance of deformity. The motor pathways in the spinal cord terminate in a pool of neurones, and each tract neurone communicates with many anterior horn cells. If, say, half of these cells are destroyed, the connections of this neuronal pool have to become extensively reorganised, and it is probable that the only effective method of getting the best out of this reorganisation is through the patient's determined and repeated attempts to move the muscle groups which appear to be paralysed. This provides a physiological explanation for the well-known fact that it is the patients who try hard who recover most. I would submit that the current orthopædic practice of discouraging activity in weak muscles for several months is likely to lose the opportunity to retrain the spinal connections in the optimum direction, and that under such methods the disconnected neurones of the spinal tracts are likely to be diverted more to muscles which are strong than weak, as the patient's spontaneous movements in bed are likely to be directed first to the movements he can make.

It is for such reasons that I and others advise early active movements to the weak and important muscle groups, which the patient practises himself after being shown how to do it. There is no substitute for the patient's will to move a muscle as far as the central nervous system is concerned. Fear of muscle fatigue after the acute stage has passed is quite unreasonable to the neurophysiologist, and simple muscle measurements easily confirm the harmlessness of deliberately induced fatigue in weak muscle groups at this stage.

Mr. Hyman (April 25) reports a remarkable case he saw in 1949, in which paralysis spread 5 weeks after the acute illness. However, his conclusion that this was due to the patient exercising too much is hardly justifiable. It is more probable that the patient had a second infection with another strain of the virus. Relapsing cases occasionally occur; but the second bout of paralysis very rarely, if ever, occurs at an interval of more than a week after the first has ceased to spread; it is for fear of this second spread that complete rest and heavy sedation seem to be so desirable for the first 2–3 weeks of the acute illness. It is conceivable that this period of 2–3 weeks should be prolonged a little if other cases like Mr. Hyman's are reported; but apart from his case, existing evidence suggests that complete rest for 2 weeks is long enough.

Department of Neurology,
Radcliffe Infirmary,
Oxford.

W. RITCHIE RUSSELL.

SIR,—I have been interested in the question of exercise in poliomyelitis since the 1947 outbreak, when I began tentatively to encourage active exercise during the third

Notes and News

EMPIRE RHEUMATISM COUNCIL

IN his report to the annual meeting of the Empire Rheumatism Council on April 29, Lord Horder, the chairman, remarked that in the past year the Council's research activities had been on a greater scale than ever before At the Hospital of St John and St Elizabeth, London, Mr A A Henly, PH D, assisted by Miss M I Potter, had continued research on steroid metabolism From this it seemed that there was no relation between urinary steroid excretion before treatment and the patient's requirements for A C T H or cortisone, but changes in the level of steroid excretion were fairly consistently related to the amount of hormone administered Experimental and clinical results had clearly shown the superior efficiency of A C T H given by continuous intravenous infusion instead of by intermittent injections Other investigators working under the ægis of the council included Dr J L Potter at the Northern General Hospital, Edinburgh, who had observed in cases of ankylosing spondylitis and rheumatoid arthritis that radiotherapy apparently caused improvement which could not be attributed to any direct effect of radiation on the diseased areas

The finance committee reported that in the year 1951–52 income amounted to *£16,965*, compared with *£20,332* in 1950–51 Expenditure totalled £14,553

COOPERATION IN THE HEALTH SERVICE

A YEAR ago the Ministry of Health proposed that a conference should be held to discuss measures for promoting coöperation between the administrative authorities of the National Health Service The London County Council and the regional hospital boards have since stated that they consider that liaison between the branches of the service is adequate, but they suggest that if any new consultative machinery is needed it should be based on hospital management committees The Metropolitan Boroughs' Standing Joint Committee also does not think it necessary to set up an independent consultative body, for it is satisfied with the present methods of cross representation, consultation between officers, and exchange of documents But it feels that there would be an advantage in councils having direct representation on H M C S At present, though councils are consulted about the membership of H M C s, there is no guarantee that their nominees will be elected At its meeting on April 23, the London Executive Council expressed its agreement with the views of the joint committee

AN UNNECESSARY VISIT

A PATIENT's offer to pay her National Health Service doctor a fee for a domiciliary visit made out of consideration for her convenience rather than her health was reported at a meeting of the London Executive Council on April 23 The patient stated frankly that she was well enough to go to her doctor's surgery, but preferred that he should visit her in her own home For this privilege she was willing to pay him a fee The Executive Council explained that the doctor by his terms of service was precluded from accepting such a fee, though he was free if he wished to visit a patient, even when it was not strictly necessary, he could make no charge for doing so The patient then referred the problem to the Ministry of Health on the grounds that, though the regulations forbade a doctor to accept payment for "medical treatment," travelling to a patient's home was not "treatment" The Minister, however, held that travelling was always involved when a doctor visited a patient and was part of the doctor's normal expenses on which his remuneration was based The Minister was unwilling to accept the responsibility for distinguishing between necessary and unnecessary visits and added that in his view to do so would "inevitably lead to misunderstandings, complaints and abuses, it would place a new and unwelcome burden of responsibility on doctors, and, at the same time, bring the Service into disrepute"

NEW PLANS AT OXFORD

BUILDING restrictions have hampered the growth of the clinical school established at Oxford in 1946, but there is now encouraging news The university and the board of governors of the United Oxford Hospitals have agreed in principle to a plan for building on the site of the Radcliffe Infirmary The plan awaits approval by the Ministry of Health It will strengthen the school in two ways Firstly, all the beds of the Nuffield professor of clinical medicine will be at the Radcliffe Infirmary, at present half of them are at the Churchill Hospital, where they are less useful for teaching The new department of clinical medicine will include improved laboratory accommodation Secondly, the board of the faculty of medicine has lately recommended that the next Nuffield professor of surgery, to be appointed in succession to the late Sir Hugh Cairns, should be a general surgeon, and the plan provides for a new department of surgery, also in the Radcliffe Infirmary, with about 50 beds, an operating theatre, and laboratories Both clinical research and teaching will benefit from the proposed changes The board of governors is making temporary arrangements, which will increase the number of beds at the Radcliffe Infirmary, until the new building is complete

OLD PEOPLE IN LIVERPOOL

ELDERLY Liverpudlians seem to be cautious of invoking statutory attentions, benevolent though these may be The Liverpool Personal Service Society, in conjunction with the department of social science of Liverpool University, during a survey [1] made between September, 1951, and January, 1952, found for instance that old people needing nursing care had not always applied for a nurse, though well aware they could have one if they liked They summed up their distrust in the remark "You never know what's for the best you might be worse off in the end" These independent tastes were probably responsible for the fact that the demand for social services among the elderly people was small Of the 500 interviewed—344 women over 60 and 155 men over 65 (in one case the sex was not recorded)—only 5 were found to be seriously short of friendly or neighbourly help

The old people visited were living in five areas in various parts of Liverpool The interviewers went from house to house in the areas chosen until they found they had visited 100 old people in each Only 47 of the 500 were living alone in houses or self contained flats, and only 42 alone in rooms, the rest were living with a spouse or with other relatives, or as members of families not their own Only 40 were out of touch with their relations, and 24 of these were living alone Most of them, however, had good friends or neighbours, or were visited by members of their church or club Indeed the interviewers record that they were not able to confirm the belief that services to elderly people are no longer rendered freely by good neighbours many of those visited had friends who called in at least once a day "to see that they were all right" Where there were family ties these were strong

Some old people, however, were lonely and unhappy at times, and the interviewers draw attention to the need for more friendly visiting of housebound old people, and because the recipients have no great enthusiasm for official visits, this visiting should as far as possible be arranged as a voluntary service, and done by people they know already Leaders of churches are urged to consider ways of increasing visiting of the old The old people's welfare committees, by encouraging the formation of clubs and community centres, can give more old people an interest in life for many of them are housebound merely because they feel there is nothing to go out for The visiting officers of the National Assistance Board, the surveyors suggest, might encourage those who appear lonely or isolated to join the appropriate church, club, or community centre of their region And these officers might also take the opportunity, it is thought, of tactfully reminding old people who are beginning to find their housework too much for them that an allowance is payable for domestic help and laundry where these are needed

Two unnecessary frustrations came to light which old people might well be spared Benches in the parks and pleasanter streets or open places give a target for a little walk and provide meeting places for cronies, but there are not nearly enough of them A modest outlay on benches by the local authority would bring many old people out in sunny weather, to the benefit of their health and spirits The other common frustration is over coal supplies one in seven of the old people had trouble, either because deliveries were irregular and the coal men pressed them to take several weeks' ration at a time, or because coal merchants refused to deliver coal upstairs or made an extra charge for doing so, or because the old people were not able to get or afford the full ration or the extra allocation for those over 75, or because they had nowhere to store coal These are points which the old people's welfare committees might well take up and set right

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[1] Social Contacts in Old Age Liverpool The University Press 1953 Pp 35 2*s*

REMEDY FOR ANÆMIA

SIR,—Dr. Mennie (April 18) seems to think that most of the anæmic people in Britain today are getting too little food or the wrong sort of food. He also seems to believe that nutritional megaloblastic anæmias are common. Both these beliefs are erroneous.

In Britain today iron-deficiency anæmia is usually caused by pregnancy or by pathological bleeding, not by malnutrition. Most iron-deficient patients who fail to respond to iron salts by mouth respond quite well to saccharated iron hydroxide intravenously; they do not respond to liver or to folic acid. Slight differences in the speed of response to treatment are of little practical importance, because oral therapy with iron should be continued for some weeks even after apparent cure, and the dosage of intravenous iron is determined by the initial hæmoglobin level and the body-weight.

Nutritional megaloblastic anæmias are very rare. I have never seen that of pellagra nor that of infancy, and but 5 cases of megaloblastic anæmia of pregnancy among over 13,000 pregnant women. In Britain our common megaloblastic anæmia is pernicious anæmia, which is not a nutritional anæmia. Pernicious anæmia is better controlled by vitamin B_{12} than by liver.[1] It is well known that folic acid may precipitate subacute combined degeneration of the cord in a previously untreated patient suffering from pernicious anæmia. Suboptimal treatment of pernicious anæmia produces peculiar non-specific blood and bone-marrow changes which make diagnosis difficult or impossible.

Can Dr. Mennie wonder if I maintain that the remedy under discussion is unnecessary and probably dangerous, and that its introduction was against the best interests both of the patient and of the country?

Central Middlesex Hospital,
London, N.W.10.

GEORGE DISCOMBE.

CARCINOMA OF THE BLADDER

SIR,—The article by Mr. Winsbury-White (April 18) calls for some comment from radiotherapists.

I feel sure that nearly all radiotherapists have obtained good results from radon-seed implants, mostly, I admit, in non-infiltrating growths, but with a reasonable percentage of success in the infiltrating type confined to the bladder. Permanent disappearance of bladder cancer can be obtained also by well-planned X-ray therapy, including rotation methods. To attempt a bladder implantation without a good reserve supply of radon seeds is, of course, tragic; but this should never happen with adequate preliminary cystoscopy.

I would cite the five-year survival-rates in 95 patients published by the Holt Radium Institute, Manchester, in 1945:

Method	*Early*	*Late*
Cystotomy and intravesical radon..	59%	7%
X-ray therapy	60%	17%

London, W.1.

ANTHONY GREEN
Radiotherapist, Royal Northern Hospital.

SIR,—Mr. Winsbury-White's remarks about vesical papillomata interested and consoled me. I have been treating a woman, now aged 71, for this condition since 1931. Diathermy keeps her symptom-free. A short trial of podophyllin, applied locally, gave little relief to either party. An unusual complication afflicted another patient.

She first came under my care in 1933 when she was a patient in a mental hospital. Her age was 63 and she had undergone an open operation for vesical papilloma in 1928. Cystoscopy showed numerous papillomata covering the base of the bladder. These responded well to diathermy; her mental condition improved, and she was able to leave hospital.

She remained under regular observation and treatment until March, 1949. During this period she was known to have a lump, about the size of a walnut, in the suprapubic scar. She said there was occasional discharge from it but preferred not to have it examined. In January, 1944, she was admitted to a nursing-home bleeding freely from the tumour, which had increased in size. After a blood-transfusion had been given I excised the tumour, which was made up of two superimposed cysts with ossification in the walls. The pathologist's report was: "Implantation of papilloma into scar with calcification and ossification."

This patient made a good immediate recovery, but a few months later her mental disorder recurred, and she died with uræmic symptoms.

Northampton.

C. C. HOLMAN.

POLIOMYELITIS VACCINES

SIR,—Recent articles and reviews dealing with research on poliomyelitis virus and with poliomyelitis vaccines do not mention the work of G. Blanc and L. A. Martin at the Pasteur Institute of Morocco. These workers claim to have adapted the poliomyelitis virus (both the Brunhilde and the Lansing types) to the rabbit.[1] In this animal the virus causes a sharp febrile illness without paralysis, and the virus—recovered from the spleen—can be transmitted from rabbit to rabbit almost indefinitely.

The laboratory diagnosis of human non-paralytic poliomyelitis has been achieved by inoculation of the rabbit with specimens of fæces from the patients.[2]

These workers have also shown that this rabbit-fixed virus can be inoculated into hundreds of men, women, and children without any harm; and that when given in large quantities orally, it multiplies in the alimentary tract and behaves like an authentic poliomyelitis virus.[3] Admittedly their findings have not yet been confirmed, and they have yet to show that the rabbit-fixed virus can induce an active immunity against the human field-virus of poliomyelitis, but their work is full of so many far-reaching possibilities that it deserves at least a passing reference.

Park Hospital,
Hither Green,
London, S.E.13.

L. J. MAURICE LAURENT.

PROFESSIONALISM IN THE HEALTH SERVICE

SIR,—On Mr. Farrer-Brown's strictures (April 11) upon our professional standards and behaviour I would not dare to comment; but anyone, I think, is entitled to discuss whether the N.H.S. is an industry or not. Mr. Farrer-Brown says it is an industry "with the noblest of purposes." Wisely enough he leaves this purpose undefined; but, be it what it may, is not production, rather than purpose, the essential feature of an industry? Must it not have a product—coal, cocoa, or what you will?

What is the product of the N.H.S.? The only likely answer is "health" or "healthy citizens." But if this be so, why does it patch and keep alive so many cripples and "crocks," and why are not the homes, food, schools, occupations, and recreations of the citizens, on which their health chiefly depends, its foremost concern? I am sure the answer is that it is *not* an industry. Its supposed product, health, is only a by-product. If it is an industry, so are the educational services and the Royal Navy. It is a service, and not a health service but a medical service (or perhaps a medical and dental service).

It exists to give medical aid, comfort, and advice to those citizens who need or ask for it. The medical and fretful His skull circumference was $17\frac{1}{2}$ in and the fontanelle sunken There was no meningism Lumbar puncture produced purulent c s f, but organisms were not seen on direct smear and cultures were sterile

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[1] Brewerton, D. A., Asher, R. A. J. *Lancet*, 1952, ii, 265.

[1] Blanc, G., Martin, L. A. *Arch. Inst. Pasteur Maroc*, 1950, 4, 19.

[2] Martin, L. A., Delon, J., Grevin, J., Catala, L., Félix, J. *Pr. méd.* 1952, 60, 1179.

[3] Blanc, G., Martin, L. A. *Bull. Acad. nat. Méd.* 1952, 136, 655.

Intravenous fluids were started, and sulphadiazine 0 5 g six-hourly, penicillin 250,000 units six hourly, and streptomycin 100 mg b d were given The general condition improved a little, but the c s f remained abnormal, with increased cell and protein content A Mantoux test was negative in a dilution of 1 in 100

Towards the end of November it was noticed that the child's eyes had a fixed glazed appearance, the neck was slightly stiff, and there was a tendency to athetoid movements of the arms His head circumference was $17\frac{3}{4}$ in. Bilateral subdural taps were done, but no subdural fluid was obtained His general condition deteriorated, and on Dec 7 he had a generalised convulsion, which was controlled with chloral hydrate and phenobarbitone There were no further convulsions, but he lapsed into semicoma An air ventriculogram at this time showed severe symmetrical dilatation of both lateral ventricles and the third ventricle He was transferred to a neurosurgical unit for decompression, but died on Jan 2, 1952, before this could be done Necropsy was refused

Case 4 —A boy, aged 2 months, was admitted on Jan 1, 1952 He had been quite well up to the previous evening, when he developed a cough In the morning he refused his feeds and looked greyish A little later he had a generalised convulsion

On admission he was very ill and in respiratory distress His temperature was 98°F, his respirations were rapid and grunting, the alæ nasi were active, and there was slight cyanosis The eyes were rather staring, and there was an internal strabismus The anterior fontanelle was level and under normal tension, and there was no neck rigidity Kernig's sign was absent There was some diminished movement of the right lower chest, and crepitations were heard over the right lower lobe

TABLE II—SUMMARY OF CASES SHOWING NO "CLASSICAL" SIGNS OF MENINGITIS

Organism	No of cases	Symptoms					Recovered	Died
		Vomiting	Irritability	Anorexia	Drowsiness	Convulsions		
Meningococcus	3	0	1	2	0	1	2	1
Pneumococcus	2	2	0	0	1	0	1	1
Bact coli	4	2	1	0	0	0	0	4
H influenzæ	1	0	1	0	0	0	1	0
No organism isolated	3	1	2	2	0	0	2	1
Total	13	5	5	4	1	1	6	7

Treatment and Progress —Pneumonia was diagnosed, the child was put in an oxygen tent, and penicillin 50,000 units six hourly and sulphadiazine 0 25 g four hourly were given Next day the child was worse, and signs of bronchial spasm were noted in the right lower lobe, but otherwise the physical signs were unchanged and there was still no meningism. Streptomycin was substituted for sulphadiazine, and the dosage of penicillin was increased to 100,000 units six hourly, but his condition continued to deteriorate and he died on Jan 3

Necropsy —The meninges over the surface of the brain were covered with thick greenish pus The c s f was cloudy and contained numerous pus cells, with a few intracellular and extracellular gram-negative diplococci resembling

TABLE I—SUMMARY OF CASE-HISTORIES OF SEVEN INFANTS WITH NO "CLASSICAL" SIGNS OF MENINGITIS

Case no	Age	Symptoms before admission	Physical signs on admission	Treatment	Progress	Necropsy findings	Causal organism	Comments
7	$6\frac{1}{2}$ mos	Vomiting for 1 day	Acutely ill apathetic child in respiratory distress Signs of right upper lobe pneumonia Temp 102°F, fontanelle level, no meningism	Penicillin. Sulpha *dimidine*	Died 4 hr after admission	Purulent meningitis with flecks of pus in sulci and exudate over tip of temporal lobes and base of brain, lungs congested	*Bact coli*	Diagnosed post mortem
8	6 wk	Intermittent pyrexia for 5 weeks, failure to gain weight, relaxed stools	Wasting and dehydration No localising signs	—	Died 1 day after admission following a convulsion	Recent meningitis with opacity of basal meninges	*Bact coli*	In another hospital L P and subdural taps had been done with negative results, diagnosed post mortem
9	2 mos	Anorexia and irritability for 2 days	Irritability, facial pallor, mottling of body and limbs Temp 101°F, fontanelle level, no neck stiffness	Sulphadiazine. 'Eucortone'	Uneventful recovery	—	Meningococcus	L P done because baby looked more ill than could be explained by the physical signs
10	2 mos	Irritability, screaming attacks, and feverishness for 3 days	Fairly healthy looking baby Temp 99 6°F No localising signs Fontanelle level, no meningism	Sulphadiazine	Rapid recovery from meningitis, but convalescence prolonged by mild gastro-enteritis	—	Unknown	Sulphonamide given before admission, L P done because of history of irritability
11	6 wk	Irritability, vomiting relaxed stools and fever for 5 days	Ill child, slight dehydration, crepitations in chest, penile hypospadias Fontanelle level, no meningism	—	A few hours after admission had a left-sided convulsion and died about 10 hr later	Exudate over hemispheres, left kidney absent right kidney hypertrophied, containing abscesses, and ureter stenosed	*Bact coli*	Diagnosed post mortem
12	5 mos	Coryza and cough for 1 week, anorexia and pallor for 2 days	Pale fretful, drowsy, and wasted Temp 102°F, fontanelle level, no meningism	Sulphadiazine Penicillin	Vomiting caused dehydration Convalescence delayed by drip sepsis and anæmia Recovery complete	—	Meningococcus	—
13	5 mos	Irritability, vomiting and constipation for 1 day	Pale, blotchy rash, and a few petechiæ Signs of pneumonia Temp 101°F, fontanelle slightly depressed, no meningism	Sulphadiazine Penicillin	Eventual complete recovery delayed by gastro enteritis	—	Unknown (presumed meningococcus)	L P done because of petechial rash

L P = Lumbar puncture

ly at the headquarters ambulance station, ready to be ispatched immediately to the scene of a serious accident. This vehicle and the equipment it carried were of great elp at Stratford.

Obituary

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He was born at Wigan, the son of John Pendlebury, J.P. At Pembroke College, Cambridge, he was prizeman, exhibitioner, and scholar, and he took a double first in the natural sciences tripos in 1893. He entered St. George's Hospital with a university scholarship and he qualified in 1896, proceeding to the F.R.C.S. the following year.

After holding a demonstratorship in anatomy at St. George's, he was appointed to the staff in 1900. He also joined the staffs of the Royal Waterloo Hospital for Children and Women and the Kensington Dispensary and Children's Hospital. He held the lectureship on surgery at St. George's, and he was for some years a member of the court of examiners of the Royal College of Surgeons of England and an examiner for the University of Cambridge and the Society of Apothecaries.

Outside his surgical career Pendlebury was an administrator and organiser of considerable ability. With the late Dr. Arthur Latham he was largely responsible for the amalgamation of the London medical societies which led to the formation of the Royal Society of Medicine. He held the offices of honorary secretary and honorary treasurer in the early years of the society and in recognition of his services he was admitted to its exclusive honorary fellowship. Some twenty years later, as first honorary secretary of the Association of Surgeons of Great Britain and Ireland, he had the responsibility of the initial organisation of that body, whose progress from strength to strength he watched with interest all his life.

C. F., who was his first dresser at St. George's, writes: "Pendlebury retired from practice and from London about a quarter of a century ago, and there are not many left who knew him in his prime. To his generation he was a surgeon of great dexterity, quick and neat in his operating, and willing to take risks when needed. His punctuality was a byword among residents and students, who soon learned that it was wise to be ready at least five minutes before any appointed time. His teaching was clear and definite and left no doubt in the minds of the students as to the correct answer: in consequence his lectures and ward rounds were always fully attended or even overcrowded. To his friends and associates 'Pen' was a staunch colleague and he was always ready to help his juniors. On a holiday or at the dinner-table he made an ideal companion."

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He was a son of the late H. W. Massingham, the well-known editor of the *Nation* and of the *Daily Chronicle*, and he was educated at University College and University College Hospital. After qualifying in 1924 he joined the staff of the old London Fever Hospital in Liverpool Road, Islington, where he became senior resident medical officer. He interested himself in the diagnosis and treatment of fevers and worked in collaboration with the late Dr. Charles Box, who was consultant to the hospital. In 1937 he published a paper on the Use and Abuse of Drugs in Acute Specific Fevers.

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Dr. Massingham is survived by his wife and an infant son.

Our obituary notice of Dr. Edridge-Green last week should have stated that he had two sons. One died in childhood and the other, a regular officer, in the 1914–18 war.

Appointments

Adam, John, M.B. Aberd., D.M.R.D.: registrar in radiology, Queen Mary's (Roehampton) Hospital, London.

Boothroyd, L. S. A., M.S. Lond., F.R.C.S.: senior surgical registrar, Exeter clinical area.

Harrison, G. J., L.R.C.P.I., D.P.M.: medical superintendent (consultant), Winwick Hospital.

Murray, David, M.B. St. And., D.P.H., D.I.H.: asst. M.O., Edinburgh school health service.

Newsam, P. N., M.B. Belf., D.P.H.: registrar in surgery, Mossley Hill Hospital, Liverpool.

Riley, Harold, M.B. Leeds, D.O.M.S.: part-time asst. (S.H.M.O.), eye department, The Children's Hospital, Birmingham.

Winter, John, M.B., M.RAD. Lpool, D.M.R.D.: consultant radiologist, Mill Road, Newsham General, and Bootle hospitals.

Newcastle Regional Hospital Board:

Caturani, Mario, M.D. Tufts, M.R.C.S., M.R.C.O.G.: consultant obstetrician and gynæcologist, N.W. Durham H.M.C. group.

King, J. M., M.B. Glasg., M.R.C.O.G.: consultant obstetrician and gynæcologist, Wansbeck H.M.C. group.

McClure, D. M., M.B. Glasg.: consultant pathologist, S. Shields H.M.C. group.

unwell, a blood-culture produced *Bact coli* The purulent meningitis found at necropsy was totally unsuspected

In cases 7 and 11 the infants were almost moribund on admission Their poor condition may have been responsible for absence of neck rigidity, but some increase in fontanelle tension might have been expected, especially in case 7, where there was no dehydration

In case 2 the child was dehydrated on admission, but after rehydration there were still no meningeal signs and the fontanelle was not under increased tension Lumbar puncture was performed because he seemed more ill than could be explained by the physical signs in the chest, and because of the disturbed level of consciousness and the convulsion

Although only 5 babies had convulsions at the onset of their illness, 9 others convulsed after admission to hospital Of the 14 who had fits, 8 died and 1 other later developed hydrocephalus and spasticity (mortality 57%), whereas of 36 babies who did not have fits only 3 died (mortality 8%) Prophylactic anticonvulsant drugs were not used as a routine The poor prognosis in infants with meningitis who develop convulsions has been emphasised by Ounsted (1951), and these figures strongly support his plea that all infants with meningitis should be given prophylactic anticonvulsant therapy

Of the 50 infants 11 died, and 7 of these, as already stated, were in the group showing no "classical" meningeal signs—which illustrates the serious prognosis among those that do not show the typical signs of meningitis All of the babies with *Bact coli* meningitis died, which agrees with the views of Randall (1948) and Ebsworth and Leys (1951) that the prognosis is poor in such infections

Descriptions of meningitis in most of the standard pædiatric textbooks do not emphasise the diagnostic difficulties For example, Wyllie and McKissock (1949) say "The onset is acute or subacute with fever 101–104°F, stiffness of the neck, muscular stiffness, Kernig's sign, twitchings, cutaneous hyperæsthesia, delirium and stupor", and Ellis (1951)

> "Stiffness of the neck is almost always present when there is meningeal involvement, but in young infants it is sometimes found that there is obvious bulging of the fontanelle with little neck stiffness Head retraction may be an early sign in infants Kernig's and Brudzinski's signs are positive
>
> Whilst the great majority of cases in early life are of abrupt onset, it is possible for the disease to appear more insidiously, with little pyrexia and few localising symptoms at the onset"

The series here reported shows that there may be no localising signs, even with an acute onset of the meningitis

"Meningism" may, of course, occur in cases without meningitis—e g, pneumonia (especially the apical type), urinary infection, and gastro enteritis

Absence of physical signs does not seem to be related to the site of the exudate In the 6 fatal cases with no meningeal signs in which necropsy was performed, the exudate was at the base of the brain in 4, around the spinal cord in 1, and mainly over the vertex in only 2 In 4 fatal cases with meningeal signs, the exudate was found around the base in all 4, over the vertex in 3, and around the cord in 1 Unfortunately the spinal cord was not examined in all the cases

In pneumococcal meningitis the lesions are mainly in the meninges of the brain, as a rule the spinal meninges are very little affected (Holt and Howland 1939, Nelson 1950) In pneumococcal meningitis, therefore, the distribution of the lesions might be the cause of absence of neck and spinal stiffness and Kernig's sign, which are presumably due to the irritation by inflammation of nerve-roots as they enter and leave the cord One case of pneumococcal meningitis in this series did, however, exhibit neck stiffness (table III) Increased tension or bulging of the fontanelle is a sign of increased intracranial pressure, but in the skulls of very young infants a moderate rise in pressure is compensated for by widening and separation of the sutures and fontanelles This compensation will be greatest in the very distensible skulls of newborn and very young babies, and will explain the absence of a bulging fontanelle in meningitis at this age In this series case 5 was the only baby under 1 month of age and she showed no such sign, and of 8 infants less than 2 months old, 3 had increased fontanelle tension and the other 5 did not, 4 of them forming part of the group of 13 without meningeal signs (table IV) A low-pressure state may occasionally develop in young infants in which the fontanelle becomes depressed and the bones of the skull may even overlap (Smith 1951)

Although the numbers of cases in each age group in table IV are too small for any definite conclusions to be drawn from them, the tendency for infants under 3 months of age to show "classical" signs less often than those in the older age-group is indicated

In conclusion, therefore, although increased tension of the fontanelle and neck stiffness may be found in infants with meningitis, they are often absent Kernig's sign is present in only about a quarter of cases and is of little value in diagnosis These cases show how varied the clinical picture may be, and "a high index of suspicion" is necessary if the mortality-rate is to be reduced Alexander (1947) goes so far as to say that stiffness of the neck and Kernig's sign are highly unreliable in the first few months of life and seldom appear before the advanced stage of meningitis She draws attention to the value of the signs of drowsiness alternating with irritability, a high-pitched cry, and a vacant look in the eyes in the diagnosis of meningitis in infants aged less than 7 months

Lumbar puncture should be done on any infant (1) who is unusually drowsy, or irritable, or has a "vacant look" in the eyes or a recent squint, (2) who is more ill than can be explained by the physical signs, or (3) who does not make the expected response to treatment for a disease such as pneumonia or gastro enteritis The "classical" signs of meningitis must not be waited for before this essential diagnostic step is taken

SUMMARY

In acute meningitis in infancy the "classical" signs of meningitis are often absent or appear late in the illness

Of a series of 50 cases of acute meningitis in infants under 1 year of age, 13 showed none of the "classical" meningeal signs 7 of these 13 cases were fatal

Review of the 50 cases supports the view that, in infants with meningitis, convulsions are of grave prognosis A plea is made for routine prophylactic anticonvulsant therapy in this disease

Delay in diagnosis is one of the main reasons why the fatality-rate of meningitis in infancy remains relatively high Diagnostic lumbar puncture should not await the development of typical meningeal signs

I wish to thank Prof N B Capon, Dr R W Brookfield, and Dr W E Crosbie for discussing this paper, and Dr S E Keidan for much help and advice

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HARRISON, G. J., L.R.C.P.I., D.P.M.: medical superintendent (consultant), Winwick Hospital.

MURRAY, DAVID, M.B. St. And., D.P.H., D.I.H.: asst. M.O., Edinburgh school health service.

NEWSAM, P. N., M.B. Belf., D.P.H.: registrar in surgery, Mossley Hill Hospital, Liverpool.

RILEY, HAROLD, M.B. Leeds, D.O.M.S.: part-time asst. (S.H.M.O.), eye department, The Children's Hospital, Birmingham.

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- **MCCLURE, D. M.**, M.B. Glasg.: consultant pathologist, S. Shields H.M.C. group.

absent The blood pressure was normal Vaginal smears of a whole cycle showed a hyperœstrogenic curve Glucose tolerance was slightly reduced

The urinary output of 17 ketosteroids was 20 mg in twenty-four hours Chromatography showed a moderate excess of 11-hydroxy 17-ketosteroids (fractions VI and VII), with unbalanced excretion of gonadal katabolites excess of androsterone (fraction IV) and absence of its isomer (fraction V)

Case 5 —A girl, aged 18, complained in March, 1952, of recent abnormal growth of hair on the face The distribution of hair on face and pubis was typically masculine Her clitoris was moderately enlarged Other clinical findings were normal, including the general physique, which remained of a feminine type

The urinary output of 17 ketosteroids was 18–20 mg in twenty-four hours Chromatography showed an excess of etiocholanolone (fraction V) and a considerable quantity of 11 hydroxy 17 ketosteroids (fractions VI and VII) Glucose tolerance and insulin sensitivity were normal Vaginal smears gave a hyperœstrogenic curve

Case 6 —The twin sister of patient no 5 had the same trouble, the distribution of hair and the other clinical findings being exactly similar Sugar metabolism was normal

The urinary output of 17-ketosteroids was 22–25 mg in twenty-four hours Chromatography showed the same abnormal excess of fraction V, with large amounts of fractions VI and VII

TREATMENT

The treatment (fig 1) in cases 1–4 was with intramuscular cortisone 50 mg daily In case 3 it was continued in a dosage of 25 mg daily, followed by 12·5 mg daily In cases 5 and 6 cortisone was given by mouth, at first in a dosage of 50 mg daily, and later 25 mg daily

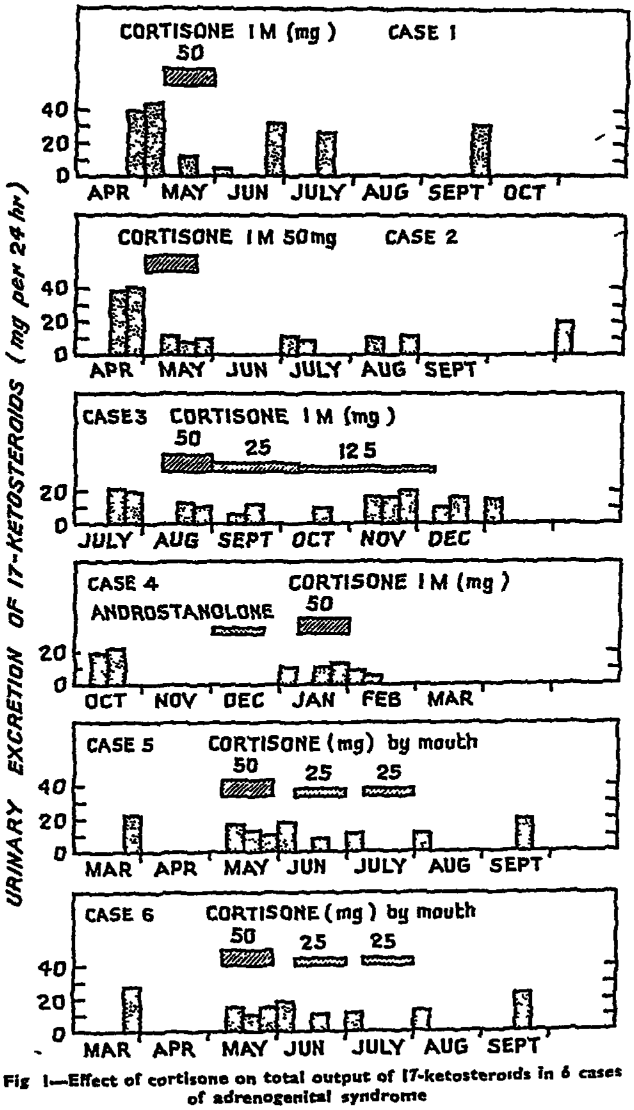

Fig 1—Effect of cortisone on total output of 17-ketosteroids in 6 cases of adrenogenital syndrome

TABLE II—INSULIN SENSITIVITY BEFORE AND AFTER CORTISONE THERAPY

Case no	Time	Blood glucose (mg per 100 ml) (% of fasting level)				
		Fasting	Time after insulin (min)			Greatest decrease (% of fasting level)
			20	30	60	
1	Before therapy	67	43 (64)	58 (87)	64 (96)	36
	" "	58	41 (71)	46 (79)	49 (84)	29
	4th day after end of therapy	47	14 (30)	5 (11)	14 (30)	89
5	Before therapy	70	37 (53)	50 (71)	70 (100)	47
	4th day after end of therapy	62	5 (8)	22 (35)	45 (73)	92
	9th day after end of therapy	75	35 (47)	32 (43)	51 (68)	57
6	Before therapy	74	62 (84)	74 (100)	80 (108)	16
	4th day after end of therapy	62	16 (26)	25 (40)	50 (81)	74
	9th day after end of therapy	47	16 (34)	12 (26)	47 (100)	74

RESULTS

Clinical

Wilkins et al (1950, 1951, 1952), Hubble (1952), and Jailer et al (1952) have shown that definite clinical improvement can be obtained only after protracted treatment Nevertheless even after short periods of cortisone therapy (the longest duration of treatment in our series was three months) some clinical results may be recorded development of breasts (cases 1 and 2), increased premenstrual tension in the breasts (case 5), and improved menstruation (cases 2 and 3) † In case 2 there was definite inhibition of hair growth, the patient having to shave only twice weekly instead of daily, and this clinical improvement lasted several months In cases 1 and 3 the patient had a dark complexion, in case 1 the quasi addisonian pigmentation was much reduced by cortisone therapy

Vaginal Smears

Before treatment the vaginal smears showed very few pyknotic and basophil cells in case 1, and an abnormally large number in case 4 In both cases the curves were without the usual inflections Under cortisone treatment a well marked cyclic inflection in the curves of both pyknotic and basophil cells appeared in cases 2, 3, and 4 In cases 5 and 6 cortisone restored the "hyperœstrogenic" curve to normal

Carbohydrate Metabolism

In cases 1, 5, and 6, after the end of treatment, the insulin sensitivity was considerably increased and a low fasting blood sugar level was observed (table II)

In case 4 cortisone had a definite diabetogenic effect the fasting blood sugar level rose from 64 to 83 mg per 100 ml and glucose tolerance was lessened

Urinary 17 Ketosteroids

The effect of cortisone on the urinary excretion of 17 ketosteroids is shown in fig 1 Daily doses of 50 mg and 25 mg given to these young adults had a definitely depressant action, whereas doses of 12 5 mg daily had no such effect The greatest effects were obtained in cases 1 and 2, where initial values were high

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† Since this paper was submitted for publication, cortisone treatment has been resumed in case 1 25 mg was injected daily from September, 1952, till March, 1953, with the unexpected result that in this case of pseudo hermaphroditism, regular normal menses occurred on Dec 18, Jan 30, and March 3

THE DIAGNOSIS OF ACUTE MENINGITIS IN INFANCY

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Although the prognosis in acute purulent meningitis in infancy has improved remarkably since the discovery and use of the sulphonamides and antibiotics, the fatality-rate is still alarmingly high. The report of the Department of Health for Scotland (1944) on "Sulphonamides in Meningococcal Meningitis" gave a fatality-rate of 28·3% in infants under the age of 1 year, compared with 2·6% in older children, aged 10–14. More recent statements indicate that the prognosis in meningococcal meningitis is little better now (Banks 1952), and it is noteworthy that, of 288 total deaths from meningococcal infection in England and Wales in 1949, 112 were of infants under 1 year of age and 202 were of children under 5 years (Registrar-General 1951).

One of the factors causing this high case-mortality is the delay in diagnosis of acute meningitis at this age. The classical clinical features, such as stiffness of neck and spine and Kernig's and Brudzinski's signs, are often absent in the early stages; or may appear at a time when treatment is no longer effective. Increased tension of the anterior fontanelle is a sign of the utmost importance; but this, too, may be absent, especially if the baby is at all dehydrated. This difficulty in diagnosis has been emphasised by Alexander (1947), Jackson (1950), and Smith (1951).

Present Investigation

Experience of several cases in which the diagnosis was made too late for effective treatment, or not until necropsy, prompted me to examine the case-sheets of the last 50 infants under the age of 12 months admitted to Alder Hey Children's Hospital with acute purulent meningitis. The admissions were between July, 1949, and April, 1952. The infection was meningococcal in 24 and pneumococcal in 5; in 4 it was caused by *Hæmophilus influenzæ*, and in 5 by *Bacterium coli;* and in 12 no organisms were isolated. Most of the unidentified infections were presumed to be meningococcal, many having been treated before admission.

The chief symptoms recorded in the routine admission history of the cases were:

Vomiting	31	Drowsiness	9
Irritability	28	Convulsions	5
Anorexia	16		

The physical signs were:

Neck rigidity	31
Tense or bulging fontanelle	22
Positive Kernig's sign	13
Squint or "vacant look" in the eyes	6

In 13 cases there were no signs of meningitis.

It must be stated that the observers were often junior house-officers, and perhaps more experienced pædiatricians might have noted evidence of meningitis in many more cases. Judgment of abnormal tension of the anterior fontanelle requires considerable experience of the normal.

Table II summarises the symptoms of the 13 cases showing no meningeal signs, and table III the signs and symptoms of the 37 cases showing obvious signs of meningitis in relation to the causal organism. Table IV summarises the signs and symptoms of the 50 cases in relation to age.

The case-histories of the 13 infants who showed no meningeal signs are reported, 7 in summary in table I, and the 6 others in more detail to illustrate the varied clinical picture of the disease at this age and the difficulties of diagnosis. Of this group 7 died, and in 5 the diagnosis was made post mortem.

Illustrative Cases

Case 1.—A girl, aged 3 months, was admitted on July 24, 1950. For five days she had been pale and listless and had been vomiting her feeds. She had had a cough for a few days.

On admission she was acutely ill, with a rectal temperature of 101°F. Respirations were rapid, the alæ nasi were active, there was slight intercostal indrawing, and occasional moist sounds were heard at both lung bases. The fontanelle was level and there was no neck rigidity. Kernig's sign was absent.

Treatment and Progress.—Pneumonia was diagnosed, and she was treated with sulphadimidine and penicillin. She remained very ill for a few days but then gradually improved; by July 29 her temperature was normal and her chest was clear both clinically and radiographically On July 30 fever returned, and twitchings of the face were observed. She became drowsy, and next day she had a generalised convulsion. There was still no neck stiffness or Kernig's sign. The cerebrospinal fluid (C.S.F.) was purulent, and pneumococci were grown on culture. Intrathecal penicillin 10,000 units was given on July 31, and again on Aug. 1. Neck rigidity was observed for the first time on Aug. 1 and even some head-retraction. Next day the C.S.F. was under very low pressure, which was not raised by jugular compression. Ventricular puncture was therefore done on Aug. 3, and penicillin 10,000 units was given into both ventricles. This was repeated on the next three days, but the child's condition deteriorated and she died on Aug. 6.

Necropsy.—Both frontal lobes were covered with a thick film of yellowish-green pus, and similar material was present in the basal cisterns and around the cord. There was a large hæmatoma in the left lateral ventricle, but no source of this hæmorrhage was found, and there was no evidence of excessive damage due to the ventricular puncture.

Case 2.—A boy, aged 3 months, was admitted on Oct. 18, 1951, with a day's history of irritability and refusal of feeds. There had been no previous illness.

On admission he looked very ill with a weak cry. His rectal temperature was 101°F. Severe dehydration and peripheral circulatory failure were evident. Scattered adventitia were heard in the chest. There was no neck rigidity, Kernig's sign was absent, and the fontanelle was level and not under increased tension.

Treatment and Progress.—Gastro-enteritis was diagnosed and intravenous fluid therapy started. Next day the temperature was still high. The baby was of good colour but drowsy, and became cyanotic when taken out of oxygen. Evidence of consolidation was present in the left lower lobe. He cried when disturbed but was not fully conscious. Later the same day he had a generalised convulsion, which was well controlled with chloral hydrate. Lumbar puncture produced opalescent C.S.F. under increased pressure and contained protein 80 mg. and sugar 89 mg. per 100 ml. Numerous pus cells and organisms resembling *H. influenzæ* were seen on direct film, but culture was sterile. Treatment with intrathecal and intramuscular streptomycin 100 mg. b.d. was started, and sulphadiazine 0·5 g. four-hourly was given by mouth. Intrathecal streptomycin 100 mg. was given daily for seven days, during which time the child's condition gradually improved, and the temperature fell to normal after five days. There were no further convulsions and eventually he made a full recovery.

Case 3.—A boy, aged 10 months, was admitted on Oct. 31, 1951. He was a twin and had been born three weeks prematurely after a normal pregnancy and delivery; his birth weight was 5 lb. 9 oz. For four weeks he had not been well with screaming attacks, diarrhœa, and vomiting. He improved for a time, but vomiting returned a few days before admission. His stools were then normal. He had been taking his feeds fairly well but refusing solids. His weight gain had been very unsatisfactory for several weeks.

On admission he was very fretful and weighed 16 lb. 12 oz. He was slightly dehydrated, but otherwise there were no abnormal physical signs. There was no neck rigidity or Kernig's sign.

Treatment and Progress.—He continued to vomit persistently and lost weight. On Nov. 16, he was dehydrated, irritable, with cortisone Some workers (Gardner and Migeon 1952, Bishop et al 1952) have measured the excretion of dehydro-iso androsterone in the adrenogenital syndrome treated with cortisone , but this single separation of one of the fractions of 17-ketosteroids may not have much significance Dehydro-iso androsterone (fraction III of the chromatogram) appears to be partly a result of hot acid hydrolysis of iso-androstenolone (Dingemanse's compound II), and an increased amount of it in the urine is no constant feature of the adrenogenital syndrome (Devis 1951b)

As shown by our chromatographic analysis in this disease, the output both of fractions II and III and of fractions V, VI, and VII may be increased Cortisone treatment definitely reduces the excretion of all these fractions, the effect being greatest on the fractions which are in greatest excess

SUMMARY

Six cases of adrenogenital syndrome treated with cortisone are reported

Clinical benefit was obtained decrease of hair growth in one case, regression of masculine physique in three cases, development of breasts in two cases, return to normal menses in two cases, and unexpected occurrence of normal menstruation in the case (no 1) of pseudo-hermaphroditism In one case skin pigmentation, resembling that of Addison's disease, regressed

The total amount of urinary 17-ketosteroids was much reduced in all six patients

Chromatography showed that this reduction affected all the adrenal fractions of the urinary 17-ketosteroids, especially those which were in great excess

The theoretical implications of these findings are discussed

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" The life span being thus extended and healthiness being assured to the senescent, the relation between the chronological and the physiological age of the individual will need to be reviewed Manifestly the school-leaving age and the age on retiral in a population in which the life expectancy is 75 years might well be much higher than in one with a life expectancy of 45 years But there will be much need for knowledge on which the education of the middle aged in the art of growing old can be based, for senescents guidance clinics, for the development of a system whereby the process of withdrawal from society and from work as the power of adjustment and adaptation wanes is as gradual as the process of entrance into society by the infant "—Prof F A E CREW, F R S , in the Hastings lecture at the British Medical Association on May 6

ASSESSMENT OF PORTAL VENOUS HYPERTENSION BY CATHETERISATION OF HEPATIC VEIN

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Myers and Taylor (1951) have described a method of estimating portal venous pressure by measuring the pressure in a catheter blocking a hepatic vein, and both they and Friedman and Weiner (1951) have shown that the technique is valid, at least in laboratory animals, by recording pressures from catheters placed simultaneously in the portal and hepatic veins The method is similar to that used by Dexter and his colleagues for measuring left auricular pressure with a catheter blocking a pulmonary arteriole (Hellems et al 1948) We have extended the technique of hepatic-vein catheterisation to study portal venous pressure in patients with liver disease

METHOD

Observations were made on fasting patients at rest ' Sodium amytal ' gr 3 (0 2 g) was given thirty minutes before the catheterisation Under fluoroscopic control a radio-opaque ' Nylon ' catheter was passed via an antecubital vein into a hepatic vein (Bearn et al 1951) The catheter was then advanced to the periphery of the liver until it met resistance about 10 cm beyond the mouth of the vein This was called the " occluded " position (fig 1) It was important at this stage to be certain that the catheter was passed to the periphery, since false records may be obtained if the catheter is obstructed at a venous junction

Pressures were then recorded by a strain gauge, the zero level being taken at a point 5 cm below the sternal angle with the patient supine Blood samples were taken from the occluded position for estimation of oxygen unsaturation, and the catheter was then withdrawn, under fluoroscopic control, about 5 cm to the "free" position (fig 2), where further pressure measurements and blood samples were taken If possible, the catheter was inserted into more than one hepatic vein radicle to obtain comparable pressure records Oxygen unsaturation was measured without delay on 5 ml samples by the Haldane blood gas apparatus

Catheterisation of a hepatic vein is not difficult and can be carried out in any centre equipped for cardiac catheterisation , it causes little discomfort to the patient, and the whole procedure rarely lasts longer than forty five minutes It is, moreover, as safe as right atrial catheterisation, and our experience totals 210 hepatic vein catheterisations without untoward incident

In some patients submitted to operation the opportunity was taken to measure the pressure in the portal vein more directly A ' Polythene ' tube, internal diameter 1 mm , was inserted at operation into a small tributary of the portal vein and tied in position , at the end of the operation it was brought out through a separate stab wound and stitched to the skin A drip containing physiological saline solution was used to keep the polythene tube patent , and, if necessary, other therapeutic fluids, including blood, could be given by this route In the first few days after operation pressures were measured with the strain gauge, and the polythene tube could then be removed without danger (Blakemore and Fitzpatrick 1951) meningococci. There was no bacterial growth on culture. The lungs showed patchy areas of collapse, especially in the left lower lobe, and an acute pyogenic bronchiolitis. Coliform bacilli were cultured from the bronchus of the left upper lobe. A left-sided hydronephrosis was present due to stenosis at the pelvi-ureteric junction.

Case 5.—A girl, aged 3 days, was admitted on Jan. 14, 1952. She was three weeks' premature and had been born after a normal pregnancy and delivery. Her birth weight was 5 lb. 11 oz. She was the first child of healthy parents, and there had been no stillbirths or miscarriages. She had appeared normal at birth, but jaundice developed a few hours later and deepened up to the time of admission. She had not taken her feeds well. Her stools had been normal in consistence and colour.

On admission she weighed only 5 lb. $3^1/_2$ oz. She was moderately jaundiced but not obviously anæmic, and she was quite vigorous. A few spasmodic contractions of the left orbicularis oculi were noted shortly after admission. The umbilicus was dry, the liver and spleen were not enlarged, and there were no signs of meningeal irritation. Bilateral cataracts were present.

TABLE III—SUMMARY OF CASES WITH "CLASSICAL" SIGNS OF MENINGITIS

Organism	No. of cases	Signs			Symptoms					Recovered	Died
		Increased fontanelle tension	Neck stiffness	Kernig's sign	Vomiting	Irritability	Anorexia	Drowsiness	Convulsions		
Meningococcus	21	13	20	8	16	16	5	2	1	19	2
Pneumococcus	3	2	1	0	1	2	2	2	1	3	0
Bact. coli ..	1	1	1	0	1	0	1	0	0	0	1
H. influenzæ ..	3	2	3	1	3	1	2	1	1	3	0
No organism isolated ..	9	4	6	4	5	4	2	3	1	8	1
Total ..	37	22	31	13	26	23	12	8	4	33	4

Investigations.—Hæmoglobin 100% (14·8 g. per 100 ml.). A blood smear showed 104 nucleated red cells per 100 leucocytes. The blood-group was O, Rh positive. Reticulocytes 14%. The Coombs test was negative on two occasions. The serum-bilirubin level was 18·4 mg. per 100 ml. The Wassermann reaction was negative. Cold agglutinins were absent. The red-cell fragility was within normal limits. The urine was normal and contained no bile salts, bile pigments, or reducing substances. The mother's blood-group was O, Rh positive, and no antibodies were detected in the serum.

Course.—During the next few days the baby took her feeds well, but she vomited occasionally and her stools were rather loose. However, she gained weight slowly, and the jaundice was fading. On Jan. 26 there was only slight jaundice, but she looked pale. Her hæmoglobin was 73% (10·7 g. per 100 ml.), but it steadily decreased to 56% (8·2 g. per 100 ml.), and 150 ml. of blood was transfused intravenously on Jan. 30. Shortly after this she developed pyrexia and was obviously unwell. She began to lose weight and had more diarrhœa and vomiting. On Feb. 2 she suddenly had a generalised convulsion, which was controlled fairly well with chloral hydrate. Blood for culture was taken at this time and later yielded a growth of *Bact. coli*. Treatment with streptomycin 60 mg. b.d. was started, but she continued to have convulsions until she died on Feb. 5.

Necropsy.—A thick greenish exudate overlay the cerebellum and base of the brain. Culture grew *Bact. coli*. No abnormality or disease of the organs was found.

Case 6.—A girl, aged 4 weeks, was admitted on March 1, 1952. She was born at full term after a normal pregnancy and delivery and had weighed 6 lb. 7 oz. at birth. Shortly after birth she had a "cold," which rapidly cleared, and she was gaining weight steadily. On the night before admission she had vomited a feed, but otherwise seemed quite normal and went to sleep. In the morning she was heard to be making a "noise in her throat"; she looked pale and refused her morning feed.

On admission she looked rather ill and had a rectal temperature of 100°F. She weighed 8 lb. 2 oz. She seemed to be unaware of her surroundings, her respirations were grunting and distressed, and she had a high-pitched cry. There was a variable internal strabismus—sometimes with the right eye and sometimes with the left—and the eyes were making continuous roving movements. Both upper eyelids were a little retracted, showing a rim of sclera above the cornea. The left pupil was a little larger than the right, but both reacted well to light. There was no wasting or dehydration. The fontanelle was pulsating, flush with the scalp, and apparently not under increased tension. There was no neck rigidity, and Kernig's sign was absent. No other abnormalities were found.

TABLE IV—SIGNS AND SYMPTOMS IN RELATION TO AGE

Age on admission (mos.)	No. of cases	Signs			Symptoms					Recovered	Died
		Increased fontanelle tension	Neck stiffness	Kernig's sign	Vomiting	Irritability	Anorexia	Drowsiness	Convulsions		
0–1	1	—	—	—	—	—	—	—	—	—	1
1–2	7	3	1	1	4	4	2	—	—	5	2
2–3	5	2	2	1	1	3	3	1	1	4	1
3–6	16	10	11	7	8	8	7	2	1	15	1
6–9	12	6	9	2	10	6	3	3	2	8	4
9–12	9	1	8	2	8	7	1	3	1	7	2
Total ..	50	22	31	13	31	28	16	9	5	39	11

Treatment and Progress.—Lumbar puncture produced about 1 ml. of turbid C.S.F., which dripped out very slowly. Penicillin 10,000 units was injected intrathecally and 100,000 units intramuscularly, followed by 50,000 units six-hourly. The C.S.F. showed polymorphs and gram-positive diplococci on smear, and pneumococci grew on culture; pneumococci were also grown from a throat swab. Radiography of the chest showed consolidation at the right lung base.

Next day the child appeared a little brighter but was still taking feeds very reluctantly. There was no meningism. Lumbar puncture produced only a few drops of blood, but cisternal puncture produced turbid C.S.F. under normal pressure. Pencillin was again injected intrathecally. Only a very little xanthochromic C.S.F., with high protein content, was obtained by lumbar puncture in the next three days, but a free flow of C.S.F. was obtained on cisternal puncture, indicating a spinal block. Penicillin was given cisternally. On the seventh day a further lumbar puncture produced a free flow of almost clear C.S.F. under normal pressure.

The child remained febrile until the tenth day, but then made an uneventful recovery. Penicillin was given intramuscularly for fourteen days. The C.S.F. a week before discharge contained 35 leucocytes (mononuclears 60%) per c.mm. and protein 40 mg. per 100 ml. Radiography of the chest showed resolution of the pneumonia. When seen a month later in the outpatient department the child was very well and had progressed normally.

Discussion

Of the 50 cases studied, 13 (26%) showed none of the "classical" signs of meningitis, though both cases 4 and 6 had rather vacant and staring eyes and a squint. It was because of these signs in case 6 that meningitis was suspected and lumbar puncture performed. In 5 of the 13 cases (nos. 4, 5, 7, 8, and 11), meningitis was not diagnosed during life, and of the other 8 cases 1 and 3 were diagnosed too late for effective treatment.

Case 5 was especially interesting. The baby was admitted to hospital at the age of 3 days with moderately severe jaundice. No other signs were found apart from bilateral cataracts. The patient presented a difficult diagnostic problem because the usual causes of jaundice at this age were thought to have been excluded. Several blood examinations revealed no incompatibility between the baby's blood and that of the mother, the red-cell fragility was within normal limits, and the Wassermann reaction was negative. Although septicæmia was considered, it was thought improbable in view of the child's excellent general condition. However, when, after three weeks, the infant began to lose weight and was obviously

CORTISONE TREATMENT IN ADRENOGENITAL SYNDROME*

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THE depressant action of cortisone on adrenal cortical secretion was first used by Wilkins et al. (1950) to correct the hypercorticism of pseudohermaphroditism in children; and the effects of this treatment in older patients with adrenogenital syndrome have been described by Wilkins et al. (1951, 1952), Bárrter et al. (1951), Thorn (1950), Bastenie et al. (1951), Laroche et al. (1952), Bishop et al. (1952), Simpson (1952), and Hubble (1952). The number of cases so far treated is small, and methods of therapy, dosage, and the mechanism of action of cortisone are still debatable.

We report here our observations in six cases of adrenogenital syndrome, including details of the different fractions of the urinary 17-ketosteroids, estimated by repeated chromatography before and after cortisone treatment.

MATERIAL, METHODS, AND TECHNIQUES

The patients, mostly ambulant, were studied partly during short stays at the clinic. The clinical examination included the anthropological measurements proposed by Decourt and Doumic (1950). The urinary output (total and fractionated) of 17-ketosteroids, the glucose tolerance (50 g. by mouth), the insulin sensitivity (intravenous insulin 0·1 unit per kg. body-weight), and vaginal smears were tested before, during, and three or four days after the end of cortisone therapy.

For the fractionation of 17-ketosteroids we used the chromatographic method of Dingemanse, as fully described by Dingemanse et al. (1952). The clinical interpretation of this fractionation has been discussed by Devis (1951a) and Albeaux-Fernet et al. (1951). Dingemanse's chromatographic analysis divides the urinary 17-ketosteroids into eight fractions, every one of which is composed of definite compounds most of whose chemical formulæ have been established (Dingemanse et al. 1952, Devis 1951a, Huis in't Veld 1948). Table I indicates their presumed relationship and origins.

The chromatogram of classical adrenogenital syndrome shows a heavy excess of fractions II and III (Devis 1951a, Dingemanse et al. 1946). When this syndrome is due to an adrenal tumour, fraction II nearly always accounts for at least half the total output of 17-ketosteroids. When it is caused by simple hyperfunction, typical adrenogenital syndrome may give a chromatographic pattern showing excess of fractions VI and VII (Devis 1951a).

The strict observance of Dingemanse's method as described by its authors allows us to apply the conclusions drawn from their chemical characterisations (Huis in't Veld 1948).

CASE-RECORDS

Case 1.—When first seen in 1947, at the age of 11 years, this girl had the typical features of android pseudohermaphroditism: accelerated body growth, muscular development, precocious epiphyseal ossification, early growth of sexual hair, progressive virilism leading to masculine aspect of the face and body, absence of breasts and vagina, and hypertrophy of the clitoris. Exploratory laparotomy revealed a small uterus and two large ovaries, a biopsy specimen of which showed a dense and strongly vascularised stroma, no germinative epithelium, but rare small primary follicles in the cortex.

In 1948 the left adrenal and two-thirds of the right adrenal, together with a small cortical adenoma, were removed. Microscopy showed enlargement of the reticular zone, which contained basophilic inclusions and brown pigment. After operation the clinical picture was not significantly changed, although the urinary output of 17-ketosteroids decreased, on an average, to 40 mg. in twenty-four hours.

Chromatography showed a heavy excess of fraction III, an insufficiency of fractions IV and V, and large, although still normal, amounts of fractions VI and VII. Insulin sensitivity was decreased (maximal decrease in glucose 30%).

Case 2.—A woman, aged 25, complained of scanty and irregular periods. At the age of 15 a masculine growth of hair had appeared on her face. In March, 1951, when she was admitted with acute appendicitis, definite virilism was detected: masculine gait and physique, male growth of hair on face and abdomen, undeveloped breasts, and a much enlarged clitoris.

The daily urinary output of 17-ketosteroids was 32·4–41·5 mg. Chromatography showed an excessive amount of 11-hydroxy compounds (fractions VI and VII) with androsterone and its isomer (fractions IV and V) at the lower normal limit.

Case 3.—This patient was first seen at the age of 18, when she complained of abnormal growth of hair on her face. She had begun to menstruate at 17, but her periods were irregular and scanty. She was of very dark complexion and moderately obese (weight 12 st. 4 lb., height 5 ft. $3^1/_2$ in.), with accumulation of fat greatest on trunk, shoulders, and thighs. Hirsutism was well marked on face and pubis. A few reddish striæ were seen on both flanks. The genitalia were normal, and the clitoris not enlarged, but the general physique was of masculine type. The blood-pressure (130/80 mm. Hg) and other clinical findings were normal. The fasting blood-sugar level and a glucose-tolerance curve were normal.

The total urinary output of 17-ketosteroids was slightly increased (19 mg. in twenty-four hours). Chromatography showed a great excess of fraction V (etiocholanolone) and a substantial output of 11-hydroxy compounds (fractions VI and VII), giving the curve the same shape as in Cushing's syndrome.

Case 4 was first seen in October, 1951, at the age of 25, complaining of abnormal growth of hair on the face, asthenia, and excessive menses. She was not obese (weight 9 st. 6 lb., height 5 ft. $4^3/_4$ in.). Her general physique was of masculine pattern, with large shoulders, slender pelvis, and long legs. There were moderate hirsutism on the face, a slight excess of body hair, and a typical masculine distribution of sexual hair. The clitoris was slightly enlarged. Striæ and osteoporosis were

TABLE I—RELATION BETWEEN HORMONES AND DINGEMANSE'S CHROMATOGRAPHIC FRACTIONS OF 17-KETOSTEROIDS

Fraction no.	Compound	Origin		Values in normal adults (% of total excreted)
		Hormone	Gland	
I	Δ^2Androstene-17-one Δ^3 Chloro-5-androstene-17-one Δ^3 5-Androstadiene-17-one	Artefact due to hydrolysis	..	3–30
II	Iso-androstene-6 ol-17-one	N hormone	Adrenal (androgenic function)	0–21
III	Dehydro-iso-androsterone			3–30
IV	Androsterone	Testosterone	Gonads	30–60
V	Etiocholan-3α ol-17-one	Partially testosterone	Gonads and adrenal cortex	
VI	11 Hydroxy-androsterone	11-oxy-compounds	Adrenal (metabolic function)	3–23
VII	11 Hydroxy-etiocholanolone			
VIII	Unidentified 17-keto-steroid	..	..	3–20

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Fig. 2 shows how this action affected the different chromatographic fractions of the 17-ketosteroids. The excretion of the adrenal androgens (fractions II and III) was considerably inhibited in case 1, but in this case, as well as in cases 2 and 4, the effect was greatest on etiocholanolone and on 11-hydroxy 17-ketosteroids (fractions V, VI, and VII). In case 3 the action mainly affected fraction V, whereas it was masked for fractions VI and VII by the presence of cortisone katabolites, which are eluted in these fractions.

DISCUSSION

The results obtained by Wilkins et al. (1950, 1951, 1952) with several months' cortisone treatment have emphasised its practical value both in pseudohermaphroditism in children and in adrenogenital syndrome in young females. Our results obtained with a short treatment confirm those of Wilkins et al. and of Hubble (1952).

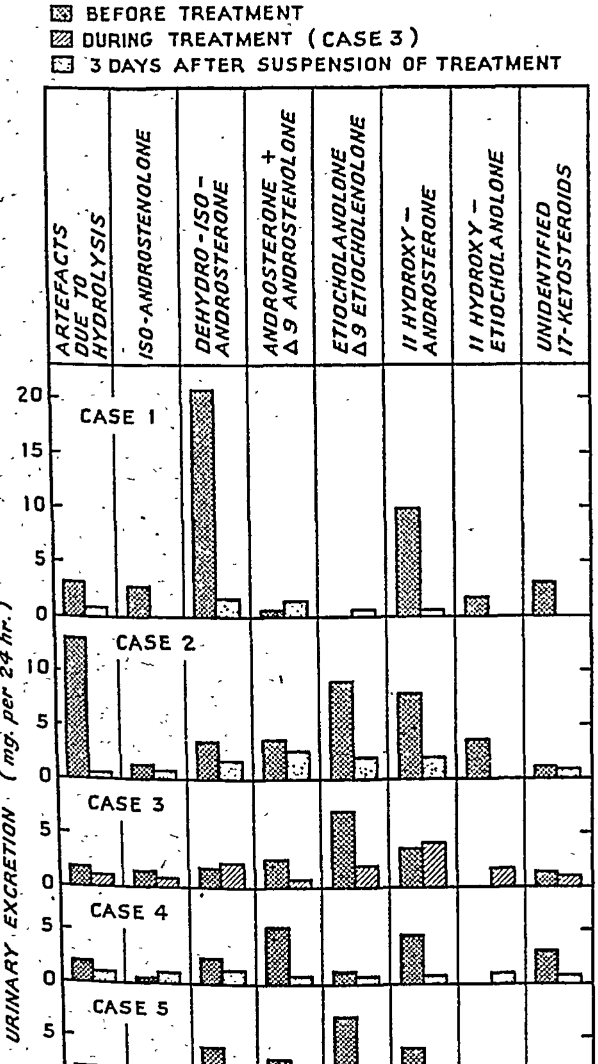

Fig. 2—Chromatographic analysis of urinary 17-ketosteroids in 6 cases of adrenogenital syndrome, with effect of cortisone shown in the first 4 cases. The absence of a histogram means none of the substance in question was found on analysis.

Wilkins et al. (1950, 1951, 1952) found that the smallest dose that would reduce the daily urinary output of 17-ketosteroids to 4–8 mg. a day was 25–50 mg. in infants and 50–100 mg. in older patients. The daily maintenance doses in patients aged more than 8 years were 25 mg. for intramuscular injection and 75 mg. for oral administration. In our cases 25–50 mg. by intramuscular injection sufficed to lower the output in adults to 10 mg. or less per twenty-four hours. This finding is in accordance with that of Hubble (1952).

Doses of 100 mg. or more, used by several workers (Bishop et al. 1952, Simpson 1952), may be unnecessary. Katabolites of the administered cortisone are partly excreted as 17-ketosteroids, which fact may account for an apparently insufficient decrease in urinary 17-ketosteroids when larger doses are used.

As shown in fig. 1, and as is evident from the observation of Bishop et al. (1952), adrenal cortical depression, judged by the urinary output of 17-ketosteroids, may last for several weeks. However, further experience will be necessary to ascertain whether oral administration of 25–50 mg. per day for twenty days each month is enough to depress cortical hyperactivity.

The suppression of adrenal cortical activity by cortisone treatment gives rise to interesting theoretical considerations. It is clear from anatomo-pathological findings, clinical investigations, and experimental studies that this effect is due to inhibition of the secretion of corticotropin (A.C.T.H.) by the pituitary gland. Barrter et al. (1951) suggest that two metabolic disturbances play a part in the pathogenesis of the adrenogenital syndrome:

1. A decreased ability of the adrenal cortex to respond to corticotropin, with an increased output of carbohydrate active steroids.
2. As a consequence of this abnormality, an increased production of corticotropin leading to abnormally high secretion of adrenal androgens.

According to Barrter et al. (1951) the biological and clinical features of adrenogenital syndrome are thus in sharp opposition to those of Cushing's syndrome.

Our observations do not seem to support this conception. Although some cases of adrenogenital syndrome and of Cushing's syndrome may give very different (nearly opposite) pictures, intermediate cases are common (see case 3).

In Hubble's (1952) case there was no evidence of deficiency of 11-oxysteroids "either under ordinary conditions or in response to A.C.T.H." Glucose-tolerance tests and insulin-sensitivity tests detected no such deficiency in the present cases. Further, in all our cases the urinary excretion of fractions V, VI, and VII was high, sometimes above the normal limit.

Fractions VI and VII are composed by 11-hydroxy-17-ketosteroids, especially 11-hydroxy-androsterone and its isomer 11-hydroxy-etiocholanolone. Fraction V contains a Δ^9 derivative of 11-hydroxy-etiocholanolone. These various compounds are believed to be metabolites of the glucocorticoids. They are absent in Addison's disease and are specifically increased both in Cushing's disease and in normal persons treated with corticotropin (Dingemanse and Huis in't Veld 1950).

Moreover, katabolites of cortisone administered to normal persons are eluted in these chromatographic fractions of 17-ketosteroids (Devis 1951b) (see fig. 2, case 3). Dobriner and Lieberman (1950) observed an increase of these substances during administration of "cortin." The occurrence, during steroid katabolism, of oxygenation in the C11 position of compounds which had no such oxygen is considered by these workers to be highly improbable.

Hitherto no attempt has been made to separate the various fractions of 17-ketosteroids in patients treated

Pressure tracings were measured by planimetry and represent the mean of the inspiratory and expiratory variations.

Readings were made in a group of patients without liver disease when catheterisation was otherwise indicated for a necessary assessment of cardiovascular, metabolic, or renal function.

RESULTS

Values for the occluded hepatic-vein pressure showed good agreement with those subsequently obtained from a portal-vein radicle (table I).

Pressure readings taken from different hepatic-vein radicles in the same liver also agreed well (table II).

The oxygen unsaturation of the hepatic-vein blood in 13 patients without liver disease was 59 ml. per litre, with a standard error of ±1·25, and in 9 patients with cirrhosis was 63·2 ml. per litre, with a standard error of ±8·2. There was therefore no significant difference between the oxygen unsaturation of the hepatic venous blood in patients without liver disease and in patients with cirrhosis.

Occluded Hepatic Venous Pressure in Portal Cirrhosis (Intrahepatic Portal Hypertension)

The occluded hepatic-vein pressure in this group was always greater than that in patients without hepatic disease (table III). The highest figure obtained in the latter group was 11·2 mm. Hg, and the lowest figure in a patient with portal cirrhosis was 15·4 mm. Hg; hence there was no overlap between the two groups. There was, moreover, a sharp gradient between the occluded and the free hepatic-vein pressures in patients with cirrhosis; and the sudden drop in pressure as the catheter is withdrawn can be well shown in a continuous tracing (fig. 3). Pressures in the free vein were usually slightly higher than similar pressures in patients without liver disease.

Case 1.—A housewife, aged 33, with post-hepatitis cirrhosis had ascites, spider nævi, and an enlarged spleen and liver two years after infective hepatitis. There was no radiological evidence of œsophageal varices. Liver-function tests showed positive flocculation tests and a reversal of the albumin/globulin ratio. Hepatic-vein catheterisation gave a high occluded pressure of 24 mm. Hg and a free pressure of 10 mm. Hg (fig. 3).

One patient with *hæmochromatosis* had an occluded hepatic-vein pressure of 15·6 mm. Hg, which suggests portal hypertension. Liver biopsy showed moderate fibrosis and distortion of lobules.

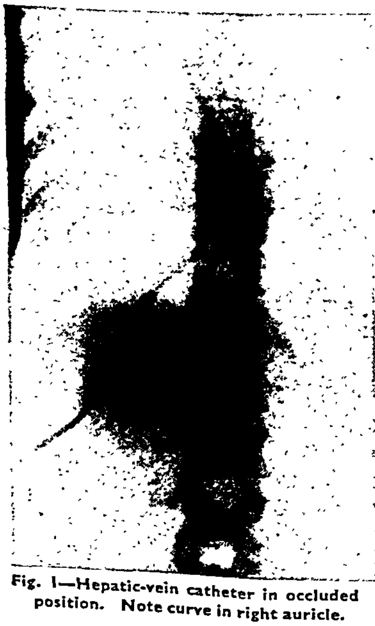

Fig. 1—Hepatic-vein catheter in occluded position. Note curve in right auricle.

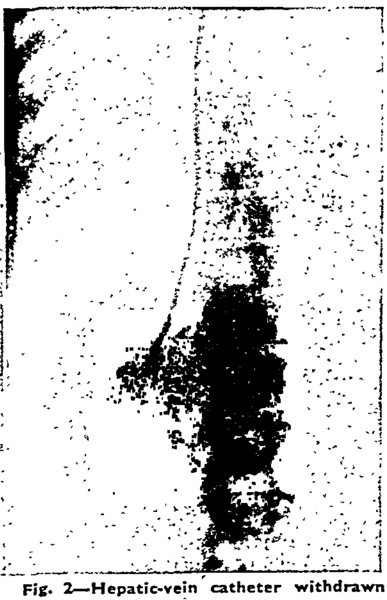

Fig. 2—Hepatic-vein catheter withdrawn to free position.

TABLE I—AGREEMENT BETWEEN PRESSURES OBTAINED FROM "OCCLUDED" HEPATIC VEIN AND FROM PORTAL-VEIN TRIBUTARY

Case no.	Pressures (mm. Hg)	
	Occluded hepatic vein	Portal-vein tributary
6	2·5	2·0
7	5·9	6·8
8	11·8	11·1
9	14·6	15·7

Extrahepatic Portal Hypertension

The occluded hepatic-vein pressure was normal in 3 patients with clinical evidence of portal hypertension. Extrahepatic portal obstruction was found at operation, and in each case the pressure measured in a portal-vein tributary was high. These patients are reported in more detail:

Case 2.—A girl, aged 16, with obliteration of the portal vein, had had recurrent hæmatemeses since the age of 13; gastroscopy revealed œsophageal and gastric varices. The spleen was enlarged. Liver-function tests and aspiration liver biopsy were normal. Hepatic-vein catheterisation showed a mean occluded pressure of 4·3 mm. Hg in three different hepatic-vein radicles (table II). At operation the portal vein was represented by a mass of tortuous dilated veins (fig. 4), and the mean pressure in a portal tributary measured postoperatively was 21·2 mm. Hg.

TABLE II—AGREEMENT BETWEEN OCCLUDED HEPATIC-VEIN PRESSURES MEASURED IN DIFFERENT RADICLES IN SAME PATIENT

Case no.	Occluded pressure (mm. Hg) in different radicles of hepatic vein		
	1	2	3
6	2·1	2·4	2·9
2	3·9	3·9	5·2
10	8·3	8·5	8·5
11	13·5	12·5	—
9	13·8	15·4	—
12	14·7	16·5	—
13	18·9	20·0	22·2
14	27·5	29·2	—

Case 3.—A lorry-driver, aged 43, with portal hypertension had had two severe hæmatemeses thought to be due to peptic ulcer, although radiography after a barium meal and gastroscopy were consistently normal. Liver-function tests and hepatic-vein pressures were also normal, the occluded pressure being 7·8 mm. Hg. Laparotomy revealed gastric and œsophageal varices, the cause of which was not found; the liver was normal. The pressure in a portal-vein radicle was 20·3 mm. Hg.

Case 4.—A man, aged 31, with hepatic cirrhosis, had undergone splenectomy six years previously for gastro-intestinal bleeding. Bleeding from œsophageal varices continued after operation. Hepatic-vein catheterisation showed a pressure of 11·7 mm. Hg in the occluded vein. At operation hepatic cirrhosis was seen and the portal vein was thrombosed. Direct measurement of the portal-vein pressure gave a very high reading of 39 mm. Hg. A portacaval anastomosis could not be undertaken.

This case demonstrates that, where portal thrombosis occurs in the presence of cirrhosis, normal pressures may be found in the occluded hepatic vein.

Obstructive Jaundice

In extrahepatic biliary obstruction both occluded and free hepatic-vein pressures were normal in 9 patients, none of whom showed evidence of biliary cirrhosis.

In intrahepatic biliary obstruction (primary biliary cirrhosis) in 3 patients the occluded hepatic-vein pressure was normal, and none showed clinical evidence of portal